Filed pursuant to 424(b)(4)
Registration Nos. 333-257820 and 333-258285

PROSPECTUS

12,000,000 Shares

Common Stock

Tenaya Therapeutics, Inc. is offering 12,000,000 shares of our common stock. This is the initial public offering, and no public market currently exists for our shares of common stock. The initial public offering price is $15.00 per share.

Our common stock has been approved for listing on the Nasdaq Global Select Market under the symbol "TNYA".

We are an "emerging growth company" as defined under the federal securities laws. Investing in our common stock involves risks. See the section titled "Risk Factors" beginning on page 16.

PRICE $15.00 A SHARE

	Price to Public	***Underwriting Discounts and Commissions(1)***	***Proceeds to Tenaya Therapeutics, Inc.***
Per Share	*$15.00*	*$1.05*	*$13.95*
Total	*$180,000,000*	*$12,600,000*	*$167,400,000*

(1) See the section titled "Underwriters" for a description of the compensation payable to the underwriters.

We have granted the underwriters the right to purchase up to 1,800,000 additional shares of our common stock to cover over-allotments, if any.

Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares against payment in New York, New York, on or about August 3, 2021.

Morgan Stanley *Cowen* *Piper Sandler*

Chardan

July 29, 2021

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Neither we nor the underwriters have authorized anyone to provide you any information or make any representations other than that contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the underwriters are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus is accurate only as of the date on the front cover of this prospectus. Our business, financial condition, results of operations and prospects may have changed since that date.

Through and including August 23, 2021 (the 25th day after the date of this prospectus), all dealers effecting transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to an unsold allotment or subscription.

For investors outside of the United States: we have not, and the underwriters have not, done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. Persons outside of the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside of the United States.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus carefully, especially the section titled "Risk Factors" and our financial statements and the related notes appearing elsewhere in this prospectus, before making an investment decision. As used in this prospectus, unless the context otherwise requires, references to "we," "us," "our," "our company," and "Tenaya" refer to Tenaya Therapeutics, Inc.

Overview

We are a biotechnology company committed to a bold mission: to discover, develop and deliver curative therapies that address the underlying drivers of heart disease. Our vision is to change the treatment paradigm for heart disease, the leading cause of death in the world, and in doing so improve and extend the lives of millions of individuals and families. We are advancing a pipeline of disease-modifying therapies developed using our product platforms and core internal capabilities to target defined sub-populations of patients with both rare and highly prevalent forms of heart disease.

Founded by leading cardiovascular scientists from Gladstone Institutes and University of Texas Southwestern Medical Center (UTSW), we are developing therapies through scientific advancements in three distinct but interrelated product platforms: Gene Therapy, Cellular Regeneration and Precision Medicine. While our Gene Therapy and Cellular Regeneration platforms focus on the use of viral vectors for drug delivery, our Precision Medicine platform enables us to identify promising targets and product candidates in a modality-agnostic manner, including gene therapies, small molecules, and biologics.

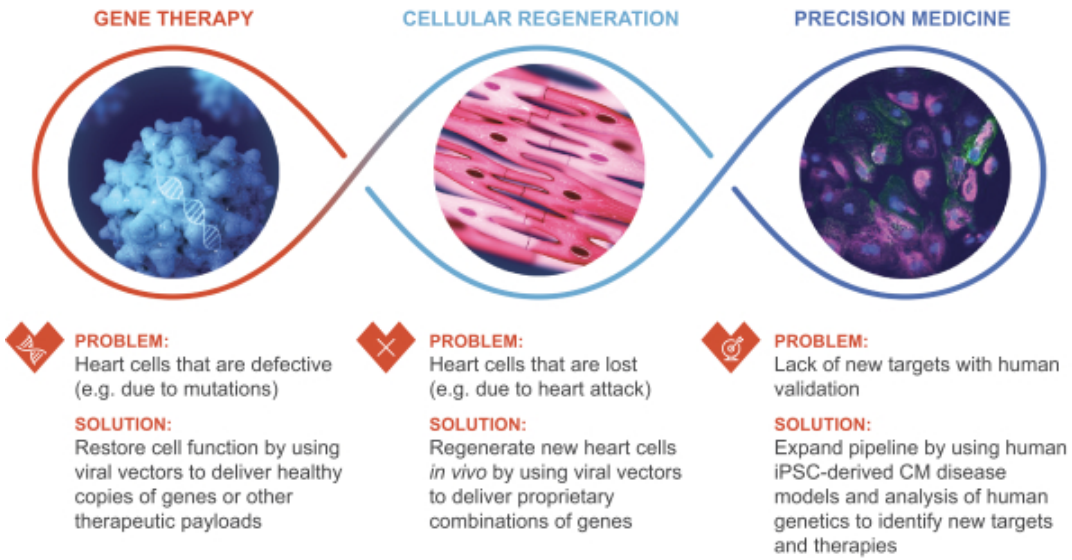
We are advancing a deep and diverse pipeline that includes both gene therapies and small molecules. In 2022, we intend to submit an investigational new drug application (IND) or a clinical trial application (CTA) to the U.S. Food and Drug Administration (FDA) or European Medicines Agency (EMA), respectively, for the most advanced product candidate from our Gene Therapy platform, TN-201, an adeno-associated virus (AAV)-based gene therapy to address genetic hypertrophic cardiomyopathy (gHCM) caused by Myosin Binding Protein C3 (*MYBPC3*) gene mutations. TN-201, currently in IND-enabling studies, is designed to deliver a fully functional *MYBPC3* gene driven by our proprietary heart-specific promoter to restore normal levels of MYBPC3 protein. We also intend to submit an IND to the FDA in 2022 for the most advanced product candidate from our Precision Medicine platform, TYA-11631, a highly specific small molecule inhibitor of histone deacetylase 6 (HDAC6i). TYA-11631, currently in IND-enabling studies, has potentially broad utility in both heart failure (HF) with preserved ejection fraction (HFpEF) as well as genetic dilated cardiomyopathy (gDCM). Our PKP2 program involves using an AAV-based gene therapy to address genetic arrhythmogenic right ventricular cardiomyopathy (gARVC) caused by plakophilin 2 (*PKP2*) gene mutations, and is currently at the candidate selection stage. Our DWORF program, an AAV-based gene therapy designed to express the Dwarf Open Reading Frame (*DWORF)* gene in the heart, has potentially broad utility in dilated cardiomyopathy (DCM) and HF with reduced ejection fraction (HFrEF), and is currently at the candidate selection stage. Our Reprogramming program for cardiac regeneration can potentially replace heart cells lost in patients experiencing HF due to prior myocardial infarction (MI), and is currently at the candidate selection stage. In addition, we have numerous earlier-stage programs emerging from our product platforms to address other forms of HF.

Our Product Platforms

We have established three distinct but interrelated product platforms to discover novel therapies for various forms of heart disease. These platforms bring together differentiated science, capabilities, and intellectual property to enable multi-modality drug discovery. As displayed below, each of our product platforms is designed

to address different problems that have historically plagued the development of therapies for heart disease. We believe these three product platforms together yield better insight into disease processes, create more opportunities for successful drug development, mitigate scientific risks, and differentiate our efforts relative to competitors.

Our Product Platforms Powering Multi-Modality Drug Discovery



1. Our ***Gene Therapy*** platform uses AAVs to deliver genes to specific cells in the heart to correct or compensate for functional defects. We have the ability to use both known AAV capsids as well as novel capsids identified through our internal capsid engineering capabilities to target cardiomyocytes (CMs), cardiac fibroblasts (CFs) or other cells important to the proper functioning of the heart. The product candidates arising from this platform are intended to overcome the shortcomings of traditional therapies that are not able to address the underlying problems that contribute to heart disease. We believe this platform has potentially broad utility for both genetic and non-genetic forms of heart disease.

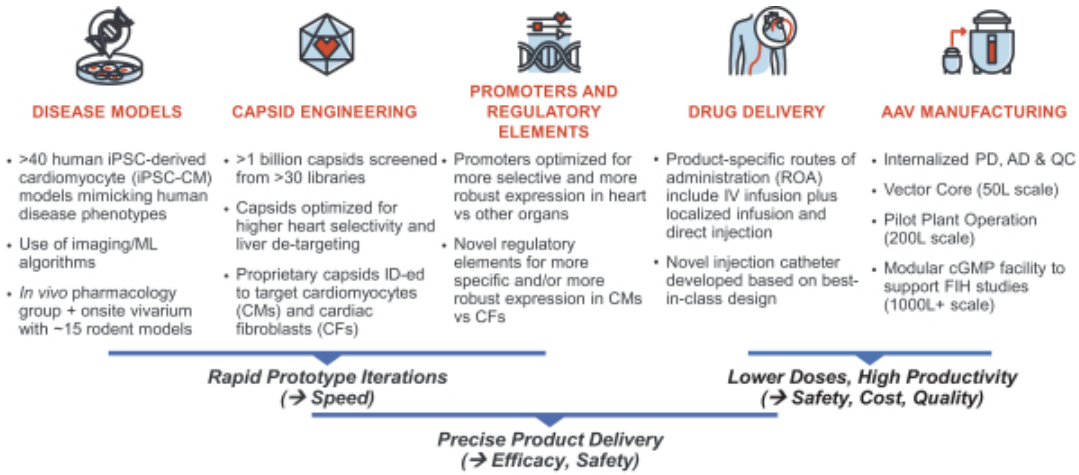
2. Our ***Cellular Regeneration*** platform uses viral vectors to deliver specific combinations of genes to existing cells in the heart to regenerate CMs *in vivo*. The product candidates arising from this platform are intended to overcome the shortcomings of traditional therapies that address symptoms but are not able to address the irreversible loss of CMs. We believe this platform has potentially broad utility across a range of heart conditions that result in the loss of CMs, including MI, chemotherapy-related toxicity, and viral infection.

3. Our ***Precision Medicine*** platform uses human induced pluripotent stem cell-derived CMs (hiPSC-CMs) as proprietary disease models combined with analysis of human genetics and the use of machine learning algorithms for the identification of new targets, validation of known targets, and high-throughput screening for drug discovery. This platform is intended to overcome the shortcomings of traditional drug development efforts that rely more heavily on insights from animal models to identify targets and to develop therapies intended for human heart disease. We believe this platform has potentially broad utility for the identification of targets and therapies in a modality-agnostic manner—including gene therapy, small molecules, and biologics—for both genetic and non-genetic forms of heart disease.

Our Approach and Capabilities

We have internalized and integrated core capabilities, as displayed below, to support our product platforms and our pipeline programs. We believe these capabilities provide us with several advantages and differentiate our efforts relative to competitors, particularly for our AAV-based drug development efforts. We believe these capabilities can collectively support rapid product development, precise product delivery, and efficient production, which ultimately improves the probability of technical and regulatory success of our product candidates.

Our Core Capabilities Supporting Our Differentiated Product Platforms



Our five core capabilities include:

1. ***Disease Models***. We have internalized the ability to create and integrate proprietary *in vitro* and *in vivo* models within our research organization. For our *in vitro* hiPSC-CM disease models, we use multiple methods to induce phenotypes within cell lines that simulate human diseases and then use these models for high throughput target identification and drug discovery. For our *in vivo* disease models, we have a dedicated onsite *in vivo* pharmacology group and vivarium, where we have established approximately 15 rodent heart disease models, both genetic and non-genetic, and can dose animals, perform heart surgeries, and use non-invasive imaging to assess the impact of our therapies under development.

2. ***Capsid Engineering***. We have established in-house AAV capsid engineering capabilities and have successfully screened over one billion variants from more than 30 diverse, proprietary AAV libraries in multiple *in vitro*, *in vivo*, and *in silico* models to discover novel AAV capsids that can target the different types of cells in the heart. These capsids are designed to have desirable properties including the ability to more selectively target the heart versus other organs as well as lower susceptibility to neutralizing antibodies. We believe our capsid engineering efforts will be critical in supporting the successful clinical development of our product candidates and enabling those product candidates, if approved, to reach more patients.

3. ***Promoters and Regulatory Elements***. We have created novel promoters and regulatory elements to support our gene therapy and cellular regeneration programs. We use these innovations to help ensure more precise and more robust expression of therapeutic payloads in the different cell types of the heart as compared to what can be achieved with currently available methods. We believe our innovations can

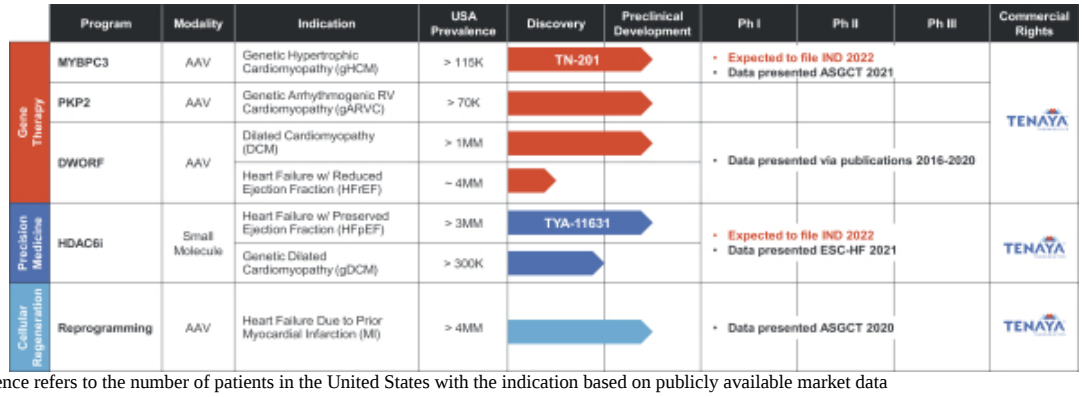
support successful clinical development in part by improving the efficacy and safety profile of our product candidates.

4. ***Drug Delivery***. We are actively exploring different routes of administration (ROAs) as well as different infusion- and injection-based methods for delivering our AAV-based therapies. We have designed a new catheter to support more targeted delivery and more efficient uptake of therapeutic payloads in the heart. We believe our discoveries in drug delivery can help widen the therapeutic index of our product candidates by reducing the dose required for a therapeutic benefit.

5. ***Manufacturing***. We have taken important steps towards internalizing both current Good Manufacturing Practice (cGMP) and non-GMP AAV manufacturing capabilities to support our emerging portfolio of gene therapy and cellular regeneration product candidates. This includes a growing in-house team of approximately 25 personnel that can support process development (PD), analytical development (AD), quality assurance (QA) and quality control (QC). We have produced non-clinical material involving both parental and novel AAV capsids at the 50L and 200L scales to support early research and IND-enabling studies in small and large animal models. We have initiated construction of a current cGMP facility in the San Francisco Bay Area near our research labs to enable smooth scale-up of production to support first-in-human (FIH) studies, initially at the 1000L scale. We expect this facility will be operational in the first half of 2022.

Our Pipeline

We are advancing a deep and diverse pipeline of therapeutic programs intended for rare diseases, such as gHCM and gARVC, as well as for more prevalent forms of heart disease, such as DCM and HFpEF. We have exclusive worldwide rights to all of our programs. Our current pipeline is summarized in the diagram below.



* USA Prevalence refers to the number of patients in the United States with the indication based on publicly available market data

- **MYBPC3 Program for gHCM**. We are developing an AAV-based gene therapy designed to deliver a functional *MYBPC3* gene in adults and children with gHCM due to *MYBPC3* gene mutations, estimated to affect more than 115,000 patients in the United States. These mutations can cause the heart walls of affected individuals to become significantly thickened, leading to fibrosis, abnormal heart rhythms, cardiac dysfunction, HF, and sudden cardiac death in some adults and children. Based on publicly available information to date, we believe there are currently no approved treatments that address the underlying genetic cause of this disease. Our product candidate, TN-201, uses a differentiated approach designed to enable robust expression of the *MYBPC3* gene in the heart. We have demonstrated significant and durable disease reversal and survival benefit in a relevant murine model after a single dose, as well as tolerability in mice and non-human primates (NHPs). The program is currently in IND-enabling studies, and we have obtained feedback from multiple regulatory agencies,

including the FDA, to guide our path to clinical development. TN-201 has also been granted Orphan Drug Designation (ODD) by the FDA. We intend to submit an IND or CTA to the FDA or EMA, respectively, in 2022.

- **HDAC6i Program for HFpEF**. We are developing an HDAC6i small molecule for various forms of HF, including HFpEF. This disease involves systemic inflammation, left ventricular hypertrophy, fibrosis, and diastolic dysfunction resulting in high morbidity and mortality in affected individuals. HFpEF is one of the greatest areas of unmet need in heart disease with more than three million patients in the United States and currently no approved disease-modifying therapies. Our product candidate, TYA-11631, is a differentiated compound with unique chemical structures and high specificity for HDAC6. We have demonstrated *in vivo* activity of our HDAC6i molecules in multiple animal models, including significant disease reversal in two different models of HFpEF as well as tolerability in mice and NHPs. Based on publicly available information to date, we believe TYA-11631 is the first HDAC6i being developed for heart disease. We have initiated IND-enabling activities and intend to submit an IND to the FDA in 2022.
- **PKP2 Program for gARVC**. We are developing an AAV-based gene therapy designed to deliver a functional *PKP2* gene in adults with gARVC due to *PKP2* gene mutation, estimated to affect more than 70,000 patients in the United States. These mutations can cause enlargement of the right ventricle (RV) in affected individuals, replacement of heart muscle with fibrotic tissue and fatty deposits, and severely abnormal heart rhythms (arrhythmia) that can make it harder for the heart to function properly and result in sudden cardiac death in some adults and children. Based on publicly available information to date, we believe there are currently no approved treatments that address the underlying genetic cause of this disease. We have demonstrated prevention of disease progression and survival benefit in a murine model after a single dose. Based on publicly available information to date, we believe these data are the first known demonstrations of durable disease modification, survival benefit, and prevention of arrhythmia using an AAV:PKP2 gene therapy construct. This program is currently at the candidate selection stage.
- **DWORF Program for DCM**. We are developing an AAV-based gene therapy designed to deliver the *DWORF* gene for patients with DCM, estimated to affect about one million patients in the United States. DCM is a progressive and life-threatening disease that causes left ventricle (LV) enlargement, LV wall thinning, insufficient contraction, reduced blood flow, ventricular arrhythmias, and can result in premature morbidity and need for heart transplant in affected individuals. DWORF is a muscle-specific micro-peptide first discovered by our co-founder Eric Olson, Ph.D. that acts on the sarcoplasmic/endoplasmic reticulum Ca2+ ATPase 2a (SERCA2a) pathway, widely considered to be a promising target in HF. We and our academic collaborators have accumulated significant preclinical *in vivo* proof-of-concept evidence for the therapeutic benefit of over-expression of the *DWORF* gene in multiple murine models, including models of gDCM and HFrEF, as well as tolerability in murine models. Based on publicly available information to date, we believe these are the first demonstrations of the potential benefit of AAV:DWORF. This program is currently at the candidate selection stage.
- **Reprogramming Program for HF due to prior MI**. We are developing an AAV-based approach to cellular regeneration that involves converting (or reprogramming) existing CFs within the heart to turn into new CMs and to replace cells permanently lost due to MI. There are estimated to be more than four million patients in the United States living with HF due to prior MI. The loss of CMs in affected individuals permanently impairs heart contraction, leading to HF and potentially fatal arrhythmias, and the death of approximately 5% to 10% of MI survivors within the first year. There are currently no approved treatments that address the underlying loss of heart tissue. The potential utility of our unique approach to creating new CMs was first demonstrated by our co-founder Deepak Srivastava, M.D. We have discovered a proprietary combination of three genes that can drive robust *in vivo* reprogramming of CFs to CMs when delivered together in a single AAV capsid. We have demonstrated significant and

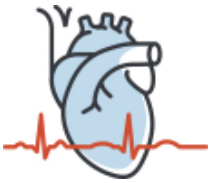
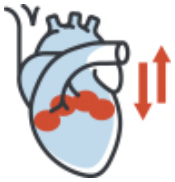
durable disease reversal as well as tolerability in multiple small and large animal models. Based on publicly available information to date, we believe our results in a pig model of HF due to prior MI represent the first-ever successful demonstration of the potential benefit of this approach in a human-sized heart. This program is currently at the candidate selection stage.

Overview of Heart Disease

Heart disease is the leading cause of death in the world, accounting for more deaths than from all cancers combined. In the United States, more than 30 million adults, or approximately 12% of the adult population, are diagnosed with heart disease. In addition, an adult dies from a cardiovascular-related health condition, such as a heart attack every 36 seconds, a gruesome statistic that translates to 31% of all deaths in the United States each year. The picture is equally bleak at the other end of the age spectrum, as approximately 35,000 children are born in the United States every year with congenital heart disease (CHD), and CHD is the leading cause of birth defect-related morbidity and mortality. There are over 250 known genetically defined disorders where the primary source of morbidity and mortality involves the heart, but there are few approved products that target the underlying cause of such diseases. Recent analysis has shown that after decades of reduction in the mortality rate due to HF, these rates are once again rising, highlighting the need for improved treatments.

The heart is a complex organ due to its biological structure as well as its tightly regulated and coordinated electrophysiological and biomechanical properties. Heart disease comes in many forms, affects individuals at many ages, and is a result of many factors. As depicted in the below table, heart disease can be generally categorized as either directly resulting from problems associated with the heart organ, for example, HF, arrhythmia, and heart valve disease, or indirectly resulting from problems associated with the vasculature, for example, coronary artery disease (CAD). In each case, the underlying cause could be genetic, or due to normal aging or due to environmental factors.

The table below illustrates four broad categories of heart disease:

CATEGORIES	DESCRIPTION
 Heart Failure (HF)	HF is a heart condition in which the heart's pumping capacity is not adequate to meet the demands for blood and oxygen required by the rest of the body. HF can be the result of a range of conditions that lead to weakening of the heart muscle. Conditions that can be associated with the development of HF include a heart attack, uncontrolled high blood pressure, congenital heart disease (heart defects present at birth), and genetic cardiomyopathies.
 Arrhythmia	Arrhythmia is one of the most common heart conditions and is described as any change in the heart's normal electrical impulses. Electrical impulses from within the heart initiate each heartbeat and ensure its normal pumping function. Arrhythmias can cause the heart to beat too quickly, too slowly or irregularly, resulting in a broad range of symptoms as well as sudden death and stroke.
 Heart Valve Disease	Heart value disease occurs when there is a problem with one or more of the four valves that normally work in unison to make sure that blood is pumped in the proper direction through the four chambers of the heart.
 Coronary Artery Disease (CAD)	CAD is among the most common type of heart disease and occurs when plaque grows in the walls of the coronary arteries, limiting the blood flow to the heart's muscle. CAD can ultimately lead to a heart attack.

Current Challenges in the Development of Novel Therapies for Heart Disease

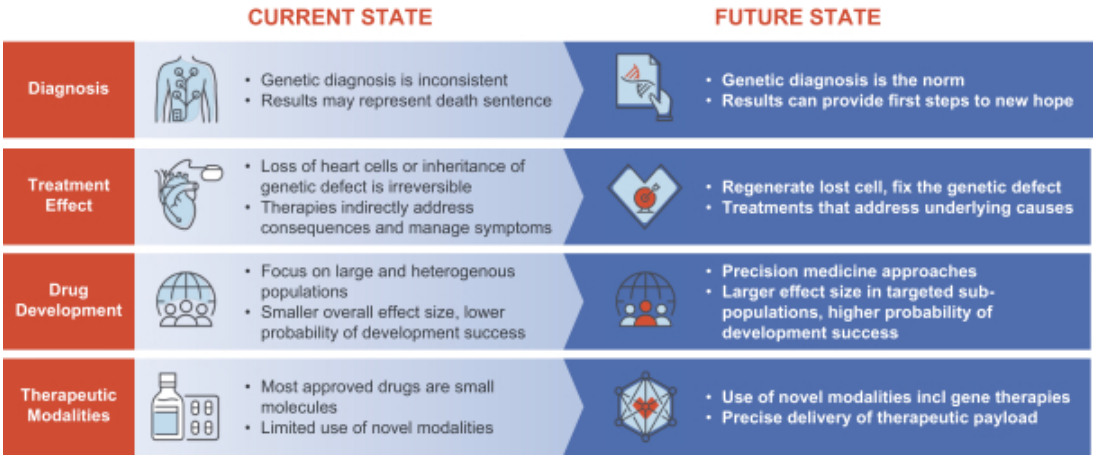
While there is significant unmet need in the field of heart disease, historically there have been challenges in developing novel therapies for the different forms of heart disease. These challenges include, but are not limited to:

- Most development efforts focus on treating symptoms rather than targeting the underlying causes of diseases;
- Identifying new disease-modifying targets is challenging;
- Genetic diagnosis and genetic counseling are limited;

- Regenerative therapy science is still in its early stages;
- Gene therapy science for the heart is still maturing;
- Regulatory requirements are stringent;
- Costs of development are high; and
- Patient access barriers are challenging.

These factors have contributed to a decline in successful heart disease drug development. However, there are recent signs of improvement. There is increasing insight into the genetic causes of heart disease and a greater push for more consistent genetic testing and family counseling supported by (1) updated clinical practice guidelines such as 2020 American College of Cardiology (ACC) and American Heart Association (AHA) recommendations for patients with hypertrophic cardiomyopathy (HCM), (2) the push by patient advocacy organizations for mandatory screening of young athletes, and (3) increased availability of accessible genetic testing covering more than 150 relevant genes associated with inherited arrhythmia and cardiomyopathy conditions. We believe with the evolving understanding of heart disease in the scientific community and general public, there are significant opportunities where we can benefit from and support the evolution towards more precise diagnosis, drug development, and treatment for heart disease, as depicted in the diagram below.

The Evolving Landscape of Heart Disease



Our Strategy

Our goal is to become a leading, fully integrated biotechnology company delivering next-generation therapies that address the underlying causes of heart disease identified through our multi-modality product platforms. We are taking advantage of an expanded understanding of heart biology and scientific advancements to discover, develop, manufacture and ultimately commercialize a deep and diverse pipeline of novel therapies. The key components of our strategy to achieve these goals are:

- Focus exclusively on heart disease;
- Develop disease-modifying therapies;
- Discover novel therapies using three product platforms in parallel;
- Target defined sub-populations of patients most likely to respond to our therapies;

- Advance a deep and diverse pipeline of therapies;
- Internalize and integrate core capabilities to support our innovation; and
- Become a fully integrated biopharmaceutical company with commercial capabilities.

Our History and Team

We were incorporated in August 2016 by The Column Group, in partnership with leading scientific and clinical researchers in cardiovascular genetics and muscle biology at Gladstone Institutes and UTSW. Since our founding, we have attracted a talented group of industry experts and scientists as part of a highly innovative organization that, as of June 30, 2021, comprises over 85 employees.

We are led by a team of executives and directors with significant experience in the discovery, development, manufacture, and commercialization of novel therapeutics, specifically in the fields of rare diseases, gene therapies, and heart disease. Faraz Ali, M.B.A., our Chief Executive Officer since 2018, previously served as the Chief Business Officer at REGENXBIO, and prior to that accumulated relevant experiences at industry-leading companies in gene therapy and orphan drug development including at bluebird bio and Genzyme Corporation.

Since inception, we have raised approximately $248 million in equity financing from leading venture, strategic and public investors, including The Column Group, Casdin Capital, SymBiosis II, LLC, Fidelity Management & Research Company, RTW Investments, and others who share our vision to build a highly innovative, integrated biotechnology company delivering next-generation therapies that address the underlying causes of heart disease.

Risks Associated with Our Business

Our ability to execute on our business strategy is subject to a number of risks, which are discussed more fully in the section titled “Risk Factors.” You should carefully consider these risks before making an investment in our common stock. These risks include, among others, the following:

- We are early in our development efforts, with a limited operating history, have not initiated or completed any clinical trials, and have no products approved for commercial sale, which may make it difficult for you to evaluate our current business and likelihood of success and future viability.
- We have not generated any product revenue to date, have incurred significant net losses since our inception, and expect to continue to incur significant net losses for the foreseeable future.
- Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve several objectives relating to the discovery, development and commercialization of our product candidates, if approved.
- Even if this offering is successful, we will require substantial additional capital to finance our operations. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate one or more of our research and drug development programs or future commercialization efforts.
- Our operations and financial results could be adversely impacted by the COVID-19 pandemic in the United States and the rest of the world.
- Our product candidates are in the early stages of development and we have no products approved for commercial sale. If we are unable to successfully develop, receive regulatory approval for, manufacture and commercialize our product candidates, or successfully develop any other product candidates, or experience significant delays in doing so, our business will be harmed.

- We intend to identify and develop gene therapy product candidates based on novel technology, and because the regulatory landscape that governs any product candidates we may develop is rigorous, complex, uncertain and subject to change, we cannot predict the time and cost of obtaining regulatory approval, if we receive it at all, for any product candidates we may develop.
- The mechanisms of action of our product candidates are unproven, and we do not know whether we will be able to develop any drug of commercial value.
- Preclinical and clinical drug development involves a lengthy and expensive process with an uncertain outcome. The clinical trials of our product candidates may not demonstrate safety and efficacy to the satisfaction of the FDA, EMA or other comparable foreign regulatory authorities or otherwise produce positive results and the results of preclinical studies and early clinical trials may not be predictive of future results. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.
- Our product candidates may cause serious adverse events, toxicities or other undesirable side effects when used alone or in combination with other approved products or investigational new drugs that may result in a safety profile that could prevent regulatory approval, prevent market acceptance, limit their commercial potential or result in significant negative consequences.
- Due to the significant resources required for the development of product candidates, and depending on our ability to access capital, we must prioritize development of certain programs and product candidates. Moreover, we may expend our limited resources on programs or product candidates that do not yield a successful product and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.
- We are in the process of building out a manufacturing facility to support future production of certain of our product candidates. We have no experience in manufacturing, and there can be no assurance that we will be able to complete our manufacturing facility or, if completed, we will be able to successfully manufacture product candidates.
- The regulatory approval processes of the FDA, EMA and other comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable. If we are ultimately unable to obtain regulatory approval of our product candidates, we will be unable to generate product revenue and our business will be substantially harmed.
- As of July 1, 2021, we have in-licensed one issued U.S. patent, own one issued U.S. patent, and own one allowed U.S. patent application relating to our technology and product candidates. If we are unable to obtain, maintain, protect, defend and enforce patent and other intellectual property coverage for our technology and product candidates, our competitors could develop and commercialize technology and product candidates similar or identical to ours, and our ability to commercialize our technology and product candidates may be adversely affected.
- Our commercial success depends significantly on our ability to operate without infringing, misappropriating or otherwise violating the patents and other intellectual property and proprietary rights of third parties. Claims by third parties that we infringe, misappropriate or otherwise violate their intellectual property or proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts, and could have a material adverse effect on the success of our business.
- We rely on third parties to conduct our preclinical studies, and plan to rely on third parties to conduct clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research and studies or to comply with applicable regulatory requirements, which may harm our business.

Corporate Information

We were incorporated in Delaware in August 2016. Our principal executive offices are located at 171 Oyster Point Boulevard, 5th Floor, South San Francisco, CA 94080. Our telephone number is (650) 825-6990. Our website address is www.tenayatherapeutics.com. Information contained on, or accessible through, our website is not incorporated by reference into this prospectus and should not be considered to be part of this prospectus. The inclusion of our website address in this prospectus is an inactive textual reference only.

Trademarks

We use the Tenaya logo and other marks as unregistered trademarks in the United States and certain other countries. This prospectus contains references to our trademarks and to those belonging to other entities. Solely for convenience, trademarks and trade names referred to in this prospectus, including logos, artwork and other visual displays, may appear without a trademark symbol, but such references are not intended to indicate in any way that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable owner of these trademarks and trade names. We do not intend our use or display of other entities' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other entity.

Implications of Being an Emerging Growth Company and a Smaller Reporting Company

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, as amended (JOBS Act). We will remain an emerging growth company until the earliest to occur of: (i) the last day of the fiscal year in which we have more than $1.07 billion in annual revenue; (ii) the date we qualify as a "large accelerated filer," with at least $700 million of equity securities held by non-affiliates; (iii) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period; and (iv) the last day of the fiscal year ending after the fifth anniversary of our initial public offering. As a result of this status, we have taken advantage of reduced reporting requirements in this prospectus and may elect to take advantage of other reduced reporting requirements in our future filings with the U.S. Securities and Exchange Commission. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards, delaying the adoption of these accounting standards until they would apply to private companies. We have elected to use the extended transition period to enable us to comply with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date on which we (1) are no longer an emerging growth company and (2) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

We are also a "smaller reporting company," meaning that the market value of our stock held by non-affiliates plus the proposed aggregate amount of gross proceeds to us as a result of this offering is less than $700 million and our annual revenue was less than $100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company after this offering if either (i) the market value of our stock held by non-affiliates is less than $250 million or (ii) our annual revenue was less than $100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

THE OFFERING

Common stock offered by us	12,000,000 shares.
Option to purchase additional shares	We have granted the underwriters an option for a period of 30 days to purchase up to 1,800,000 additional shares of our common stock.
Common stock to be outstanding immediately after this offering	39,324,727 shares (or 41,124,727 shares if the underwriters exercise in full their option to purchase additional shares).
Use of proceeds	We estimate that the net proceeds from this offering will be approximately $163.7 million, or $188.8 million if the underwriters exercise in full their option to purchase additional shares of common stock, at the initial public offering price of $15.00 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. We currently intend to use the net proceeds from this offering, together with our existing cash and cash equivalents, to fund our ongoing and planned preclinical and clinical development of our most advanced product candidates in our MYBPC3 and HDAC6i programs, the continued development of our other programs, including our PKP2, DWORF and Reprogramming programs, the expansion of our manufacturing capabilities and facilities and the remainder, if any, for working capital and other general corporate purposes. See the section titled “Use of Proceeds.”
Risk factors	See the section titled “Risk Factors” for a discussion of factors that you should carefully consider before deciding to invest in shares of our common stock.
Nasdaq Global Select Market trading symbol	“TNYA”

The number of shares of our common stock to be outstanding after this offering is based on 27,324,727 shares of our common stock outstanding as of March 31, 2021 (including our convertible preferred stock on an as-converted basis), and excludes:

- 1,727,968 shares of common stock issuable upon exercise of options outstanding as of March 31, 2021 with a weighted-average exercise price of $3.06 per share;
- 835,473 shares of common stock issuable upon exercise of options granted after March 31, 2021, with a weighted-average exercise price of $10.00 per share;
- 379,271 shares of common stock reserved for future issuance under our Amended and Restated 2016 Equity Incentive Plan, as amended, as of March 31, 2021;
- 4,000,000 shares of common stock reserved for future issuance under our 2021 Equity Incentive Plan (2021 Plan), which became effective on the business day immediately prior to the date of effectiveness of the registration statement of which this prospectus forms a part, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan; and
- 800,000 shares of common stock reserved for future issuance under our 2021 Employee Stock Purchase Plan (2021 ESPP), which became effective on the business day immediately prior to the date of effectiveness of the registration statement of which this prospectus forms a part, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan.

Unless otherwise indicated, this prospectus reflects and assumes the following:

- a 1-for-6 reverse stock split of our outstanding common and preferred stock effected on July 23, 2021;
- no exercise of the outstanding options referred to above;
- no exercise by the underwriters of their option to purchase up to an additional 1,800,000 shares of common stock from us in this offering;
- the automatic conversion of all outstanding shares of our convertible preferred stock as of March 31, 2021 into an aggregate of 26,102,278 shares of our common stock immediately prior to the completion of this offering; and
- the filing and effectiveness of our amended and restated certificate of incorporation and the adoption of our amended and restated bylaws, each of which will occur immediately prior to the completion of this offering.

SUMMARY FINANCIAL DATA

The following tables set forth our summary financial data for the periods and as of the dates indicated. We have derived the summary statements of operations data for the years ended December 31, 2019 and 2020 from our audited financial statements included elsewhere in this prospectus. The summary statements of operations data for the three months ended March 31, 2020 and 2021 and the summary balance sheet data as of March 31, 2021 are derived from our unaudited interim condensed financial statements included elsewhere in this prospectus. We have prepared the unaudited interim condensed financial statements on the same basis as the audited financial statements. We have included, in our opinion, all adjustments, consisting only of normal recurring adjustments that we consider necessary for a fair presentation of the financial information set forth in those unaudited interim condensed financial statements.

You should read the following summary financial data together with the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and the related notes included elsewhere in this prospectus. The summary financial data in this section are not intended to replace our financial statements and are qualified in their entirety by our financial statements and related notes included elsewhere in this prospectus. Our historical results are not necessarily indicative of the results that may be expected in the future, and our results for the three months ended March 31, 2021 are not necessarily indicative of results to be expected for the full year.

	Year Ended December 31,		Three Months Ended March 31,	
	2019	2020	2020	2021
	(in thousands, except share and per share data)			
Statements of Operations Data:				
Operating expenses:				
Research and development	$ 23,148	$ 31,099	$ 7,297	$ 9,590
General and administrative	4,564	7,813	1,969	3,515
Total operating expenses	27,712	38,912	9,266	13,105
Loss from operations	(27,712)	(38,912)	(9,266)	(13,105)
Other income (expense), net:				
Interest income	453	87	57	9
Change in fair value of convertible preferred stock tranche liability	11	75	(19)	—
Other income (expense), net	1,017	355	177	(2)
Total other income	1,481	517	215	7
Net loss before income tax expense	(26,231)	(38,395)	(9,051)	(13,098)
Income tax expense	—	—	—	—
Net loss	$ (26,231)	$ (38,395)	$ (9,051)	$ (13,098)
Net loss per share, basic and diluted	$ (34.71)	$ (39.50)	$ (10.15)	$ (11.93)
Weighted-average shares used in computing net loss per share, basic and diluted	755,779	972,091	891,990	1,097,805
Pro forma net loss per share, basic and diluted(1)		$ (1.42)		$ (0.48)
Weighted-average shares used in computing pro forma net loss per share, basic and diluted(1)		27,074,369		27,200,083

(1) The unaudited pro forma net loss per share for the year ended December 31, 2020 and the three months ended March 31, 2021 was computed using the weighted-average number of shares of common stock outstanding, including the pro forma effect of the conversion of all outstanding shares of our convertible preferred stock into shares of common stock, as if such conversion had occurred at the beginning of the most recently completed fiscal year.

	As of March 31, 2021		
	Actual	Pro Forma(1)	Pro Forma as adjusted(2)
		(in thousands)	
Balance Sheet Data:			
Cash and cash equivalents	$128,439	$ 128,439	$ 292,139
Working capital(3)	123,840	123,840	287,614
Total assets	159,757	159,757	323,383
Convertible preferred stock	240,735	—	—
Additional paid-in capital	2,054	242,786	406,485
Accumulated deficit	(95,910)	(95,910)	(95,910)
Total stockholders' (deficit) equity	(93,943)	146,792	310,492

(1) The pro forma balance sheet data gives effect to: (i) the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of 26,102,278 shares of our common stock immediately prior to the completion of this offering, as if such conversion had occurred on March 31, 2021; (ii) the related reclassification of our convertible preferred stock aggregate carrying value to permanent equity; and (iii) the filing and effectiveness of our amended and restated certificate of incorporation immediately prior to the closing of this offering.

(2) The pro forma as adjusted balance sheet data gives effect to: (i) the pro forma adjustments set forth in footnote (1) above; and (ii) the issuance and sale of 12,000,000 shares of our common stock in this offering at the initial public offering price of $15.00 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

(3) We define working capital as current assets less current liabilities. See our financial statements and the related notes included elsewhere in this prospectus for further details regarding our current assets and current liabilities.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this prospectus, including our audited financial statements and the related notes included elsewhere in this prospectus and the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations and the market price of our common stock.

Risks Related to Our Financial Position, Need for Additional Capital and Limited Operating History

We are early in our development efforts, with a limited operating history, have not initiated or completed any clinical trials, and have no products approved for commercial sale, which may make it difficult for you to evaluate our current business and likelihood of success and future viability.

We are a preclinical stage biotechnology company with a limited operating history upon which you can evaluate our business and prospects. We commenced operations in 2016, have not initiated or completed any clinical trials, have no products approved for commercial sale and have not generated any revenue. We are developing therapies that address the underlying drivers of heart disease, which is an unproven and highly uncertain undertaking and involves a substantial degree of risk. All of our product candidates are still in preclinical development and have never been tested in humans. Since our inception in 2016, we have devoted substantially all of our focus and financial resources to developing our gene therapy, cellular regeneration and precision medicine platforms, identifying and developing product candidates, conducting preclinical studies, acquiring technology, organizing and recruiting management and technical staff, business planning, establishing our intellectual property portfolio, raising capital, and providing general and administrative support for these operations.

We have not yet demonstrated our ability to successfully initiate and complete any clinical trials, obtain marketing approvals, manufacture a clinical- or commercial-scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. As a result, it may be more difficult for investors to accurately predict our likelihood of success and viability than it could be if we had a longer operating history.

In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors and risks frequently experienced by early-stage biotechnology companies in rapidly evolving fields. We also may need to transition from a company with a research and development focus to a company capable of supporting commercial activities. We have not yet demonstrated an ability to successfully overcome such risks and difficulties, or to make such a transition. If we do not adequately address these risks and difficulties or successfully make such a transition, our business will suffer.

We have not generated any product revenue to date, have incurred significant net losses since our inception, and expect to continue to incur significant net losses for the foreseeable future.

We have incurred significant net losses since our inception, have not generated any product revenue to date and have financed our operations through private placements of our convertible preferred stock. Our net loss was $38.4 million for the year ended December 31, 2020 and $13.1 million for the three months ended March 31, 2021. As of March 31, 2021, we had an accumulated deficit of $95.9 million. Substantially all of our losses have resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We are still in the early stages of development of our

product candidates and have not yet initiated or completed any clinical trials. Our product candidates will require substantial additional development time and resources before we will be able to apply for regulatory approvals and, if approved, begin generating revenue from product sales. As a result, we expect that it will be several years, if ever, before we receive approval to commercialize a product and generate revenue from product sales. Even if we succeed in receiving marketing approval for and commercializing one or more of our product candidates, we expect that we will continue to incur substantial research and development and other expenses in order to discover, develop and market additional potential products.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter such that a period-to-period comparison of our results of operations may not be a good indication of our future performance, particularly since we expect our expenses to increase if and when our product candidates progress through clinical development as product candidates in later stages of clinical development generally have higher development costs than those in earlier stages, primarily due to the increased size and duration of later-stage clinical trials. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our working capital, our ability to fund the development of our product candidates and our ability to achieve and maintain profitability and the performance of our stock.

Our ability to generate revenue and achieve profitability depends significantly on our ability to achieve several objectives relating to the discovery, development and commercialization of our product candidates, if approved.

We rely on our multi-modality drug discovery platforms to identify and develop product candidates. Our business depends entirely on the success of these platforms and the successful development, regulatory approval, manufacturing and commercialization of product candidates that we discover with these platforms. Our ability to generate revenue and achieve profitability depends significantly on our ability, or any future collaborator's ability, to achieve several objectives, including:

- successful and timely completion of preclinical and clinical development of product candidates and programs in our Gene Therapy, Cellular Regeneration and Precision Medicine platforms, and our other future product candidates and programs;
- obtaining regulatory approval to commence clinical trials of our product candidates;
- establishing and maintaining relationships with contract research organizations (CROs) and clinical sites for the clinical development of our product candidates and any other future product candidates;
- the initiation and successful patient enrollment and completion of clinical trials on a timely basis;
- acceptable frequency and severity of adverse events in the clinical trials;
- the efficacy and safety profiles that are satisfactory to the U.S. Food and Drug Administration (FDA) or any comparable foreign regulatory authority for marketing approval;
- timely receipt of marketing approvals from applicable regulatory authorities for any product candidates for which we successfully complete clinical development;
- complying with any required post-marketing approval commitments to applicable regulatory authorities;
- establishing and operating a manufacturing facility and developing an efficient and scalable manufacturing process for our product candidates;
- establishing and maintaining commercially viable supply and manufacturing relationships with third parties that can provide adequate, in both amount and quality, products and services to support clinical development and meet the market demand for our product candidates, if approved;

- successful commercial launch following any marketing approval, including the development of a commercial infrastructure, whether in-house or with one or more collaborators;
- successful outputs from our capsid engineering and promotor and regulator elements efforts;
- a continued acceptable safety profile following any marketing approval of our product candidates;
- commercial acceptance of our product candidates by patients, the medical community and third-party payors;
- satisfying any required post-marketing approval commitments to applicable regulatory authorities;
- identifying, assessing and developing new product candidates;
- obtaining, maintaining, and expanding patent and other intellectual property protection, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- protecting and enforcing our rights in our intellectual property portfolio;
- defending against third-party infringement, misappropriation, or other claims, if any;
- entering into, on favorable terms, any collaboration, licensing or other arrangements that may be necessary or desirable to develop, manufacture or commercialize our product candidates;
- obtaining coverage and adequate reimbursement by third-party payors for our products and patients' willingness to pay in the absence of such coverage and adequate reimbursement;
- obtaining additional funding to develop, manufacture and commercialize our product candidates;
- addressing any competing therapies and technological and market developments;
- managing costs, including any unforeseen costs, that we may incur as a result of nonclinical study or clinical trial delays due to COVID-19 or other causes; and
- attracting, hiring and retaining qualified personnel including clinical, scientific, management and administrative personnel.

We may never be successful in achieving our objectives and, even if we are, may never generate revenue that is significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to maintain or further our research and development efforts, raise additional necessary capital, grow our business and continue our operations.

We may also experience delays in establishing our manufacturing facility, developing a sustainable, reproducible and scalable manufacturing process or transferring that process to commercial partners, which may prevent us from initiating and completing our planned clinical trials or commercializing our product candidates on a timely or profitable basis, if at all.

Even if this offering is successful, we will require substantial additional capital to finance our operations. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate one or more of our research and drug development programs or future commercialization efforts.

As of March 31, 2021, we had $128.4 million in cash and cash equivalents. Based on our current operating plan, we believe that the net proceeds from this offering, together with our existing cash and cash equivalents, will be sufficient to fund our operations through at least the next 24 months from the date of our unaudited interim condensed financial statements included elsewhere in this prospectus. Our estimate as to how long we expect the net proceeds from this offering, together with our existing cash and cash equivalents, to be able to continue to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. Our operations have consumed substantial amounts of cash since inception, and we expect our expenses to increase in connection with our ongoing activities, particularly as we initiate and conduct clinical trials of, and seek marketing approval for, our programs as well as develop our proprietary drug discovery platforms. Even if one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with sales, marketing, manufacturing and distribution activities. Our expenses could increase beyond expectations if we are required by the FDA, the EMA or other regulatory agencies to perform clinical trials or preclinical studies in addition to those that we currently anticipate. Other unanticipated costs may also arise. Because the design and outcome of our planned and anticipated preclinical studies and clinical trials are highly uncertain, we cannot reasonably estimate the actual amount of resources and funding that will be necessary to successfully complete the development and commercialization of any product candidate we develop. We are not permitted to market or promote any product candidate before we receive marketing approval from the FDA. Following this offering, we also expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in order to continue our operations.

Our future capital requirements will depend on may factors, including, but not limited to:

- the scope, progress, results and costs of researching, developing and testing our product candidates including conducting preclinical studies and clinical trials;
- the costs, timing and outcome of regulatory review of our product candidates or any future candidates;
- the number and characteristics of other product candidates that we pursue or acquire;
- the costs of future activities, including product sales, medical affairs, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;
- the costs of establishing and operating our own manufacturing facility;
- the costs of manufacturing commercial-grade products and sufficient inventory to support commercial launch;
- the cost of commercialization activities, include the cost of building a sales force in anticipation of product commercialization and distribution costs;
- the revenue, if any, received from commercial sale of our products, should any of our product candidates receive marketing approval;
- the cost and timing of hiring new employees to support our continued growth;
- the costs of preparing, filing and prosecuting patent applications, maintaining, protecting and enforcing our intellectual property rights and defending intellectual property-related claims;
- the effect of competing products that may limit market penetration of our products;
- the ability to establish and maintain collaborations on favorable terms, if at all;
- the extent to which we acquire or in-license other product candidates and technologies;
- the timing, receipt and amount of sales of, or milestone payments related to or royalties on, our current or future product candidates, if any;
- our need to implement additional internal systems and infrastructure, including financial and reporting systems;
- the compliance and administrative costs associated with being a public company; and
- the extent to which we acquire or invest in businesses, products, or technologies, although we currently have no commitments or agreements relating to any of these types of transactions.

A change in the outcome of any of these or other factors with respect to the development of any of our product candidates could significantly change the costs and timing associated with the development of that product candidate, and many of these factors are outside of our control. Identifying potential product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory and marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives.

We currently plan to use the net proceeds from this offering, together with our existing resources, as described in the section titled "Use of Proceeds." Advancing the development of our programs will require a significant amount of capital. The net proceeds from this offering, together with our cash and cash equivalents, will not be sufficient for us to fund any of our product candidates through regulatory approval, and we will need to raise additional capital to complete the development and commercialization of our product candidates.

We may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Attempting to secure additional financing may divert our management from our day-to-day activities, which may adversely affect our ability to develop our product candidates. Our failure to raise capital as and when needed or on acceptable terms would have a negative impact on our financial condition and our ability to pursue our business strategy, and we may have to delay, reduce the scope of, suspend or eliminate one or more of our platforms, programs, planned clinical trials or future commercialization efforts.

Our operations and financial results could be adversely impacted by the COVID-19 pandemic in the United States and the rest of the world.

In March 2020, the World Health Organization declared the novel coronavirus disease (COVID-19) outbreak a global pandemic. To limit the spread of COVID-19, governments have taken various actions including the issuance of stay-at-home orders and physical distancing guidelines. Accordingly, businesses have adjusted, reduced or suspended operating activities. Beginning in March 2020, the majority of our workforce began working from home. Disruptions caused by the COVID-19 pandemic, including the effects of the stay-at-home orders and work-from-home policies, have impacted productivity, have resulted in increased operational expenses, certain adjustments to our operations, delays in our development efforts, and delays in certain supply chain activities. We may experience further disruptions as a result of COVID-19 that could severely impact our business, including:

- interruptions, difficulties or delays arising in our existing operations and company culture as a result of all of our employees working remotely, including those hired during the COVID-19 pandemic;
- delays in the build out of our manufacturing facility;
- delays in receiving approval from local regulatory authorities to initiate our planned clinical trials;
- delays or difficulties in enrolling and retaining patients in clinical trials and incurrence of additional costs as a result of preclinical study and clinical trial delays and adjustments;
- challenges related to ongoing and increased operational expenses related to the COVID-19 pandemic;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- delays, difficulties or increased costs to comply with COVID-19 protocols at our leased facilities and clinical sites;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals that may serve as our potential clinical trial sites and hospital staff supporting the conduct of clinical trials;

- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others;
- limitations in resources that would otherwise be focused on the conduct of our business or our clinical trials, including because of sickness or the desire to avoid contact with large groups of people or as a result of government-imposed "Stay-at-Home" orders or similar working restrictions;
- delays in preclinical and clinical sites receiving the supplies and materials needed to conduct our planned clinical trials;
- interruption in global shipping that may affect the transport of clinical trial materials, such as investigational drug product to be used in our clinical trials;
- changes in regulations as part of a response to the COVID-19 pandemic which may require us to change the ways in which our clinical trials are conducted, or to discontinue clinical trials altogether, or which may result in unexpected costs;
- delays in necessary interactions with regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government or contractor personnel;
- refusal of the FDA to accept data from clinical trials in affected geographies outside the United States;
- increased competition for CROs, contract development and manufacturing organizations (CDMOs), suppliers and vendors; and
- delays in collecting, receiving and analyzing data from patients enrolled in our clinical trials due to limited staff at potential clinical trial sites, limitation or suspension of on-site visits by patients, or patients' reluctance to visit the clinical trial sites during the pandemic.

We will continue to assess the impact that COVID-19 may have on our ability to effectively conduct our business operations as planned and there can be no assurance that we will be able to avoid a material impact on our business from the spread of COVID-19 or its consequences, including disruption to our business and downturns in business sentiment generally or in our industry.

Additionally, certain third parties with whom we engage or may engage, including our collaborators, CROs, third-party manufacturers, suppliers, clinical trial sites, regulators and other third parties with whom we conduct business have similarly adjusted their operations and are assessing their capacity in light of the COVID-19 pandemic. If these third parties experience shutdowns or continued business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively impacted. For example, as a result of the COVID-19 pandemic, we experienced delays in the procurement of materials needed to conduct our preclinical studies. Additionally, certain preclinical studies are conducted by CROs, some of which were delayed as a result of the COVID-19 pandemic and which could be discontinued or further delayed as the pandemic continues. Research and development expenses and general and administrative expenses may vary significantly if there is an increased impact from COVID-19 on the costs and timing associated with the conduct of our business. As we continue to actively advance our programs, we are assessing the impact of the COVID-19 pandemic, our expected timelines and costs on an ongoing basis.

Three vaccines for COVID-19 have been granted Emergency Use Authorization by the FDA, and more are likely to be authorized in the coming months. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, has made it more difficult to obtain materials and manufacturing slots for our product candidates needed for our preclinical studies and clinical trials, which could lead to delays in these studies and trials.

The global outbreak of COVID-19 continues to rapidly evolve. The extent to which the COVID-19 pandemic impacts our business will depend on future developments such as the rate of the spread of the disease,

travel restrictions and social distancing in the United States and other countries, business closures or business disruptions, supply of and demand for vaccines, and the effectiveness of actions taken in the United States and other countries to contain and treat the disease and to address its impact, including on financial markets or otherwise. Further, a lack of coordinated response on risk mitigation and vaccination deployment with respect to the COVID-19 pandemic could result in significant increases to the duration and severity of the pandemic and could have a corresponding negative impact on our business. While the extent of the impact of the current COVID-19 pandemic on our business and financial results is uncertain, a continued and prolonged public health crisis such as the COVID-19 pandemic could have a material negative impact on our business, financial condition and operating results.

To the extent the COVID-19 pandemic adversely affects our business, financial condition and operating results, it may also have the effect of heightening many of the risks described in this “Risk Factors” section.

Raising additional capital will cause dilution to our stockholders, including purchasers of our common stock in this offering, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial revenues, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources, which may dilute our stockholders or restrict our operating activities. We do not have any committed external source of funds. Adequate additional financing may not be available to us on acceptable terms, or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making acquisitions, engaging in acquisition, merger or collaboration transactions, selling or licensing our assets, making capital expenditures, redeeming our stock, making certain investments, declaring dividends or encumbering our assets to secure future indebtedness. Such restrictions could adversely impact our ability to conduct our operations and execute our business plan.

If we raise additional funds through upfront payments or milestone payments pursuant to strategic collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or intellectual property, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes to offset future taxable income may be limited.

Our net operating loss (NOL) carryforwards may be unavailable to offset future taxable income because of restrictions under U.S. tax law. Our NOLs generated in tax years ending on or prior to December 31, 2017 are only permitted to be carried forward for 20 taxable years under applicable U.S. federal tax law, and therefore could expire unused. Under tax legislation commonly referred to as the Tax Cuts and Jobs Act (Tax Act) as amended by the Coronavirus Aid, Relief, and Economic Security Act (CARES Act), our federal NOLs generated in tax years beginning after December 31, 2017 may be carried forward indefinitely, but for taxable years beginning after December 31, 2020, the deductibility of federal NOLs generated in tax years beginning after December 31, 2017 is limited to 80% of our current year taxable income. It is uncertain if and to what extent various states will conform to the Tax Act. As of December 31, 2020, we had available federal NOL carry forwards of approximately $78.5 million, of which $75.4 million do not expire.

In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (Code), if a corporation undergoes an "ownership change" (generally defined as a cumulative change in the corporation's ownership by "5-percent shareholders" that exceeds 50 percentage points over a rolling three-year period), the corporation's ability to use its pre-change NOLs and certain other pre-change tax attributes to offset its post-change taxable income may be limited. Similar rules may apply under state tax laws. We have experienced such ownership changes in the past, and we may experience ownership changes in the future as a result of this offering or subsequent shifts in our stock ownership, some of which are outside our control. As of December 31, 2020, a formal study was conducted and concluded that we experienced an ownership change during 2020. As a result, we have removed $3.1 million of deferred tax assets related to NOLs and research tax credit carryforwards due to Section 382 limitations. Our ability to utilize our remaining NOLs and certain other tax attributes could be further limited by a future "ownership change" as described above and consequently, we may not be able to utilize a material portion of our NOLs and certain other tax attributes, which could have a material adverse effect on our cash flows and results of operations.

Risks Related to the Discovery, Development, Manufacturing and Commercialization of Our Product Candidates

Our product candidates are in the early stages of development and we have no products approved for commercial sale. If we are unable to successfully develop, receive regulatory approval for, manufacture and commercialize our product candidates, or successfully develop any other product candidates, or experience significant delays in doing so, our business will be harmed.

We are very early in our development efforts. We have not initiated clinical trials for any of our programs. We do not have any products that are approved for commercial sale, and we may never be able to develop or commercialize marketable products. Before we generate any revenue from product sales, each of our programs and product candidates will require additional preclinical and clinical development, expansion of manufacturing capabilities and expertise, regulatory approval, building a commercial organization or successfully outsourcing commercialization, substantial investment and significant marketing efforts. We are not permitted to market or promote any product candidates before we receive approval from the FDA or comparable foreign regulatory authorities, and we many never receive such approval. Because our product candidates are in an early stage of development, there is a high risk of failure and we may never succeed in developing marketable products.

If we do not successfully initiate and complete our planned clinical trials in a timely manner or fail to achieve favorable results from the trial, we may experience significant delays or other issues in advancing our programs. We cannot be certain that our clinical trials will be initiated and completed on time, if at all, or whether our planned clinical strategy will be acceptable to the FDA or comparable foreign regulatory authorities. There is a high failure rate for biopharmaceutical products proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials even after achieving promising results in earlier stage clinical trials. Data obtained from preclinical studies and clinical trials are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, regulatory delays or rejections may be encountered as a result of many factors, including changes in regulatory policy during the period of product development.

Because of the early stage of development of our programs, our ability to eventually generate significant revenues from our product candidates, which we do not expect will occur for several years, if ever, will depend on a number of factors, including:

- the successful and timely completion of our ongoing preclinical studies;
- generating sufficient data to support the initiation or continuation of clinical trials;
- addressing any delays, necessary adjustments and additional costs in preclinical studies and clinical trials resulting from factors related to the COVID-19 pandemic;

- submission of INDs or other regulatory applications for our planned clinical trials and authorizations from regulators to initiate clinical trials;
- contracting with the necessary parties to conduct clinical trials;
- successful enrollment in, and completion of, clinical trials on a timely basis;
- achieving favorable results from clinical trials;
- the timely manufacture of sufficient quantities of a product candidate for use in clinical trials and, if approved, commercialization;
- successful outputs from our capsid engineering and promotor and regulator elements efforts;
- sufficiency of our financial and other resources to complete the necessary preclinical studies and clinical trials and commercialization activities;
- the frequency and severity of adverse events in clinical trials;
- demonstrating efficacy, safety and tolerability profiles that are satisfactory to the FDA, EMA or any comparable foreign regulatory authority for marketing approval;
- the timely receipt of marketing approvals from applicable regulatory authorities;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- operational, technical and clinical development challenges associated with pediatric indications that we may pursue, including challenges associated with recruiting and enrolling eligible pediatric patients in clinical trials;
- additional clinical trials and other requirements imposed by regulatory authorities for expanding drug labeling to include pediatric populations or for approval a pediatric product candidate, including formulation changes, additional bridging studies, manufacturing changes, dosage and administration changes, among others;
- the maintenance of existing or the establishment of new supply arrangements with third-party drug product suppliers and manufacturers for clinical development and, if approved, commercialization;
- maintaining consistent quality, purity, and potency across clinical supplies and commercial supplies for any approved products;
- obtaining and maintaining patent and other intellectual property protection, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- protecting, enforcing and defending our rights in our intellectual property portfolio;
- our ability to expand into multiple indications;
- the successful launch of commercial sales following any marketing approval;
- a continued acceptable safety profile and sustained therapeutic effect of our therapies following any marketing approval;
- the actual market-size, ability to identify patients and the demographics of patients eligible for our product candidates, which may be different than expected;
- commercial acceptance by patients, the medical community and third-party payors, particularly since the product candidates we develop may be novel; and
- our ability to compete with other therapies.

We do not have control over many of these factors, including certain aspects of preclinical and clinical development and the regulatory submission process and potential threats to our intellectual property rights. If we are not successful with respect to one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business.

To become and remain profitable, we must develop, obtain approval for and eventually commercialize products candidates, if approved, that generate significant revenue. We do not expect to receive approval of any product candidates for many years and may never succeed in these activities. In addition, it is not uncommon for product candidates to exhibit unforeseen safety issues or inadequate efficacy when tested in humans despite promising results in preclinical animal models, and we may ultimately be unable to demonstrate adequate safety and efficacy of our product candidates to obtain marketing approval. Even if we obtain approval and begin commercializing one or more of our product candidates, we may never generate revenue that is significant or large enough to achieve profitability.

Even if we succeed in commercializing one or more of our product candidates, we will continue to incur substantial research and development, manufacturing and other expenditures to develop and market additional product candidates. Our failure to become or remain profitable would decrease the value of the company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations.

Even if we successfully discover and advance product candidates into clinical development, their success will be subject to all of the clinical, regulatory and commercial risks described elsewhere in this “Risk Factors” section. Accordingly, we cannot assure you that we will ever be able to discover, develop, obtain regulatory approval of, manufacture, commercialize or generate significant revenue from any product candidates.

We intend to identify and develop gene therapy product candidates based on novel technology, and because the regulatory landscape that governs any product candidates we may develop is rigorous, complex, uncertain and subject to change, we cannot predict the time and cost of obtaining regulatory approval, if we receive it at all, for any product candidates we may develop.

We intend to discover, develop, manufacture, and commercialize gene therapy product candidates for the heart. Our product candidates may use both known capsids, such as AAV9, as well as proprietary capsids developed in-house through our own capsid engineering efforts or licensed from third parties. Furthermore, our product candidates may also use novel heart-specific promoters and we may explore different routes-of-administration involving infusion- or injection-based catheters to support targeted delivery and efficient uptake of gene therapies for the heart. We are also establishing proprietary manufacturing processes for our product candidates. Our future success depends on the successful development of these novel therapeutic approaches.

To date, only three products that utilize AAV-mediated gene transfer have been approved in the United States or Europe, including Novartis Pharmaceuticals’ Zolgensma (developed by AveXis), Roche’s Luxturna (developed by Spark Therapeutics), and uniQure’s Glybera. No AAV-based gene therapies have yet been approved for the heart, much less therapies for the heart using novel capsids or promoters or delivery methods. It is therefore difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in the United States, the European Union or other jurisdictions.

The regulatory requirements that will govern any novel gene therapy product candidates we develop are not entirely clear, have changed over time and are subject to further change. Within the broader genetic medicine field, very few therapeutic products have received marketing authorization from the FDA, the EMA or comparable foreign regulatory authorities. Even with respect to more established products that fit into the categories of gene therapies or cell therapies, the regulatory landscape is still developing. Regulatory requirements governing gene therapy products and cell therapy products have changed frequently and will likely continue to change in the future. Changes in the regulatory authorities’ data requirements and risk mitigation methods, including requirements resulting from safety concerns raised by regulatory authorities in clinical programs of unrelated companies in the gene therapy and cardiovascular fields in general, could have a material impact on our clinical development, increase our costs, and delay regulatory approval of our product candidates. Moreover, there is substantial overlap in those responsible for regulation of existing gene therapy products and

cell therapy products. For example, in the United States, the FDA has established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research (CBER) to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review.

Our product candidates will need to meet safety and efficacy standards applicable to any new biologic under the regulatory framework administered by the FDA. In addition to FDA oversight and oversight by institutional review boards (IRBs), under guidelines promulgated by the National Institutes of Health (NIH), gene therapy clinical trials are also subject to review and oversight by an institutional biosafety committee (IBC), a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment. While the NIH guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH guidelines voluntarily follow them. Although the FDA decides whether individual gene therapy protocols may proceed, the review process and determinations of other reviewing bodies can impede or delay the initiation of a clinical trial, even if the FDA has reviewed the trial and approved its initiation.

The same applies in the European Union. The EMA's Committee for Advanced Therapies (CAT) is responsible for assessing the quality, safety, and efficacy of advanced-therapy medicinal products. Advanced-therapy medicinal products include gene therapy medicines, somatic-cell therapy medicines and tissue-engineered medicines. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for a gene therapy medicinal candidate that is submitted to the EMA. In the European Union, the development and evaluation of a gene therapy product must be considered in the context of the relevant EU guidelines. The EMA may issue new guidelines concerning the development and marketing authorization for gene therapy products and require that we comply with these new guidelines. As a result, the procedures and standards applied to gene therapy products and cell therapy products may be applied to any gene therapy product candidate we may develop, but that remains uncertain at this point.

Approvals by the EMA may not be indicative of what the FDA may require for approval. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approvals necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue and our business, financial condition, results of operations and prospects could be materially harmed.

Adverse developments in preclinical studies or clinical trials conducted by others in the field of gene therapy and gene regulation products may cause the FDA, the EMA, and other regulatory bodies to revise the requirements for the conduct of the clinical studies and approval of any product candidates we may develop or limit the use of products utilizing gene regulation technologies, either of which could harm our business. In addition, the clinical trial requirements of the FDA, the EMA, and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty, and intended use and market of the potential products. The regulatory approval process for product candidates such as ours can be more expensive and take longer than for other, better known, or more extensively studied pharmaceutical or other product candidates. Further, as we are developing novel potential treatments for diseases in which, in some cases, there is little clinical experience with potential new endpoints and methodologies, there is heightened risk that the FDA, the EMA or other regulatory bodies may not consider the clinical trial endpoints to provide clinically meaningful results, and the resulting clinical data and results may be more difficult to analyze. In addition, we may not be able to identify or develop appropriate animal disease models to enable or support planned clinical development. Any natural history studies that we may conduct or rely upon in our clinical development may not be accepted by the FDA, EMA or other regulatory authorities. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of products utilizing gene regulation technology in a timely manner or under technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in

expenses, delays, or other impediments to our research programs or the commercialization of resulting products. Further, approvals by one regulatory agency may not be indicative of what other regulatory agencies may require for approval.

The regulatory review committees and advisory groups described above and the new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional preclinical studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates, or lead to significant post-approval limitations or restrictions. As we advance our research programs and develop future product candidates, we will be required to consult with these regulatory and advisory groups and to comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of any product candidates we identify and develop. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all.

The mechanisms of action of our product candidates are unproven, and we do not know whether we will be able to develop any drug of commercial value.

We have discovered and are developing product candidates that have what we believe are novel mechanisms of action. Because no currently-approved drugs appear to operate via the same biochemical mechanisms as our compounds, we cannot be certain that our product candidates will result in commercially viable drugs that safely and effectively treat the indications for which we intend to develop them. The results we have seen for our compounds in preclinical models may not translate into similar results in humans, and results of early clinical trials in humans may not be predictive of the results of larger clinical trials that may later be conducted with our product candidates. As an example, patients may develop antibodies against the product candidates, or the product candidates may otherwise have a more limited duration of therapeutic effect than anticipated, resulting in decreased efficacy over time, which could delay approval and, if approved, limit the ultimate commercial value. Even if we are successful in developing and receiving regulatory approval for a product candidate for the treatment of a particular disease, we cannot be certain that it will be accepted by prescribers or be reimbursed by insurers or that we will also be able to develop and receive regulatory approval for that or other product candidates for the treatment of other diseases. If we are unable to successfully develop and commercialize our product candidates, our business will be materially harmed.

Moreover, in the event any of our competitors were to develop their own product candidates that have a similar mechanism of action to any of our product candidates, any efficacy or safety concerns identified during the development of such similar product candidates may have an adverse impact on the development of our product candidates. For example, if our competitors' product candidate having a similar mechanism of action as any of our product candidates is shown in clinical trials to give rise to serious safety concerns or have poor efficacy when administered to the target patient population, the FDA or other regulatory bodies may subject our product candidates to increased scrutiny, leading to additional delays in development and potentially decreasing the chance of ultimate approval of our product candidates.

Preclinical and clinical drug development involves a lengthy and expensive process with an uncertain outcome. The clinical trials of our product candidates may not demonstrate safety and efficacy to the satisfaction of the FDA, EMA or other comparable foreign regulatory authorities or otherwise produce positive results and the results of preclinical studies and early clinical trials may not be predictive of future results. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

It is impossible to predict when or if any product candidate that we develop will prove effective or safe in humans or will receive marketing approval. Before obtaining marketing approval from the FDA, EMA or other

comparable foreign regulatory authorities for the sale of our product candidates, we must complete preclinical development and extensive clinical trials to demonstrate with substantial evidence the safety and efficacy of such product candidates.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and its ultimate outcome is uncertain. We cannot guarantee that any of our clinical trials will be conducted as planned or completed on schedule, or at all. Clinical trials can fail at any stage of testing and failure may result from a multitude of factors, including, among other things, flaws in study design, dose selection issues, placebo effects, patient enrollment criteria and failure to demonstrate favorable safety or efficacy traits. The outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later clinical trials. For example, our product candidates may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies or having successfully advanced through initial clinical trials. As a result, we cannot assure you that any clinical trials that we conduct will demonstrate consistent or adequate efficacy and safety to support marketing approval.

To the extent we pursue any pediatric indications or expand any approved drug product labeling to include pediatric populations, we may face additional challenges associated with clinical testing in pediatric populations, which can increase our operational costs, delay regulatory approval and commercialization, or expose us to additional liability. For example, finding qualified clinical sites that have access to sufficient pediatric populations and that are interested in participating in our clinical trials may take additional time than adult indications. There may be fewer eligible patients with the target genetic disorder or heart disease or condition applicable to our product candidate for our planned clinical trials. This may increase the time needed to enroll patients for our planned pediatric clinical trials, increase our clinical development timelines, delay approval for such pediatric indications, and increase our operational costs. We may also be required to modify the formulation or other aspects of the product candidate, as compared to the comparable product candidate intended for adult patient populations, make manufacturing changes, modify route of administration, and conduct additional clinical studies, such as bridging studies and additional safety studies, before we can commence our clinical trials in pediatric populations. Any delays in our planned clinical development activities for pediatric patients could have an adverse effect on our business operations.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier-stage clinical trials, and we cannot be certain that we will not face similar setbacks. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their drugs. This is particularly true for clinical trials in very rare diseases, such as with certain indications we are pursuing, where the very small patient population makes it difficult or impossible to conduct two traditional, adequate and well-controlled studies, and therefore the FDA or comparable foreign regulatory authorities are often permitted to exercise flexibility in approving therapies for such diseases. Moreover, results acceptable to support approval in one jurisdiction may be deemed inadequate by another regulatory authority to support regulatory approval in that other jurisdiction. To the extent that the results of the trials are not satisfactory to the FDA or comparable foreign regulatory authorities for support of a marketing application, we may be required to expend significant resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates. Furthermore, the failure of any of our product candidates to demonstrate safety and efficacy in any clinical trial could negatively impact the perception of our other product candidates and/or cause the FDA or comparable regulatory authorities to require additional testing before approving any of our product candidates.

To date, we have not initiated or completed any clinical trials required for the approval of our product candidates. We may experience numerous unforeseen events during, or as a result of, preclinical studies or clinical trials that could delay or prevent receipt of marketing approval or our ability to commercialize our product candidates, including:

- inability to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation of clinical trials;
- delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for advanced clinical trials, including our natural history studies;
- receipt of feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- clinical trial observations or results that require us to modify the design of our clinical trials;
- negative or inconclusive clinical trial results that may require us to conduct additional clinical trials or abandon certain drug development programs;
- obtaining approval from one or more IRBs;
- the number of patients required for clinical trials being larger than anticipated, enrollment in these clinical trials being slower than anticipated or participants dropping out of these clinical trials at a higher rate than anticipated;
- any failure or delay in reaching an agreement with CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- the suspension or termination of our clinical trials for various reasons, including non-compliance with regulatory requirements or a finding that our product candidates have undesirable side effects or other unexpected characteristics or risks;
- changes to clinical trial protocol;
- clinical sites deviating from trial protocol or dropping out of a trial;
- the cost of clinical trials of our product candidates being greater than anticipated;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates being insufficient or inadequate;
- subjects experiencing severe or unexpected drug-related adverse effects;
- selection of clinical end points that require prolonged periods of clinical observation or analysis of the resulting data;
- a facility manufacturing our product candidates or any of their components being ordered by the FDA or comparable foreign regulatory authorities to temporarily or permanently shut down due to violations of current good manufacturing practice (cGMPs), regulations or other applicable requirements, or infections or cross-contaminations of product candidates in the manufacturing process;
- any changes to our manufacturing process that may be necessary or desired;
- third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, good clinical practices (GCP) or other regulatory requirements;
- third-party contractors not performing data collection or analysis in a timely or accurate manner;
- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications;
- regulators revising the requirements for approving our product candidates;

- absence in some countries of established groups with sufficient regulatory expertise for review of AAV gene therapy protocols; and
- the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing in a timely manner, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may incur unplanned costs, be delayed in seeking and obtaining marketing approval, if we receive such approval at all, receive more limited or restrictive marketing approval, be subject to additional post-marketing testing requirements or have the drug removed from the market after obtaining marketing approval.

Moreover, in the future, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. Moreover, our product development costs will also increase if we experience delays in preclinical studies or clinical trials or in obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. We may also determine to change the design or protocol of one or more of our clinical trials, which could result in increased costs and expenses and/or delays. Any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues.

In addition, many of the factors that cause, or lead to, termination or suspension of, or a delay in the commencement or completion of, clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. Any delays to our clinical trials that occur as a result could shorten any period during which we may have the exclusive right to commercialize our product candidates and our competitors may be able to bring products to market before we do, and the commercial viability of our product candidates could be significantly reduced. Any of these occurrences may harm our business, financial condition and prospects significantly.

Our product candidates may cause serious adverse events, toxicities or other undesirable side effects when used alone or in combination with other approved products or investigational new drugs that may result in a safety profile that could prevent regulatory approval, prevent market acceptance, limit their commercial potential or result in significant negative consequences.

We are developing novel therapies for the treatment of heart disease. As a result, there is uncertainty as to the safety profile of product candidates we may develop. If our product candidates are associated with undesirable side effects or have unexpected characteristics in preclinical studies or clinical trials we may need to interrupt, delay or abandon their development or limit development to more narrow uses or subpopulations in

which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Treatment-related side effects could also affect patient recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. There is no guarantee that our product candidates will not have side effects similar to those seen in other gene therapies or that we will be able to prevent side effects from escalating to an unsafe level for our patients. Any of these occurrences may prevent us from achieving or maintaining market acceptance of the affected product candidate and may harm our business, financial condition and prospects significantly.

Patients in our planned clinical trials may in the future suffer other serious adverse events or other side effects not observed in our preclinical studies or previous clinical trials. Patients treated with our other product candidates may also be undergoing other therapies which can cause side effects or adverse events that are unrelated to our product candidate but may still impact the success of our clinical trials. The inclusion of critically ill patients in our clinical trials may result in deaths or other adverse medical events due to other therapies or medications that such patients may be using or due to the gravity of such patients' illnesses. For example, it is expected that some of the patients enrolled in our clinical trials will die or experience major clinical events either during the course of our clinical trials or after participating in such trials.

If further serious adverse events or other side effects are observed in any of our current or future clinical trials, we may have difficulty recruiting patients to the clinical trials, patients may drop out of our trials, or we may be required to abandon the trials or our development efforts of that product candidate altogether. We, the FDA, EMA, other comparable regulatory authorities or an IRB may suspend clinical trials of a product candidate at any time for various reasons, including a belief that subjects in such trials are being exposed to unacceptable health risks or adverse side effects. Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early-stage trials have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude the product candidate from obtaining or maintaining marketing approval, undesirable side effects may inhibit market acceptance due to its tolerability versus other therapies. Any of these developments could materially harm our business, financial condition and prospects. Further, if any of our product candidates obtains marketing approval, toxicities associated with such product candidates previously not seen during clinical testing may also develop after such approval and lead to a requirement to conduct additional clinical safety trials, additional contraindications, warnings and precautions being added to the drug label, significant restrictions on the use of the product or the withdrawal of the product from the market. We cannot predict whether our product candidates will cause toxicities in humans that would preclude or lead to the revocation of regulatory approval based on preclinical studies or early stage clinical trials.

The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and the results of our clinical trials may not satisfy the requirements of the FDA, EMA or other comparable foreign regulatory authorities.

We will be required to demonstrate with substantial evidence through well-controlled clinical trials that our product candidates are safe and effective for use in a diverse population before we can seek marketing approvals for their commercial sale. Success in preclinical studies and early-stage clinical trials does not mean that future clinical trials will be successful. For instance, we do not know whether any of our product candidates will perform in our current or future preclinical studies or future clinical trials as it has in prior preclinical studies or earlier clinical trials. Product candidates in clinical trials may fail to demonstrate sufficient safety and efficacy to the satisfaction of the FDA, EMA and other comparable foreign regulatory authorities despite having progressed through preclinical studies. Regulatory authorities may also limit the scope of later-stage trials until we have demonstrated satisfactory safety, which could delay regulatory approval, limit the size of the patient population to which we may market our product candidates, or prevent regulatory approval.

In some instances, there can be significant variability in safety and efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in

size and type of the patient populations, differences in and adherence to the dose and dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. Patients treated with our product candidates may also be undergoing other therapies and may be using other approved products or investigational new drugs, which can cause side effects or adverse events that are unrelated to our product candidates. As a result, assessments of efficacy can vary widely for a particular patient, and from patient to patient and site to site within a clinical trial. This subjectivity can increase the uncertainty of, and adversely impact, our clinical trial outcomes.

We do not know whether any clinical trials we may conduct will demonstrate consistent or adequate efficacy and safety sufficient to obtain approval to market any of our product candidates.

If we experience delays or difficulties in the enrollment and/or maintenance of patients in clinical trials, our regulatory submissions or receipt of necessary marketing approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials to such trial's conclusion as required by the FDA, EMA or other comparable foreign regulatory authorities. Patient enrollment is a significant factor in the timing of clinical trials. Our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate.

We may experience delays if our clinical trial sites limit their onsite staff or temporarily close as a result of the COVID-19 pandemic. In addition, patients may not be able to visit clinical trial sites for dosing or data collection purposes due to limitations on travel and physical distancing imposed or recommended by federal or state governments or patients' reluctance to visit the clinical trial sites during the pandemic. These factors resulting from the COVID-19 pandemic could delay the anticipated readouts from our clinical trials and our regulatory submissions.

We are developing product candidates for the treatment of heart disease, including for certain indications, such as rare genetic diseases, with limited patient pools from which to draw for clinical trials. We also may encounter difficulties in identifying and enrolling patients with a stage of disease appropriate for our planned clinical trials and monitoring such subjects adequately during and after treatment. The process of finding and diagnosing patients may prove costly. Further, the treating physicians in our clinical trials may also use their medical discretion in advising patients enrolled in our clinical trials to withdraw from our studies to try alternative therapies.

We expect patient enrollment to be affected because our competitors have ongoing clinical trials for programs that are under development for the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials could instead enroll in clinical trials of our competitors' programs. Patient enrollment for our current or any future clinical trials may be affected by other factors, including:

- size and nature of the patient population;
- challenges associated with recruiting pediatric patient population, including, but not limited to, identifying clinical sites that are qualified to participate in pediatric clinical trials, smaller number of eligible pediatric patients who are interested in participating within the target age groups, or under-diagnosis or challenges associated with diagnosing pediatric populations with the applicable target disease or condition;
- perceived risks and benefits of novel, unproven approaches;
- severity of the disease under investigation;
- availability and efficacy of approved drugs for the disease under investigation;
- patient eligibility criteria for the trial in question as defined in the protocol;

- perceived risks and benefits of the product candidate under study;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new products that may be approved or other product candidates being investigated for the indications we are investigating;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- the activities of key opinion leaders (KOLs) and patient advocacy groups;
- proximity and availability of clinical trial sites for prospective patients; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion or, because they may have an advanced disease, will not survive the full terms of the clinical trials.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates and jeopardize our ability to obtain marketing approval for the sale of our product candidates. Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining participation in our clinical trials through the treatment and any follow-up periods.

Due to the significant resources required for the development of product candidates, and depending on our ability to access capital, we must prioritize development of certain programs and product candidates. Moreover, we may expend our limited resources on programs or product candidates that do not yield a successful product and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Due to the significant resources required for the development of product candidates, in particular our product candidates in IND-enabling studies and those that begin clinical trials, we must decide which programs, product candidates and indications to pursue and advance and the amount of resources to allocate to each. Our decisions concerning the allocation of research, development, collaboration, management and financial resources toward particular programs, product candidates or therapeutic areas may not lead to the development of any viable commercial product and may divert resources away from better opportunities. Similarly, our potential decisions to delay, terminate or collaborate with third parties in respect of certain platforms, programs or product candidates may subsequently also prove to be less than optimal and could cause us to miss valuable opportunities. If we make incorrect determinations regarding the viability or market potential of any of our programs or product candidates or misread trends in the biotechnology industry, in particular in the field of cardiology, our business could be seriously harmed. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other programs, product candidates or other diseases that may later prove to have greater commercial potential than those we choose to pursue, or relinquish valuable rights to our platforms or product candidates through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain sole development and commercialization rights.

We face significant competition and if our competitors develop and market technologies or products more rapidly than we do or that are more effective, safer or less expensive than the products we develop, our commercial opportunities will be negatively impacted.

The biotechnology and biopharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary and novel products and product candidates. Our competitors have developed, are developing or may develop products, product candidates and processes competitive with our product candidates. Any product candidates that we successfully develop and

commercialize will compete with existing therapies and new therapies that may become available in the future. We believe that a significant number of products are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may attempt to develop product candidates.

We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies, emerging and start-up companies, universities and other research institutions. We also compete with other organizations to recruit management, scientists and clinical development personnel, which could negatively affect our level of expertise and our ability to execute our business plan. We will also face competition in establishing clinical trial sites, enrolling subjects for clinical trials and in identifying and in-licensing new product candidates.

We expect to face competition from existing products and products in development for each of our programs. We anticipate substantial direct competition from a variety of competitors, including:

- General cardiovascular drug development: Companies known to have approved product and active drug development efforts for cardiovascular disease include but are not limited to AstraZeneca, Bayer, Bristol Myers Squibb, Cytokinetics, Eli Lilly, Johnson & Johnson/Janssen, Maze Therapeutics, Merck, Novartis, and Novo Nordisk;
- Gene Therapy platform: Companies known to be pursuing gene therapy approaches for the heart include but are not limited to 4D Molecular Therapeutics, Bayer, Bristol Myers Squibb, BioMarin Pharmaceutical, DiNAQOR, Nuevocor, Precigen, Renova Therapeutics, Renovacor, Rocket Pharmaceuticals, Sardicor, Stride Bio, and uniQure;
- Cellular Regeneration platform: Companies known to be pursuing approaches to cellular regeneration for the heart include but are not limited to AstraZeneca, Bayer, BioCardia, Cardior Pharmaceuticals, Jaan Biotherapeutics, Khloris Biosciences, Mesoblast, Mogrify, Sana Biotechnologies and Xylocor Therapeutics; and
- Precision Medicine platform: Companies known to be pursuing approaches to drug discovery for the heart using disease models based on iPSC-CMs include but are not limited to DiNAQOR and Tara Biosystems.

Many of these current and potential competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources and commercial expertise than we do. Large pharmaceutical and biotechnology companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients and manufacturing biotechnology products. These companies also have significantly greater research and marketing capabilities than we do and may also have products that have been approved or are in late stages of development, and collaborative arrangements in our target markets with leading companies and research institutions. Established pharmaceutical and biotechnology companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make the product candidates that we develop obsolete. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies, as well as in acquiring technologies complementary to, or necessary for, our programs. As a result of all of these factors, our competitors may succeed in obtaining approval from the FDA, EMA or other comparable foreign regulatory authorities or in discovering, developing and commercializing products in our field before we do.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer side effects, are more convenient, have a broader label, are marketed more effectively, are more widely reimbursed or are less expensive than any products that we may develop. Our competitors also may obtain marketing approval from the FDA, EMA or other comparable foreign regulatory authorities for their products more rapidly than we may obtain approval for ours, which could result in

our competitors establishing a strong market position before we are able to enter the market. Even if the product candidates we develop achieve marketing approval, they may be priced at a significant premium over competitive products if any have been approved by then, resulting in reduced competitiveness. Technological advances or products developed by our competitors may render our technologies or product candidates obsolete, less competitive or not economical. If we are unable to compete effectively, our opportunity to generate revenue from the sale of our products we may develop, if approved, could be adversely affected.

Interim, topline and preliminary data from our clinical trials that we announce or publish may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary, interim or topline data from our clinical trials. These interim updates are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data is available. In addition, we may report interim analyses of only certain endpoints rather than all endpoints. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse changes between interim data and final data could significantly harm our business and prospects. Further, additional disclosure of interim data by us or by our competitors in the future could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the preliminary or topline data that we report differ from late, final or actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, financial condition, results of operations and prospects.

We may not be successful in our efforts to utilize our proprietary drug discovery platforms to develop a pipeline of product candidates.

A key element of our strategy is to leverage our proprietary drug discovery platforms to develop a pipeline of product candidates to treat heart disease. In order to do so, we must continue to invest in our proprietary drug discovery platforms and development capabilities, including our internal disease modeling and capsid engineering efforts, our in-house cassette engineering capabilities to create novel promoters and regulatory elements to support our programs, and targeted drug delivery approaches for efficient uptake of gene therapies for the heart. Although our research and development efforts to date have resulted in a pipeline of product candidates, these product candidates may not be safe and effective. Our capsid engineering, promoter and regulatory elements may not be successful. In addition, although we expect that our proprietary drug discovery platforms and development capabilities will allow us to develop a diverse pipeline of product candidates, we may not prove to be successful at doing so. Furthermore, we may also find that the uses of our proprietary drug discovery platforms are limited because alternative uses of our therapeutics prove not to be safe or effective.

Even if we are successful in building our pipeline, the potential product candidates that we identify may not be suitable for clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to be products that will receive marketing approval or achieve market acceptance. Further, because our product candidates and programs are based on our proprietary drug discovery platforms, adverse developments with respect to one of our programs may have a significant adverse impact on the actual or perceived likelihood of success and value of our other programs.

In addition, the biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies. Our future success will depend in part on our ability to maintain a competitive position with our approach. If we fail to stay at the forefront of technological change in utilizing our proprietary drug discovery platforms to create and develop programs and product candidates, we may be unable to compete effectively. Our competitors may render our approach obsolete or limit the commercial value of our product candidates, by advances in existing technological approaches or the development of new or different approaches, potentially eliminating the advantages in our drug discovery process that we believe we derive from our research approach and proprietary technologies. By contrast, adverse developments with respect to other companies that attempt to use a similar approach to our approach may adversely impact the actual or perceived value of our proprietary drug discovery platforms and potential of our programs and product candidates. If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations.

The manufacture of drugs is complex, and we or our third-party manufacturers may encounter difficulties in production. If we or any of our third-party manufacturers encounter such difficulties, our ability to provide adequate supply of our product candidates for preclinical studies or clinical trials or our products for patients, if approved, could be delayed or prevented.

Manufacturing drugs, especially in large quantities, is complex and may require the use of innovative technologies. Each lot of an approved drug product must undergo thorough testing for safety identity, strength, quality, purity and potency. Manufacturing drugs requires key materials and facilities specifically designed for and validated for this purpose, as well as sophisticated QA and QC procedures. Slight deviations anywhere in the manufacturing process, including manufacturing drug substance, drug product filling, labeling, packaging, storage and shipping and quality control and testing, may result in lot failures or product recalls. When changes are made to the manufacturing process, we may be required to provide preclinical and clinical data showing the comparable quality and efficacy of the products before and after such changes. If we or our third-party manufacturers are unable to produce sufficient quantities for preclinical studies or clinical trials or for commercialization as a result of these challenges, or otherwise, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

Gene therapies are novel, complex and difficult to manufacture. We could experience production problems that result in delays in development or commercialization of our product candidates, limit the supply of our products, if approved, or otherwise seriously harm our business.

Our gene therapy product candidates require processing steps that are more complex than those required for most chemical and protein pharmaceuticals. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as ours generally cannot be fully characterized. As a result, assays of the finished product may not be sufficient to ensure that the product will perform in the intended manner. Accordingly, we need to employ multiple steps to control our manufacturing process to assure that the process works and the product candidate is made strictly and consistently in compliance with the process. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims or insufficient inventory, which could delay or prevent the initiation of clinical trials or receipt of regulatory approvals. We may encounter problems achieving adequate quantities and quality of clinical-grade materials that meet FDA, or other

comparable applicable foreign regulatory authorities standards or specifications with consistent and acceptable production yields and costs.

In addition, the FDA and other comparable foreign regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA or other comparable foreign regulatory authorities may require that we not distribute a lot until the agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. Lot failures or product recalls could cause us to delay clinical trials or product launches which could be costly to us and otherwise seriously harm our business.

We also may encounter problems hiring and retaining the experienced scientific, quality control and manufacturing personnel needed to operate our manufacturing process which could result in delays in our production or difficulties in maintaining compliance with applicable regulatory requirements.

Any problems in our manufacturing process or facilities or the facilities with which we contract could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies, which could limit our access to additional attractive development programs. Problems in manufacturing process or facilities also could restrict our ability to meet market demand for our products, if approved. Additionally, should our agreement or agreements with other parties with whom we have manufacturing agreements be terminated for any reason, there are a limited number of manufacturers who would be suitable replacements, and it would take a significant amount of time to transition the manufacturing to a replacement.

We are in the process of building out a manufacturing facility to support future production of certain of our product candidates. We have no experience in manufacturing, and there can be no assurance that we will be able to complete our manufacturing facility or, if completed, we will be able to successfully manufacture product candidates.

We have historically relied on third parties to manufacture supplies of our product candidates. We plan to fully integrate and internalize AAV manufacturing capabilities to support our Gene Therapy and Cellular Regeneration platforms. We have established an in-house Pilot Plant Operation facility that operates at the 200L scale to support all non-clinical studies including IND-enabling pharmacology (efficacy) and toxicology (safety) studies. We have initiated construction of a dedicated cGMP facility for drug product manufacturing in the San Francisco Bay Area that we expect will be operational in the first half of 2022. The facility will initially produce drug product at the 1000L scale to support FIH studies for TN-201, the most advanced product candidate from our MYBPC3 program. To optimize our use of resources and utilize extensive third-party experience in small molecule manufacturing, we intend to work with CDMOs for our small molecule programs. We intend to initiate cGMP manufacturing for our HDAC6 inhibitor program, TYA-11631, before the end of 2021.

Although some of our employees have experience in the manufacturing of biopharmaceutical products from prior employment at other companies, we as a company have no prior experience in manufacturing. We may face delays or increased costs in the build out of our manufacturing facility or the production of clinical supply at our manufacturing facility, once operational, and cannot guarantee when our facility will be able to produce sufficient quantities of product candidates needed to support our preclinical studies and planned clinical trials. In addition, government approvals will be required for us to operate our manufacturing facility and can be time-consuming to obtain, and there can be no assurance that such approval will be obtained. As a manufacturer of pharmaceutical products, we also will be required to demonstrate and maintain compliance with cGMP requirements related to production processes, quality control and assurance and recordkeeping. Furthermore, establishing and maintaining manufacturing operations may require a reallocation of other resources and management time, as well as potentially significant capital expenditures, particularly in areas relating to operations, quality, regulatory, facilities and information technology. We also may encounter problems hiring and retaining the experienced scientific, quality control and manufacturing personnel needed to operate our manufacturing processes. If we experience unanticipated

employee shortage or turnover in any of these areas, we may not be able to effectively manage our ongoing manufacturing operations and we may not achieve the operating efficiencies that we anticipate from developing these capabilities, which may negatively affect our product development timelines or result in difficulties in maintaining compliance with applicable regulatory requirements.

Any delays in developing our internal manufacturing capabilities may disrupt or delay the supply of our product candidates if we have not maintained a sufficient back-up supply of such product candidates through third-party manufacturers. Moreover, changing manufacturing facilities during the clinical development process may also require that we conduct additional studies, make notifications to regulatory authorities, make additional filings to regulatory authorities, and obtain regulatory authority approval for the new facilities, which may be delayed or which we may never receive.

Any failure or delay in the development of our manufacturing facility or capabilities may hamper our ability to further process improvement, maintain quality control, limit our reliance on contract manufacturers and protect our trade secrets and other intellectual property, and could adversely impact the development or commercialization of our product candidates.

Our manufacturing facilities will be subject to significant government regulations and approvals, which are often costly and could result in adverse consequences to our business if we fail to comply with the regulations or maintain the approvals.

We will need to comply with the FDA's and applicable foreign regulatory authorities' cGMP requirements for the production of product candidates for clinical trials and, if approved, commercial supply. We may encounter difficulties in achieving QC and QA and may experience shortages in qualified personnel. We will be subject to inspections by the FDA and comparable agencies in other jurisdictions to confirm compliance with applicable regulatory requirements. These requirements include the qualification and validation of our manufacturing equipment and processes. Any failure to follow cGMP or other regulatory requirements or delay, interruption or other issues that arise in the manufacture of our product candidates as a result of a failure of our facilities or the facilities or operations of our third-party suppliers to comply with regulatory requirements or pass any regulatory authority inspection could significantly impair our ability to develop and commercialize our product candidates, including leading to significant delays in the availability of our product candidates for our clinical trials or the termination or hold on a clinical trial, or the delay or prevention of a filing or approval of marketing applications for our product candidates. Significant noncompliance could also result in the imposition of sanctions, including fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals for our product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could damage our reputation. If we are not able to maintain regulatory compliance, we may not be permitted to market our product candidates and/or may be subject to product recalls, seizures, injunctions, or criminal prosecution.

We may not be able to successfully manufacture our product candidates in sufficient quality and quantity, which would delay or prevent us from developing our product candidates and commercializing resulting approved products, if any.

To date, our product candidates have been manufactured in quantities adequate for preclinical studies. In order to conduct clinical trials for a product candidate and for commercialization of the resulting product if that product candidate is approved for sale, we will need to manufacture product candidates in larger quantities. We may not be able to successfully repeat or increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner or at all. Significant changes or scale-up of manufacturing may require additional validation studies, which are costly and which regulatory authorities must review and approve. In addition, quality issues may arise during those changes or scale-up activities. If we are unable to successfully manufacture of any of our product candidates in sufficient quality and quantity, the development of that product candidate and regulatory approval or commercial launch for any resulting products may be delayed or there may be a shortage in supply, which could significantly harm our business.

Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates progress through preclinical studies and clinical trials to marketing approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize yield and manufacturing batch size, minimize costs and achieve consistent quality and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commercialize our product candidates, if approved, and generate revenue.

Even if approved, we may not successfully commercialize our product candidates.

Our product candidates are subject to the risks of failure inherent in the development of pharmaceutical products based on new technologies, and our failure to develop safe, commercially viable products would severely limit our ability to become profitable or to achieve significant revenues. Even if one or more of our product candidates is approved, we may be unable to successfully commercialize our product candidates for several reasons, including:

- some or all of our product candidates may be found to be unsafe or ineffective or otherwise fail to meet applicable regulatory standards or receive necessary regulatory clearances; our product candidates, if safe and effective, may nonetheless not be able to be developed into commercially viable products;
- it may be difficult to manufacture or market our product candidates on a scale that is necessary to ultimately deliver our products to end-users;
- intellectual property and proprietary rights of third parties may preclude us from marketing our product candidates;
- the nature of our indications as rare diseases means that the potential market size may be limited; and
- third parties may market superior or equivalent drugs which could adversely affect the commercial viability and success of our product candidates.

Our product candidates may not achieve adequate market acceptance among physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

Even if our product candidates receive regulatory approval, they may not gain adequate market acceptance among physicians, patients, third-party payors and others in the medical community. If we are unable to demonstrate sufficient safety to permit a broader use of our product candidates, we may not generate significant product revenue and we may not become profitable. The degree of market acceptance of any of our approved product candidates will depend on a number of factors, including:

- the efficacy and safety profile as demonstrated in clinical trials compared to alternative treatments;
- the size of the relevant pediatric patient population if approved for a pediatric indication, including challenges associated with diagnosing or identifying pediatric populations with the applicable target disease or condition;
- perceive safety and efficacy profile and ease of use for pediatric patient population if approved for a pediatric indication;
- the timing of market introduction of the product candidate as well as competitive products;
- the clinical indications for which a product candidate is approved;

- restrictions on the use of product candidates in the labeling approved by regulatory authorities, such as boxed warnings or contraindications in labeling, or a risk evaluation and mitigation strategy, if any, which may not be required of alternative treatments and competitor products;
- physicians, hospitals, treatment centers and patients considering our product candidates as a safe, pure and effective treatment;
- the perceived prevalence and severity of any side effects for our product candidates compared to the prevalence and severity of any side effects for conventional products and other gene therapies;
- the potential and perceived advantages of our product candidates over alternative treatments;
- the cost of treatment in relation to alternative treatments;
- relative convenience and ease of administration;
- the willingness of the target patient population or their caregivers to try new therapies and of physicians to prescribe these therapies;
- the availability of coverage and adequate reimbursement by third-party payors, including government authorities;
- patients' willingness to pay for these therapies in the absence of such coverage and adequate reimbursement;
- the effectiveness of sales and marketing efforts;
- support from KOLs and patient advocacy groups;
- unfavorable publicity relating to our product candidates; and
- the approval of other new therapies for the same indications.

If any of our product candidates are approved but do not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors and patients, we may not generate or derive sufficient revenue from that product candidate and our financial results could be negatively impacted.

Adverse public perception or regulatory scrutiny of gene therapy technology or precision medicine for the treatment of heart diseases may negatively impact the developmental progress or commercial success of product candidates that we develop.

The developmental and commercial success of product candidates that we develop will depend in part on public acceptance of the use of gene therapy technology, including the use of AAVs, and precision medicine for the prevention or treatment of human diseases. Adverse public perception of gene therapies or precision medicine may negatively impact our ability to raise capital or enter into strategic agreements for the development of product candidates.

Gene therapy and precision medicine remain novel technologies. The commercial success of our products, if successfully developed and approved, may be adversely affected by claims that gene therapy or precision medicine is unsafe, unethical or immoral. This may lead to unfavorable public perception and the inability of any of our product candidates to gain the acceptance of the public or the medical community. Unfavorable public perceptions may also adversely impact our ability to enroll clinical trials for our product candidates. Moreover, success in commercializing any product candidates that receive regulatory approval will depend upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of such product candidates in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available.

Publicity of any adverse events in, or unfavorable results of, preclinical studies or clinical trials for any current or future product candidates, or with respect to the studies or trials of our competitors or of academic

researchers utilizing similar technologies, even if not ultimately attributable to our technology or product candidates, could negatively influence public opinion. Negative public perception about the use of AAV technology in human therapeutics or precision medicine, whether related to our technology or our competitor's technology, could result in increased governmental regulation, delays in the development and commercialization of product candidates or decreased demand for the resulting products, any of which may seriously harm our business.

The limited number of patients who have the diseases for which our product candidates are being developed may make it more difficult for us to enroll or complete clinical trials or may result in findings in our clinical trials that do not reach levels of statistical significance sufficient for marketing approval. Even if such product candidates achieve marketing approval, because such target patient populations are small and the addressable patient population may be even smaller, we must be able to successfully identify patients and capture a significant market share to achieve profitability and growth.

Some of the indications for which we plan to evaluate our product candidates in clinical trials are rare genetic diseases. Accordingly, there are limited patient pools from which to draw for clinical trials. In addition to the rarity of these diseases, the eligibility criteria of our planned clinical trials will further limit the pool of available study participants as we will require that patients have specific characteristics that we can measure to assure their disease is either severe enough or not too advanced to include them in a trial. Moreover, the effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. We may not be able to initiate or continue clinical trials on a timely basis or at all for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in the trials as required by applicable regulations or as needed to provide appropriate statistical power for a given trial. Similarly, because some of the conditions we intend to treat are rare in nature, we plan to design and conduct clinical trials utilizing a small number of patients in order to evaluate the safety and therapeutic activity of our product candidates. Conducting trials in smaller subject populations increases the risk that any safety or efficacy issues observed in only a few patients could prevent such trials from reaching statistical significance or otherwise meeting their specified endpoints, which could require us to conduct additional clinical trials, or delay or prevent our product candidates from receiving regulatory approval, which would seriously harm our business.

Additionally, the potentially addressable patient population for our product candidates may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our product candidates, because the potential target populations are very small, we may never achieve profitability despite obtaining such significant market share.

Any product candidates we develop may become subject to unfavorable third-party coverage and reimbursement practices, as well as pricing regulations.

The availability and extent of coverage and adequate reimbursement by third-party payors including government health administration authorities, private health coverage insurers, managed care organizations and other third-party payors is essential for most patients to be able to afford expensive treatments. The indications we are initially pursuing have small patient populations. For product candidates that are designed to treat smaller patient populations to be commercially viable, the reimbursement for such product candidates must be higher, on a relative basis, to account for the lack of volume. Accordingly, we will need to implement a coverage and reimbursement strategy for any approved product candidate that accounts for the smaller potential market size.

Sales of any of our product candidates that receive marketing approval will depend substantially, both in the United States and internationally, on the extent to which the costs of such product candidates will be covered and reimbursed by third-party payors. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved

reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize an adequate return on our investment. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not successfully commercialize any product candidate for which we obtain marketing approval.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved products. In the United States, for example, principal decisions about reimbursement for new products are typically made by the Centers for Medicare & Medicaid Services (CMS), an agency within the U.S. Department of Health and Human Services (HHS). CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare, and private third-party payors often follow CMS's decisions regarding coverage and reimbursement to a substantial degree. However, one third-party payor's determination to provide coverage for a product candidate does not assure that other payors will also provide coverage for the product candidate or at the same level of reimbursement. As a result, the coverage determination process is often time-consuming and costly. This process will require us to provide scientific and clinical support for the use of our products to each third-party payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Further, such payors are increasingly challenging the price, examining the medical necessity and reviewing the cost effectiveness of medical product candidates. There may be especially significant delays in obtaining coverage and reimbursement for newly approved drugs. Third-party payors may limit coverage to specific product candidates on an approved list, known as a formulary, which might not include all FDA-approved drugs for a particular indication. We may need to conduct expensive pharmaco-economic studies to demonstrate the medical necessity and cost effectiveness of our products. Nonetheless, our product candidates may not be considered medically necessary or cost effective. We cannot be sure that coverage and reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be.

Outside the United States, the commercialization of therapeutics is generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost containment initiatives in Europe, Canada and other countries has and will continue to put pressure on the pricing and usage of therapeutics such as our product candidates. In many countries, particularly the countries of the European Union, medical product prices are subject to varying price control mechanisms as part of national health systems. In these countries, pricing negotiations with governmental authorities can take considerable time after a product receives marketing approval. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. In general, product prices under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

If we are unable to establish or sustain coverage and adequate reimbursement for any product candidates from third-party payors, the adoption of those products and sales revenue will be adversely affected, which, in turn, could adversely affect the ability to market or sell those product candidates, if approved. Coverage policies and third-party payor reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Our business entails a significant risk of product liability and if we are unable to obtain sufficient insurance coverage, such inability could have an adverse effect on our business and financial condition. If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our products.

Our business exposes us to significant product liability risks inherent in the development, testing, manufacturing and marketing of therapeutic treatments. We currently have no product liability insurance. Any insurance we have or may obtain may not provide sufficient coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance at a reasonable cost to protect us against losses caused by product liability claims that could have an adverse effect on our business and financial condition. Also, our insurance policies may have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

We may be sued if any of our product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical testing, manufacturing, marketing, or sale post-approval. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, or a breach of warranties. Claims could also be asserted under state consumer protection laws. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit testing and commercialization of our products. Even successful defense would require significant financial and management resources.

Regardless of the merits or eventual outcome, liability claims may result in:

- delays in the development of our product candidates;
- FDA, EMA or other regulatory authority investigation of the safety and effectiveness of our products, our manufacturing processes and facilities or our marketing programs;
- decreased or interrupted demand for our products;
- injury to our reputation;
- withdrawal of clinical trial participants and inability to continue clinical trials;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- a diversion of management’s time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing, or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources; and
- the inability to commercialize any products.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

The regulatory approval processes of the FDA, EMA and other comparable foreign regulatory authorities are lengthy, time consuming and inherently unpredictable. If we are ultimately unable to obtain regulatory approval of our product candidates, we will be unable to generate product revenue and our business will be substantially harmed.

Our product candidates are and will continue to be subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, safety, efficacy, approval, recordkeeping, reporting, labeling, storage, packaging, advertising and promotion, pricing, marketing and distribution of drugs. Rigorous preclinical testing and clinical trials and an extensive regulatory approval process must be successfully completed in the United States and in many foreign jurisdictions before a new drug can be approved for marketing. Obtaining approval by the FDA, EMA and other comparable foreign regulatory authorities is costly, unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the type, complexity and novelty of the product candidates involved. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other data. Even if we eventually complete clinical testing and receive approval for our product candidates, the FDA, EMA and other comparable foreign regulatory authorities may approve our product candidates for a more limited indication or a narrower patient population than we originally requested or may impose other prescribing limitations or warnings that limit the product's commercial potential. We have not submitted for, or obtained, regulatory approval for any product candidate, and it is possible that none of our product candidates will ever obtain regulatory approval. Further, development of our product candidates and/or regulatory approval may be delayed for reasons beyond our control. We cannot provide any assurance that any product candidate we may develop will progress through required clinical testing and obtain the regulatory approvals necessary for us to begin selling them.

We have not initiated, conducted, managed or completed any clinical trials nor managed the regulatory approval process with the FDA or any other regulatory authority. Applications for our product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA, EMA or other comparable foreign regulatory authorities may disagree with the design, implementation or results of our clinical trials;
- the FDA, EMA or other comparable foreign regulatory authorities may determine that our product candidates are not safe and effective, are only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use;
- the population studied in the clinical trial may not be sufficiently broad or representative to assure efficacy and safety in the full population for which we seek approval;
- the FDA, EMA or other comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- we may be unable to demonstrate to the FDA, EMA or other comparable foreign regulatory authorities that our product candidate's risk-benefit ratio for its proposed indication is acceptable;
- the FDA, EMA or other comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA, EMA or other comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations and prospects. Any delay or failure in seeking or obtaining required approvals would have a material and adverse effect on our ability to generate revenue from any particular product candidates we are developing and for which we are seeking approval. Furthermore, any regulatory approval to market a drug may be subject to significant limitations on the approved uses or indications for which we may market, promote and advertise the drug or the labeling or other restrictions. In addition, the FDA has the authority to require a Risk Evaluation and Mitigation Strategy (REMS) plan as part of approving an NDA, or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug. These requirements or restrictions might include limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria and requiring treated patients to enroll in a registry. These limitations and restrictions may significantly limit the size of the market for the drug and affect reimbursement by third-party payors.

We are also subject to numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign regulatory approval process varies among countries, and generally includes all of the risks associated with FDA and EMA approval described above as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval.

The FDA, EMA and other comparable foreign regulatory authorities may not accept data from trials conducted in locations outside of their jurisdiction.

We are planning on undertaking clinical trials in the United States and additional clinical trials internationally. The acceptance of study data by the FDA, EMA or other comparable foreign regulatory authority from clinical trials conducted outside of their respective jurisdictions may be subject to certain conditions. In cases where data from U.S. clinical trials are intended to serve as the basis for marketing approval in the foreign countries outside the United States, the standards for clinical trials and approval may be different. There can be no assurance that any U.S. or foreign regulatory authority would accept data from trials conducted outside of its applicable jurisdiction. If the FDA, EMA or any applicable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval or clearance for commercialization in the applicable jurisdiction.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction. For example, even if the FDA or EMA grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion and reimbursement of the product candidate in those countries. However, a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from those in the United States, including additional preclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval.

Obtaining foreign regulatory approvals and establishing and maintaining compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the

introduction of our products in certain countries. If we or any future collaborator fail to comply with the regulatory requirements in international markets or fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our potential product candidates will be harmed.

Even if we successfully complete the necessary preclinical studies and clinical trials, we cannot predict when, or if, we will obtain regulatory approval to commercialize a product candidate and the approval may be for a narrower indication than we seek.

We cannot commercialize a product candidate until the appropriate regulatory authorities have reviewed and approved the product candidate. We have not received approval from regulatory authorities in any jurisdiction to market any of our product candidates. Even if our product candidates meet their safety and efficacy endpoints in clinical trials, the regulatory authorities may not complete their review processes in a timely manner, issue a complete response letter, or ultimately, we may not be able to obtain regulatory approval. In addition, we may experience delays or rejections if an FDA Advisory Committee recommends disapproval or restrictions on use. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative actions, or changes in regulatory authority policy during the period of product development, clinical trials and the review process. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of data obtained from preclinical and clinical testing could delay, limit or prevent the receipt of marketing approval for a product candidate.

Regulatory authorities also may approve a product candidate for more limited indications than requested or they may impose significant limitations in the form of narrow indications, warnings or other labeling changes. These regulatory authorities may require precautions or contra-indications with respect to conditions of use or they may grant approval subject to the performance of costly post-marketing clinical trials. Regulatory authorities may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a REMS or equivalent requirement. In addition, regulatory authorities may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates and materially harm our business, financial condition, results of operations and prospects.

Even if our product candidates receive regulatory approval, they will be subject to significant post-marketing regulatory requirements and oversight.

Any regulatory approvals that we may receive for our product candidates will require the submission of reports to regulatory authorities and on-going surveillance to monitor the safety and efficacy of the product candidate, may contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, and may include burdensome post-approval study or risk management requirements and regulatory inspection. For example, the FDA may require a REMS in order to approve our product candidates, which could entail requirements for a medication guide, physician training and communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or foreign regulatory authorities approve our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as on-going compliance with cGMPs and GCPs for any clinical trials that we conduct post-approval. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with cGMP regulations and standards. If we or a regulatory agency discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the

facilities where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. In addition, failure to comply with FDA, EMA and other comparable foreign regulatory requirements may subject our company to administrative or judicially imposed sanctions, including:

- delays in or the rejection of product approvals;
- restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials;
- restrictions on the products, manufacturers or manufacturing process;
- warning or untitled letters;
- civil and criminal penalties;
- injunctions;
- suspension or withdrawal of regulatory approvals;
- product seizures, detentions or import bans;
- voluntary or mandatory product recalls and publicity requirements;
- total or partial suspension of production; and
- imposition of restrictions on operations, including costly new manufacturing requirements.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates, if approved, and generate revenue. Furthermore, non-compliance by us or any future collaborator with regulatory requirements, including safety monitoring and with requirements related to the development of products for the pediatric population can also result in significant financial penalties.

We may not be able to obtain orphan drug designation or obtain or maintain orphan drug exclusivity for our product candidates and, even if we do, that exclusivity may not prevent the FDA, EMA or other comparable foreign regulatory authorities, from approving competing products.

Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. Similarly, in Europe, the European Commission, upon the recommendation of the EMA's Committee for Orphan Medicinal Products, grants orphan drug designation to promote the development of drugs that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than five in 10,000 persons in Europe and for which no satisfactory method of diagnosis, prevention, or treatment has been authorized (or the product would be a significant benefit to those affected). Additionally, designation is granted for drugs intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in Europe would be sufficient to justify the necessary investment in developing the drug. In Europe, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers. However, there can be no assurances that we will be able to obtain orphan designations for our product candidates.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such

designation, the product is entitled to orphan drug exclusivity. Orphan drug exclusivity in the United States provides that the FDA may not approve any other applications, including a full NDA, to market the same drug for the same indication for seven years, except in limited circumstances. The applicable exclusivity period is ten years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified.

The FDA has granted orphan drug designation for TN-201, the most advanced product candidate from our MYBPC3 program, and we may seek orphan drug designation for other product candidates in the United States, Europe and other jurisdictions. Even if we obtain orphan drug designation for a product candidate, we may not be able to obtain or maintain orphan drug exclusivity for that product candidate. We may not be the first to obtain marketing approval of any product candidate for which we have obtained orphan drug designation for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to ensure that we will be able to manufacture sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties may be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care or the manufacturer of the product with orphan exclusivity is unable to maintain sufficient product quantity. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the product candidate any advantage in the regulatory review or approval process or entitles the product candidate to priority review.

We may face difficulties from changes to current FDA and healthcare regulations and future legislation.

Existing regulatory policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the current U.S. administration may impact our business and industry, which could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict how current and future legislation, executive actions, and litigation, including the executive orders referenced below, will be implemented, and the extent to which they will impact our business, our clinical development, and the FDA's and other agencies' ability to exercise their regulatory authority, including FDA's pre-approval inspection and timely review of any regulatory filings or applications we submit to the FDA. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course or constraints on our business operations, including operations of our contractors, our business may be negatively impacted.

For example, in March 2010, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the ACA), was passed, which substantially changed the way healthcare is financed by both the government and private insurers, and continues to significantly impact the U.S. pharmaceutical industry. Since its enactment, there have been judicial and

Congressional challenges to certain aspects of the ACA. For example, various portions of the ACA have been the subject of legal and constitutional challenges in the U.S. Supreme Court. In June 2021, the U.S. Supreme Court held that Texas and other challengers had no legal standing to challenge the ACA, dismissing the case without specifically ruling on the constitutionality of the ACA. On January 28, 2021, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. We cannot predict how this Supreme Court decision or future litigation will impact our business, or what other healthcare measures and regulations will ultimately be implemented at the federal or state level or the effect of any future legislation or regulation may have on our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, effective April 1, 2013, which will remain in effect through 2030, with the exception of a temporary suspension implemented under various COVID-19 relief legislation from May 1, 2020 through the end of 2021, unless additional congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our drugs, if approved, and accordingly, our financial operations.

Moreover, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, in 2020, HHS and CMS issued various rules that are expected to impact, among others, price reductions from pharmaceutical manufacturers to plan sponsors under Part D, fee arrangements between pharmacy benefit managers and manufacturers, manufacturer price reporting requirements under the Medicaid Drug Rebate Program, including regulations that affect manufacturer-sponsored patient assistance programs subject to pharmacy benefit manager accumulator programs and Best Price reporting related to certain value-based purchasing arrangements. Multiple lawsuits have been brought against the HHS challenging various aspects of the rules. In January 2021, the Biden administration issued a "regulatory freeze" memorandum that directs department and agency heads to review new or pending rules of the prior administration. It is unclear whether these new regulations will be withdrawn or when they will become fully effective under the Biden administration. Under the American Rescue Plan Act of 2021, effective January 1, 2024, the statutory cap on Medicaid Drug Rebate Program rebates that manufacturers pay to state Medicaid programs will be eliminated. Elimination of this cap may require pharmaceutical manufacturers to pay more in rebates than it receives on the sale of products, which could have a material impact on our business. The impact of these lawsuits as well as legislative, executive, and administrative actions of the Biden administration on us and the pharmaceutical industry as a whole is unclear.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. We are unable to predict the future course of federal or state healthcare legislation in the United States directed at broadening the availability

of healthcare and containing or lowering the cost of healthcare. These and any further changes in the law or regulatory framework that reduce our revenue or increase our costs could also have a material and adverse effect on our business, financial condition and results of operations.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our product candidates. It is also possible that additional governmental action is taken to address the COVID-19 pandemic.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for biotechnology products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

We are subject to stringent laws, rules, regulations, policies, industry standards and contractual obligations regarding data privacy and security and may be subject to additional related laws and regulations in jurisdictions into which we expand. Many of these laws and regulations are subject to change and reinterpretation and could result in claims, changes to our business practices, monetary penalties, increased cost of operations or other harm to our business.

The regulatory framework for privacy and personal information security issues worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. The U.S. federal and various state, local and foreign government bodies and agencies have adopted or are considering adopting laws, rules, regulations and standards limiting, or laws, rules, regulations and standards regarding, the collection, distribution, use, disclosure, storage, security and other processing of personal information.

Outside of the United States, legal requirements relating to the collection, storage, processing and transfer of personal data continue to evolve. For example, the collection and use of health data and other personal data is governed in the European Union by the General Data Protection Regulation (GDPR), which extends the geographical scope of EU data protection law to entities and operations outside of the European Union under certain conditions and imposes substantial obligations upon companies and new rights for individuals, and by certain EU member state-level legislation. For example, the GDPR requires data controllers to implement stringent operational requirements for processors and controllers of personal data, including transparent and expanded disclosure to data subjects about how their personal data is to be used, limitations on retention of information, mandatory data breach notification requirements, and higher standards for data controllers to demonstrate that they have obtained valid consent for certain data processing activities. Failure to comply with the GDPR may result in fines up to €20,000,000 or 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, and other administrative penalties. The GDPR may increase our responsibility and liability in relation to personal data that we may process, and we may be required to implement additional measures in an effort to comply with the GDPR and with other laws, rules, regulations and standards in the European Union, including those of EU member states, relating to privacy and data protection. This may be onerous and if our efforts to comply with GDPR or other applicable EU laws, rules, regulations and standards are not successful, or are perceived to be unsuccessful, it could adversely affect our business. Further, in July 2020, the European Court of Justice (ECJ) invalidated the EU-U.S. Privacy Shield, which had enabled the transfer of personal data from the European Union to the United States for companies that had self-certified to the Privacy Shield. The ECJ decision also raised questions about the continued validity of one of the primary

alternatives to the EU-U.S. Privacy Shield, namely the European Commission's Standard Contractual Clauses, and EU regulators have issued additional guidance regarding considerations and requirements that we and other companies must consider and undertake when using the Standard Contractual Clauses. Although the European Union has presented a new draft set of contractual clauses, at present, there are few, if any, viable alternatives to the EU-U.S. Privacy Shield and the Standard Contractual Clauses and it remains to be seen whether additional means for lawful data transfers will become available. To the extent that we were to rely on the EU-U.S. or Swiss-U.S. Privacy Shield programs, we will not be able to do so in the future, and the ECJ's decision and other regulatory guidance or developments otherwise may impose additional obligations with respect to the transfer of personal data from the European Union and Switzerland to the United States, each of which could restrict our activities in those jurisdictions, limit our ability to provide our products and services in those jurisdictions, or increase our costs and obligations and impose limitations upon our ability to efficiently transfer personal data from the European Union and Switzerland to the United States.

Further, the exit of the United Kingdom from the European Union, often referred to as Brexit, has created uncertainty with regard to data protection regulation in the United Kingdom. Specifically, the United Kingdom exited the European Union on January 1, 2020, subject to a transition period that ended December 31, 2020. The United Kingdom has implemented legislation similar to the GDPR, referred to as the UK GDPR, which provides for significant fines of up to the greater of £17.5 million or 4% of global turnover and exposes us to two parallel regimes with potentially divergent enforcement actions for certain violations. With respect to transfers of personal data, on June 28, 2021, the European Commission issued an adequacy decision in respect of the United Kingdom's data protection framework, enabling data transfers from EU member states to the United Kingdom to continue without requiring organizations to put in place contractual or other measures in order to lawfully transfer personal data between the territories. While it is intended to last for at least four years, the European Commission may unilaterally revoke the adequacy decision at any point, and if this occurs it could lead to additional costs and increase our overall risk exposure. The relationship between the United Kingdom and European Union in relation to aspects of data protection law in the medium and longer term remains unclear, including with respect to cross-border data transfers and the role of the UK Information Commissioner's Office with respect to the European Union, which exposes us to further compliance risk. We may incur liabilities, expenses, costs, and other operational losses relating to the GDPR, the UK GDPR, and other laws and regulations in the European Union and United Kingdom relating to privacy and data protection, including those of applicable EU member states in connection with any measures we take to comply with them.

Finally, federal, state and foreign laws, rules, regulations and standards may apply generally to the privacy and security of information we maintain, and may differ from each other in significant ways, thus complicating compliance efforts and potentially requiring us to undertake additional measures to comply with them. In the United States, there are a broad variety of data privacy, protection and security laws, rules, regulations and standards that may apply to our activities, such as state data breach notification laws, state personal data privacy laws (for example, the California Consumer Privacy Act of 2018 (CCPA)), state health information privacy laws, and federal and state consumer protection laws (for example, Section 5(c) of the Federal Trade Commission Act). A range of enforcement agencies exist at both the state and federal levels that can enforce these laws, rules, regulations and standards. For example, the CCPA, which took effect on January 1, 2020, requires covered businesses that process personal information of California residents to disclose their data collection, use and sharing practices. Further, the CCPA provides California residents with new data privacy rights (including the ability to opt out of certain disclosures of personal information), imposes new operational requirements for covered businesses, provides for significant civil penalties for violations as well as a private right of action for certain data breaches and statutory damages (that is expected to increase data breach class action litigation and result in significant exposure to costly legal judgements and settlements). Aspects of the CCPA and its interpretation and enforcement remain uncertain. In addition, California voters passed the California Privacy Rights Act of 2020 (CPRA) in November 2020, which becomes effective in most material respects on January 1, 2023. The CPRA will, among other things, give California residents the ability to limit use of certain sensitive personal information, further restrict the use of cross-contextual advertising, establish restrictions on the retention of personal information, expand the types of data breaches subject to the CCPA's private right of action, provide

for increased penalties for CPRA violations concerning California residents under the age of 16, and establish a new California Privacy Protection Agency to implement and enforce the new CCPA and CPRA. Although there are limited exemptions for clinical trial data under the CCPA, the CCPA and other similar laws could impact our business activities, depending on their interpretation. Further, laws in all 50 states require businesses to provide notice to customers whose personal data has been disclosed as a result of a data breach.

With the GDPR, CCPA, CRPA and other laws, regulations and other obligations relating to privacy and data protection imposing new and relatively burdensome obligations, and with substantial uncertainty over the interpretation and application of these and other obligations, we may face challenges in addressing their requirements and making necessary changes to our policies and practices, and may incur significant costs and expenses in an effort to do so. We are currently in the process of developing and updating our policies and procedures in accordance with requirements under the CCPA and the GDPR, as well as other applicable data privacy and protection laws and regulations. Additionally, the CPRA and the CCPA may lead other states to pass comparable legislation, with potentially greater penalties and more rigorous compliance requirements relevant to our business. Additionally, if third parties we work with, such as vendors or service providers, violate applicable laws, rules or regulations or our policies, such violations may also put our or our customers' data, including personal data, at risk, which could in turn have an adverse effect on our business.

We make public statements about our use, collection, disclosure and other processing of personal data through our privacy policies, information provided on our website and press statements. Although we endeavor to comply with our public statements and documentation, we may at times fail to do so or be alleged to have failed to do so. The publication of our privacy policies and other statements that provide promises and assurances about data privacy and security can subject us to potential government or legal action if they are found to be deceptive, unfair or misrepresentative of our actual practices. Any failure or perceived failure by us or our vendors or service providers to comply with our applicable policies or notices relating to privacy or data protection, our contractual or other obligations to third parties, or any of our other legal obligations, laws, rules, regulations and standards relating to privacy or data protection, may result in governmental investigations or enforcement actions, litigation, claims and other proceedings, harm our reputation, and could result in significant liability.

Inadequate funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the U.S. Securities and Exchange Commission (SEC) and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, in recent years, including in 2018 and 2019, the U.S. government shut down several times and certain regulatory agencies, such as the FDA and the SEC, had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, upon completion of this offering and in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Our relationships with healthcare professionals, clinical investigators, CROs and third-party payors in connection with our current and future business activities may be subject to federal and state healthcare fraud and abuse laws, false claims laws, transparency laws, government price reporting, and health information privacy and security laws, which could expose us to significant losses, including, among other things, criminal sanctions, civil penalties, contractual damages, exclusion from governmental healthcare programs, reputational harm, administrative burdens and diminished profits and future earnings.

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, clinical investigators, CROs, third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we research, as well as market, sell and distribute our products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations may include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- the federal false claims laws, including the civil False Claims Act, which can be enforced by private citizens through civil whistleblower or qui tam actions, and civil monetary penalties laws, prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), prohibits, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- the Civil Monetary Penalty Act of 1981 and implementing regulations, which impose penalties against any person or entity that, among other things, is determined to have presented or caused to be presented a claim to a federal healthcare program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent, or offered or transferred remuneration to a federal healthcare beneficiary that a person knows or should know is likely to influence the beneficiary's decision to order or receive items or services reimbursable by the government from a particular provider or supplier;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH) and their implementing regulations, also imposes obligations, including mandatory contractual terms, on covered entities, which are health plans, healthcare clearinghouses, and certain health care providers, as those terms are defined by HIPAA, and their respective business associates and their subcontractors, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to annually report to CMS information regarding payments and other transfers of value to physicians, defined to include doctors, dentists, optometrists, podiatrists and chiropractors, and teaching hospitals as well as information regarding ownership and investment interests held by physicians and their immediate family members. Beginning with data reporting in 2022, reporting obligations with respect to covered recipients will be

expanded to include physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists and anesthesiologist assistants, and certified nurse midwives for payments and transfers of value made during the previous year; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance regulations promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures, or drug pricing; state and local laws that require the registration of pharmaceutical sales and medical representatives; state laws that govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our current and future business arrangements with third parties will comply with applicable healthcare and data privacy and security laws and regulations will involve substantial ongoing costs, and may require us to undertake or implement additional policies or measures. We may face claims and proceedings by private parties, and claims, investigations and other proceedings by governmental authorities, relating to allegations that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations, and it is possible that courts or governmental authorities may conclude that we have not complied with them, or that we may find it necessary or appropriate to settle any such claims or other proceedings. In connection with any such claims, proceedings, or settlements, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings and the curtailment or restructuring of our operations. Defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, CDMOs, suppliers and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, CDMOs, suppliers and vendors may engage in misconduct or other improper activities. Misconduct by these parties could include failures to comply with FDA regulations, provide accurate information to the FDA, comply with federal and state health care fraud and abuse laws and regulations, accurately report financial information or data or disclose unauthorized activities to us. In particular, research, sales, marketing and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct by these parties could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a code of conduct, but it is not always possible to identify and deter misconduct by these parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or

regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings and the curtailment or restructuring of our operations.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses, we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of hazardous and flammable materials, including chemicals and biological materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Our business activities may be subject to the U.S. Foreign Corrupt Practices Act and similar anti-bribery and anti-corruption laws of other countries in which we operate, as well as U.S. and certain foreign export controls, trade sanctions, and import laws and regulations. Compliance with these legal requirements could limit our ability to compete in foreign markets and subject us to liability if we violate them.

Our business activities are subject to the U.S. Foreign Corrupt Practices Act of 1977, as amended (FCPA), the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate. These laws generally prohibit companies and their employees, agents, representatives, business partners, and third-party intermediaries from, directly or indirectly, offering, promising, giving or authorizing others to give anything of value, either directly or indirectly, to recipients in the public or private sector in order to influence official action or otherwise obtain or retain business. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, hospitals are owned and operated by the government, and doctors and other hospital employees would be considered foreign officials under the FCPA. Recently, the SEC and Department of Justice (DOJ) have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies.

We sometimes leverage third parties to assist with the conduct of our business abroad. We, our employees, agents, representatives, business partners and our third-party intermediaries may have direct or indirect interactions with officials and employees of government agencies or state-owned or affiliated entities and may be held liable for the corrupt or other illegal activities of these employees, agents, representatives, business partners

or third-party intermediaries even if we do not explicitly authorize such activities. We cannot assure you that all of our employees, agents, representatives, business partners and third-party intermediaries will not take actions in violation of applicable law for which we may be ultimately held responsible. As we increase our international sales and business, our risks under these laws may increase.

These laws also require that we make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls and compliance procedures designed to prevent violations of anti-corruption laws. There is no certainty that all of our employees, agents, representatives, business partners and third-party intermediaries, or those of our affiliates, will comply with applicable laws and regulations, for which we may be ultimately held responsible.

Violations of these laws and regulations could result in whistleblower complaints, fines, severe civil or criminal sanctions, settlements, prosecution, enforcement actions, damages, adverse media coverage, investigations, loss of export privileges, disgorgement, and other remedial measures and prohibitions on the conduct of our business including our ability to offer our products in one or more countries. Responding to any investigation or action will likely result in a materially significant diversion of management's attention and resources and significant defense costs and other professional fees. As a general matter, investigations, enforcement actions and sanctions could damage our reputation, our brand, our international activities, our ability to attract and retain employees and our business, prospects, operating results and financial condition.

In addition, our products may be subject to U.S. and foreign export controls, trade sanctions and import laws and regulations. Governmental regulation of the import or export of our products, or our failure to obtain any required import or export authorization for our products, when applicable, could harm our international sales and adversely affect our revenue. Compliance with applicable regulatory requirements regarding the export of our products may create delays in the introduction of our products in international markets or, in some cases, prevent the export of our products to some countries altogether. Furthermore, U.S. export control laws and economic sanctions prohibit the shipment of certain products and services to countries, governments, and persons targeted by U.S. sanctions. If we fail to comply with export and import regulations and such economic sanctions, penalties could be imposed, including fines and/or denial of certain export privileges. Moreover, any new export or import restrictions, new legislation or shifting approaches in the enforcement or scope of existing regulations, or in the countries, persons, or products targeted by such regulations, could result in decreased use of our products by, or in our decreased ability to export our products to, existing or potential customers with international operations. Any decreased use of our products or limitation on our ability to export or sell our products would likely adversely affect our business.

Comprehensive U.S. tax reform legislation could increase the tax burden on our orphan drug programs and adversely affect our business and financial condition.

In 2017, the U.S. government enacted the Tax Act, which as modified by the CARES Act, includes significant changes to the taxation of business entities. These changes include, among others, (i) a permanent reduction to the corporate income tax rate, (ii) a partial limitation on the deductibility of business interest expense and NOL carryforwards and (iii) a shift of the U.S. taxation of multinational corporations from a tax on worldwide income to a territorial system (along with certain rules designed to prevent erosion of the U.S. income tax base). Further, the comprehensive tax legislation reduces the orphan drug tax credit from 50% to 25% of qualifying expenditures. When and if we become profitable, this reduction in tax credits may result in an increased federal income tax burden on our orphan drug programs as it may cause us to pay federal income taxes earlier under the revised tax law than under the prior law and, despite being partially off-set by a reduction in the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, may increase our total federal tax liability attributable to such programs. Additionally, President Biden has proposed an increase of the corporate tax rate from 21% to 28%, which, if enacted would further increase our total federal tax liability when and if we become profitable.

Notwithstanding the changes in the corporate income tax rate, the overall impact of this comprehensive tax legislation resulted in an overall reduction in our deferred tax assets, and our business and financial condition could still be adversely affected as additional guidance and regulations are issued with respect to the original tax law change. In addition, it is uncertain if and to what extent various states will conform to this comprehensive tax legislation, and states may enact suspensions or limitations on the use of NOLs and tax credits (including, without limitation, California legislation enacted in 2020 that suspends the use of California NOLs and limits the use of certain California tax credits for certain periods). The impact of this comprehensive tax legislation on holders of our common stock is also uncertain and could be adverse. Investors should consult with their legal and tax advisors with respect to this comprehensive tax legislation and the potential tax consequences of investing in or holding our common stock.

Risks Related to Employee Matters, Managing Our Growth and Other Risks Related to Our Business

Our success is highly dependent on our ability to attract and retain highly skilled executive officers and employees.

To succeed, we must recruit, retain, manage and motivate qualified clinical, scientific, technical and management personnel, and we face significant competition for experienced personnel. We are highly dependent on the principal members of our management and scientific and medical staff, particularly Faraz Ali, M.B.A., our Chief Executive Officer. Additionally, the COVID-19 pandemic may interfere with our ability to hire or retain personnel. If we do not succeed in attracting and retaining qualified personnel, particularly at the management level, it could adversely affect our ability to execute our business plan and harm our operating results. In particular, the loss of one or more of our executive officers could be detrimental to us if we cannot recruit suitable replacements in a timely manner. We do not maintain “key person” insurance for any of our executives or other employees. We could in the future have difficulty attracting and retaining experienced personnel and may be required to expend significant financial resources in our employee recruitment and retention efforts.

Many of the other biotechnology companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide higher compensation, more diverse opportunities and better prospects for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high-quality personnel, the rate and success at which we can discover, develop and commercialize our product candidates will be limited and the potential for successfully growing our business will be harmed.

Additionally, we rely on our scientific founders and other scientific and clinical advisors and consultants to assist us in formulating our research, development and clinical strategies. These advisors and consultants are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. In addition, these advisors and consultants typically will not enter into non-compete agreements with us. If a conflict of interest arises between their work for us and their work for another entity, we may lose their services. Furthermore, our advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours. In particular, if we are unable to maintain consulting relationships with our scientific founders or if they provide services to our competitors, our development and commercialization efforts will be impaired and our business will be significantly harmed.

In order to successfully implement our plans and strategies, we will need to grow the size of our organization, and we may experience difficulties in managing this growth.

As of June 30, 2021, we had more than 85 full-time employees. Of these employees, approximately 47 are engaged in research and development activities and approximately 25 are engaged in manufacturing activities. In order to successfully implement our development and commercialization plans and strategies, and as we transition into operating as a public company, we expect to need additional managerial, operational, sales,

marketing, financial and other personnel. Future growth would impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining and motivating additional employees;
- managing our internal development efforts effectively, including the clinical, FDA, EMA and other comparable foreign regulatory agencies' review process for our product candidates, while complying with any contractual obligations to contractors and other third parties we may have; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to successfully develop and, if approved, commercialize our product candidates will depend, in part, on our ability to effectively manage any future growth, and our management may also have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services, including key aspects of our research and development, clinical development, manufacturing and operations. We cannot assure you that the services of independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by third-party service providers is compromised for any reason, our preclinical studies and the initiation and conduct of our planned clinical trials may be extended, delayed or terminated, and we may not be able to obtain marketing approval of our product candidates or otherwise advance our programs and business. We cannot assure you that we will be able to manage our existing third-party service providers or find other competent outside contractors and consultants on economically reasonable terms, or at all.

If we are not able to effectively expand our organization by hiring new employees and/or engaging additional third-party service providers, we may not be able to successfully implement the tasks necessary to develop and commercialize our product candidates and, accordingly, may not achieve our research, development and commercialization goals.

If we are unable to establish sales or marketing capabilities or enter into agreements with third parties to sell or market our product candidates, we may not be able to successfully sell or market our product candidates that obtain regulatory approval.

We currently do not have and have never had a marketing or sales team. In order to commercialize any product candidates, if approved, we must build marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services for each of the territories in which we may have approval to sell or market our product candidates. We may not be successful in accomplishing these required tasks.

Establishing an internal sales or marketing team with technical expertise and supporting distribution capabilities to commercialize our product candidates will be expensive and time-consuming and will require significant attention of our executive officers to manage. Any failure or delay in the development of our internal sales, marketing and distribution capabilities could adversely impact the commercialization of any of our product candidates that we obtain approval to market, if we do not have arrangements in place with third parties to provide such services on our behalf. Alternatively, if we choose to collaborate, either globally or on a territory-by-territory basis, with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems, we will be required to negotiate and enter into arrangements with such third parties relating to the proposed collaboration and such arrangements may prove to be less profitable than commercializing the product

on our own. If we are unable to enter into such arrangements when needed, on acceptable terms, or at all, we may not be able to successfully commercialize any of our product candidates that receive regulatory approval, or any such commercialization may experience delays or limitations. If we are unable to successfully commercialize our approved product candidates, either on our own or through collaborations with one or more third parties, our future product revenue will suffer, and we may incur significant additional losses.

Our computer systems, or those of any of our CROs, manufacturers, contractors, consultants or other third parties or potential future collaborators, may fail or suffer security incidents or data privacy breaches or other unauthorized or improper access to, use of, or destruction of our proprietary or confidential data, employee data, or personal data, which could result in additional costs, loss of revenue, significant liabilities, harm to our brand and material disruption of our operations.

Despite the implementation of security measures in an effort to protect systems that store our information, given their size and complexity and the increasing amounts of information maintained on our internal information technology systems, and those of our third-party CROs, other contractors (including sites performing our clinical trials), consultants and other third parties, such systems are vulnerable to breakdown or other damage or interruption from, among other things, service interruptions, system malfunctions, natural disasters, terrorism, war, telecommunication and electrical failures, security breaches from inadvertent or intentional actions by our employees, contractors, consultants, business partners, and other third parties, cyber-attacks by malicious third parties (including supply chain cyber-attacks or attacks by nation-state or nation-state supported actors, or the deployment of harmful malware, ransomware, denial-of-service attacks, phishing attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information), which may compromise our system infrastructure or lead to the loss, destruction, alteration, prevention of access to, disclosure, dissemination of, or damage or unauthorized access to, our data (including trade secrets or other confidential information, intellectual property, proprietary business information and personal data) or data that is processed or maintained on our behalf, or other assets, which could result in financial, legal, business and reputational harm to us.

We have in the past and may in the future experience phishing attempts, and companies have, in general, experienced an increase in phishing and social engineering attacks from third parties in connection with the COVID-19 pandemic, and the increase in remote working further increases security threats. To the extent that any data breach, disruption or security incident were to result in any loss, destruction, unavailability, alteration, disclosure, dissemination of, or damage or unauthorized access to, our personal data, applications, assets or any other data processed or maintained on our behalf, or for it to be believed or reported that any of the foregoing occurred, we could incur significant liability, financial harm and reputational damage and the development and commercialization of our product candidates could be delayed. We cannot ensure that our data protection efforts and our investment in information technology, or the efforts or investments of CROs, consultants or other third parties, will prevent breakdowns or breaches in our or their systems or other cybersecurity incidents that cause loss, destruction, unavailability, alteration, dissemination of, or damage or unauthorized access to, our data, including personal data, assets and other data processed or maintained on our behalf, that could have a material adverse effect upon our reputation, business, operations or financial condition. We also rely on third parties to manufacture our product candidates, and any data breaches or other security events relating to their computer systems could also have a material adverse effect on our business. Controls employed by our information technology department and our CROs, consultants and other third parties could prove inadequate, and our ability to monitor such third parties' data security practices is limited. Due to applicable laws, rules, regulations and standards or contractual obligations, we may be held responsible for any information security failure or cyber-attack attributed to our third-party service providers as they relate to the information we share with them.

If any data breach or other security incident were to occur and cause interruptions in our operations, it could result in a material disruption of our programs and the development of our product candidates could be delayed. In addition, the loss of clinical trial data for our product candidates could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data. Further, any such event that

leads to loss, damage, or unauthorized access to, or use, alteration, disclosure or dissemination of, personal data, including personal data regarding our clinical trial subjects or employees, could harm our reputation directly, compel us to comply with federal and state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, and otherwise subject us to substantial liability under laws, rules, regulations and standards that protect the privacy and security of personal data, which could result in significant legal and financial exposure and reputational damages that could potentially have an adverse effect on our business. Additionally, we do not currently maintain cybersecurity insurance and therefore the successful assertion of one or more large claims against us in connection with a breach or other cybersecurity-related matter could adversely affect our business, financial condition, results of operations and prospects.

Notifications and follow-up actions related to a data breach or other security incident could impact our reputation and cause us to incur significant costs, including significant legal expenses and remediation costs. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the lost data. We expect to incur significant costs in an effort to detect and prevent security incidents, and we may face increased costs and requirements to expend substantial resources in the event of an actual or perceived security incident. However, we cannot guarantee that we will be able to detect or prevent any such incidents, or that we can remediate any such incidents in an effective or timely manner. Our efforts to improve security and protect data from compromise may also identify previously undiscovered instances of data breaches or other cybersecurity incidents. To the extent that any data breach, disruption or security incident were to result in any loss, destruction, or alteration of, damage, unauthorized access to or inappropriate or unauthorized disclosure of or dissemination of, our data, including personal data, or other information that is processed or maintained on our behalf, we could be exposed to litigation and governmental investigations and inquiries, the further development and commercialization of our product candidates could be delayed, and we could be subject to significant fines or penalties for any noncompliance with certain state, federal and international privacy and security laws, rules, regulations and standards.

Our operations are vulnerable to interruption by fire, earthquakes, power loss, telecommunications failure, terrorist activity, pandemics and other events beyond our control, which could harm our business.

Our facilities are located in the San Francisco Bay Area. We have not undertaken a systematic analysis of the potential consequences to our business and financial results from a major flood, blizzard, wildfire, earthquake, power loss, terrorist activity, pandemics or other disasters and do not have a recovery plan for such disasters. In addition, we do not carry sufficient insurance to compensate us for actual losses from interruption of our business that may occur, and any losses or damages incurred by us could harm our business. Also, our CDMOs and suppliers' facilities are located in multiple locations where other natural disasters or similar events which could severely disrupt our operations, could expose us to liability and could have a material adverse effect on our business. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

A variety of risks associated with marketing our product candidates internationally could materially adversely affect our business.

We may seek regulatory approval of our product candidates outside of the United States and, accordingly, we expect that we will be subject to additional risks related to operating in foreign countries if we obtain the necessary approvals, including:

- differing regulatory requirements and reimbursement regimes in foreign countries;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;

- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the FCPA or comparable foreign regulations;
- challenges obtaining, maintaining, protecting, defending and enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

These and other risks associated with our international operations may materially adversely affect our ability to attain or maintain profitable operations.

Risks Related to Our Intellectual Property

We have in-licensed one issued U.S. patent, own one issued U.S. patent, and own one allowed U.S. patent application relating to our technology and product candidates. If we are unable to obtain, maintain, protect, defend and enforce patent and other intellectual property coverage for our technology and product candidates, our competitors could develop and commercialize technology and product candidates similar or identical to ours, and our ability to commercialize our technology and product candidates may be adversely affected.

Our commercial success depends in large part on our ability to obtain, maintain, protect, defend and enforce patents, trade secrets and other intellectual property for our product candidates and proprietary technologies and their uses, as well as our ability to operate without infringing, misappropriating or otherwise violating the intellectual property and proprietary rights of others. We rely on patent, copyright, trade secret and trademark laws in the United States and certain other countries to protect our proprietary technology, and we generally seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates, proprietary technologies and their uses that are important to our business. We also seek to protect our proprietary position by acquiring or in-licensing relevant issued patents or pending applications from third parties, but the efforts we and our licensors take to protect our intellectual property may provide only limited protection. In particular, the development of our product candidates and technology is at an early stage and consequently, our patent portfolio is also at an early stage. Presently, we own one issued U.S. patent, one allowed U.S. patent application and one other pending non-provisional U.S. patent application, seven non-expired Patent Cooperation Treaty (PCT) applications, nine pending foreign patent applications and at least five pending provisional U.S. patent applications. There can be no assurance that we or our licensors will obtain any additional issued patents or that any issued patents we or our licensors obtain will provide us with any competitive advantage. Any failure to obtain adequate patent protection for our product candidates and technology would have a material adverse effect on our business, financial condition, results of operations and prospects.

Pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, patents issue from such applications, and then only to the extent the issued

claims cover the technology. There can be no assurance that our patent applications or the patent applications of our licensors will result in additional patents being issued or that any such issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents issued will not be infringed, designed around, or invalidated by third parties.

Even issued patents may later be found invalid or unenforceable or may be modified, narrowed in scope, or revoked in proceedings instituted by third parties before various patent offices or in courts in the United States and abroad. The degree of future protection for our and our licensor's intellectual property and proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. These uncertainties and limitations in our ability to properly protect the intellectual property rights relating to our product candidates could have a material adverse effect on our financial condition and results of operations.

We cannot be certain that the claims in our U.S. pending patent applications, corresponding international patent applications and patent applications in certain foreign jurisdictions, or those of our licensors, will be considered patentable by the United States Patent and Trademark Office (USPTO), courts in the United States or by the patent offices and courts in foreign countries, nor can we be certain that any issued claims will not be found invalid or unenforceable if challenged. Additionally, our provisional applications may never result in issued patents. A U.S. provisional patent application expires twelve months from its filing date, and its subject matter can only be claimed in an issued patent if, among other things, we file a non-provisional patent application making a valid priority claim to that provisional patent application before it expires. If we do not timely file a non-provisional patent application, we may lose the benefit of the priority dates of our provisional patent application, and intervening prior art may jeopardize patent protection on the inventions disclosed in such a provisional patent application. While we intend to timely file non-provisional patent applications claiming the benefit of the priority dates of our provisional patent applications, and otherwise diligently prosecute our patent rights, we cannot predict whether any of our future patent applications for our technology and product candidates will result in the issuance of patents that effectively protect our technology and product candidates. Additionally, our owned pending PCT patent applications are not eligible to become issued patents until, among other things, we file a national stage patent application within 30 months in the countries in which we seek patent protection. If we do not timely file any national stage patent applications, we may lose our priority date with respect to our PCT patent applications and any patent protection on the inventions disclosed in such PCT patent applications. If we or our licensors do not successfully obtain patent protection, or if the scope of the patent protection we or our licensors obtain is not sufficiently broad, valid, and enforceable, we may be unable to prevent others from using our technology, developing or commercializing similar or identical technology and products, or marketing competing products and technologies. Any failure to obtain or maintain patent protection with respect to our technology and product candidates would have a material adverse effect on our business, financial condition, results of operations and prospects.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our potential future licensors or collaborators will be successful in protecting our product candidates by obtaining and defending adequate patent coverage. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;
- patent applications may not result in any patents being issued;
- patents may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable, narrowed in scope or otherwise may not provide any competitive advantage;
- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained

patents that will limit, interfere with or eliminate our ability to make, use and sell our potential product candidates;

- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates and limiting the scope of our protection in countries outside the United States.

The patent prosecution process is also expensive and time-consuming, and we and our licensors may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions where protection may be commercially advantageous. It is also possible that we or our licensors will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. We may not be able to obtain or maintain patent applications and patents due to the subject matter claimed in such patent applications and patents being in disclosures in the public domain.

In addition, although we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, outside scientific collaborators, CROs, third-party manufacturers, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. Consequently, we may not be able to prevent any third parties, including our competitors, from using any of our technology that is in the public domain to compete with our technology and product candidates.

Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If the scope of any patent protection we obtain is not sufficiently broad, or if we lose any of our patent protection, our ability to prevent our competitors from commercializing similar or identical product candidates would be adversely affected.

The patent position of biotechnology companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications and those of our licensors may not result in patents being issued which protect our product candidates or which effectively prevent others from commercializing competitive product candidates or otherwise provide any commercial advantage.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we own or in-license currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Our competitors or other third parties may avail themselves of safe harbor under the Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Amendments) to conduct research and clinical trials and may be able to circumvent our patent rights by developing similar or alternative technologies or products in a non-infringing manner. Any patents that we may own or in-license may be challenged or circumvented by third parties or may be narrowed, rendered unenforceable, or invalidated as a result of challenges by third parties. Consequently, we do not know whether our product candidates will be

protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our potential future patents or the patents of our licensors by developing similar or alternative technologies or products in a non-infringing manner which could materially adversely affect our business, financial condition, results of operations and prospects.

While we believe our intellectual property allows us to pursue our current development programs, several companies and academic institutions are pursuing alternate approaches to gene therapy and have built intellectual property around these approaches and methods. In addition, we may not be aware of all third-party intellectual property rights potentially relating to our technology and product candidates. Publications of discoveries in the scientific literature often lag the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in any owned or any licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. If a third party can establish that we or our licensors were not the first to make or the first to file for patent protection of such inventions, our owned or licensed patent applications may not issue as patents and even if issued, may be challenged and invalidated or rendered unenforceable. Furthermore, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States may remain confidential until a patent issues.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and the inventorship, scope, validity or enforceability of our potential future patents or the patents of our licensors may be challenged in the courts or patent offices in the United States and abroad. For example, we may be subject to a third-party pre-issuance submission of prior art to the USPTO, or become involved in opposition, derivation, revocation, reexamination, post-grant review (PGR) and inter partes review (IPR), or other similar proceedings challenging any patents that we may own or in-license. Such submissions may also be made prior to a patent's issuance, precluding the granting of a patent based on one of our owned or licensed pending patent applications. A third party may also claim that our potential future owned patents or licensed patent rights are invalid or unenforceable in a litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our potential future owned patents or licensed patent rights, allow third parties to commercialize our product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Moreover, our potential future patents or the patents of our licensors may become subject to post-grant challenge proceedings, such as oppositions in a foreign patent office, that challenge our priority of invention or other features of patentability with respect to our potential future patents and patent applications and those of our licensors. Such challenges may result in loss of patent rights, loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our product candidates. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. In addition, if the breadth or strength of protection provided by our potential future patents and patent applications or the patents and patent applications of our licensors is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of current and future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to develop products that are similar to our product candidates but that are not covered by the claims of the patent applications that we own or license;

- we or our current or future licensors or collaborators might not have been the first to make the inventions covered by the patent applications that we own or license now or may own or license in the future;
- we or our current or future licensors or collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that the pending patent applications we own or license will not lead to issued patents;
- issued patents that we may hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors or other third parties;
- others may have access to the same intellectual property rights licensed to us in the future on a nonexclusive basis;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may have an adverse effect on our business; and
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third-party may subsequently file a patent covering such intellectual property.

Should any of these events occur, it could significantly harm our business, results of operations and prospects.

Our commercial success depends significantly on our ability to operate without infringing, misappropriating or otherwise violating the patents and other intellectual property and proprietary rights of third parties. Claims by third parties that we infringe, misappropriate or otherwise violate their intellectual property or proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts, and could have a material adverse effect on the success of our business.

Our commercial success depends in part on avoiding infringement, misappropriation or other violation of the patents, intellectual property and proprietary rights of third parties. However, our research, development and commercialization activities may be subject to claims that we infringe, misappropriate or otherwise violate patents or other intellectual property rights owned or controlled by third parties. Other entities may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our product candidates and products that may be approved in the future, or impair our competitive position. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology industry, including patent infringement lawsuits, oppositions, reexaminations, IPR proceedings and PGR proceedings before the USPTO and corresponding foreign patent offices. Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields in which we are developing product candidates. There are and in the future may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Given the vast number of patents in our field of technology, we cannot be certain or guarantee that we do not infringe existing patents or that we will not infringe patents that may be granted in the future.

For example, we are aware of third-party patent rights that could be construed to cover the use of our TN-201 product candidate. We believe that if these third-party patent rights were to be asserted against us, we would

have valid defenses against such assertions, including that such patent rights are invalid and not infringed. However, if such third-party patent rights were asserted against us and found to be valid, enforceable and infringed, we could be liable for damages and be required to obtain a license to such patent rights prior to commercializing TN-201 in the United States, and such license may not be available on commercially reasonable terms or at all. Additionally, we are aware of third-party patent rights related to the use of certain AAV vectors, which have been asserted against others, including in at least one instance against a company for pre-approval activities. If these patent rights were to be asserted against us, we believe we would have valid defenses to such assertions, however such defenses may not be successful and we could be liable for damages and need to secure a license to such patent rights, which may not be available on commercially reasonable terms or at all. In the event any of the foregoing were to occur, we may be prevented from further developing and commercializing any affected product candidates, including TN-201.

As the biotechnology industry expands and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement, misappropriation or other violation of the patent or other intellectual property rights of third parties. If any third-party claims that we infringe any of the above-referenced patent rights or any other patent rights, such claims would be time consuming and could:

- result in costly litigation that may cause negative publicity;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing any of our product candidates until the asserted patent expires or is held finally invalid or not infringed in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis;
- subject us to significant liability and damages to third parties, including treble damages if we are found to willfully infringe third-party intellectual property; or
- require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all, or which might be non-exclusive, which could result in our competitors gaining access to the same technology.

Although no third party has asserted a claim of patent infringement against us as of the date of this prospectus, there can be no assurance that we will not be subject to claims of patent or other intellectual property infringement in the future that could prevent our product candidates from being marketed. Furthermore, we may fail to identify relevant patents or patent applications or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patent applications may issue with claims of relevance to our technology. In addition, we may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by our activities. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technology and product candidates. Because patent applications are maintained as confidential for a certain period of time, until the relevant application is published, we may be unaware of third-party patents that may be infringed by commercialization of any of our product candidates, and we cannot be certain that we were the first to file a patent application related to a product candidate or technology. Moreover, because patent applications can take many years to issue, there may be currently-pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, identification of third-party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. There is also no assurance that there is not prior art of which we are aware, but which we do not believe is relevant to our business, which may, nonetheless, ultimately be found to limit our ability to make, use, sell, offer for sale or import our products that may be approved in the future, or impair our competitive position. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents.

Third parties may assert claims of patent infringement against us directed at any of our product candidates based on our existing patent applications or patents that may be granted in the future, regardless of their merit. Any patent-related legal action against us claiming damages and seeking to enjoin commercial activities relating to our products, treatment indications, or processes could subject us to significant liability for damages, including treble damages if we were determined to willfully infringe, and require us to obtain a license to manufacture or market our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of management and employee resources from our business. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. Moreover, even if we or our future strategic partners were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. In addition, we cannot be certain that we could redesign our product candidates, treatment indications, or processes to avoid infringement, if necessary, and we could encounter delays in our product introductions while we attempt to develop alternative technology and product candidates to avoid infringing third-party intellectual property rights. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing our product candidates, which could harm our business, financial condition and operating results. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our product candidates and technology.

Parties making claims against us may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

Because of the inevitable uncertainty in intellectual property litigation, we could lose a patent infringement or other action asserted against us regardless of our perception of the merits of the case. Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. There is no assurance that a court would find in our favor on questions of infringement, validity, enforceability, or priority. A court of competent jurisdiction could hold that these third-party patents are valid, enforceable, and infringed, which could materially and adversely affect our ability to commercialize any future products we may develop and any other future products or technologies covered by the asserted third-party patents. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent or find that our technology did not infringe any such claims. Further, even if we were successful in defending against any such claims, such claims could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

We may in the future pursue invalidity proceedings with respect to third-party patents. The outcome following legal assertions of invalidity is unpredictable. Even if resolved in our favor, these legal proceedings may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such proceedings adequately. Some of these third parties may be able to sustain the costs of such proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting

from the initiation and continuation of patent proceedings could compromise our ability to compete in the marketplace. If we do not prevail in the patent proceedings the third parties may assert a claim of patent infringement directed at our product candidates.

In addition, our agreements with some of our suppliers or other entities with whom we do business require us to defend or indemnify these parties to the extent they become involved in infringement claims, including the types of claims described above. We could also voluntarily agree to defend or indemnify third parties in instances where we are not obligated to do so if we determine it would be important to our business relationships. If we are required or agree to defend or indemnify third parties in connection with any infringement claims, we could incur significant costs and expenses that could adversely affect our business, operating results or financial condition.

We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.

Many pharmaceutical companies, biotechnology companies, and academic institutions may have patents and patent applications potentially relevant to our business. We may find it necessary or prudent to obtain licenses to such patents from such third-party intellectual property holders, for example, in order to avoid infringing these third-party patents. We may also require licenses from third parties for certain technologies for use with future product candidates. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also expect that competition for the in-licensing or acquisition of third-party intellectual property rights for future products that are attractive to us may increase in the future, which may mean fewer suitable opportunities for us as well as higher acquisition or licensing costs. We may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We may be involved in lawsuits to protect or enforce our potential future patents or our licensors' patents, which could be expensive, time consuming and unsuccessful. Further, our potential future patents or our licensors' patents could be found invalid or unenforceable if challenged in court.

Competitors and other third parties may infringe, misappropriate or otherwise violate our intellectual property rights. To prevent infringement, misappropriation, unauthorized use or other violation, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, our potential future patents also may become involved in inventorship, priority or validity disputes. In a patent infringement proceeding, a court may decide that a patent we may own or in-license is not valid, is unenforceable or is not infringed, or may refuse to stop the other party from using the technology at issue on the grounds that our potential future patents do not cover such technology. If we or any of our potential future collaborators were to initiate legal proceedings against a third party to enforce a patent directed at one of our product candidates, the defendant could counterclaim that our potential future patent or the patent of our licensor is invalid or unenforceable in whole or in part. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, lack of sufficient written description, non-enablement, or obviousness-type double patenting. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution.

Third parties may also raise similar invalidity claims before the USPTO or patent offices abroad, even outside the context of litigation. Such mechanisms include re-examination, PGR, IPR, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in the revocation or cancellation of or amendment to our potential future patents in such a way that they no longer cover our technology or product candidates or prevent third parties from competing with our technology or product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we, our licensor, and the patent examiners are unaware during prosecution. There is also no assurance that there is not prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim in our potential future patents and patent applications or the patents and patent applications of our licensors, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our technology or proprietary drug discovery platform, or any product candidates that we may develop. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations and prospects.

In addition, if the breadth or strength of protection provided by our patent applications or the patents and patent applications of our licensors is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

In addition, the issuance of a patent does not give us the right to practice the patented invention. Third parties may have blocking patents that could prevent us from marketing our own potential future patented product and practicing our own potential future patented technology.

Intellectual property litigation may lead to unfavorable publicity that harms our reputation and causes the market price of our common shares to decline.

During the course of any intellectual property litigation, there could be public announcements of the initiation of the litigation as well as results of hearings, rulings on motions, and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our existing products, programs or intellectual property could be diminished. Accordingly, the market price of shares of our common stock may decline. Such announcements could also harm our reputation or the market for our future products, which could have a material adverse effect on our business.

Derivation proceedings may be necessary to determine priority of inventions, and an unfavorable outcome may require us to cease using the related technology or to attempt to license rights from the prevailing party.

Derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patent applications or the patents or patent

applications of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all. Our defense of derivation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with such proceedings could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us bring our product candidates to market.

Changes in U.S. patent law, or laws in other countries, could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology and pharmaceutical industries involve a high degree of technological and legal complexity. Therefore, obtaining and enforcing biotechnology and pharmaceutical patents is costly, time consuming and inherently uncertain. Changes in either the patent laws or in the interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property and may increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. We cannot predict the breadth of claims that may be allowed or enforced in our potential future patents or in third-party patents. In addition, Congress or other foreign legislative bodies may pass patent reform legislation that is unfavorable to us.

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. In 2011, the Leahy-Smith America Invents Act (Leahy-Smith Act) was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and also may affect patent litigation. These also include provisions that switched the United States from a first-to-invent system to a first inventor-to-file system, allow third-party submission of prior art to the USPTO during patent prosecution and set forth additional procedures to attack the validity of a patent by the USPTO administered post grant proceedings, including post-grant review, *inter partes* review and derivation proceedings. Under a first-inventor-to-file system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to the patent on an invention regardless of whether another inventor was the first to invent the claimed invention. The USPTO recently developed new regulations and procedures to govern administration of the Leahy- Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first-to-file provisions, became effective in 2013. The Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition and results of operations. In addition, patent reform legislation may pass in the future that could lead to additional uncertainties and increased costs surrounding the prosecution, enforcement and defense of our patent applications.

Furthermore, the U.S. Supreme Court and the U.S. Court of Appeals for the Federal Circuit have made, and will likely continue to make, changes in how patent laws in the United States are interpreted. The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Similarly, foreign courts have made, and will likely continue to make, changes in how the patent laws in their respective jurisdictions are interpreted. We cannot predict future changes in the interpretation of patent laws or changes to patent laws that might be enacted into law by United States and foreign legislative bodies. Depending on decisions by the U.S. Congress, the U.S. federal courts, the USPTO, or similar authorities in foreign jurisdictions, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patent and the patents we might obtain or license in the future.

We may be subject to claims challenging the inventorship or ownership of our owned patent applications or in-licensed patent rights and other intellectual property.

We or our licensors may be subject to claims that former employees or other third parties have an ownership interest in our owned patent applications or in-licensed patents, trade secrets or other intellectual property rights as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or other third parties who are involved in developing our current or future products. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership of our patent applications or our licensors' owned or in-licensed patents, trade secrets or other intellectual property rights. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property rights that are important to our current or future product candidates. It may be necessary or we may desire to enter into a license to settle any such claim; however, there can be no assurance that we would be able to obtain a license on commercially reasonable terms, if at all. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and distraction to management and other employees, and any litigation or the threat of litigation may adversely our reputation, or affect our ability to hire employees or contract with independent contractors.

In addition, while it is our policy to require our employees, consultants, advisors, contractors and other third parties who may be involved in the conception or development of intellectual property rights to execute agreements assigning such intellectual property rights to us, we or our licensors may be unsuccessful in executing such agreements with each party who, in fact, conceives or develops intellectual property rights that we regard as our own. The assignment of intellectual property rights may not be self-executing or sufficient in scope, or the assignment agreements may be breached, and we or our licensors may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property rights. Furthermore, individuals executing agreements with us may have preexisting or competing obligations to a third party, such as an academic institution, and thus an agreement with us or our licensors may be ineffective in perfecting ownership of inventions developed by that individual. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If we do not obtain patent term extension for our product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, one or more of our U.S. patents or those of our licensors may be eligible for limited patent term restoration under the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. A maximum of one patent may be extended per FDA approved product as compensation for the patent

term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Patent term extension may also be available in certain foreign countries upon regulatory approval of our product candidates.

We may not be granted any extensions for which we apply in the United States or any other jurisdiction because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. In addition, to the extent we wish to pursue patent term extension based on a patent that we in-license from a third party, we would need the cooperation of that third party. If we are unable to obtain patent term extension or restoration, or the foreign equivalent, or if the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States, even in jurisdiction where we do pursue patent protection. Consequently, we may not be able to prevent third parties from practicing our or our licensors' inventions in all countries outside the United States, even in jurisdictions where we or our licensors due pursue patent protection, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our product candidates, and our potential future patents, the patents of our licensors, or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of many foreign countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, which could make it difficult for us to stop the infringement of our potential future patents or our licensor's patents, if pursued and obtained, or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our or our licensors' patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our potential future patents or the patents of our licensors at risk of being invalidated or interpreted narrowly and our patent applications or the patent applications of our licensors at risk of not issuing and could provoke third parties to assert claims against us. We or our licensors may not prevail in any lawsuits that we or our licensors initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by regulations and governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or patent applications will be due to the USPTO and various foreign patent offices outside of the United States at various points over the lifetime of our potential future patents and patent applications and those of our licensors. We have systems in place to remind us to pay these fees, and we rely on our outside patent annuity service to pay these fees when due. Additionally, the USPTO and various foreign patent offices require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. An inadvertent lapse or non-compliance with such requirements can sometimes be cured by payment of a late fee or by other means in accordance with rules applicable to the particular jurisdiction. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If such an event were to occur, it could have a material adverse effect on our business, financial condition and results of operations.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

We intend to use registered or unregistered trademarks or trade names to brand and market ourselves and our products, but we do not yet own a U.S. registered trademark for our corporate name, “Tenaya”. Our future trademark applications in the United States and in foreign jurisdictions may not be allowed or may subsequently be opposed. Once filed and registered, our potential future trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these potential future trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. As a means to enforce our potential future trademark rights and prevent infringement, we may be required to file trademark claims against third parties or initiate trademark opposition proceedings, which can be expensive and time-consuming. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our potential future registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively, and our business may be adversely affected.

Additionally, our potential future registered trademarks may not be maintained or enforced. During trademark registration proceedings, we may receive rejections. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our potential future trademark applications and registrations, and our potential future trademarks may not survive such proceedings. If we do not secure registrations for our potential future trademarks, we may encounter more difficulty in enforcing them against third parties than we otherwise would. Our efforts to enforce or protect our proprietary rights related to trademarks, domain names or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our financial condition or results of operations.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patent protection to protect the intellectual property underlying our technology and product candidates, we also rely on the protection of our trade secrets, including unpatented know-how, technology and other proprietary information to maintain our competitive position. Although we have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties who have access to such information, and confidential information and invention assignment agreements with employees, consultants, advisors and other third parties involved in the development of intellectual property, we cannot guarantee that we and our licensors have entered into such agreements with each party that may have had access to our trade secrets or proprietary information or that has been involved in the development of intellectual property. Additionally, we cannot provide any assurances that all such agreements have been duly executed, and any of these parties may breach such agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. We may not be able to prevent the unauthorized disclosure or use of our technical know-how or other trade secrets by the parties to these agreements. Monitoring unauthorized uses and disclosures is difficult and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets.

Moreover, third parties may still obtain this information or may come upon this or similar information independently, and we would have no right to prevent them from using that technology or information to compete with us. Furthermore, we expect these trade secrets, know-how and proprietary information to over time be disseminated within the industry through independent development, the publication of journal articles describing the methodology and the movement of personnel from academic to industry scientific positions. Consequently, we may be unable to prevent our proprietary technology from being exploited in the United States and abroad, which could affect our ability to expand in domestic and international markets or require costly efforts to protect our technology. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems, but such security measures may be breached, and we may not have adequate remedies for any such breach. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced, and our competitive position would be harmed. If we do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

We may be subject to claims that we or our employees, consultants, advisors or contractors have wrongfully used or disclosed alleged confidential information or trade secrets.

We have entered into and may enter in the future into non-disclosure and confidentiality agreements to protect the proprietary positions of third parties, such as outside scientific collaborators, CROs, third-party manufacturers, consultants, advisors, potential partners, lessees of shared multi-company property and other third parties. We may become subject to litigation where a third party asserts that we or our employees or other third parties inadvertently or otherwise breached the agreements and used or disclosed trade secrets or other information proprietary to the third parties. Defense of such matters, regardless of their merit, could involve substantial litigation expense and be a substantial diversion of employee resources from our business. We cannot predict whether we would prevail in any such actions. Moreover, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our product candidates and technology. Failure to defend against any such claim could subject us to significant liability for monetary damages or prevent or delay our developmental and commercialization efforts, which could adversely affect our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team and other employees.

Parties making claims against us may be able to sustain the costs of complex intellectual property litigation more effectively than we can because they have substantially greater resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, operating results, financial condition and prospects.

We may be subject to claims that we have wrongfully hired an employee from our competitors or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industry, in addition to our employees, we engage the services of consultants to assist us in the development of our product candidates. Many of these consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other biotechnology and pharmaceutical companies including our competitors or potential competitors. We may become subject to claims that we, our employees or consultants inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or their former or current clients. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely affect our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team and other employees.

Our rights to develop and commercialize our technology and product candidates may be subject, in part, to the terms and conditions of licenses granted to us by others.

We have entered into a license agreement with UTSW pursuant to which we have acquired the exclusive right to certain patents and patent applications relating to therapeutics overexpressing the peptide named Dwarf Open Reading Frame, and have entered into various other license agreements with other third parties. We may enter into additional license agreements in the future with other third parties to advance our research or allow commercialization of product candidates. These and other licenses may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future.

In addition, subject to the terms of any such license agreements, we may not have the right to control the preparation, filing, prosecution, maintenance, enforcement, and defense of patents and patent applications covering the technology that we license from third parties. In such an event, we cannot be certain that these patents and patent applications will be prepared, filed, prosecuted, maintained, enforced, and defended in a manner consistent with the best interests of our business. If our licensors fail to prosecute, maintain, enforce, and defend such patents, or lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated, and our right to develop and commercialize any of our products that are subject of such licensed rights could be adversely affected.

Our licensors may have relied on third-party consultants or collaborators or on funds from third parties such that our licensors are not the sole and exclusive owners of the patents we in-licensed. If other third parties have ownership rights to our in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Additionally, our licenses may be subject to certain rights of third parties, and, as a result, our current and future licenses may not provide us with exclusive rights to use the licensed intellectual property and technology.

For example, the intellectual property we license from UTSW is subject to certain non-commercial rights reserved by UTSW and certain rights retained by the U.S. government, including march-in rights. Patents licensed to us could be put at risk of being invalidated or interpreted narrowly in litigation filed by or against our licensors or another licensee or in administrative proceedings brought by or against our licensors or another licensee in response to such litigation or for other reasons. As a result, we may not be able to prevent competitors or other third parties from developing and commercializing competitive products, including in territories covered by our licenses.

It is possible that we may be unable to obtain additional licenses at a reasonable cost or on reasonable terms, if at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business, financial condition, results of operations, and prospects significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current technology, manufacturing methods, product candidates, or future methods or products resulting in either an injunction prohibiting our manufacture or future sales, or, with respect to our future sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties, which could be significant.

Our current licenses impose, and our future licenses likely will impose, various diligence, royalty payment, milestone payment, insurance and other obligations on us. If we fail to comply with any of these or other obligations in our license agreements, we may be required to pay damages and the licensor may have the right to terminate the licenses. Termination by the licensor would cause us to lose valuable rights, and could prevent us from developing and commercializing our product candidates and proprietary technologies. Our business would be seriously harmed if any current or future licenses terminate, if the licensors fail to abide by the terms of the license, if the licensors fail to enforce licensed patents against infringing third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. Furthermore, if any current or future licenses terminate, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties may gain the freedom to seek regulatory approval of, and to market, products identical to ours. If our license agreements terminate, or we experience a reduction or elimination of licensed rights under these agreements, we may have to negotiate new or reinstated licenses with less favorable terms or we may not have sufficient intellectual property rights to operate our business.

Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. In addition, while we cannot currently determine the amount of royalty obligations we would be required to pay on the sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in product candidates that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize any product candidates, we may be unable to achieve or maintain profitability.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

Disputes may arise between us and our current or future licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;

- our right to sublicense patents and other rights to third parties;
- whether third parties are entitled to compensation or equitable relief, such as an injunction, for our use of the intellectual property rights without their authorization;
- our involvement or lack of involvement in the prosecution, defense, and enforcement of licensed patents and our licensors' overall patent enforcement strategy;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the amounts of royalties, milestones or other payments due under the license agreement;
- our right to transfer or assign the license;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, or are insufficient to provide us the necessary rights to use the intellectual property rights, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects.

In spite of our efforts, our current and future licensors might conclude that we have materially breached our obligations under our license agreements and might therefore terminate such license agreements, thereby removing our ability to develop and commercialize products and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products identical to ours. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

The patent protection and patent prosecution for some of our product candidates may be dependent on third parties.

While we normally seek to obtain the right to control prosecution, maintenance and enforcement of the patents relating to our product candidates, there may be times when the filing and prosecution activities for patents relating to our product candidates are controlled by our licensor, potential licensors or collaboration partners. If any of our licensor, potential licensors or collaboration partners fail to prosecute, maintain and enforce such patents and patent applications in a manner consistent with the best interests of our business, including by payment of all applicable fees for patents covering our product candidates, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products. In addition, even where we have the right to control patent prosecution of patents and patent applications we have licensed to and from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensees, our licensors and their counsel that took place prior to the date upon which we assumed control over patent prosecution.

Intellectual property discovered through government funded programs may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies. Compliance with such regulations may limit our exclusive rights and limit our ability to contract with non-U.S. manufacturers.

We have in-licensed certain patents and patent applications that were generated through the use of U.S. government funding or grants, and we may acquire or license in the future intellectual property rights that have been generated through the use of U.S. government funding or grants. Pursuant to the Bayh-Dole Act of 1980, the U.S. government has certain rights in inventions developed with government funding. These U.S. government rights include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right, under certain limited circumstances, to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third-party if it determines that: (1) adequate steps have not been taken to commercialize the invention; (2) government action is necessary to meet public health or safety needs; or (3) government action is necessary to meet requirements for public use under federal regulations (also referred to as march-in rights). For example, the intellectual property we license from UTSW is subject to certain rights retained by the U.S. government, including march-in rights. If the U.S. government exercises its march-in rights in our current or future intellectual property rights that are generated through the use of U.S. government funding or grants, we could be forced to license or sublicense intellectual property developed by us or that we license on terms unfavorable to us, and there can be no assurance that we would receive compensation from the U.S. government for the exercise of such rights. The U.S. government also has the right to take title to these inventions if the grant recipient fails to disclose the invention to the government or fails to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us or the applicable licensor to expend substantial resources. In addition, the U.S. government requires that any products embodying any of these inventions or produced through the use of any of these inventions be manufactured substantially in the United States. This preference for U.S. industry may be waived by the federal agency that provided the funding if the owner or assignee of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. industry may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. Any failure by us to comply with federal regulations regarding intellectual property rights that were developed through the use of U.S. government funding could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct our preclinical studies, and plan to rely on third parties to conduct clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research and studies or to comply with applicable regulatory requirements, which may harm our business.

We utilize and depend upon independent investigators and collaborators, such as medical institutions, CROs and strategic partners to conduct and support our preclinical studies and plan to continue to do so for our future clinical trials. These third parties have had and will continue to have a significant role in the conduct of our preclinical studies and planned clinical trials and the subsequent collection and analysis of data.

These third parties are not our employees, and except for remedies available to us under our agreements with such third parties, we have limited ability to control the amount or timing of resources that any such third party will devote to our preclinical studies or our planned clinical trials. Furthermore, the competition for third parties has increased as a result of COVID-19. The third parties we rely on for these services may also have relationships with other entities, some of which may be our competitors, for whom they may also be conducting

clinical trials or other drug development activities, which could affect their performance on our behalf. Some of these third parties may terminate their engagements with us at any time. We also expect to have to negotiate budgets and contracts with CROs and clinical trial sites and we may not be able to do so on favorable terms, which may result in delays to our development timelines and increased costs. If we need to enter into alternative arrangements with, or replace or add any third parties, it would involve substantial cost and require extensive management time and focus, or involve a transition period, and may delay our drug development activities, as well as materially impact our ability to meet our desired clinical development timelines.

Our heavy reliance on these third parties for such drug development activities will reduce our control over these activities. As a result, we will have less direct control over the conduct, timing and completion of preclinical studies and clinical trials and the management of data developed through preclinical studies and clinical trials than would be the case if we were relying entirely upon our own staff. Nevertheless, we are responsible for ensuring that each of our studies and trials is conducted in accordance with applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with GCP standards, regulations for conducting, recording and reporting the results of clinical trials to assure that data and reported results are reliable and accurate and that the rights, integrity and confidentiality of trial participants are protected. The EMA also requires us to comply with similar standards. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. There can be no assurance that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials substantially comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under current cGMP regulations and will require a large number of test patients. Our failure or any failure by these third parties to comply with these regulations or to recruit a sufficient number of patients, may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

We contract with third parties for the production of our product candidates for preclinical studies and expect to continue to do so for additional preclinical studies, clinical trials and ultimately for commercialization for certain of our product candidates. This reliance on third parties increases the risk that we will not have sufficient quality and quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not currently have the infrastructure or internal capability to manufacture supplies of our product candidates for use in development and commercialization. We plan to fully integrate and internalize AAV manufacturing capabilities to support our Gene Therapy and Cellular Regeneration platforms, and have initiated construction of a cGMP manufacturing facility. Until our manufacturing facility is complete and operational, we will continue to rely on third-party manufacturers for our Gene Therapy and Cellular Regeneration platforms. Moreover, to optimize our use of resources and utilize extensive third-party experience in small molecule manufacturing, we intend to continue to rely on third-party manufacturers for our small molecule programs.

Competition for third-party manufacturers and supplies has increased as a result of COVID-19. Changing third-party manufacturers could result in delays in our manufacturing supply chain which could delay or otherwise impact development of our programs and result in increased costs.

We do not have long-term supply agreements, and we purchase our required drug product on a purchase order basis, which means that aside from any binding purchase orders we have from time to time, our supplier could cease supplying to us or change the terms on which it is willing to continue supplying to us at any time. If we were to experience an unexpected loss of supply of our product candidates for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, any pending or ongoing preclinical studies or clinical trials.

We may be unable to maintain or establish required agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the failure of the third party to manufacture our product candidates according to our schedule and specifications, or at all, including if our third-party contractors give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them;
- the termination or nonrenewal of arrangements or agreements by our third-party contractors at a time that is costly or inconvenient for us;
- the breach by the third-party contractors of our agreements with them;
- the failure of third-party contractors to comply with applicable regulatory requirements, including cGMPs;
- the failure of the third party to manufacture our product candidates according to our specifications;
- the mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;
- clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and
- the infringement, misappropriation or other violation of our intellectual property or proprietary information, including our trade secrets and know-how.

We do not have complete control over all aspects of the manufacturing process of our CDMOs and are dependent on these CDMOs for compliance with cGMP regulations for manufacturing active pharmaceutical ingredients (API), drug substance and finished drug products. We are in the process of developing our supply chain for each of our product candidates and intend to put in place framework agreements under which CDMOs will generally provide us with necessary quantities of API, drug substance and drug product on a project-by-project basis based on our development needs. As we advance our product candidates through development, we will consider our lack of redundant supply for the API, drug substance and drug product for each of our product candidates to protect against any potential supply disruptions. However, we may be unsuccessful in putting in place such framework agreements or protecting against potential supply disruptions.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. If our CDMOs cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, EMA or others, they will not be able to secure and/or maintain marketing approval for their manufacturing facilities. In addition, we do not have control over the ability of our CDMOs to maintain adequate QC, QA, facilities, equipment and qualified personnel. If the FDA, EMA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we will need to find alternative manufacturing facilities, and those new facilities would need to be inspected and approved by FDA, EMA or comparable regulatory authority prior to commencing manufacturing, which would significantly impact our ability to develop, obtain marketing approval for or market our product candidates, if approved. Our failure,

or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates or drugs and harm our business and results of operations.

We rely on third-party suppliers for the raw materials required for the production of our product candidates for all of our programs. Our reliance on third-party supplies will continue even after we operationalize our cGMP manufacturing facility to support our Gene Therapy and Cellular Regeneration platforms. Our dependence on these third-party suppliers and the challenges we may face in obtaining adequate supplies of raw materials involve several risks, including limited control over pricing, availability, quality and delivery schedules. As a small company, our negotiation leverage is limited and we are likely to get lower priority than our competitors who are larger than we are. We cannot be certain that our suppliers will continue to provide us with the quantities of these raw materials that we require or satisfy our anticipated specifications and quality requirements. Any interruption in supply of raw materials could materially harm our ability to manufacture our product candidates until a new source of supply, if any, could be identified and qualified. We may be unable to find a sufficient alternative supplier in a reasonable time or on commercially reasonable terms. Any performance failure on the part of our suppliers could delay the development and potential commercialization of our product candidates, including limiting supplies necessary for clinical trials and regulatory approvals, which would seriously harm our business.

Our current and anticipated future dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins and our ability to commercialize any product candidates that receive marketing approval on a timely and competitive basis.

Our reliance on third parties may require us to share our trade secrets, which increases the possibility that our competitors will discover them or that our trade secrets will be misappropriated or disclosed.

Because we currently rely on third parties in the course of our business, we may share our proprietary technology and confidential information, including trade secrets, with them. We seek to protect our proprietary technology, in part, by entering into confidentiality agreements, and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements, invention assignment or other similar agreements with our collaborators, advisors, employees, consultants and other third parties prior to beginning research or disclosing trade secrets or proprietary information. These agreements typically limit the rights of the third parties to use or disclose our trade secrets and confidential information. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are intentionally or inadvertently incorporated into the technology of others or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets and despite our efforts to protect our trade secrets, our competitors' discovery of our proprietary technology, trade secrets or confidential information or other unauthorized use or disclosure of such information would impair our competitive position and may have a material adverse effect on our business, financial condition, results of operations and prospects.

If we engage in future acquisitions or strategic partnerships, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks.

From time to time, we evaluate various acquisition opportunities and strategic partnerships, including licensing or acquiring complementary products, intellectual property rights, technologies or businesses. Any potential acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;

- the assumption of additional indebtedness or contingent liabilities;
- the issuance of our equity securities;
- assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing programs and initiatives in pursuing such a strategic merger or acquisition;
- retention of key employees, the loss of key personnel and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and marketing approvals; and
- our inability to generate revenue from acquired technology and/or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

In addition, if we undertake acquisitions or pursue partnerships in the future, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense.

If we decide to establish collaborations, but are not able to establish those collaborations on commercially reasonable terms, we may have to alter our development and commercialization plans.

Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. We strategically evaluate collaborations and partnerships with biopharmaceutical companies that may have more robust and complementary capabilities and resources to accelerate the development and maximize the availability and potential of our product candidates, particularly for more prevalent indications. The relationships may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business.

We would face significant competition in seeking appropriate collaborators and the negotiation process is time-consuming and complex. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA, EMA or comparable foreign regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing drugs, the existence of uncertainty with respect to our ownership of intellectual property and industry and market conditions generally. The potential collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such collaboration could be more attractive than the one with us for our product candidate. Further, we may not be successful in our efforts to establish a collaboration or other alternative arrangements for product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view them as having the requisite potential to demonstrate safety and efficacy.

In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. Even if we are successful in entering into a collaboration, the terms and conditions of that collaboration may restrict us from entering into future agreements on certain terms with potential collaborators.

If and when we seek to enter into collaborations, we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

We may enter into collaborations with third parties for the development and commercialization of product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

If we enter into any collaboration arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements. Collaborations involving our product candidates would pose numerous risks to us, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to, and the manner in which they perform their obligations under, these collaborations and may not perform their obligations as expected;
- collaborators may deemphasize or not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus, including as a result of a business combination or sale or disposition of a business unit or development function, or available funding or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- a collaborator with marketing and distribution rights to multiple products may not commit sufficient resources to the marketing and distribution of our product relative to other products;
- we may grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- collaborators may not properly obtain, maintain, defend, protect or enforce our intellectual property rights or may use our proprietary information and intellectual property in such a way as to invite litigation or other intellectual property-related proceedings that could jeopardize or invalidate our proprietary information and intellectual property or expose us to potential litigation or other intellectual property related proceedings;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates;

- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all;
- collaborators may not provide us with timely and accurate information regarding development progress and activities under the collaboration or may limit our ability to share such information, which could adversely impact our ability to report progress to our investors and otherwise plan our own development of our product candidates;
- collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property; and
- a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings.

If we enter into collaborations to develop and potentially commercialize any product candidates, we may not be able to realize the benefit of such transactions if we or our collaborator elect not to exercise the rights granted under the agreement or if we or our collaborator are unable to successfully integrate a product candidate into existing operations and company culture. In addition, if our agreement with any of our collaborators terminates, our access to technology and intellectual property licensed to us by that collaborator may be restricted or terminate entirely, which may delay our continued development of our product candidates utilizing the collaborator's technology or intellectual property or require us to stop development of those product candidates completely. We may also find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. Any collaborator may also be subject to many of the risks relating to product development, regulatory approval, and commercialization described in this "Risk Factors" section, and any negative impact on our collaborators may adversely affect us.

If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any product candidates we may develop, we may not be successful in commercializing those product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to third parties. In the future, we may choose to build a focused sales, marketing and commercial support infrastructure to sell, or participate in sales activities with collaborators for, some of our product candidates if and when they are approved.

There are risks involved with both establishing our own commercial capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force or reimbursement specialists is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and other commercialization capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our commercialization personnel.

Factors that may inhibit our efforts to commercialize any approved product on our own include:

- our inability to recruit and retain adequate numbers of effective sales, marketing, reimbursement, compliance, customer service, medical affairs and other support personnel;
- our inability to recruit and build a commercial infrastructure due to the impacts of COVID-19;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future approved products;

- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement, and other acceptance by payors;
- the inability to price our products at a sufficient price point to ensure an adequate and attractive level of profitability;
- restricted or closed distribution channels that make it difficult to distribute our products to segments of the patient population;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent commercialization organization.

If we enter into arrangements with third parties to perform sales, marketing, commercial support and distribution services, our product revenue or the profitability of product revenue may be lower than if we were to market and sell any products we may develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to commercialize our product candidates or may be unable to do so on terms that are favorable to us. We may have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish commercialization capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates if approved and our business would be seriously harmed.

Risks Related to This Offering and Ownership of Our Common Stock

We do not know whether an active, liquid and orderly trading market will develop for our common stock or what the market price of our common stock will be and as a result it may be difficult for you to sell your shares of our common stock.

Prior to this offering, no market for shares of our common stock existed and an active trading market for our shares may never develop or be sustained following this offering. We determined the initial public offering price for our common stock through negotiations with the representatives of the underwriters, and the negotiated price may not be indicative of the market price of our common stock after this offering. The market value of our common stock may decrease from the initial public offering price. As a result of these and other factors, you may be unable to resell your shares of our common stock at or above the initial public offering price. The lack of an active market may impair your ability to sell your shares at the time you wish to sell them or at a price that you consider reasonable. The lack of an active market may also reduce the fair market value of your shares. Furthermore, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic collaborations or acquire companies, technologies or other assets by using our shares of common stock as consideration.

The price of our stock may be volatile, and you could lose all or part of your investment.

The trading price of our common stock following this offering is likely to be highly volatile and subject to wide fluctuations in response to various factors, some of which we cannot control. The stock market in general, and pharmaceutical and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies.

Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In addition to the factors discussed in this “Risk Factors” section and elsewhere in this prospectus, these factors include:

- the timing and results of preclinical studies and clinical trials of our product candidates, those conducted by third parties or those of our competitors;

- the success of competitive products or announcements by potential competitors of their product development efforts;
- regulatory actions with respect to our products or our competitors' products;
- actual or anticipated changes in our growth rate relative to our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other intellectual property or proprietary rights;
- the recruitment or departure of key personnel;
- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures, collaborations or capital commitments;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- market conditions in the pharmaceutical and biotechnology sector;
- changes in the structure of healthcare payment systems;
- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or our other stockholders;
- expiration of market stand-off or lock-up agreements;
- the impact of any natural disasters or public health emergencies, such as the COVID-19 pandemic;
- the availability of fiscal and monetary stimulus measures to counteract the impact of natural disasters or public health emergencies, such as the COVID-19 pandemic; and
- general economic, political, industry and market conditions.

The realization of any of the above risks or any of a broad range of other risks, including those described in this "Risk Factors" section, could have a dramatic and adverse impact on the market price of our common stock.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or our guidance.

Our quarterly and annual operating results may fluctuate significantly in the future, which makes it difficult for us to predict our future operating results. From time to time, we may enter into license or collaboration agreements or strategic partnerships with other companies that include development funding and significant upfront and milestone payments and/or royalties, which may become an important source of our revenue. These upfront and milestone payments may vary significantly from period to period and any such variance could cause a significant fluctuation in our operating results from one period to the next.

In addition, we measure compensation cost for stock-based awards made to employees at the grant date of the award, based on the fair value of the award as determined by our board of directors, and recognize the cost as an expense over the employee's requisite service period. As the variables that we use as a basis for valuing these awards change over time, including, after the closing of this offering, our underlying stock price and stock price volatility, the magnitude of the expense that we must recognize may vary significantly.

Furthermore, our operating results may fluctuate due to a variety of other factors, many of which are outside of our control and may be difficult to predict, including the following:

- the timing and cost of, and level of investment in, research and development activities relating to our programs, product candidates and any future programs and product candidates, which will change from time to time;
- our ability to enroll patients in clinical trials and the timing of enrollment;
- the cost of establishing and operating a manufacturing facility and manufacturing our product candidates and any future product candidates, which may vary depending on FDA, EMA or other comparable foreign regulatory authority guidelines and requirements, the quantity of production and the terms of our agreements with manufacturers;
- expenditures that we will or may incur to acquire or develop additional product candidates and technologies or other assets;
- the timing and outcomes of clinical trials for our product candidates, or competing product candidates;
- the need to conduct unanticipated clinical trials or trials that are larger or more complex than anticipated;
- competition from existing and potential future products that compete with our programs and product candidates, and changes in the competitive landscape of our industry, including consolidation among our competitors or partners;
- any delays in regulatory review or approval of our product candidates;
- the level of demand for our product candidates, if approved, which may fluctuate significantly and be difficult to predict;
- the risk/benefit profile, cost and reimbursement policies with respect to our product candidates, if approved, and existing and potential future products that compete with any of our product candidates;
- our ability to commercialize any of our product candidates, if approved, inside and outside of the United States, either independently or working with third parties;
- our ability to establish and maintain collaborations, licensing or other arrangements;
- our ability to adequately support future growth;
- potential unforeseen business disruptions that increase our costs or expenses;
- future accounting pronouncements or changes in our accounting policies;
- the changing and volatile global economic and political environment; and
- increased impact from COVID-19 on the costs and timing associated with the conduct of our clinical trial and other related business activities.

The cumulative effect of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated guidance we may provide.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

As of June 30, 2021, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately 66.3% of our common stock and, upon the closing of this offering, that same group will beneficially own approximately 46.5% of our outstanding common stock (based on the number of shares of common stock outstanding as of June 30, 2021 assuming no exercise of the underwriters' option to purchase additional shares, no exercise of outstanding options and no purchases of shares in this offering by any of this group), in each case assuming the conversion of all outstanding shares of our convertible preferred stock into shares of our common stock immediately prior to the closing of this offering. These stockholders, acting together, may be able to control matters requiring stockholder approval. For example, they may be able to control elections of directors, amendments of our organizational documents or approval of any merger, sale of assets or other major corporate transactions. This concentration of ownership control may delay, discourage or prevent a change of control, including unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders, entrench our management and board of directors or delay or prevent a merger, consolidation, takeover or other business combination involving us that other stockholders may desire. The interests of this group of stockholders may not always coincide with your interests or the interests of other stockholders and they may act in a manner that advances their best interests and not necessarily those of other stockholders, including seeking a premium value for their common stock, and might affect the prevailing market price for our common stock.

Participation in this offering by our existing stockholders and/or their affiliated entities may reduce the public float for our common stock.

To the extent certain of our existing stockholders who are our affiliates or their affiliated entities participate in this offering, such purchases would reduce the non-affiliate public float of our common stock after this offering, which is the number of shares of our common stock that are not held by officers, directors and affiliated stockholders. A reduction in the public float could reduce the number of shares that are available to be traded at any given time, thereby adversely impacting the liquidity of our common stock and depressing the price at which you may be able to sell shares of common stock purchased in this offering.

You will incur immediate and substantial dilution as a result of this offering.

If you purchase common stock in this offering, you will incur immediate and substantial dilution of approximately $7.10 per share, representing the difference between the initial public offering price of $15.00 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, and our pro forma net tangible book value per share as of March 31, 2021 after giving effect to this offering and the automatic conversion of all outstanding shares of our convertible preferred stock immediately prior to the closing of this offering. As of March 31, 2021, there were 1,727,968 shares subject to outstanding options with a weighted-average exercise price of $3.06 per share. To the extent that these outstanding options or other options that we have issued or may issue in the future are ultimately exercised or the underwriters exercise their option to purchase additional shares, you will incur further dilution. See the section of this prospectus titled "Dilution" for a further description of the dilution you will experience immediately after this offering.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. After this offering, we will have 39,324,727 outstanding shares of common stock, based on the number of shares outstanding as of March 31, 2021, assuming: (1) no exercise of the underwriters' option to purchase additional shares and (2) the conversion of all outstanding shares of our convertible preferred stock into shares of common stock immediately prior to the closing of this offering. This includes the shares that we sell in this offering, which may be resold in the public market immediately

without restriction, unless purchased by our affiliates. Of the remaining shares, 27,324,727 shares of our common stock are currently restricted as a result of securities laws or market stand-off or lock-up agreements but will be able to be sold after this offering as described in the "Shares Eligible for Future Sale" section of this prospectus. Moreover, after this offering, holders of an aggregate of 26,102,278 shares of our common stock will have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also intend to register all shares of common stock that we may issue under our equity incentive plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements described in the "Underwriters" section of this prospectus.

Our executive officers, directors and the holders of substantially all of our capital stock and securities convertible into or exchangeable for our capital stock have entered into market stand-off agreements with us and lock-up agreements with the underwriters under which they have agreed, subject to specific exceptions described in the section titled "Underwriters," not to sell, directly or indirectly, any shares of common stock without the permission of the underwriters for a period of 180 days following the date of this prospectus. We refer to such period as the lock-up period or restricted period. When the lock-up period expires, we and our securityholders subject to a lock-up agreement or market stand-off agreement will be able to sell our shares in the public market. In addition, the underwriters may, in their sole discretion, release all or some portion of the shares subject to lock-up agreements at any time and for any reason. See the description of the market stand-off agreement with us and the lock-up agreement with the underwriters in the section of this prospectus titled "Shares Eligible for Future Sale" for more information. Sales of a substantial number of such shares upon expiration of the lock-up and market stand-off agreements, the perception that such sales may occur, or early release of these agreements, could cause our market price to fall or make it more difficult for you to sell your common stock at a time and price that you deem appropriate.

We are an "emerging growth company" and a "smaller reporting company" and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies and smaller reporting companies will make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012 (JOBS Act). For as long as we continue to be an emerging growth company, we intend to take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure in this prospectus;
- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended (Sarbanes-Oxley Act);
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation in this prospectus and our periodic reports and proxy statements; and
- exemptions from the requirements of holding nonbinding advisory stockholder votes on executive compensation and stockholder approval of any golden parachute payments not previously approved.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to avail ourselves of this exemption from new or revised accounting standards and, therefore, will not be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. As a result, our

financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

We will remain an emerging growth company until the earliest to occur of: (1) the last day of the fiscal year in which we have more than $1.07 billion in annual revenue; (2) the date we qualify as a "large accelerated filer," with at least $700.0 million of equity securities held by non-affiliates; (3) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period; and (4) the last day of the fiscal year ending after the fifth anniversary of our initial public offering.

Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company," as defined in the Securities Exchange Act of 1934, as amended (Exchange Act), which would allow us to continue to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in this prospectus and our periodic reports and proxy statements.

We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

If securities or industry analysts do not publish research or reports, or if they publish adverse or misleading research or reports, regarding us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that securities or industry analysts publish about us, our business or our market. We do not currently have and may never obtain research coverage by securities or industry analysts. If no or few securities or industry analysts commence coverage of us, the stock price would be negatively impacted. In the event we obtain securities or industry analyst coverage, if any of the analysts who cover us issue adverse or misleading research or reports regarding us, our business model, our intellectual property, our stock performance or our market, or if our operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

We will incur increased costs as a result of operating as a public company, and our management will devote substantial time to related compliance initiatives. Additionally, if we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.

As a public company, we will incur significant legal, accounting and other expenses that we did not incur as a private company, and these expenses may increase even more after we are no longer an "emerging growth company." We will be subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Protection Act, as well as rules adopted, and to be adopted, by the SEC and the Nasdaq Stock Market LLC (Nasdaq). Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, we expect these rules, regulations and standards to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly, which will increase our operating expenses. For example, we expect these rules, regulations and standards to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain sufficient coverage, particularly in light of recent cost increases related to coverage. We cannot accurately predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

In addition, as a public company we will be required to incur additional costs and obligations in order to comply with SEC rules that implement Section 404 of the Sarbanes-Oxley Act. Under these rules, beginning with our second annual report on Form 10-K after we become a public company, we will be required to make a formal assessment of the effectiveness of our internal control over financial reporting, and once we cease to be an emerging growth company, we will be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaging in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially continue to engage outside consultants and adopt a detailed work plan to assess and document the adequacy of our internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are designed and operating effectively, and implement a continuous reporting and improvement process for internal control over financial reporting.

The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation to meet the detailed standards under the rules. During the course of its testing, our management may identify material weaknesses or deficiencies which may not be remedied in time to meet the deadline imposed by the Sarbanes-Oxley Act.

Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our stock could decline and we could be subject to sanctions or investigations by the stock exchange on which our common stock is listed, the SEC or other regulatory authorities.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

Upon the closing of this offering, we will become subject to the periodic reporting requirements of the Exchange Act. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the facts that judgments in decision-making can be faulty and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

We will have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in "Use of Proceeds," and you will be relying on the judgment of our management regarding the application of these proceeds, who could spend the proceeds in ways that do not

improve our results of operations or enhance the value of our common stock. You will not have the opportunity, as part of your investment decision, to assess whether we are using the proceeds appropriately. Our management might not apply the net proceeds in ways that ultimately increase the value of your investment. If we do not invest or apply the net proceeds from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

We may be subject to securities litigation, which is expensive and could divert management attention.

The market price of our common stock may be volatile and, in the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. This risk is especially relevant for us because biotechnology companies have experienced significant stock price volatility in recent years and we may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

We do not intend to pay dividends on our common stock in the foreseeable future, so any returns will be limited to the value of our common stock.

We have never declared or paid any cash dividends on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to any appreciation in the value of their stock.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws, as they will be in effect upon closing of this offering, and Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the market price of our common stock.

Our amended and restated certificate of incorporation and amended and restated bylaws, as they will be in effect upon closing of this offering, will contain provisions that could depress the market price of our common stock by acting to discourage, delay or prevent a change in control of our company or changes in our management that the stockholders of our company may deem advantageous. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. These provisions, among other things:

- establish a classified board of directors so that not all members of our board are elected at one time;
- permit only the board of directors to establish the number of directors and fill vacancies on the board;
- provide that directors may only be removed "for cause" and only with the approval of two-thirds of our stockholders;
- authorize the issuance of "blank check" preferred stock that our board could use to implement a stockholder rights plan (also known as a poison pill);
- eliminate the ability of our stockholders to call special meetings of stockholders;
- prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders;
- prohibit cumulative voting;
- authorize our board of directors to amend the bylaws;
- establish advance notice requirements for nominations for election to our board or for proposing matters that can be acted upon by stockholders at annual stockholder meetings; and

- require a super-majority vote of stockholders to amend or repeal specified provisions of our amended and restated certificate of incorporation and amended and restated bylaws, as they will be in effect upon closing of this offering.

In addition, Section 203 of the General Corporation Law of the State of Delaware (DGCL), prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

Any provision of our amended and restated certificate of incorporation, amended and restated bylaws or Delaware law that has the effect of delaying or preventing a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our capital stock and could also affect the price that some investors are willing to pay for our common stock.

Our amended and restated bylaws that will become effective upon the closing of this offering provide that the Court of Chancery of the State of Delaware and the federal district courts of the United States of America will be the exclusive forums for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated bylaws that will become effective upon the closing of this offering provide that the Court of Chancery of the State of Delaware (or, if the Court of Chancery does not have jurisdiction, another State court in Delaware or the federal district court for the District of Delaware) is the exclusive forum for the following (except for any claim as to which such court determines that there is an indispensable party not subject to the jurisdiction of such court (and the indispensable party does not consent to the personal jurisdiction of such court within 10 days following such determination), which is vested in the exclusive jurisdiction of a court or forum other than such court or for which such court does not have subject matter jurisdiction):

- any derivative action or proceeding brought on our behalf;
- any action asserting a claim of breach of fiduciary duty;
- any action asserting a claim against us arising under the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws; and
- any action asserting a claim against us that is governed by the internal-affairs doctrine.

This provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act or any other claim for which the U.S. federal courts have exclusive jurisdiction.

Our amended and restated bylaws further provide that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act.

These exclusive-forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage lawsuits against us and our directors, officers and other employees. In addition, these exclusive-forum provisions may impose additional litigation costs for stockholders who determine to pursue any such lawsuits against us.

Any person or entity purchasing or otherwise acquiring any interest in any of our securities shall be deemed to have notice of and consented to these provisions. There is uncertainty as to whether a court would enforce such provisions, and the enforceability of similar choice of forum provisions in other companies' charter documents has been challenged in legal proceedings. It is possible that a court could find these types of provisions to be inapplicable or unenforceable, and if a court were to find either exclusive-forum provision in our amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could seriously harm our business.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements. All statements other than statements of historical facts contained in this prospectus, including statements regarding our future results of operations and financial position, business strategy, development plans, planned preclinical studies and clinical trials, future results of clinical trials, expected research and development costs, regulatory strategy, timing and likelihood of success, as well as plans and objectives of management for future operations, are forward-looking statements. In some cases, investors can identify forward-looking statements by terms such as “may,” “will,” “should,” “would,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential” or “continue” or the negative of these terms or other similar expressions. Forward-looking statements contained in this prospectus include, but are not limited to, statements about:

- the ability of our preclinical studies and planned clinical trials to demonstrate safety and efficacy of our product candidates, and other positive results;
- the timing, progress and results of preclinical studies and planned clinical trials for our current product candidates and other product candidates we may develop, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, and the period during which the results of the studies or trials will become available;
- the timing, scope and likelihood of regulatory filings and approvals, including timing of INDs, CTAs, FDA approvals, and final regulatory approval of our current product candidates and any other future product candidates;
- our ability to develop and advance our current product candidates and programs into, and successfully complete, clinical studies;
- our manufacturing, commercialization, and marketing capabilities and strategy and the timing of our facilities becoming operational;
- our plans relating to commercializing our product candidates, if approved;
- the need to hire additional personnel and our ability to attract and retain such personnel;
- the size of the market opportunity for our product candidates, including our estimates of the number of patients who suffer from the diseases we are targeting;
- our competitive position and the success of competing therapies that are or may become available;
- the beneficial characteristics, and the potential safety, efficacy and therapeutic effects of our product candidates and our approach;
- our plans relating to the further development of our product candidates, including the biomarkers and endpoints that we may evaluate and additional indications and targets we may pursue;
- the impact of existing laws and regulations and regulatory developments in the United States, Europe and other jurisdictions;
- our expectations regarding the impact of the COVID-19 pandemic on our business, including our preclinical studies and clinical trials;
- our intellectual property position, including the scope of protection we are able to establish and maintain for intellectual property rights covering our current product candidates and other product candidates we may develop, including the extensions of existing patent terms where available, the validity of intellectual property rights held by third parties, and our ability not to infringe, misappropriate or otherwise violate any third-party intellectual property rights;
- our continued reliance on third parties to conduct additional preclinical studies and planned clinical trials of our product candidates, and for the development and manufacture of our product candidates for preclinical studies and clinical trials;

- our ability to obtain, and negotiate favorable terms of, any collaboration, partnership, licensing or other arrangements that may be necessary or desirable to develop, manufacture or commercialize our product candidates;
- the pricing and reimbursement of our current product candidates and other product candidates we may develop, if approved, including any increase in demand as a result of the availability of reimbursement from the government and third-party payors;
- the rate and degree of market acceptance and clinical utility of our current product candidates and other product candidates we may develop;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our financial performance;
- the period over which we estimate our existing cash and cash equivalents will be sufficient to fund our future operating expenses and capital expenditure requirements;
- our expectations regarding the period during which we will remain an emerging growth company under the JOBS Act; and
- our anticipated use of our existing resources and the net proceeds from this offering.

We have based these forward-looking statements largely on our current expectations and projections about our business, the industry in which we operate and financial trends that we believe may affect our business, financial condition, results of operations and prospects, and these forward-looking statements are not guarantees of future performance or development. These forward-looking statements speak only as of the date of this prospectus and are subject to a number of risks, uncertainties and assumptions described in the section titled “Risk Factors” and elsewhere in this prospectus. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, investors should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein until after we distribute this prospectus, whether as a result of any new information, future events or otherwise.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

MARKET, INDUSTRY AND OTHER DATA

This prospectus contains estimates, projections and other information concerning our industry, our business and the markets for our product candidates, including data regarding the estimated size of such markets and the incidence of certain medical conditions. We obtained the industry, market and similar data set forth in this prospectus from our internal estimates and research and from academic and industry research, publications, surveys and studies conducted by third parties, including governmental agencies. In some cases, we do not expressly refer to the sources from which this data is derived. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Investors are cautioned not to give undue weight to any such information, projections and estimates.

USE OF PROCEEDS

We estimate that the net proceeds to us from the sale of the shares of our common stock in this offering will be approximately $163.7 million, or approximately $188.8 million if the underwriters exercise their option to purchase additional shares in full, based upon the initial public offering price of $15.00 per share, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

The principal purposes of this offering are to obtain additional capital to support our operations, establish a public market for our common stock and facilitate our future access to the public capital markets. We currently intend to use the net proceeds from this offering, together with our existing cash and cash equivalents, as follows:

- approximately $35 million to $40 million to fund our ongoing and planned preclinical and clinical development of our product candidate TN-201 in our MYBPC3 program, including initiation of the planned Phase 1/2 clinical trial;
- approximately $10 million to $15 million to fund our ongoing and planned preclinical and clinical development of our product candidate TYA-11631 in our HDAC6i program through initiation of the planned Phase 1 clinical trial;
- approximately $25 million to $35 million to fund the continued development of our other programs, including our PKP2, DWORF and Reprogramming programs;
- approximately $40 million to $50 million to fund the expansion of our manufacturing capabilities and facilities; and
- the remaining amounts, if any, for working capital and other general corporate purposes.

Our expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the completion of this offering or the amounts that we will actually spend on the uses set forth above and we may require additional funds in order to fully accomplish the specified uses listed above. We believe opportunities may exist from time to time to expand our current business through licenses with or acquisitions of, or investments in, complementary businesses, products, intellectual property or technologies. While we have no current agreements, commitments or understandings for any specific licenses, acquisitions or investments at this time, we may use a portion of the net proceeds for these purposes. As a result, our management will have broad discretion over the use of the net proceeds from this offering.

Based on our current operating plan, we believe that the net proceeds from this offering, together with our existing cash and cash equivalents, will be sufficient to fund our operating expenses and capital expenditures through at least the next 24 months from the date of our unaudited interim condensed financial statements included elsewhere in this prospectus. The net proceeds from this offering, together with our existing cash and cash equivalents, will not be sufficient to fund any of our product candidates through regulatory approval, and we anticipate needing to raise additional capital to complete the development of and commercialize our product candidates. It is difficult to predict the cost and timing required to complete development and obtain regulatory approval of, and commercialize, our product candidates due to, among other factors, our lack of experience as a company with initiating, conducting and completing clinical trials, and uncertainty regarding the scope and design of clinical trials required to obtain regulatory approval for our product candidates, the rate of subject enrollment in our planned clinical trials, filing requirements with various regulatory agencies, clinical trial results, and the actual costs of manufacturing, supplying and commercializing our product candidates. The amounts and timing of our expenditures will depend upon numerous factors including the cost and results of our research and development efforts, the timing, cost and success of preclinical studies and any clinical trials we may commence in the future, the timing of regulatory submissions, our ability to obtain additional financing, the amount of cash obtained through our existing collaborations and future collaborations, if any, and any unforeseen cash needs. We also may elect to raise additional capital opportunistically.

Pending their use, we intend to invest the net proceeds of this offering in short- and intermediate-term interest-bearing obligations, including U.S. government money market funds, U.S. Treasury obligations, U.S. agency and government-sponsored entity obligations, corporate debt obligations, and taxable and tax-exempt municipal obligations.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain any future earnings and do not expect to pay any dividends in the foreseeable future. Any future determination to declare cash dividends will be made at the discretion of our board of directors, subject to applicable laws, and will depend on a number of factors, including our financial condition, results of operations, capital requirements, contractual restrictions, general business conditions and other factors that our board of directors may deem relevant.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and capitalization as of March 31, 2021:

- on an actual basis;
- on a pro forma basis to give effect to: (i) the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of 26,102,278 shares of our common stock immediately prior to the completion of this offering, as if such conversion had occurred on March 31, 2021; (ii) the related reclassification of our convertible preferred stock aggregate carrying value to permanent equity; and (iii) the filing and effectiveness of our amended and restated certificate of incorporation immediately prior to the closing of this offering; and
- on a pro forma as adjusted basis to give further effect to the sale by us of 12,000,000 shares of our common stock in this offering, at the initial public offering price of $15.00 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this information in conjunction with our financial statements and the related notes appearing elsewhere in this prospectus, the section titled “Management’s Discussion and Analysis of Financial Condition and Results of Operations”, and other financial information contained in this prospectus.

	As of March 31, 2021 (in thousands, except share and per share data)		
	Actual	Pro Forma	Pro Forma as adjusted
Cash and cash equivalents	$128,439	$128,439	$292,139
Convertible preferred stock, par value $0.0001; 26,102,301 shares authorized, 26,102,278 issued and outstanding, actual; no shares authorized, issued and outstanding, pro forma and pro forma as adjusted	240,735	—	—
Stockholders’ (deficit) equity:			
Preferred stock, par value $0.0001; no shares authorized, issued and outstanding, actual; 200,000,000 shares authorized, no shares issued and outstanding, pro forma and pro forma as adjusted	—	—	—
Common stock, par value $0.0001; 30,330,000 shares authorized, 1,222,449 shares issued and outstanding, actual; 1,000,000,000 shares authorized, 27,324,727 shares issued and outstanding, pro forma; 1,000,000,000 shares authorized, 39,324,727 shares issued and outstanding, pro forma as adjusted	—	3	4
Additional paid-in capital	2,054	242,786	406,485
Notes receivable from stockholders	(87)	(87)	(87)
Accumulated deficit	(95,910)	(95,910)	(95,910)
Total stockholders’ (deficit) equity	$ (93,943)	$146,792	$310,492
Total capitalization	$146,792	$146,792	$310,492

The number of shares of our common stock issued and outstanding, pro forma and pro forma as adjusted, in the table above are based on 27,324,727 shares of our common stock outstanding as of March 31, 2021 (including conversion of all of our outstanding shares of convertible preferred stock into 26,102,278 shares of our common stock), and excludes:

- 1,727,968 shares of our common stock issuable upon the exercise of options outstanding as of March 31, 2021, with a weighted-average exercise price of $3.06 per share;
- 835,473 shares of our common stock issuable upon the exercise of options granted subsequent to March 31, 2021, with a weighted-average exercise price of $10.00 per share;
- 379,271 shares of our common stock reserved for future grant or issuance under our Amended and Restated 2016 Equity Incentive Plan as of March 31, 2021;
- 4,000,000 shares of our common stock reserved for future issuance under our 2021 Equity Incentive Plan, which became effective on the business day immediately prior to the date of effectiveness of the registration statement of which this prospectus forms a part, as well as any automatic increases in the number of shares of our common stock reserved for future issuance pursuant to this plan; and
- 800,000 shares of common stock reserved for future issuance under our 2021 ESPP, which became effective on the business day immediately prior to the date of effectiveness of the registration statement of which this prospectus forms a part, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan.

DILUTION

If you invest in our common stock in this offering, your ownership will be immediately diluted to the extent of the difference between the initial public offering price per share and the pro forma as adjusted net tangible book value per share of our common stock after this offering.

As of March 31, 2021, we had a historical net tangible book value (deficit) of $(94.0) million, or $(76.91) per share of common stock. Our historical net tangible book value (deficit) represents our total tangible assets, less our total liabilities and convertible preferred stock, which is not included within stockholders' equity (deficit), divided by the total number of shares of our common stock outstanding as of March 31, 2021.

Our pro forma net tangible book value as of March 31, 2021, was $146.7 million, or $5.37 per share. Pro forma net tangible book value per share represents our total tangible assets, less our total liabilities, divided by the total number of shares of common stock outstanding as of March 31, 2021, after giving effect to the conversion of our convertible preferred stock into an aggregate of 26,102,278 shares of our common stock.

After giving further effect to the sale and issuance by us of the 12,000,000 shares of our common stock in this offering, at the initial public offering price of $15.00 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of March 31, 2021 would be $310.5 million, or $7.90 per share. This represents an immediate increase in pro forma net tangible book value to our existing stockholders of $2.53 per share and an immediate dilution to new investors of $7.10 per share. Dilution per share to new investors represents the difference between the price per share to be paid by new investors for the shares of common stock sold in this offering and the pro forma as adjusted net tangible book value per share immediately after this offering. The following table illustrates this per share dilution:

Initial public offering price per share		$15.00
Historical net tangible book value (deficit) per share as of March 31, 2021	$(76.91)	
Pro forma increase in historical net tangible book value (deficit) per share as of March 31, 2021	82.28	
Pro forma net tangible book value per share as of March 31, 2021	5.37	
Increase in pro forma net tangible book value per share attributable to new investors participating in this offering	2.53	
Pro forma as adjusted net tangible book value per share after this offering		7.90
Dilution in pro forma as adjusted net tangible book value per share to new investors participating in this offering		$ 7.10

If the underwriters' over-allotment option is exercised in full, the pro forma as adjusted net tangible book value per share of our common stock would be $8.16 per share, and the dilution in pro forma net tangible book value per share to new investors in this offering would be $6.84 per share, in each case at the initial public offering price of $15.00 per share.

The following table summarizes, as of March 31, 2021, on a pro forma as adjusted basis, the number of shares of common stock purchased from us, the total consideration paid, or to be paid, and the average price per share paid, or to be paid, by existing stockholders and by the new investors, at the initial public offering price of $15.00 per share, before deducting underwriting discounts and commissions and estimated offering expenses payable by us:

	Shares Purchased		Total Consideration		Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders	27,324,727	69.5%	$248,159,975	58.0%	$ 9.08
New investors	12,000,000	30.5	180,000,000	42.0	$ 15.00
Total	39,324,727	100.0%	$428,159,975	100.0%	

The above table assumes no exercise of the underwriters' over-allotment option. If the underwriters' over-allotment option were exercised in full, our existing stockholders would own 66.4% and our new investors would own 33.6% of the total number of shares of our common stock outstanding upon completion of this offering.

The number of shares of our common stock issued and outstanding, in the tables above are based on 27,324,727 shares of our common stock outstanding as of March 31, 2021 (including conversion of all of our outstanding shares of convertible preferred stock into 26,102,278 shares of our common stock), and excludes:

- 1,727,968 shares of our common stock issuable upon the exercise of options outstanding as of March 31, 2021, with a weighted-average exercise price of $3.06 per share;
- 835,473 shares of our common stock issuable upon the exercise of options granted subsequent to March 31, 2021, with a weighted-average exercise price of $10.00 per share;
- 379,271 shares of our common stock reserved for future grant or issuance under our Amended and Restated 2016 Equity Incentive Plan as of March 31, 2021;
- 4,000,000 shares of our common stock reserved for future issuance under our 2021 Equity Incentive Plan, which became effective on the business day immediately prior to the date of effectiveness of the registration statement of which this prospectus forms a part, as well as any automatic increases in the number of shares of our common stock reserved for future issuance pursuant to this plan; and
- 800,000 shares of common stock reserved for future issuance under our 2021 ESPP, which became effective on the business day immediately prior to the date of effectiveness of the registration statement of which this prospectus forms a part, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this plan.

To the extent that stock options are exercised, new stock options are issued under our equity incentive plan or we issue additional shares of common stock in the future, there will be further dilution to investors participating in this offering. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

SELECTED FINANCIAL DATA

The following tables set forth our selected financial data for the periods and as of the dates indicated. We have derived the selected statements of operations data for the years ended December 31, 2019 and 2020, and the selected balance sheet data as of December 31, 2019 and 2020, from our audited financial statements appearing elsewhere in this prospectus. The selected statements of operations data for the three months ended March 31, 2020 and 2021 and the selected balance sheet data as of March 31, 2021 are derived from our unaudited interim condensed financial statements included elsewhere in this prospectus. We have prepared the unaudited interim condensed financial statements on the same basis as the audited financial statements. We have included, in our opinion, all adjustments, consisting only of normal recurring adjustments that we consider necessary for a fair presentation of the financial information set forth in those unaudited interim condensed financial statements.

You should read the following selected financial data together with the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and the related notes appearing elsewhere in this prospectus. The selected financial data in this section are not intended to replace our financial statements and are qualified in their entirety by our financial statements and related notes appearing elsewhere in this prospectus. Our historical results are not necessarily indicative of our future results, and our results for the three months ended March 31, 2021 are not necessarily indicative of results to be expected for the full year.

	Year Ended December 31,		Three Months Ended March 31,	
	2019	2020	2020	2021
	(in thousands, except share and per share data)			
Statements of Operations Data:				
Operating expenses:				
Research and development	$ 23,148	$ 31,099	$ 7,297	$ 9,590
General and administrative	4,564	7,813	1,969	3,515
Total operating expenses	27,712	38,912	9,266	13,105
Loss from operations	(27,712)	(38,912)	(9,266)	(13,105)
Other income (expense), net:				
Interest income	453	87	57	9
Change in fair value of convertible preferred stock tranche liability	11	75	(19)	—
Other income (expense), net	1,017	355	177	(2)
Total other income	1,481	517	215	7
Net loss before income tax expense	(26,231)	(38,395)	(9,051)	(13,098)
Income tax expense	—	—	—	—
Net loss	$ (26,231)	$ (38,395)	$ (9,051)	$ (13,098)
Net loss per share, basic and diluted	$ (34.71)	$ (39.50)	$ (10.15)	$ (11.93)
Weighted-average shares used in computing net loss per share, basic and diluted	755,779	972,091	891,990	1,097,805
Pro forma net loss per share, basic and diluted(1)		$ (1.42)		$ (0.48)
Weighted-average shares used in computing pro forma net loss per share, basic and diluted(1)		27,074,369		27,200,083

(1) The unaudited pro forma net loss per share for the year ended December 31, 2020 and the three months ended March 31, 2021 was computed using the weighted-average number of shares of common stock outstanding, including the pro forma effect of the conversion of all outstanding shares of our convertible preferred stock into shares of common stock, as if such conversion had occurred at the beginning of the most recently completed fiscal year.

	As of December 31,		As of March 31,
	2019	2020	2021
	(in thousands)		
Balance Sheet Data:			
Cash and cash equivalents	$ 23,872	$128,535	$ 128,439
Working capital(1)	23,622	124,923	123,840
Total assets	38,001	148,161	159,757
Convertible preferred stock	73,042	220,754	240,735
Additional paid-in capital	764	1,584	2,054
Accumulated deficit	(44,417)	(82,812)	(95,910)
Total stockholders' deficit	(43,739)	(81,315)	(93,943)

(1) We define working capital as current assets less current liabilities. See our financial statements included elsewhere in this prospectus for further details regarding our current assets and current liabilities.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion of our financial condition and results of operations should be read together with the section titled "Selected Financial Data," and our financial statements and related notes included elsewhere in this prospectus. The following discussion contains forward-looking statements that reflect our plans, estimates and beliefs. Our actual results could differ materially from those discussed in the forward-looking statements. Factors that could cause or contribute to these differences include those discussed below and elsewhere in this prospectus, particularly in the section titled "Risk Factors." Our historical results are not necessarily indicative of the results that may be expected for any period in the future. See also the section of this prospectus titled "Special Note Regarding Forward-Looking Statements."

Overview

We are a biotechnology company headquartered in South San Francisco, California focused on discovering, developing and delivering curative therapies that address the underlying drivers of heart disease. We are advancing a pipeline of disease-modifying therapies developed using our product platforms and core internal capabilities to target defined sub-populations of patients with both rare and highly prevalent forms of heart disease.

We were incorporated in August 2016 and commenced operations thereafter. Our operations to date have included developing our Gene Therapy, Cellular Regeneration and Precision Medicine platforms, identifying and developing product candidates, conducting preclinical studies, acquiring technology, organizing and recruiting management and technical staff, conducting business planning, establishing our intellectual property portfolio, raising capital, and providing general and administrative support for these operations. All of our programs are currently in the preclinical stage and we do not have any products approved for sale. We have not generated any revenue.

Since our inception, we have incurred net losses each year and we expect to continue to incur significant and increasing losses for the foreseeable future as we continue to advance our platforms, programs and product candidates, and as we transition to operating as a public company. Our net losses may fluctuate significantly from period to period, depending on the timing of expenditures on our research and development activities. Our net losses were $26.2 million and $38.4 million for the years ended December 31, 2019 and 2020, respectively, and $9.1 million and $13.1 million for the three months ended March 31, 2020 and 2021, respectively. As of March 31, 2021, we had an accumulated deficit of $95.9 million. Our net losses resulted primarily from our research and development programs and, to a lesser extent, general and administrative costs associated with our operations.

We have not generated any revenue from product sales or other sources since inception. Our ability to generate product revenue sufficient to achieve profitability, if ever, will depend heavily on the successful completion and eventual commercialization of our product candidates which we expect, if it ever occurs, will take a number of years. In addition, we have leased additional space in the San Francisco Bay Area intended for future manufacturing and office space as we invest in our manufacturing capabilities.

To date, we have funded our operations primarily from the sale and issuance of our convertible preferred stock. From our inception through March 31, 2021, we raised an aggregate of $247.9 million in gross proceeds from sales of our convertible preferred stock. As of March 31, 2021, we had cash and cash equivalents of $128.4 million.

We will need substantial additional funding in the future to finance our operations, including the commercialization of any product candidates that may be approved by the FDA or comparable foreign regulatory authorities. Until such time, if ever, as we can generate significant product revenue, we expect to finance our

operations with our existing cash and cash equivalents, the net proceeds from this offering, any future equity or debt financings, and upfront and milestone and royalty payments, if any, received under future licenses or collaborations or other arrangements with other companies, or other sources of financing. We may not be able to raise additional capital on terms acceptable to us or at all. If we are unable to raise additional capital on acceptable terms when needed, our business, results of operations, and financial condition would be adversely affected, and we may have to delay, reduce or eliminate our product development or future commercialization efforts. Insufficient liquidity may also require us to relinquish rights to product candidates at an earlier stage of development or on less favorable terms than we would otherwise choose. The amount and timing of our future funding requirements will depend on many factors, including the pace and results of our development efforts. We cannot provide assurance that we will ever be profitable or generate positive cash flow from operating activities.

University of Texas Southwestern Medical Center (UTSW) License Agreement

In January 2020, we entered into a license agreement with UTSW (UTSW License), pursuant to which UTSW granted us an exclusive, royalty-bearing, sublicensable patent license and a non-exclusive, non-sublicensable license for mutually agreed upon development activities. Under the UTSW License, we are obligated to pay UTSW (i) a non-refundable upfront license fee of $0.1 million, (ii) milestone payments up to a total of $14.8 million in aggregate, which are contingent upon achieving specific development and commercialization milestone events, and (iii) low-single digits royalties on future net sales of each royalty-bearing product.

During the year ended December 31, 2020, we recorded research and development expenses of $0.1 million related to the upfront license fee payable pursuant to the UTSW License. As of March 31, 2021, we have not recognized any milestone or royalty payments under the UTSW License.

COVID-19

As a result of the COVID-19 pandemic, we could experience disruptions that could severely impact our business. Potential impacts to our business include disruptions or restrictions on our employees' ability to effectively conduct their work. In addition, some of our suppliers of certain lab materials, or service providers used in the performance of our research activities, are located in areas impacted by COVID-19, which could limit our ability to achieve planned progress. COVID-19 could adversely affect the economy and financial markets, resulting in an economic downturn that could affect our financing prospects. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which health epidemics such as COVID-19 could adversely impact our business. To date, we have experienced modest delays in the progress of our research and development activities, primarily due to extended lead times at certain suppliers and temporary and partial shutdowns at certain academic institutions as a result of statewide stay-at-home orders. However, these stay-at-home orders have largely terminated and operations have since resumed. We continue to monitor and assess the effects of the COVID-19 pandemic on our business, but the ultimate impact of the COVID-19 outbreak or a similar health epidemic is highly uncertain and subject to change. For additional details, see the section titled "Risk Factors."

Components of Operating Results

Research and Development

Research and development activities account for a significant portion of our operating expenses. Research and development expenses relate primarily to discovery and development of our platforms, programs and product candidates, and are recognized as incurred. Internal research and development costs include, among others, personnel-related costs (including salaries, benefits, travel and stock-based compensation for employees engaged in research and development functions), laboratory supplies and other non-capital equipment utilized for in-house research, allocated facilities and overhead costs. External research and development expenses include, among

others, amounts incurred to contract research organizations (CROs) that conduct research and development activities on our behalf, consulting fees and amounts owed under licensing agreements. We do not allocate our costs by platform, program or product candidate, as a significant amount of research and development expenses include internal costs, which are deployed across multiple platforms, programs, product candidates and activities.

Amounts recorded for external goods or services incurred for research and development activities that have not yet been invoiced often represent estimates. We do not currently have projects that require estimates for percentage of completion and we record estimates for amounts due but not yet invoiced based on input from external service providers.

We expect our research and development expenses to increase for the foreseeable future as we continue to invest in research and development activities related to developing our platforms, programs and product candidates and progressing through preclinical and clinical product development stages. The process of conducting the necessary research to advance to the clinical stage and ultimately obtain regulatory approval is costly and time-consuming, and the successful development of our product candidates is highly uncertain. As a result, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent we will generate revenue from the commercialization and sale of any of our product candidates.

General and Administrative

General and administrative expenses consist of personnel-related costs (including salaries, benefits, travel and stock-based compensation for our employees in executive, finance and other administrative functions), legal fees, professional fees incurred for accounting, audit, and tax services, recruiting costs, and facility costs not otherwise included in research and development expenses. Legal fees include those related to corporate and intellectual property related matters.

We expect that our general and administrative expenses will increase for the foreseeable future to support our continued research and development activities, general operations, future business development opportunities and professional fees. In addition, we expect to incur additional expenses associated with operating as a public company, including legal, accounting, insurance, exchange listing, SEC compliance, and investor relations costs.

Interest Income

Interest income primarily consists of interest earned on our cash, cash equivalents and investment balances.

Change in Fair Value of Convertible Preferred Stock Tranche Liability

The change in fair value of our convertible preferred stock tranche liability fluctuates based on remeasurements at each reporting period. Our convertible preferred stock tranche liability stems from our obligation to issue additional shares to investors upon the second and third closings of our Series B convertible preferred stock. Until settlement, fluctuations in the fair value of a convertible preferred stock tranche liability are based on the remeasurement at each reporting period. Our convertible preferred stock tranche liability was settled on the second and third closings of our Series B convertible preferred stock financing in March and August 2020, respectively.

Other Income

Other income primarily consists of sublease income for a portion of our facilities in South San Francisco during 2019 and 2020 and interest earned on cash balances.

Results of Operations

Comparison of the Three Months Ended March 31, 2020 and 2021

The following table summarizes our results of operations for the periods presented.

	Three Months Ended March 31,		$ Change	% Change
	2020	2021		
	(in thousands)			
Operating expenses:				
Research and development	$ 7,297	$ 9,590	$ 2,293	31%
General and administrative	1,969	3,515	1,546	79%
Total operating expenses	9,266	13,105	3,839	41%
Loss from operations	(9,266)	(13,105)	(3,839)	41%
Other income (expense), net:				
Interest income	57	9	(48)	(84)%
Change in fair value of convertible preferred stock tranche liability	(19)	—	19	(100)%
Other income (expense), net	177	(2)	(179)	(101)%
Total other income (expense), net	215	7	(208)	(97)%
Net loss and comprehensive loss	$ (9,051)	$(13,098)	$(4,047)	45%

Research and Development Expenses

The following table summarizes our research and development expenses for the periods presented.

	Three Months Ended March 31,		$ Change	% Change
	2020	2021		
	(in thousands)			
Facility and laboratory costs	$ 2,601	$ 4,096	$1,495	57%
Personnel-related costs	2,432	3,337	905	37%
External costs	1,957	2,043	86	4%
Other research and development expenses	307	114	(193)	(63)%
Total research and development expenses	$ 7,297	$ 9,590	$2,293	31%

Research and development expenses were $7.3 million and $9.6 million for the three months ended March 31, 2020 and 2021, respectively. The increase of $2.3 million, or 31%, was primarily due to:

- an increase of $1.5 million in facility and laboratory costs, including laboratory supplies and materials and other allocated costs, as we ramped up our research and development operations;
- an increase of $0.9 million in personnel-related costs, including stock-based compensation, primarily due to growth in the number of our research and development employees as we expanded our research and development capabilities; and
- an increase of $0.1 million in external costs, including amounts paid to CROs for research and development activities, consulting fees, preclinical studies and other external research expenses as we progressed development of our programs.

These increases were partially offset by a decrease of $0.2 million in other research and development expenses, including licensing fees.

General and Administrative

General and administrative expenses were $2.0 million and $3.5 million for the three months ended March 31, 2020 and 2021, respectively. The increase of $1.5 million, or 79%, was primarily due to a $0.8 million increase in professional service expenses and a $0.6 million increase in personnel-related expenses, including stock-based compensation, as a result of increased headcount as we grew our operations.

Interest Income

Interest income was $57,000 and $9,000 for the three months ended March 31, 2020 and 2021, respectively. The decrease of $48,000, or 84%, was primarily due to a change in our investment portfolio mix.

Change in Fair Value of Convertible Preferred Stock Tranche Liability

The change in fair value of our convertible preferred stock tranche liability for the three months ended March 31, 2020 was attributable to changes in the fair value of the underlying Series B convertible preferred stock. There was no similar expense for the three months ended March 31, 2021 as our convertible preferred stock tranche liability was settled in 2020.

Other Income (Expense), Net

Other income (expense), net of $0.2 million for the three months ended March 31, 2020 was primarily due to sublease income. We did not have any sublease agreements in place during the three months ended March 31, 2021.

Comparison of the Years Ended December 31, 2019 and 2020

The following table summarizes our results of operations for the periods presented.

	Year Ended December 31,		$	%
	2019	2020	Change	Change
	(in thousands)			
Operating expenses:				
Research and development	$ 23,148	$ 31,099	$ 7,951	34%
General and administrative	4,564	7,813	3,249	71%
Total operating expenses	27,712	38,912	11,200	40%
Loss from operations	(27,712)	(38,912)	(11,200)	40%
Other income (expense), net:				
Interest income	453	87	(366)	(81)%
Change in fair value of convertible preferred stock tranche liability	11	75	64	nmf*
Other income (expense), net	1,017	355	(662)	(65)%
Total other income (expense), net	1,481	517	(964)	(65)%
Net loss and comprehensive loss	$ (26,231)	$ (38,395)	$(12,164)	46%

* nmf—not meaningful

Research and Development Expenses

The following table summarizes our research and development expenses for the periods presented.

	Year Ended December 31,		$	%
	2019	2020	Change	Change
	(in thousands)			
Personnel-related costs	$ 7,130	$ 10,525	$3,395	48%
Facility and laboratory costs	8,786	11,798	3,012	34%
External costs	6,995	8,190	1,195	17%
Other research and development expenses	237	586	349	147%
Total research and development expenses	$ 23,148	$ 31,099	$7,951	34%

Research and development expenses were $23.1 million and $31.1 million for the years ended December 31, 2019 and 2020, respectively. The increase of $8.0 million, or 34%, was primarily due to:

- an increase of $3.4 million in personnel-related costs, including stock-based compensation, primarily due to growth in the number of our research and development employees as we expanded our research and development capabilities;
- an increase of $3.0 million in facility and laboratory costs, including laboratory supplies and materials and other allocated costs, as we ramped up our research and development operations;
- an increase of $1.2 million in external costs, including amounts paid to CROs for research and development activities, consulting fees, preclinical studies and other external research expenses as we progressed development of our programs; and
- an increase of $0.3 million in other research and development expenses, including licensing fees, due to entering into additional license agreements in 2020.

General and Administrative

General and administrative expenses were $4.6 million and $7.8 million for the years ended December 31, 2019 and 2020, respectively. The increase of $3.2 million, or 71%, was primarily due to a $1.4 million increase in personnel-related expenses, including stock-based compensation, as a result of higher headcount as we grew our operations, a $1.2 million increase in professional service expenses and a $0.3 million increase in facility related expenses to support the growth of our operations.

Interest Income

Interest income was $0.5 million and $0.1 million for the years ended December 31, 2019 and 2020, respectively. The decrease of $0.4 million, or 81%, was primarily due to lower average interest rates in 2020 as compared to 2019 and a change in our investment portfolio mix.

Change in Fair Value of Convertible Preferred Stock Tranche Liability

The $0.1 million change in fair value of our convertible preferred stock tranche liability for the year ended December 31, 2020 was attributable to changes in the fair value of the underlying Series B convertible preferred stock.

Other Income (Expense), Net

Other income (expense), net was $1.0 million and $0.4 million for the years ended December 31, 2019 and 2020, respectively. The decrease in other income of $0.7 million, or 65%, was primarily due to a $0.6 million reduction in sublease income as a result of the expiration of one of our sublease agreements in the third quarter of 2019.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, we have not generated any revenue and we have incurred significant net losses and negative cash flows from operations. To date, we have funded our operations primarily from the sale and issuance of our convertible preferred stock. From our inception through March 31, 2021, we raised an aggregate of $247.9 million in gross proceeds from sales of our convertible preferred stock. As of March 31, 2021, we had cash and cash equivalents of $128.4 million and an accumulated deficit of $95.9 million.

Funding Requirements

We expect our expenses and operating losses will increase substantially over the foreseeable future. The expected increase in expenses will be driven in large part by our ongoing activities, if and as we:

- continue to advance our Gene Therapy, Cellular Regeneration and Precision Medicine platforms;
- continue preclinical development of our product candidates and initiate additional preclinical studies;
- commence clinical trials of our product candidates;
- build out our manufacturing facilities and establish our manufacturing capabilities, including developing our contract development and manufacturing relationships;
- acquire and license technologies aligned with our Gene Therapy, Cellular Regeneration and Precision Medicine platforms;
- seek regulatory approval of our product candidates that successfully complete clinical trials;
- expand our operational, financial, and management systems and increase personnel, including personnel to support our preclinical and clinical development, manufacturing, and future commercialization efforts;
- continue to develop, grow, perfect, enforce and defend our intellectual property portfolio; and
- incur additional legal, accounting, and other expenses in operating our business, including the additional costs associated with operating as a public company.

Based on our current operating plan and without giving effect to the anticipated net proceeds from this offering, we believe that our existing cash and cash equivalents will be sufficient to meet our working capital and capital expenditure needs for at least the next twelve months.

We also believe that the anticipated net proceeds from this offering, together with our existing cash and cash equivalents, will be sufficient to fund our planned operating expenses and capital expenditure requirements through at least the next 24 months from the date of our unaudited interim condensed financial statements included elsewhere in this prospectus. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect. We may also raise additional financing on an opportunistic basis in the future. We expect to continue to expend significant resources for the foreseeable future.

In order to complete the development of our product candidates and commercialize our product candidates, if approved, we will require substantial additional funding. Until such time as we can generate significant revenue from sales of our product candidates, if ever, we expect to finance our operations through public or private equity offerings or debt financings or other capital sources, which may include strategic collaborations or other arrangements with third parties, or other sources of financing. We may not be able to raise additional capital on terms acceptable to us or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be or could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that

include covenants limiting or restricting our ability to take specific actions, including restricting our operations and limiting our ability to incur liens, issue additional debt, pay dividends, repurchase our common stock, make certain investments or engage in merger, consolidation, licensing or asset sale transactions. If we raise funds through strategic collaborations, partnerships and other similar arrangements with third parties, we may be required to grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. If we are unable to raise additional capital on acceptable terms when needed, our business, results of operations, and financial condition would be adversely affected.

Our ability to raise additional funds may be adversely impacted by potential worsening global economic conditions and the recent disruptions to, and volatility in, the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic. If we fail to obtain necessary capital when needed on acceptable terms, or at all, it could force us to delay, limit, reduce or terminate our product development programs, future commercialization efforts or other operations. Because of the numerous risks and uncertainties associated with research, product development and commercialization of product candidates, we are unable to predict the timing or amount of our working capital requirements or when or if we will be able to achieve or maintain profitability.

Cash Flows

The following table summarizes our cash flows for each of the periods indicated.

	Year Ended December 31,		Three Months Ended March 31,	
	2019	2020	2020	2021
	(in thousands)			
Net cash provided by (used in):				
Operating activities	$ (24,096)	$ (35,447)	$ (8,238)	$(15,789)
Investing activities	(5,583)	(7,010)	2,318	(4,323)
Financing activities	30,511	147,268	30,670	20,015
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 832	$ 104,811	$24,750	$ (97)

Operating Activities

Net cash used in operating activities for the three months ended March 31, 2021 was $15.8 million, which consisted primarily of a net loss of $13.1 million and a net change in net operating assets and liabilities of $4.0 million, partially offset by $1.3 million in non-cash charges. The non-cash charges primarily consisted of depreciation and amortization of $0.7 million, stock-based compensation of $0.4 million and the non-cash operating lease expense of $0.2 million. The change in net operating assets and liabilities was primarily due to an increase in other non-current assets of $3.3 million related to a security deposit for a lease entered into in February 2021, a decrease in accrued expenses and other current liabilities of $1.0 million and a decrease in operating lease liabilities of $0.4 million, partially offset by an increase in accounts payable of $0.6 million and a decrease in prepaid expenses and other current assets of $0.1 million.

Net cash used in operating activities for the three months ended March 31, 2020 was $8.2 million, which consisted primarily of a net loss of $9.1 million and a net change in net operating assets and liabilities of $21,000, partially offset by $0.8 million in non-cash charges. The non-cash charges primarily consisted of depreciation and amortization of $0.6 million and stock-based compensation of $0.2 million. The change in net operating assets and liabilities was primarily due to an increase in accounts payable of $0.7 million and a decrease in prepaid expenses and other current assets of $0.2 million, partially offset by a decrease in accrued expenses and other current liabilities of $0.5 million, a decrease in deferred rent and other lease liabilities of $0.2 million and an increase in other non-current assets of $0.2 million as we expanded our operations.

Net cash used in operating activities for the year ended December 31, 2020 was $35.4 million, which consisted primarily of a net loss of $38.4 million and a net change in net operating assets and liabilities of $0.2 million, partially offset by $3.2 million in non-cash charges. The non-cash charges primarily consisted of depreciation and amortization of $2.5 million and stock-based compensation of $0.7 million. The change in net operating assets and liabilities was primarily due to a decrease in deferred rent of $0.8 million, an increase in prepaid expenses and other current assets of $0.3 million and an increase in other non-current assets of $0.2 million, partially offset by an increase in accrued expenses and other current liabilities of $0.9 million and an increase in accounts payable of $0.1 million as we expanded our operations.

Net cash used in operating activities for the year ended December 31, 2019 was $24.1 million, which consisted primarily of a net loss of $26.2 million and a net change in net operating assets and liabilities of $0.3 million, partially offset by $2.4 million in non-cash charges. The non-cash charges primarily consisted of depreciation and amortization of $2.0 million and stock-based compensation of $0.4 million. The change in net operating assets and liabilities was primarily due to a decrease in deferred rent of $0.7 million and increase in prepaid expenses and other current assets of $0.4 million, partially offset by an increase in accounts payable of $0.4 million and an increase in accrued expenses and other current liabilities of $0.5 million as we expanded our operations.

Investing Activities

Net cash used in investing activities for the three months ended March 31, 2021 was $4.3 million, which consisted of purchases of property and equipment that primarily related to our manufacturing and office space in the San Francisco Bay Area.

Net cash provided by investing activities for the three months ended March 31, 2020 was $2.3 million, which consisted of proceeds from maturities of marketable securities of $2.8 million, partially offset by purchases of property and equipment of $0.4 million.

Net cash used in investing activities for the year ended December 31, 2020 was $7.0 million, which consisted of purchases of property and equipment of $9.8 million that primarily related to our manufacturing and office space in the San Francisco Bay Area, partially offset by proceeds from maturities of marketable securities of $2.8 million.

Net cash used in investing activities for the year ended December 31, 2019 was $5.6 million, which consisted of purchases of property and equipment of $2.9 million and net purchases of and proceeds from maturities of marketable securities of $2.7 million.

Financing Activities

Net cash provided by financing activities for the three months ended March 31, 2021 was $20.0 million, which primarily consisted of net proceeds received from the issuance of our Series C convertible preferred stock.

Net cash provided by financing activities for the three months ended March 31, 2020 was $30.7 million, which primarily consisted of net proceeds received from the sale and issuance of our Series B convertible preferred stock.

Net cash provided by financing activities for the year ended December 31, 2020 was $147.3 million, which consisted of net proceeds received from the sale and issuance of our Series B convertible preferred stock of $61.3 million and net proceeds received from the initial closing of our Series C convertible preferred stock of $86.0 million.

Net cash provided by financing activities for the year ended December 31, 2019 was $30.5 million, which consisted of net proceeds received from the sale and issuance of our Series B convertible preferred stock of $30.4 million and proceeds from the exercise of stock options of $0.1 million.

Contractual Obligations and Other Commitments

We enter into contracts in the normal course of business with contract research organizations for preclinical studies and other services, which are generally cancellable with limited notice.

The following table summarizes our contractual obligations and other commitments as of December 31, 2020:

	Payments Due by Period				
	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years	Total
	(in thousands)				
Operating lease obligations	$ 3,752	$4,489	$3,362	$ —	$11,603
Total contractual obligations	$ 3,752	$4,489	$3,362	$ —	$11,603

The obligations noted above represent our operating lease obligations related to our leased facility currently occupied in South San Francisco, California, with a lease term that expires in May 2025. The table does not include the operating lease we entered into in the San Francisco Bay Area in February 2021 for our manufacturing facility, which commenced in May 2021 and has a ten-year term. Payments associated with this operating lease agreement will result in additional operating lease obligations not included in the above table of approximately $13.9 million plus operating expenses.

We also enter into contracts in the normal course of business with various third parties for preclinical studies, manufacturing services with CDMOs and other services. These contracts generally provide for termination upon limited notice, and therefore we believe that our noncancelable obligations under these agreements are not material. These payments are not included in the table above. This table also does not include any milestone or royalty payments to third parties as the amounts, timing and likelihood of such payments are not known at this time. See Note 5 to our audited financial statements and Note 5 to our unaudited interim condensed financial statements included elsewhere in this prospectus.

Off-Balance Sheet Arrangements

Since inception, we have not engaged in any off-balance sheet arrangements as defined in the rules and regulations of the SEC.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of the financial condition and results of operations is based on our financial statements, which have been prepared in accordance with the U.S. generally accepted accounting principles, or GAAP. The preparation of our financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, expenses and related disclosures. Our estimates are based on historical experience and on various other factors that are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in the notes to our financial statements included elsewhere in this prospectus, we believe that the following accounting policies are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

Research and Development Expenses

We record research and development costs in the periods in which they are incurred. Goods or services incurred for research and development activities that have not yet been invoiced are recorded as liabilities within accrued expenses and other current liabilities on the balance sheets. Amounts recorded for unbilled services often represent estimates, which are typically based on contracted amounts for the proportion of work performed and determined through analysis with internal personnel and external service providers as to the progress or stage of completion of the associated services. We make judgments and estimates in determining the accrued and other current liabilities balance. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust accrued expenses or prepaid expenses accordingly, which impact research and development expenses. We have not experienced any material differences between accrued costs and actual costs incurred. Changes in these estimates that result in material changes to our accrued costs could materially affect our results of operations.

We have and may continue to acquire the rights to licensed technology that represents in-process research and development to use and develop in the commercialization of product candidates, if approved. The upfront payments made to acquire licenses, products or rights, or payments made related to future milestone payments are recognized as research and development expenses provided that there is no alternative future use of the rights in other research and development projects, up to the point of regulatory approval. Milestone payments are expensed when the specific milestone has been achieved.

Stock-Based Compensation

We measure and record expense related to all equity awards granted to employees and non-employees in the statements of operations based on their grant date estimated fair values, including stock options and restricted stock awards. For stock-based awards that vest subject to the satisfaction of a service requirement, the expense is recognized using the straight-line method over the requisite service period, which is generally the vesting period. Forfeitures are recognized as they occur.

The fair value of restricted stock awards is determined on the date of grant based on the estimated fair value of our common stock on that date.

For purposes of determining the estimated fair value of options granted to employees and non-employees, we use the Black-Scholes option pricing model, which requires the use of highly subjective assumptions. These assumptions include:

- *Fair Value of Common Stock*—See the subsection titled "—Common Stock Valuations" below.
- *Expected Term*—We determine the expected term, which represents the period that stock-based awards are expected to be outstanding, in accordance with the simplified method, which is presumed to be the mid-point between the contractual term and the vesting term.
- *Expected Volatility*—As there is no trading history for our common stock, we have determined our computation of expected volatility on the historical volatility of a representative group of public companies with similar characteristics to us, including stage of product development and life science industry focus. The historical volatility is calculated based on a period of time commensurate with the expected term assumption.
- *Risk-Free Interest Rate*—We base the risk-free interest rate on U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term assumption.
- *Expected Dividend*—The expected dividend yield is assumed to be zero as we have never paid and have no plans to pay dividends on our common stock.

See Note 9 to our audited financial statements and Note 9 to our unaudited interim condensed financial statements included elsewhere in this prospectus for more information concerning certain of the specific

assumptions we used in applying the Black-Scholes valuation model to determine the estimated fair value of our stock options.

For the years ended December 31, 2019 and 2020, we incurred stock-based compensation of $0.4 million and $0.7 million, respectively. For the three months ended March 31, 2020 and 2021, we incurred stock-based compensation of $0.2 million and $0.4 million, respectively. As of March 31, 2021, there was $6.4 million of total unrecognized stock-based compensation, which is expected to be recognized over a weighted-average period of approximately 3.5 years.

The intrinsic value of all outstanding options as of March 31, 2021 was $20.6 million, based on the initial public offering price of $15.00 per share, of which $7.1 million is related to vested options and $13.5 million is related to unvested options.

In June 2021, our board of directors granted options to purchase 388,475 shares of our common stock at an exercise price of $9.36 per share. We subsequently determined the grant-date fair value of these awards using an assumed underlying common stock fair value of $11.77 per share for financial reporting purposes. In July 2021, we granted options to purchase 446,998 shares of our common stock at an exercise price of $10.56 per share. We subsequently determined the grant-date fair value of these awards using an assumed underlying common stock fair value of $12.30 per share for financial reporting purposes. We expect to recognize stock-based compensation of between approximately $8.1 million to $8.6 million for these June 2021 and July 2021 awards over the vesting period, which is generally four years.

Common Stock Valuations

Historically, for all periods prior to this offering, fair values of the shares of common stock underlying our stock-based awards were approved on each grant date by our board of directors. Our board of directors considered, among other things, valuations of our common stock which were prepared by an independent third-party valuation firm in accordance with the guidance provided by the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*. The significant objective and subjective factors included, but are not limited to:

- our most recently available estimated valuations of our common stock performed by an independent third-party valuation firm;
- the prices of shares of our convertible preferred stock sold to investors in arm's length transactions, and the rights, preferences and privileges of our convertible preferred stock relative to our common stock;
- our stage of development and material risks related to our business;
- our results of operations and financial position, including our levels of available capital resources;
- progress of our research and development activities;
- the lack of marketability of our common stock as a private company;
- the likelihood of achieving a liquidity event, such as an initial public offering (IPO) or a sale of our company, given prevailing market conditions;
- trends and developments in our industry; and
- external market conditions affecting the life sciences and biotechnology industry sectors.

For the independent third-party valuations performed in October 2018 and October 2019, we used a probability-weighted expected return method (PWERM) whereby our total equity value was estimated under various exit scenarios and allocated to our different classes of equity. The PWERM included various scenarios in

which we complete an IPO, the sale of our company or dissolution of our company that considered our estimate of the timing of each scenario and were weighted based on our estimate of the probability of each event occurring. The equity value under the IPO scenarios was based on the market approach and considered recent IPO values of comparable companies. The equity value under the scenarios in which we complete the sale of our company was based on the market approach and considered recent licensing deals for programs utilizing similar technologies as us. The equity value under the dissolution scenarios was based on the market approach and considered the return on investment from failed venture capital investments. The equity value under each scenario was adjusted for anticipated future financings and the equity value allocated to our common stock was reduced by a discount for lack of marketability.

For the independent third-party valuations performed in November 2020 and April 2021, we used a hybrid method of the PWERM and the option pricing model (OPM) backsolve method to allocate our estimated equity value to our different classes of equity. The PWERM included scenarios in which we complete an IPO and a scenario in which we complete an alternative exit (OPM Scenario) that considered our estimate of the timing of each scenario and were weighted based on our estimate of the probability of each event occurring. The equity value under the IPO scenarios was based on the market approach and considered recent IPO values of comparable companies. The equity value under the OPM Scenario in the November 2020 valuation utilized the OPM backsolve method based on our Series C convertible preferred stock financing. The April 2021 valuation considered market-based adjustments to the equity value determined under this approach in the November 2020 valuation. In an OPM framework, the backsolve method for inferring the equity value implied by a recent financing transaction involves making assumptions for the expected time to liquidity, volatility, dividend yield, and risk-free rate and then solving for the value of equity such that the value for the most recent financing equals the amount paid. The equity value allocated to our common stock was reduced by a discount for lack of marketability.

For valuations after the completion of this offering, the fair value of each share of underlying common stock will be based on the closing price of our common stock as reported on the date of grant on the primary stock exchange on which our common stock is traded.

Convertible Preferred Stock Tranche Liability

The obligation to issue additional shares of our Series B convertible preferred stock on the second and third closings of our Series B convertible preferred stock was determined to be a freestanding financial instrument that should be accounted for as a liability. At issuance, we recorded the convertible preferred stock tranche liability on the balance sheet at its estimated fair value, using the estimated fair value of the underlying Series B stock and common stock (which was determined using the standard pricing model). The other inputs used to arrive at the fair value of the convertible preferred stock tranche liability was a discount rate and the expected term, which was based on the expected contractual closing date or the actual closing date.

A tranche liability is subject to remeasurement at each balance sheet date, with changes in fair value recognized as a gain or loss on remeasurement as a component of other income (expense), net in the statements of operations until settlement or extinguishment. Our convertible preferred stock tranche liability was settled upon the closing of our second and third closings of our Series B convertible preferred stock financing in March and August 2020, respectively.

Recent Accounting Pronouncements

See Note 2 to our audited financial statements and Note 2 to our unaudited interim condensed financial statements included elsewhere in this prospectus for more information about recent accounting pronouncements, the timing of their adoption, and our assessment, to the extent we have made one yet, of their potential impact on our financial condition of results of operations.

Emerging Growth Company and Smaller Reporting Company Status

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012 (JOBS Act). We will remain an emerging growth company until the earliest to occur of: (i) the last day of the fiscal year in which we have more than $1.07 billion in annual revenue; (ii) the date we qualify as a "large accelerated filer," with at least $700 million of equity securities held by non-affiliates; (iii) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period; and (iv) the last day of the fiscal year ending after the fifth anniversary of our initial public offering. As a result of this status, we have taken advantage of reduced reporting requirements in this prospectus and may elect to take advantage of other reduced reporting requirements in our future filings with the SEC. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards, delaying the adoption of these accounting standards until they would apply to private companies. We have elected to use the extended transition period to enable us to comply with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date on which we (i) are no longer an emerging growth company and (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

We are also a "smaller reporting company" meaning that the market value of our stock held by non-affiliates plus the proposed aggregate amount of gross proceeds to us as a result of this offering is less than $700 million and our annual revenue was less than $100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company after this offering if either (i) the market value of our stock held by non-affiliates is less than $250 million or (ii) our annual revenue was less than $100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation and other matters.

Interest Rate Risk

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities. We held cash and cash equivalents of $128.5 million and $128.4 million as of December 31, 2020 and March 31, 2021, respectively, which consisted of bank deposits and money market funds. Historical fluctuations in interest rates have not had a significant impact on our financial condition or results of operations. We believe that we do not have any material exposure to changes in the fair value of these assets as a result of changes in interest rates due to the short-term nature of our cash and cash equivalents.

BUSINESS

Overview

Heart disease is the leading cause of death in the world, accounting for more deaths than from all cancers combined. In the United States, more than 30 million adults are diagnosed with heart disease and approximately 35,000 children are born each year with congenital heart disease (CHD). There are over 250 known genetically defined disorders where the primary source of morbidity and mortality involves the heart, but there are few approved products that target the underlying cause of such diseases. Recent analysis has shown that mortality rates due to heart failure (HF) are rising. While there is a clear need for improved treatments, the rate of cardiovascular drug product approvals has declined in recent years.

We are a biotechnology company committed to a bold mission: to discover, develop and deliver curative therapies that address the underlying drivers of heart disease. Our vision is to change the treatment paradigm for heart disease, and in doing so improve and extend the lives of millions of individuals and families. We are advancing a pipeline of disease-modifying therapies developed using our product platforms and core internal capabilities to target defined sub-populations of patients with both rare and highly prevalent forms of heart disease.

Founded by leading cardiovascular scientists from Gladstone Institutes and University of Texas Southwestern Medical Center (UTSW), we are developing therapies through scientific advancements in three distinct but interrelated product platforms: Gene Therapy, Cellular Regeneration and Precision Medicine. While our Gene Therapy and Cellular Regeneration platforms focus on the use of viral vectors for drug delivery, our Precision Medicine platform enables us to identify promising targets and product candidates in a modality-agnostic manner, including gene therapies, small molecules, and biologics.

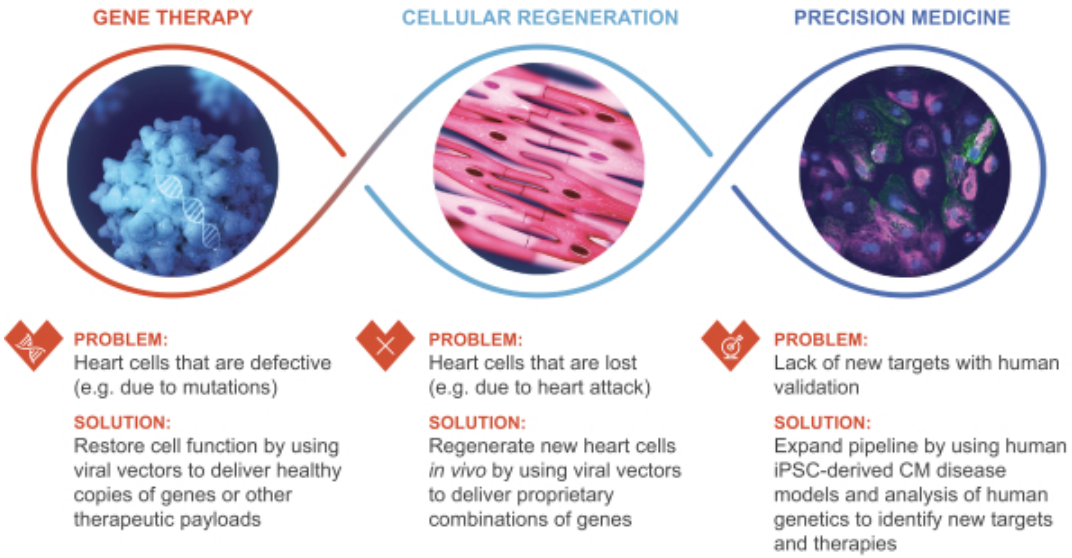
We are advancing a deep and diverse pipeline that includes both gene therapies and small molecules. In 2022, we intend to submit an investigational new drug application (IND) or a clinical trial application (CTA) to the U.S. Food and Drug Administration (FDA) or European Medicines Agency (EMA), respectively, for the most advanced product candidate from our Gene Therapy platform, TN-201, an adeno-associated virus (AAV)-based gene therapy to address genetic hypertrophic cardiomyopathy (gHCM) caused by Myosin Binding Protein C3 (*MYBPC3)* gene mutations. TN-201, currently in IND-enabling studies, is designed to deliver a fully functional *MYBPC3* gene driven by our proprietary heart-specific promoter to restore normal levels of MYBPC3 protein. We also intend to submit an IND to the FDA for the most advanced product candidate from our Precision Medicine platform, TYA-11631, a highly specific small molecule inhibitor of histone deacetylase 6 (HDAC6i). TYA-11631, currently in IND-enabling studies, has potentially broad utility in both HF with preserved ejection fraction (HFpEF) as well as genetic dilated cardiomyopathy (gDCM). Our PKP2 program involves using an AAV-based gene therapy to address genetic arrhythmogenic right ventricular cardiomyopathy (gARVC) caused by plakophilin 2 *(PKP2)* gene mutations, and is currently at the candidate selection stage. Our DWORF program, an AAV-based gene therapy designed to express the Dwarf Open Reading Frame (*DWORF*) gene in the heart, has potentially broad utility in dilated cardiomyopathy (DCM) and HF with reduced ejection fraction (HFrEF), and is currently at the candidate selection stage. Our Reprogramming program for cardiac regeneration can potentially replace heart cells lost in patients experiencing HF due to prior myocardial infarction (MI), and is currently at the candidate selection stage. In addition, we have numerous earlier-stage programs emerging from our product platforms to address other forms of HF.

Our Product Platforms

We have established three distinct but interrelated product platforms to discover novel therapies for various forms of heart disease. These platforms bring together differentiated science, capabilities, and intellectual property to enable multi-modality drug discovery. As displayed below, each of our product platforms is designed to address different problems that have historically plagued the development of therapies for heart disease. We

believe these three product platforms together yield better insight into disease processes, create more opportunities for successful drug development, mitigate scientific risks, and differentiate our efforts relative to competitors.

Our Product Platforms Powering Multi-Modality Drug Discovery



1. Our ***Gene Therapy*** platform uses AAVs to deliver genes to specific cells in the heart to correct or compensate for functional defects. We have the ability to use both known AAV capsids as well as novel capsids identified through our internal capsid engineering capabilities. Depending on the nature of the disease, we may target cardiomyocytes (CMs), cardiac fibroblasts (CFs), or other cells important to the proper functioning of the heart. The genes delivered can be a healthy copy of genes that are known to be mutated in human disease, or some other protein or construct that can exert a therapeutic effect. The product candidates arising from this platform are intended to overcome the shortcomings of traditional therapies that are not able to address the underlying problems that contribute to heart disease. We believe this platform has potentially broad utility for both genetic and non-genetic forms of heart disease.

2. Our ***Cellular Regeneration*** platform uses viral vectors to deliver specific combinations of genes to existing cells in the heart to regenerate CMs *in vivo*. We own certain intellectual property that covers two distinct approaches to achieve regeneration of new heart tissue. One approach uses AAV vectors to deliver proprietary combinations of genes that induce the resident CFs to convert to CMs. We have developed, through internal capsid engineering capabilities, novel AAV capsids with enhanced CF transduction. Another approach uses non-integrating lentiviruses to deliver proprietary combinations of genes that induce the resident CMs to undergo transient cell division. The product candidates arising from this platform are intended to overcome the shortcomings of traditional therapies that address symptoms but are not able to address the irreversible loss of CMs. We believe this platform has potentially broad utility across a range of heart conditions that result in the loss of CMs, including MI, chemotherapy-related toxicity, and viral infection.

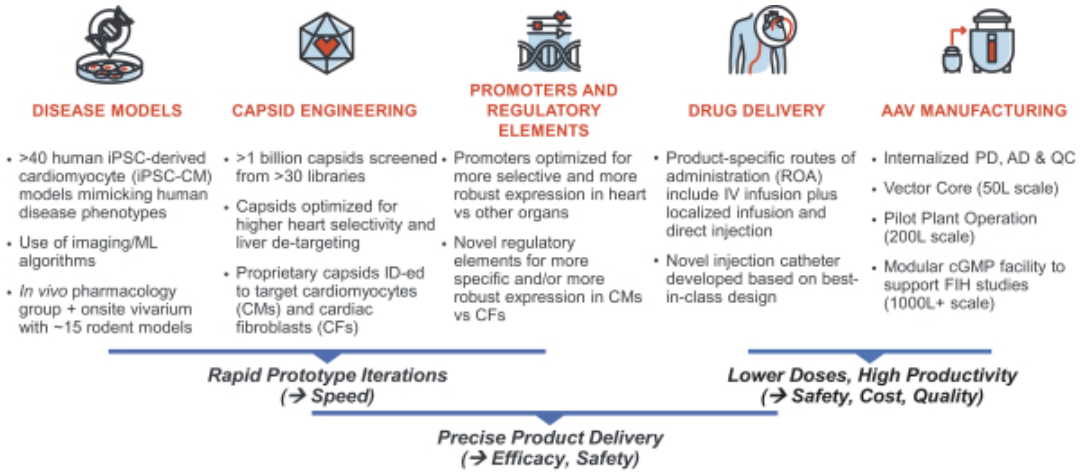
3. Our ***Precision Medicine*** platform uses human induced pluripotent stem cell-derived CMs (hiPSC-CMs) as proprietary disease models combined with analysis of human genetics and the use of machine learning algorithms for the identification of new targets, validation of known targets, and high-throughput screening for drug discovery. This platform is intended to overcome the shortcomings

of traditional drug development efforts that rely more heavily on insights from animal models to identify targets and to develop therapies intended for human heart disease. We believe this platform may also help identify promising drug targets directed to sub-populations of patients who are more likely to respond to such targeted product candidates. We believe this platform has potentially broad utility for the identification of targets and therapies in a modality-agnostic manner—including gene therapy, small molecules, and biologics—for both genetic and non-genetic forms of heart disease.

Our Approach and Capabilities

We have internalized and integrated core capabilities, as displayed below, to support our product platforms and our pipeline programs. We believe these capabilities provide us with several advantages and differentiate our efforts relative to competitors, particularly for our AAV-based drug development efforts. We believe these capabilities can collectively support rapid product development, precise product delivery, and efficient production, which ultimately improves the probability of technical and regulatory success of our product candidates.

Our Core Capabilities Supporting Our Differentiated Product Platforms



Our five core capabilities include:

1. ***Disease Models***. Having better models of human heart disease is an important capability for drug discovery. Existing models may not be adequate to assess the efficacy or safety of novel therapies. In order to achieve this, we have internalized the ability to create and integrate proprietary *in vitro* and *in vivo* models within our research organization. For our *in vitro* hiPSC-CM disease models, we use multiple methods to induce phenotypes within cell lines that simulate human diseases and then use these models for high throughput target identification and drug discovery. For our *in vivo* disease models, we have a dedicated onsite *in vivo* pharmacology group and vivarium, where we have established approximately 15 rodent heart disease models, both genetic and non-genetic, and can dose animals, perform heart surgeries, and use non-invasive imaging to assess the impact of our therapies under development.
2. ***Capsid Engineering***. We have established in-house AAV capsid engineering capabilities and have successfully screened over one billion variants from more than 30 diverse, proprietary AAV libraries in multiple *in vitro*, *in vivo*, and *in silico* models to discover novel AAV capsids that can target the different types of cells in the heart. We have generated preclinical data to support the superiority of these capsids over parental variants in multiple species—including NHPs—against multiple attributes.

These capsids are designed to have desirable properties including the ability to more selectively target the heart versus other organs as well as lower susceptibility to neutralizing antibodies. We believe our capsid engineering efforts will be critical in supporting the successful clinical development of our product candidates and enabling those product candidates, if approved, to reach more patients.

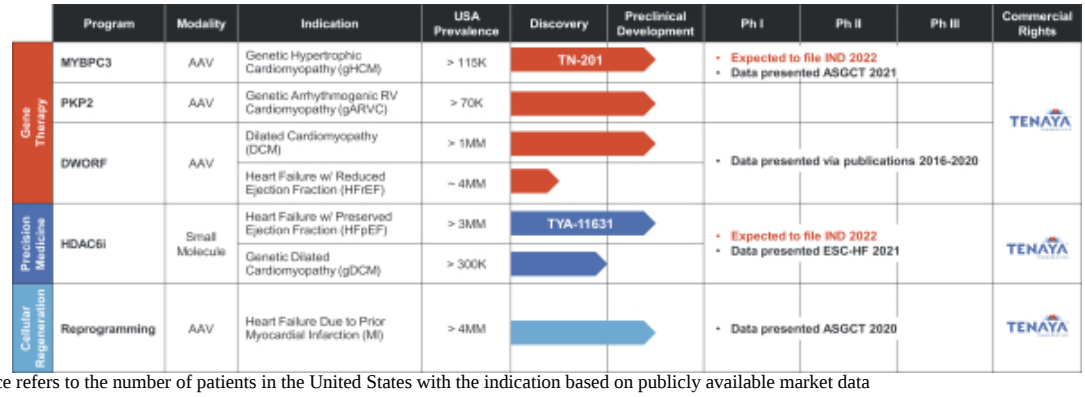
3. ***Promoters and Regulatory Elements***. We have created novel promoters and regulatory elements to support our gene therapy and cellular regeneration programs. These promoters and regulatory elements control the expression of genes within the cells. We use these innovations to help ensure more precise and more robust expression of therapeutic payloads in the different cell types of the heart as compared to what can be achieved with currently available methods. We believe our innovations can support successful clinical development in part by improving the efficacy and safety profile of our product candidates.

4. ***Drug Delivery***. We are actively exploring different routes of administration (ROAs) as well as different infusion- and injection-based methods for delivering our AAV-based therapies. We have designed a new catheter to support more targeted delivery and more efficient uptake of therapeutic payloads in the heart. We believe our discoveries in drug delivery can help widen the therapeutic index of our product candidates by reducing the dose required for a therapeutic benefit.

5. ***Manufacturing***. We have taken important steps towards internalizing both current Good Manufacturing Practice (cGMP) and non-GMP AAV manufacturing capabilities to support our emerging portfolio of gene therapy and cellular regeneration product candidates. This includes a growing in-house team of approximately 25 personnel that can support process development (PD), analytical development (AD), and quality assurance (QA) and quality control (QC). We have in-house personnel to support both upstream and downstream PD, AD, and QC efforts. We have produced non-clinical material involving both parental and novel AAV capsids at the 50L and 200L scales to support early research and IND-enabling studies in small and large animal models. We have initiated construction of a current cGMP facility in the San Francisco Bay Area near our research labs to enable smooth scale-up of production to support first-in-human (FIH) studies, initially at the 1000L scale. We expect this facility will be operational in the first half of 2022. We have in-licensed certain manufacturing intellectual property to support our programs.

Our Pipeline

We are advancing a deep and diverse pipeline of therapeutic programs intended for rare diseases, such as gHCM and gARVC, as well as for more prevalent forms of heart disease, such as DCM and HFpEF. We have exclusive worldwide rights to all of our programs. Our pipeline includes programs that have emerged from our internal efforts, including various ongoing early stage discovery efforts across our platforms, as well as programs that are based on intellectual property licensed from academic institutions.



* USA Prevalence refers to the number of patients in the United States with the indication based on publicly available market data

- ***MYBPC3 Program for gHCM***. We are developing an AAV-based gene therapy designed to deliver a functional *MYBPC3* gene in adults and children with gHCM due to *MYBPC3* gene mutations, estimated to affect more than 115,000 patients in the United States. These mutations can cause the heart walls of affected individuals to become significantly thickened, leading to fibrosis, abnormal heart rhythms, cardiac dysfunction, HF, and sudden cardiac death in some adults and children. Based on publicly available information to date, we believe there are currently no approved treatments that address the underlying genetic cause of this disease. Our product candidate, TN-201, uses a differentiated approach designed to enable robust expression of the *MYBPC3* gene in the heart. We have demonstrated significant and durable disease reversal and survival benefit in a relevant murine model after a single dose, as well as tolerability in mice and non-human primates (NHPs). The program is currently in IND-enabling studies, and we have obtained feedback from multiple regulatory agencies, including the FDA, to guide our path to clinical development. TN-201 has also been granted Orphan Drug Designation (ODD) by the FDA. We intend to submit an IND or CTA to the FDA or EMA, respectively, in 2022.
- ***HDAC6i Program for HFpEF***. We are developing an HDAC6i small molecule for various forms of HF, including HFpEF. This disease involves systemic inflammation, left ventricular hypertrophy, fibrosis, and diastolic dysfunction resulting in high morbidity and mortality in affected individuals. HFpEF is one of the greatest areas of unmet need in heart disease with more than three million patients in the United States and currently no approved disease-modifying therapies. Our product candidate, TYA-11631, is a differentiated compound with unique chemical structures and high specificity for HDAC6. We have demonstrated *in vivo* activity of our HDAC6i molecules in multiple animal models, including significant disease reversal in two different models of HFpEF as well as tolerability in mice and NHPs. Based on publicly available information to date, we believe TYA-11631 is the first HDAC6i being developed for heart disease. We have initiated IND-enabling activities and intend to submit an IND to the FDA in 2022.
- ***PKP2 Program for gARVC***. We are developing an AAV-based gene therapy designed to deliver a functional *PKP2* gene in adults with gARVC due to *PKP2* gene mutation, estimated to affect more than 70,000 patients in the United States. These mutations can cause enlargement of the right ventricle (RV) in affected individuals, replacement of heart muscle with fibrotic tissue and fatty deposits, and severely abnormal heart rhythms (arrhythmia) that can make it harder for the heart to function properly and result in sudden cardiac death in some adults and children. Based on publicly available information to date, we believe there are currently no approved treatments that address the underlying genetic cause of this disease. We have demonstrated prevention of disease progression and survival benefit in a murine model after a single dose. Based on publicly available information to date, we believe these data are the first known demonstrations of durable disease modification, survival benefit, and prevention of arrhythmia using an AAV:PKP2 gene therapy construct. This program is currently at the candidate selection stage.
- ***DWORF Program for DCM***. We are developing an AAV-based gene therapy designed to deliver the *DWORF* gene for patients with DCM, estimated to affect about one million patients in the United States. DCM is a progressive and life-threatening disease that causes left ventricle (LV) enlargement, LV wall thinning, insufficient contraction, reduced blood flow, ventricular arrhythmias, and can result in premature morbidity and need for heart transplant in affected individuals. DWORF is a muscle-specific micro-peptide first discovered by our co-founder Eric Olson, Ph.D. that acts on the sarcoplasmic/endoplasmic reticulum Ca2+ ATPase 2a (SERCA2a) pathway, widely considered to be a promising target in HF. We and our academic collaborators have accumulated significant preclinical *in vivo* proof-of-concept evidence for the therapeutic benefit of over-expression of the *DWORF* gene in multiple murine models, including models of gDCM and HFrEF, as well as tolerability in murine models. Based on publicly available information to date, we believe these are the first demonstrations of the potential benefit of AAV:DWORF. This program is currently at the candidate selection stage.

- ***Reprogramming Program for HF due to prior MI***. We are developing an AAV-based approach to cellular regeneration that involves converting (or reprogramming) existing CFs within the heart to turn into new CMs and to replace cells permanently lost due to MI. There are estimated to be more than four million patients in the United States living with HF due to prior MI. The loss of CMs in affected individuals permanently impairs heart contraction, leading to HF and potentially fatal arrhythmias, and the death of approximately 5% to 10% of MI survivors within the first year. There are currently no approved treatments that address the underlying loss of heart tissue. The potential utility of our unique approach to creating new CMs was first demonstrated by our co-founder Deepak Srivastava, M.D. We have discovered a proprietary combination of three genes that can drive robust *in vivo* reprogramming of CFs to CMs when delivered together in a single AAV capsid. We have demonstrated significant and durable disease reversal as well as tolerability in multiple small and large animal models. Based on publicly available information to date, we believe our results in a pig model of HF due to prior MI represent the first-ever successful demonstration of the potential benefit of this approach in a human-sized heart. This program is currently at the candidate selection stage.

Our Management Team and Investors

We were incorporated in August 2016 by The Column Group, in partnership with leading scientific and clinical researchers in cardiovascular genetics and muscle biology at Gladstone Institutes and UTSW. Since our founding, we have attracted a talented group of industry experts and scientists as part of a highly innovative organization that, as of June 30, 2021, comprises over 85 employees.

We are led by a team of executives and directors with significant experience in the discovery, development, manufacture, and commercialization of novel therapeutics, specifically in the fields of rare diseases, gene therapies, and heart disease. Faraz Ali, M.B.A., our Chief Executive Officer since 2018, previously served as the Chief Business Officer at REGENXBIO, and prior to that, accumulated relevant experiences at industry-leading companies in gene therapy and orphan drug development including at bluebird bio and Genzyme Corporation.

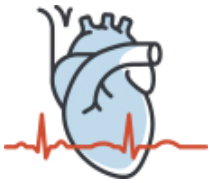
Since inception, we have raised approximately $248 million in equity financing to date from leading venture, strategic and public investors, including The Column Group, Casdin Capital, SymBiosis II, LLC, Fidelity Management & Research Company, RTW Investments, and others who share our vision to build a highly innovative, integrated biotechnology company delivering next-generation therapies that address the underlying causes of heart disease.

Overview of Heart Disease

Heart disease is the leading cause of death in the world, accounting for more deaths than from all cancers combined. In the United States, more than 30 million adults, or approximately 12% of the adult population, are diagnosed with heart disease. In addition, an adult dies from a cardiovascular-related health condition, such as a heart attack every 36 seconds, a gruesome statistic that translates to 31% of all deaths in the United States each year. The picture is equally bleak at the other end of the age spectrum, as approximately 35,000 children are born in the United States every year with CHD, and CHD is the leading cause of birth defect-related morbidity and mortality. There are over 250 known genetically defined disorders where the primary source of morbidity and mortality involves the heart, but there are few approved products that target the underlying cause of such diseases. Recent analysis has shown that after decades of reduction in the mortality rate due to HF, these rates are once again rising, highlighting the need for improved treatments.

The heart is a complex organ due to its biological structure as well as its tightly regulated and coordinated electrophysiological and biomechanical properties. Heart disease comes in many forms, affects individuals at many ages, and is a result of many factors. As depicted in the below table, heart disease can be generally categorized as either directly resulting from problems associated with the heart organ, for example, HF, arrhythmia and heart valve disease; or indirectly resulting from problems associated with the vasculature, for example, coronary artery disease (CAD). In each case, the underlying cause could be genetic, or due to normal aging or due to environmental factors.

The table below illustrates four broad categories of heart disease:

CATEGORIES	DESCRIPTION
 Heart Failure (HF)	HF is a heart condition in which the heart's pumping capacity is not adequate to meet the demands for blood and oxygen required by the rest of the body. HF can be the result of a range of conditions that lead to weakening of the heart muscle. Conditions that can be associated with the development of HF include a heart attack, uncontrolled high blood pressure, congenital heart disease (heart defects present at birth), and genetic cardiomyopathies.
 Arrhythmia	Arrhythmia is one of the most common heart conditions and is described as any change in the heart's normal electrical impulses. Electrical impulses from within the heart initiate each heartbeat and ensure its normal pumping function. Arrhythmias can cause the heart to beat too quickly, too slowly or irregularly, resulting in a broad range of symptoms as well as sudden death and stroke.
 Heart Valve Disease	Heart value disease occurs when there is a problem with one or more of the four valves that normally work in unison to make sure that blood is pumped in the proper direction through the four chambers of the heart.
 Coronary Artery Disease (CAD)	CAD is among the most common type of heart disease and occurs when plaque grows in the walls of the coronary arteries, limiting the blood flow to the heart's muscle. CAD can ultimately lead to a heart attack.

While there is significant unmet need in the field of heart disease, historically there have been challenges in developing novel therapies for the different forms of heart disease. We are currently focused on HF and arrhythmia, particularly when these diseases can be traced to some underlying genetic defect.

Current Challenges in the Development of Novel Therapies for Heart Disease

- ***Most development efforts focus on treating symptoms rather than targeting the underlying causes of diseases.*** First-line therapies for HF such as generic small molecules, including ACE inhibitors, angiotensin II receptor blockers, beta blockers, aldosterone antagonists, and diuretics, are most commonly used, irrespective of the underlying cause of the HF.
- ***Identifying new disease-modifying targets is challenging.*** There is a high reliance on animal models that are not always predictive of human heart disease. There is only a 4% to 7% overall probability of

successful drug development from Phase 1 through commercialization for heart disease, among the lowest of all therapeutic areas.

- ***Genetic diagnosis and genetic counseling are limited.*** Most patients presenting with heart disease do not currently obtain a genetic test as part of their diagnosis. Given there are almost no therapies that are targeted at the underlying genetic cause of the disease, physicians may believe a genetic test will not influence treatment and management decisions. Additionally, even when patients do receive a genetic diagnosis, genetic counseling and family screening are not commonly employed. As a result, family members who may be at risk of disease are not consistently identified early. Additionally, this also limits the availability of patients for clinical trials of genetic medicines in heart disease.
- ***Regenerative therapy science is still in its early stages.*** Historical attempts at developing cell and gene therapies for heart disease have not been successful. Much effort was devoted to regenerative medicine approaches using autologous (from self) or allogeneic (from donors) cell sources, but after more than 150 clinical studies involving thousands of patients over the last two decades, those efforts have mostly ended in failure. Factors that likely contributed to these failures include (1) an insufficient number of new cells surviving rejection by the immune system, (2) only modest efficacy from the surviving cells, and (3) arrhythmia caused by abnormal electric activity and connections between new cells and the existing cells.
- ***Gene therapy science for the heart is still maturing.*** There have been few attempts at gene therapy for heart disease. Most early gene therapy efforts used adenoviruses instead of AAV. The most well-known AAV-based effort involved the use of AAV1 to deliver SERCA2a. After promising preclinical and early clinical results, this effort was discontinued following an unsuccessful Phase 2b study. These first-generation gene therapy efforts for the heart did not have the benefit of more recent advances in capsids, promoters, delivery, and manufacturing.
- ***Regulatory requirements are stringent.*** Historically, cardiovascular drug development has involved large clinical studies to demonstrate a survival benefit over and above standard-of-care, and with very low tolerance for safety risks. Endpoints focused on functional improvements, such as change in ejection fraction (EF), have generally not been sufficient for FDA approval. This translates to a need for very large, long, and expensive randomized and placebo-controlled clinical studies. The average size of a clinical study used to support treatment recommendations for HF can involve approximately 2,000 to 8,000 patients. As an example, studies for therapies intended to treat diabetes may require safety trials involving 5,000 to 15,000 patients to rule out cardiovascular risk.
- ***Costs of development are high.*** In part due to the historical need for very large clinical studies, drug development for new therapies of heart disease has been very long and expensive. A recent analysis demonstrated that, on average, biopharmaceutical companies spent $1 billion in clinical development per cardiovascular drug product approval, the highest ratio among all therapeutic areas.
- ***Patient access barriers are challenging.*** In addition to being the leading cause of death, heart disease is one of the largest and most expensive categories for payers. The United States spends approximately $317 billion per year on heart disease alone, or nearly 17% of all U.S. healthcare spending, representing the most expensive category of chronic diseases to treat. The total direct and indirect costs of HF alone are expected to increase to $70 billion by 2030. As a result, heart disease is an area of focus for cost-containment and price sensitivity for new therapies for both private and public payers.

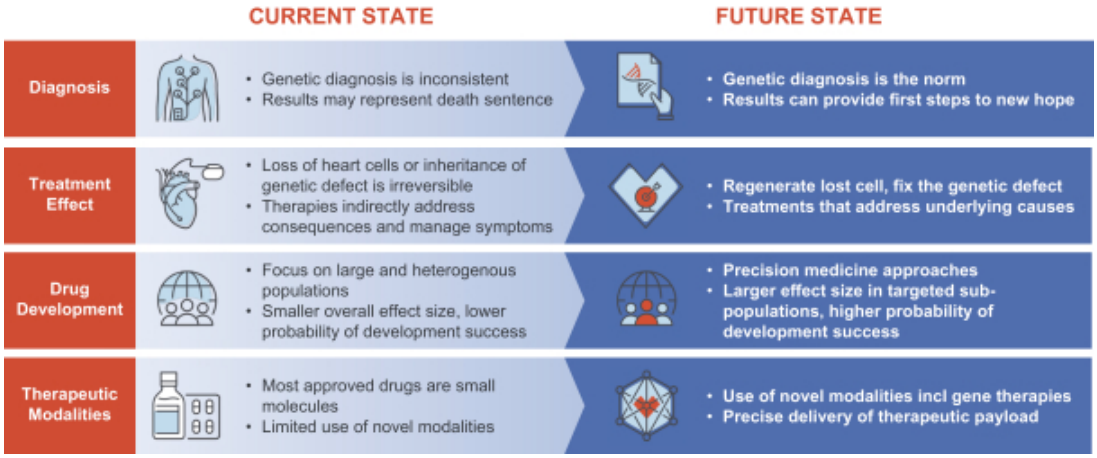
These factors have contributed to a decline in successful heart disease drug development. Between 2000 and 2009, FDA approvals for new cardiovascular drug products declined by approximately 33% compared with the prior decade. While heart disease is the leading cause of death in the world, fewer resources have been mobilized in support of new therapies for heart disease relative to investment in other therapeutic areas, such as oncology and diseases of the central nervous system.

However, there are recent signs of improvement. There is increasing insight into the genetic causes of heart disease and a greater push for more consistent genetic testing and family counseling supported by (1) updated

clinical practice guidelines such as 2020 American College of Cardiology (ACC) and American Heart Association (AHA) recommendations for patients with hypertrophic cardiomyopathy (HCM), (2) the push by patient advocacy organizations for mandatory screening of young athletes, and (3) increased availability of accessible genetic testing covering more than 150 relevant genes associated with inherited arrhythmia and cardiomyopathy conditions. There are also a small but growing number of examples of clinical success with precision medicine approaches in cardiology, including in genetic cardiomyopathies.

We believe with the evolving understanding of heart disease in the scientific community and the general public, there are significant opportunities where we can benefit from and support the evolution towards more precise diagnosis, drug development, and treatment for heart disease, as depicted in the diagram below.

The Evolving Landscape of Heart Disease



Our Strategy

Our goal is to become a leading, fully integrated biotechnology company delivering next-generation therapies that address the underlying causes of heart disease identified through our multi-modality product platforms. We are taking advantage of an expanded understanding of heart biology and advances in the science to discover, develop, manufacture and ultimately commercialize a deep and diverse pipeline of novel therapies. The key components of our strategy to achieve these goals are:

- ***Focus exclusively on heart disease.*** Heart disease is still the leading cause of death globally, more than all cancers combined, and the unmet medical need remains high. We see significant opportunity to address this sizable market with our dedicated strategy. The heart is a complex organ to target, in part due to the tightly regulated and coordinated electrophysiological and biomechanical properties that can complicate delivery of effective therapies and necessitates a deep understanding of heart biology. Our laser focus leads to insights that underpin our foundational and differentiated capabilities to address challenges that have historically presented barriers to the successful development of novel therapies for the heart.
- ***Develop disease-modifying therapies.*** We are focused on developing disease-modifying and potentially life-saving novel therapies that target the underlying causes of heart disease. We are particularly interested in areas where there is no current standard-of-care or where we believe the nature and the magnitude of the effect of our therapies will be significant relative to existing standards-of-care. For example, we believe our AAV-based gene therapies for genetically defined conditions have the potential to be curative after a single dose.

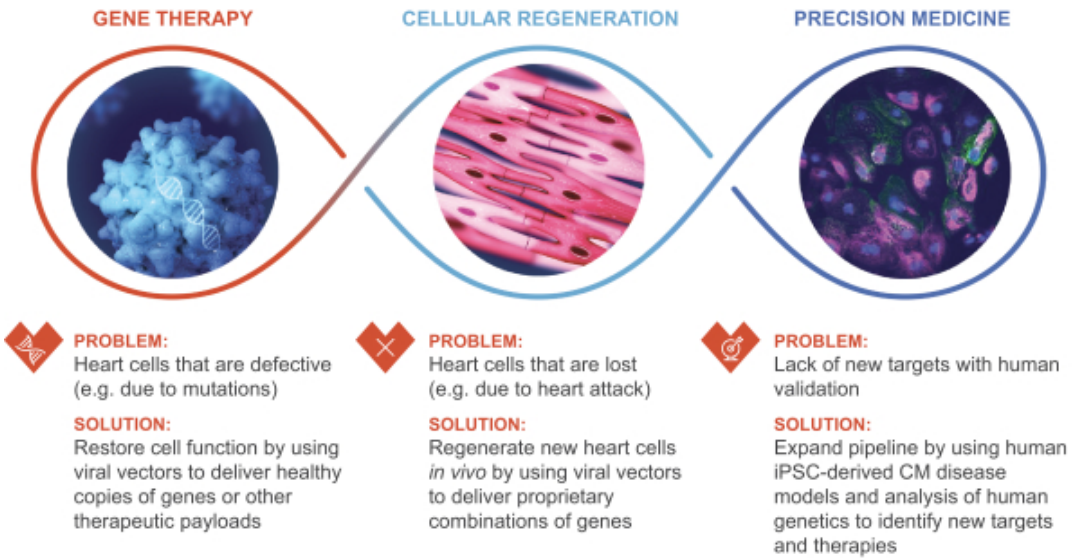
- ***Discover novel therapies using three product platforms in parallel***. To address the wide range of issues in heart diseases, we are advancing science from three distinct product platforms in parallel. Each platform tackles different problems that have historically plagued drug development in the field of cardiology: (i) our Gene Therapy platform to deliver a wide variety of therapeutic payloads more precisely to heart tissue, (ii) our Cellular Regeneration platform to replace heart cells lost to disease, and (iii) our Precision Medicine platform to discover targeted therapies in a modality-agnostic fashion. These platforms represent distinct but interrelated product engines that we believe will enable a robust pipeline of promising product candidates while also mitigating overall scientific risk.
- ***Target defined sub-populations of patients most likely to respond to our therapies*.** We seek to focus on patient populations where the genetic cause of the disease is well-established, including genetic cardiomyopathies and other monogenic disorders. We also seek to use different strategies to sub-segment larger HF populations, such as HFrEF and HFpEF, through the use of genetics or biomarkers to improve selection of patients with attributes that are more suited to the specific mechanism of action. We believe this strategy can accelerate clinical development, reduce overall development costs, and improve the probability of clinical and regulatory success.
- ***Advance a deep and diverse pipeline of therapies*.** We aim to advance potential product candidates from all three product platforms concurrently, and the current pipeline already has at least one program from each product platform. The diversity of our programs illustrates the ambition of our vision and the versatility and depth of our scientific approaches. For example, from our Gene Therapy platform we are advancing AAV-based therapies for rare, genetic forms of heart disease including (i) TN-201, our MYBPC3 product candidate for gHCM, (ii) our PKP2 product candidate for gARVC and (iii) our DWORF product candidate for DCM and HFrEF; from our Cellular Regeneration platform, we are advancing the Reprogramming approach to creating new CMs to replace cells lost in patients with HF due to prior MI; and from our Precision Medicine platform, we are advancing TYA-11631, an HDAC6i small molecule intended to address HFpEF and gDCM. We are also working on several other undisclosed programs, particularly from our Gene Therapy and Precision Medicine platforms, that we believe will add to our future pipeline opportunities.
- ***Internalize and integrate core capabilities to support our innovation*.** We have five core capabilities that we believe will enable us to rapidly discover, develop, and deliver heart therapies. These capabilities include: (i) Disease Models, (ii) Capsid Engineering, (iii) Promoter and Regulatory Elements, (iv) Drug Delivery and (v) Manufacturing. We believe the integration of our know-how and innovations in these areas will allow us to generate scientific insights more rapidly and improve the probability of technical and regulatory success of our product candidates. The internalization of these capabilities also reduces our reliance on third parties—be it academic labs, CROs, or CDMOs—providing us better control of our timelines and costs.
- ***Become a fully integrated biopharmaceutical company with commercial capabilities.*** We aim to discover, develop, manufacture, and eventually commercialize therapies. We believe this strategy can make us a partner of choice for academics and larger companies alike who wish to access deep expertise in next generation therapies for heart disease. We also strategically evaluate collaborations and partnerships with biopharmaceutical companies that may have more robust and complimentary capabilities and resources to accelerate the development and maximize the availability and potential of our product candidates, particularly for more prevalent indications.

Our Product Platforms

To unlock the full potential of novel therapies across many forms of heart disease, we are advancing science from three product platforms in parallel. Each platform is intended to address different problems that have historically plagued drug development in the field of cardiology: (i) our Gene Therapy platform to deliver a wide variety of therapeutic payloads more precisely to heart tissue, (ii) our Cellular Regeneration platform to replace heart cells lost to disease, and (iii) our Precision Medicine platform to discover targeted therapies in a modality-

agnostic fashion. We are advancing programs from these distinct but interrelated product platforms that combine different science, capabilities, and intellectual property. We believe these three product platforms together yield better insights into disease processes, create more opportunities for successful drug development, mitigate scientific risk, and differentiate our efforts relative to competitors.

Our Product Platforms Powering Multi-Modality Drug Discovery



Gene Therapy Platform

Gene therapy focuses on repairing or replacing defective or mutated genes to produce a therapeutic effect or treat a disease. AAV is a non-enveloped virus that already exists in some humans and does not cause disease. In gene therapy, the viral DNA within an AAV is replaced with new DNA to become a precisely coded vector to deliver the engineered therapeutic to specific tissues or organs within the body.

AAV vectors are the subject of significant research and development as they can be leveraged as a gene delivery vehicle for a wide range of therapeutic payloads to a wide variety of human cells. AAV-mediated gene therapy has been shown to be highly effective in targeting multiple organs, including the eye, the liver and the central nervous system. These viruses have been used to dose more than 3,300 patients in approximately 150 clinical studies around the world, and there are now several therapies that use such viruses that have been approved by the FDA and other regulatory agencies.

Recent third-party clinical studies have demonstrated that AAV serotype 9 (AAV9) can effectively transduce the hearts of infants and adults. This supports the results of several published non-clinical studies using AAV9 in murine and NHP models. Overall, most data suggest that AAV9 may be the best of the known existing parental vectors for the purpose of cardiac gene therapy where the target cells are CMs (one of the most abundant cell types in the heart responsible for contraction).

However, AAV9 has limitations. AAV9 has a well-established ability to also transduce the liver and the central nervous system, in addition to the heart, which can create safety considerations. Also, some individuals have neutralizing antibodies to AAV9, making them ineligible for AAV9-based treatments.

Cardiac-specific promoters like cardiac troponin T (cTnT) can help limit the expression of AAV-delivered genes to CMs, but do not enable targeted gene expression in other heart cells (e.g. CFs). Additionally, the level of gene expression from these promoters may not be sufficient for therapeutic effect for some targets.

Therefore, there is significant room for improvement, and we aim to improve gene therapy for the heart in ways that expand its utility. We believe our five core internal capabilities will allow us to identify, engineer, validate, deliver and manufacture novel AAV vectors to optimize the delivery and expression of therapies more selectively to cells of interest in the heart. With our capsid engineering capabilities, we have designed and screened more than one billion AAV variants to find novel capsids with higher tropism and transduction efficiency for different types of heart cells, lower transduction efficiency for the liver and other tissues, and lower susceptibility to neutralizing antibodies. We have discovered promoters and regulatory elements that enable more precise gene expression in specific heart cells. We are developing new catheters and are exploring different ROAs to more precisely deliver vectors to heart tissue. And we have established know-how to enable more optimal manufacturing, including of novel AAV capsids.

These capabilities open the opportunity to deliver novel gene therapies to patients with heart disease and to position us to become a leader in cardiac gene therapy. We are leveraging these capabilities to develop gene therapies for rare, genetic forms of heart disease, as well as to enable the transition to more prevalent forms as well.

The product candidates arising from our Gene Therapy platform are intended to overcome the shortcomings of traditional pharmacological or surgical interventions that are not able to address the underlying genetic factors contributing to heart disease. Our initial area of focus is on the delivery of a healthy copy of genes that are known to be mutated in genetic cardiomyopathies; for example, our most advanced product candidate from our Gene Therapy platform involves delivering a healthy copy of the *MYBPC3* gene to address the leading cause of gHCM. This “lock and key” gene therapy program was selected following a screen of hundreds of potential targets. We believe our MYBPC3 program is able to benefit from a variety of factors, including high disease severity and large unmet need; relatively high prevalence; emerging science supporting haploinsufficiency as the disease driver; representative disease models; and illustrative proof-of-concept evidence for gene therapy from academic labs.

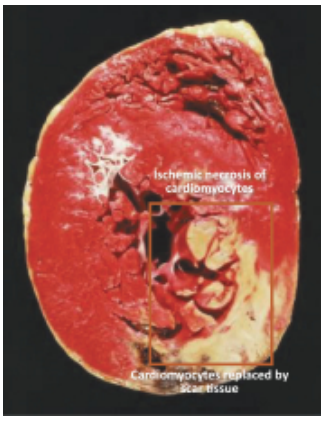
We believe the versatility of our Gene Therapy platform and related differentiated capabilities enables us to rapidly expand our portfolio of therapies beyond the initial focus. For example, our PKP2 program is another example of a “lock and key” approach to addressing the leading cause of gARVC. Our DWORF program is based on the idea of delivering the recently discovered DWORF protein targeting a well-known SERCA2a pathway that has been shown to exert a therapeutic effect in a range of disease models. We continue to explore other genetic cardiomyopathies that can potentially be addressed by our Gene Therapy platform.

Cellular Regeneration Platform

Scientists have long known that the human heart is not able to regenerate itself, unlike many other organs in the body. Acute MI—more commonly referred to as a heart attack—can kill as many as 25% of CMs from the LV, or approximately one billion cells. The heart has no natural way to replace cells that are lost slowly with age or suddenly due to disease. One reason that HF is so prevalent and the leading cause of death in the world is due to the lack of regenerative potential of the heart. Acute MI is associated with a 30% mortality rate; about 50% of the deaths occur prior to arrival at the hospital. An additional 5% to 10% of survivors die within the first year after their MI. Approximately half of all patients with an MI are rehospitalized within one year of their first MI. Finding ways to replace lost heart cells is one of the “holy grails” of regenerative medicine.

There are two abundant cell types in the heart: CMs, which are the cells that are responsible for contraction during each heartbeat, and CFs, that produce and secrete growth factors, cytokines and other signaling molecules contributing to structural, biochemical, mechanical and electrical properties of the myocardium. While CFs are

able to divide and proliferate, CMs are post-mitotic, meaning they are incapable of regenerating. CMs that are lost due to aging or disease are replaced by fibrotic scar tissue that is permanent and irreparable with currently approved therapies.

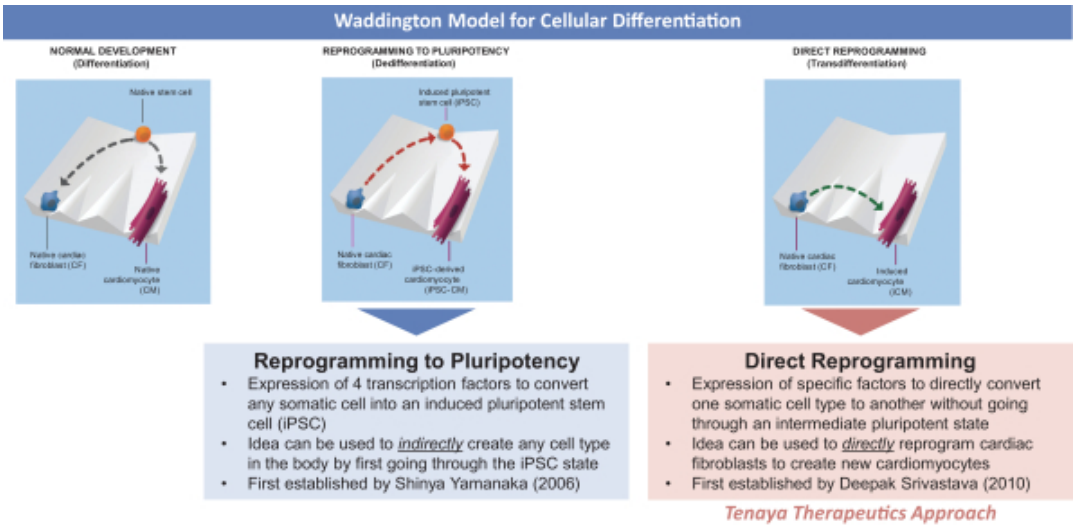


The field of cardiac regeneration has historically been dominated by *ex vivo* cell therapy approaches using autologous (from self) or allogeneic (from donors) cell sources to replace lost CMs. However, there have been no successful therapies after scores of clinical studies involving thousands of patients. Any modest efficacy seen in clinical studies are now often attributed to indirect paracrine effects rather than true cardiac regeneration. Some have tried to induce regeneration by infusion or injecting cells generated from hiPSC-CMs or human embryonic stem cells (hESCs), but that has been fraught with many challenges, as these cells have an embryonic phenotype and generate arrhythmias once injected into the heart; recipients need to be immunosuppressed to avoid rejection; and integration into the electric and mechanical connections of the heart is still imperfect.

We are advancing a cardiac regeneration approach based on research conducted by our founders at Gladstone Institutes and UTSW, who pioneered the idea of restoring heart function after a heart attack by *in vivo* regeneration of lost CMs. Our approach is intended to achieve this by using viral vectors to deliver a proprietary combination of three genes that when delivered together in a single AAV can permanently convert—or "reprogram"—a patient's own resident CFs into new CMs.

This approach was inspired by the Nobel-prize winning discoveries of Shinya Yamanaka who first discovered that human cells can be "reprogrammed" with certain specific factors—which became known as the "Yamanaka factors"—to become induced pluripotent stem cells (iPSCs), and that these newly formed iPSCs were in turn capable of differentiating to become any other human cell type in the body, including heart cells. Our founders and other academic labs built on this idea and demonstrated that it is possible to directly convert CFs to CMs without first going through the iPSC stage. Dr. Srivastava, one of our co-founders and a member of our board of directors, was the first to demonstrate proof of concept of this "direct reprogramming" approach for cardiac regeneration *in vivo* in a mouse model and *in vitro* with human cells. Several independent academic labs around the world have subsequently replicated the results with direct reprogramming for cardiac regeneration using the same factors as well as new combinations.

The figure below helps illustrate the idea of direct reprogramming of CFs to CMs using the Waddington model for cellular differentiation:



There have been several historical challenges for the field of direct reprogramming for cardiac regeneration to turn this promising scientific discovery into potentially viable therapies. Most academic efforts required anywhere from three to five factors to achieve the conversion of human CFs to CMs, and the overall conversion rate was relatively low. Some of these efforts used a combination of retroviruses and small molecules to achieve this conversion, which is not clinically applicable. The published proof-of-concept work has been demonstrated in murine models of acute MI (i.e. immediately at the time of onset of heart attack), but not in models of HF following MI (i.e. following some period of time sometime after the heart attack has already happened) which more accurately simulates the situation that would be adopted in the clinical setting.

We believe we are the first to potentially overcome these challenges. We have discovered a proprietary combination of three genes that can be co-packaged and co-expressed from a single proprietary AAV vector engineered for higher transduction of CFs when compared to existing parental capsids. We have demonstrated higher transdifferentiation rates *in vitro* using human CFs that are higher than rates reported in published studies using combinations of other factors intended to drive reprogramming. We have demonstrated robust and durable proof-of-concept of this approach in multiple rodent models of acute MI and HF post-MI. Most importantly, based on publicly available information to date, we believe our results in a pig model of HF due to prior MI represent the first-ever successful demonstration of the potential therapeutic benefit of this approach in a human-sized heart.

We believe our *in vivo* approach to cardiac regeneration may have several advantages over *ex vivo* cell therapies. Because the newly formed CMs are generated from the patients' own cells, they are not rejected by the body and no immunosuppression is needed. And since these newly formed CMs are generated from within the patient's heart tissue, it may be easier for them to electrically and mechanically connect with surrounding cells as they mature and to contribute to healthy heart function with lower risk for arrhythmias. In addition, it is easier to manufacture and to deliver AAV-based therapies and to offer them at commercially viable prices compared to cell-based therapies.

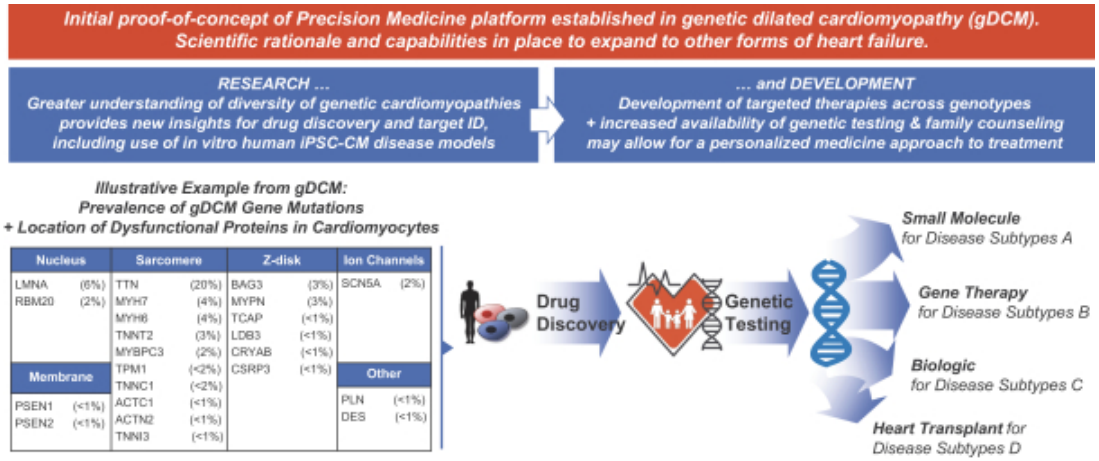
The initial focus of our Cellular Regeneration platform is on the development of disease-modifying treatments for HF due to prior MI. We believe the versatility of this product platform and related differentiated capabilities position us to expand our portfolio of therapies rapidly and pursue other indications involving loss of CMs.

Precision Medicine Platform

The idea of "precision medicine" has been around for a number of years, with the core concept of delivering the right therapy to the right patient at the right time. Recently, the idea of precision medicine has gained traction in oncology, in particular, with the benefit of a better understanding of the genetics of different tumor types, and a growing ability to match therapies to specific mutations (e.g. Genentech's Herceptin therapy for HER2+ breast cancer). We aim to bring this concept of precision medicine to the discovery and development of targeted therapies for heart disease.

There is an increasing understanding of the genetic basis for many cardiomyopathies, including DCM, HCM, restrictive cardiomyopathy (RCM) and arrhythmogenic cardiomyopathy (ACM). DCM provides an interesting case study. Mutations in more than 50 genes have been identified for gDCM, with more than 50% of patients presenting with multiple mutations. These mutations affect different parts of the cellular apparatus of patients' CMs, including the sarcomere, nucleus, ion channels, and cellular membranes. Yet mutations in proteins with diverse biology present as a common disease phenotype, suggesting common nodes of disease yet to be discovered. Despite this heterogeneity of genetic background and underlying pathophysiology, the therapies used for these patients are the same as therapies used for patients with other forms of HF. We envision a future in which therapies are more specific to the underlying cause of disease and are used to treat patients who have been categorized based on their underlying genetic mutations.

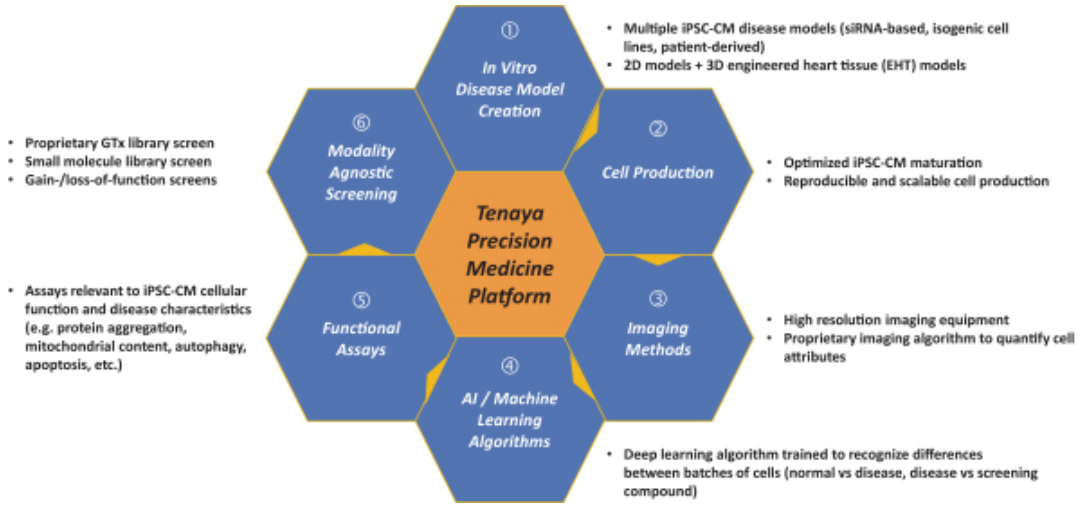
The figure below helps illustrate our vision for "precision medicine" research and development for heart disease through the lens of gDCM:



It is also necessary to have the appropriate disease models to discover new targets and to test new therapies. Unfortunately, there is still a lack of representative *in vivo* models; of the greater than 50 genes known to cause gDCM when mutated, less than ten have relevant murine models to support drug discovery. The situation is even worse for others forms of genetic cardiomyopathy. We are committed to finding new ways to model genetic cardiomyopathies, including *in vivo* but also *in vitro* models.

There is a growing body of academic literature supporting the use of hiPSC-CMs to model human heart disease and the potential cardiotoxicity of therapeutics during drug discovery. This can be helpful where animal models for specific forms of heart disease either do not yet exist or are not yet sufficiently representative of human disease. There are also a growing number of biopharmaceutical companies that are using iPSCs for phenotypic screening and drug discovery. We are advancing a novel approach of using proprietary hiPSC-CMs disease models for target identification and drug discovery specifically for heart disease.

The figure below illustrates how we have internalized and integrated six key aspects necessary to advance the discovery of precision medicine therapeutics using hiPSC-CMs:



We have demonstrated proof of concept of this approach using an hiPSC-CM disease model representing a specific gDCM mutation plus machine learning algorithms to measure variations in appearance of these cells when screened with a library of several thousand small molecule compounds. We identified several biologically relevant hits and validated HDAC6 as a specific target of interest. We have since turned our findings into a product candidate in our HDAC6i program with *in vivo* activity and tolerability demonstrated in multiple heart disease models of HFpEF and gDCM.

We are currently conducting target identification screens for both gene therapy and small molecules targets in multiple iPSC-CM disease models of gDCM. We are also expanding our efforts to different genetic backgrounds including the leading genetic causes of cardiomyopathy. We believe the versatility of our Precision Medicine platform and related capabilities enables us to rapidly expand our portfolio of product candidates beyond HDAC6i.

Our Approach and Capabilities

We utilize five core internal capabilities to support our three product platforms. Our key capabilities include the creation and development of (1) disease models to more accurately simulate human heart disease phenotypes, (2) proprietary heart-tropic AAV capsids designed to enable precise tissue targeting and increase safety, (3) proprietary promoters and regulatory elements to control gene expression, (4) fit-for-purpose drug delivery methods for more optimal uptake and distribution of our product candidates and (5) scalable AAV manufacturing to better control quality, costs, timelines and supply.

We believe integration of these in-house capabilities provides us with several advantages and differentiates our efforts relative to other drug discovery companies, especially for gene therapy drug development. Through the combination of these capabilities, we are developing product candidates that can address the complicated characteristics of heart disease. For example, we believe with our capabilities in capsids and promoter design and delivery, we can overcome the limitations faced by prior cardiac gene therapy approaches by enabling more precise delivery and more robust gene expression and lowering the risk of off-target effects. We also believe that these approaches can overcome the historical challenges of drug development for heart disease, by enabling delivery of a wide range of therapeutic approaches to specific cells in the heart.

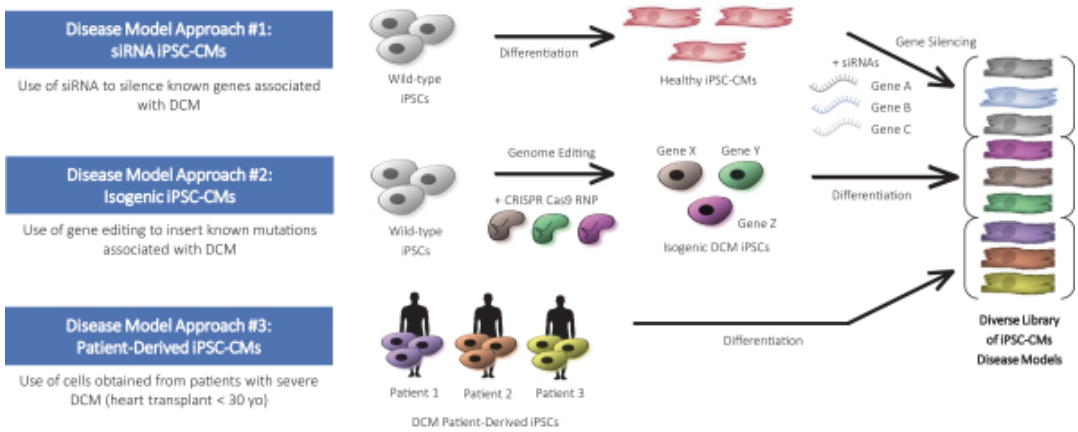
By having our capabilities in-house, we believe we are able to achieve deeper insight, shorten product development cycles, and improve the probability of technical and regulatory success for our product candidates compared to what can be achieved with a more outsourced approach. This further allows us to rapidly build a diverse pipeline of product candidates. Ultimately, we believe our differentiated capabilities can support development of product candidates that, if approved, could address the high unmet need of patients with cardiac diseases and could be delivered at a lower cost of goods than what is possible today.

1. Disease Models

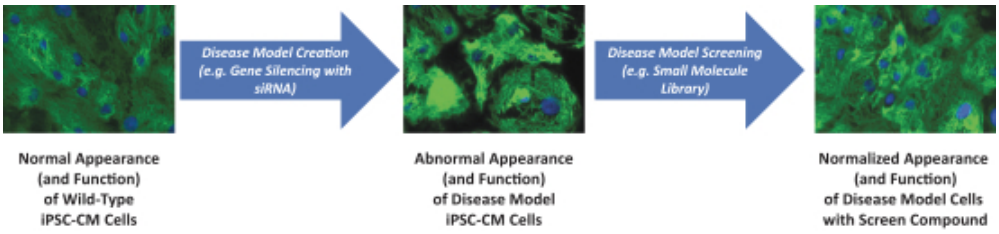
We have internalized the ability to create and integrate *in vitro* and *in vivo* models within our research organization, which allows us to simulate human heart disease phenotypes. We believe our success will be supported by the know-how we are developing and the proprietary integration of these disease models across our programs.

- *In vitro cell-based disease models*: For our *in vitro* disease models, we have leveraged the seminal discovery of methods used to generate iPSCs to establish disease models based on human iPSC-derived cardiomyocytes (iPSC-CMs). We have implemented three primary approaches to model human heart disease in this way: (i) short interfering ribonucleic acid (siRNA) constructs to silence specific genes of interest in iPSC-CMs; (ii) CRISPR-based gene editing approaches to create isogenic iPSC-cell lines where specific genes have been altered; and (iii) iPSCs derived from patients with severe heart disease, for example, severe DCM resulting in early HF and transplant, sourced from commercial and academic collaborators.

  In the figure below, we illustrate our primary disease model approaches based on iPSC-CMs:



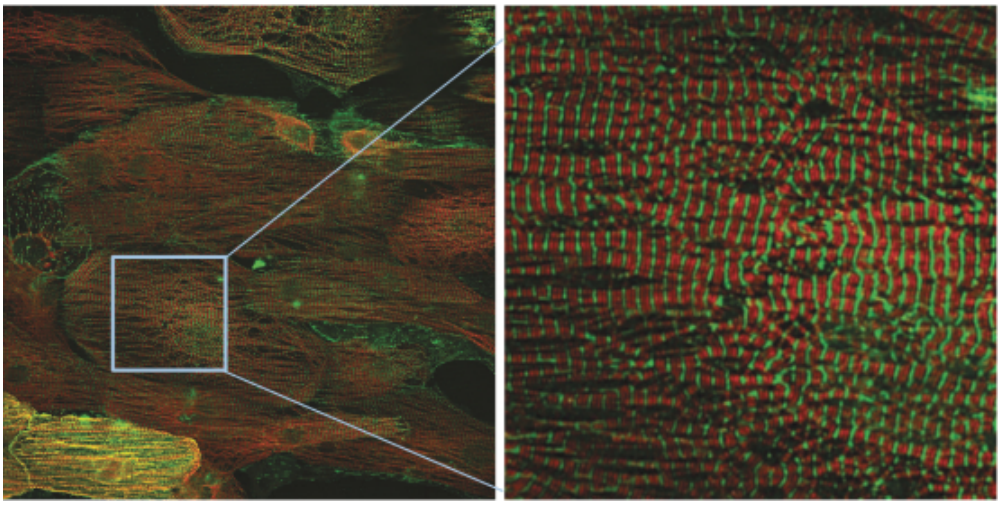
These disease models can collectively help simulate the impact of human disease-causing mutations on the appearance and function of CMs. They can also help model the impact of potentially disease-modifying treatments on such cells. In the figure below, we illustrate how, through use of gene editing and gene silencing tools, we can modify the appearance of normal iPSC-CMs to appear disorganized, and subsequently restore cell appearance with compounds from our screening library:



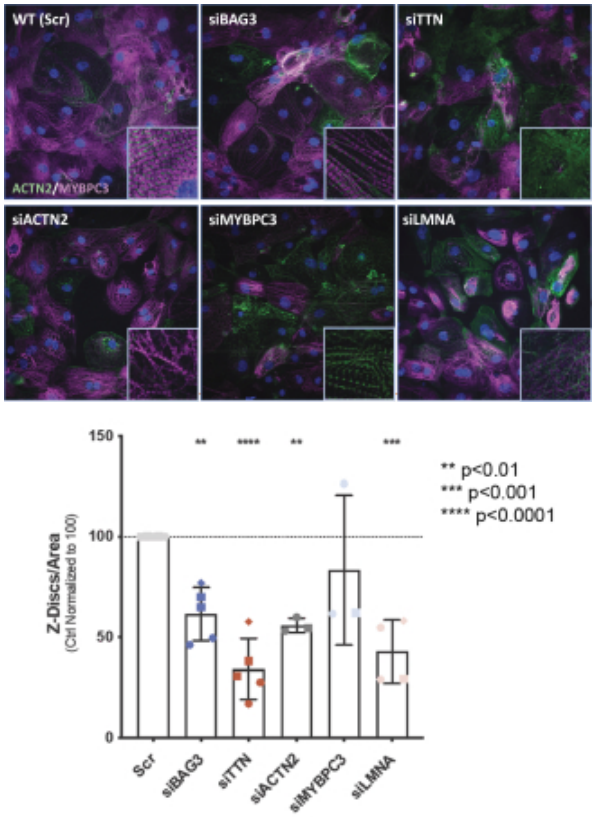
We initially used cells from these disease models plated in two-dimensional formats. We have since advanced our efforts to include three-dimensional engineered heart tissue disease models where the cells have a more mature phenotype and with contractility that can be measured more reliably.

- *iPSC production:* To conduct robust target identification and drug discovery screens using our cell-based disease models, we need to produce large volumes of these hiPSC-CMs. We have developed the necessary know-how to do so reliably and reproducibly at increasing scale.
- *Imaging techniques:* We use a combination of immunostaining, high-resolution imaging, and imaging algorithms to visualize and quantify phenotypic differences between our in-house iPSC-CM disease models. We can measure several details of the sarcomeres of these cell lines, including sarcomere density, disarray and Z-disc area.

The figure below shows the degree of automated high-resolution image capture that is possible to help visualize the details of iPSC-CM disease models such as the sarcomere structure and other characteristics:

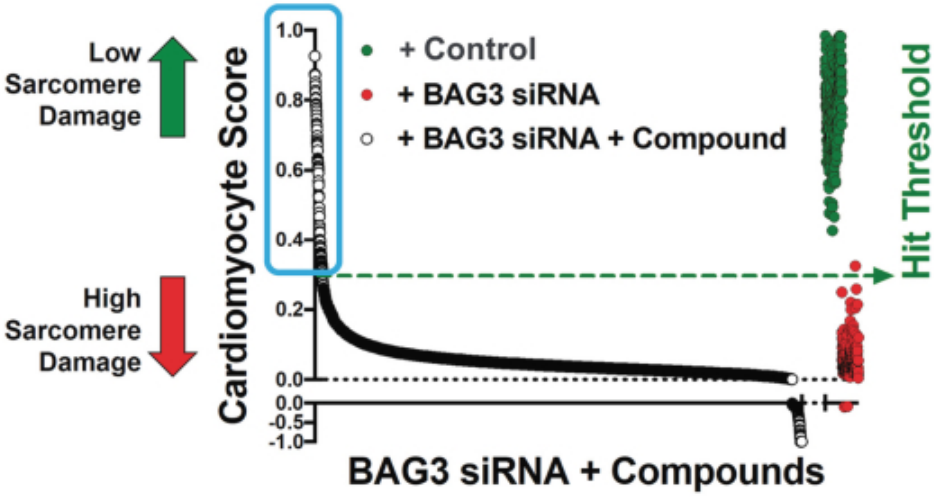


In the figure below, we show data that illustrate our ability to use proprietary imaging algorithms to quantify reproducible and statistically significant differences between particular attributes of the iPSC-CMs (e.g. Z-Disc Area of the sarcomere) across multiple disease model lines:



- *Machine learning algorithms:* We have used machine learning algorithms to support high-throughput phenotypic screening of our iPSC-CM disease models. The algorithms can rapidly and reproducibly measure subtle differences in the overall appearance between wild-type iPSC-CM cells and the different disease models, as well as differences on the disease models in response to compounds in our screening libraries.

  The figure below illustrates the output of a screen in a disease model of DCM, using siRNA silencing of the *BAG3* gene, with a curated library of greater than 5,000 small molecule compounds. A deep learning algorithm that was trained on images of the disease model and on normal cells was used to determine which compounds caused the sarcomeres within the cells to appear more disorganized, representing more sarcomere damage (red), or more organized, representing less sarcomere damage (green), as measured by a “cardiomyocyte score”:

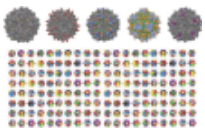
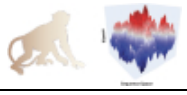
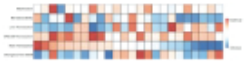


- *In vivo models:* For our *in vivo* disease models, we have a dedicated onsite *in vivo* pharmacology group and vivarium. We have established approximately 15 rodent heart disease models, both genetic and non-genetic, and continue to develop new models in-house as needed. We can dose both gene therapies as well as small molecules. We can perform heart surgeries on these rodent models and use blinded echocardiography-based imaging techniques to assess the impact of our therapies under development. The internalization of these capabilities greatly reduces our reliance on external CROs and academic organizations and significantly increases the speed and consistency with which we can iterate on product prototypes, generate data and formulate insights on our product candidates. We also work with established CROs for research efforts involving large animal models (e.g., NHPs and pigs), including for efficacy studies and evaluation of drug delivery methods. Through these efforts we have developed important insights into the advantages and limitations of specific models and have learned how to optimize the design of our experiments. This insight influences our preclinical drug development strategies and our discussions with regulatory agencies.

2. Capsid Engineering

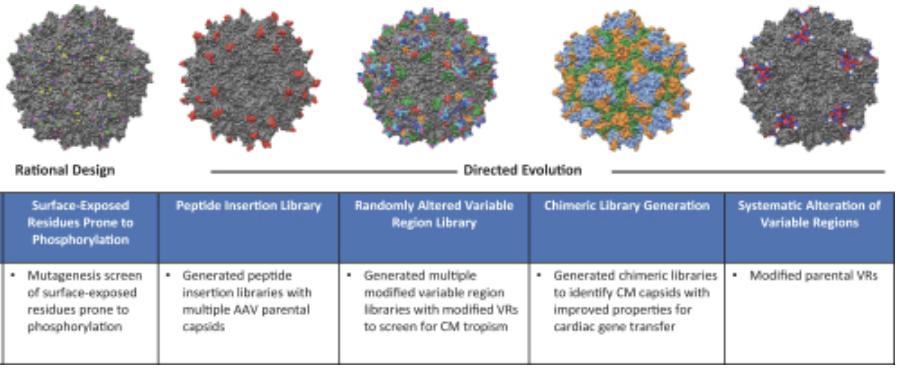
Our goal is to discover, design, and develop novel heart-tropic AAV capsids with superior attributes in order to enable more precise tissue targeting and to improve the safety profile of our product candidates. To achieve this goal, we have established in-house AAV capsid engineering capabilities and have designed and screened over one billion variants from diverse, proprietary libraries to discover, design, and develop novel capsids to support our programs.

The table below captures the breadth and depth of the focused strategies we have pursued to discover novel AAV capsids:

Focused Multi-Year AAV Screening Efforts Using Diverse Strategies		
Cell specificity		Capsid engineering efforts for both CMs and CFs
Library diversity		Screened more than one billion variants from 30 diverse libraries (rational design, peptide insertion, variable region, chimeric, etc.)
Screening models		Screening and validation in multiple models, including human iPSC-CMs, rodent models, NHPs as well as *in silico* / machine learning models
Screening criteria		Evaluating novel capsids for multiple criteria including higher heart transduction, lower liver transduction, lower antigenicity, and comparable manufacturability (as compared to relevant known serotypes)

- *Cell specificity:* We are using our capsid engineering capabilities to identify novel AAV capsids with an overall higher tropism for the heart compared to other organs and selectively target the two most abundant cell types in the heart: CMs and CFs. We already have achieved *in vivo* proof of concept for novel vectors for both cell types. Having capsids that more specifically target one cell type over another could help improve efficacy and safety and lower cost of goods for our future product candidates.
- *Library diversity:* We have screened more than one billion variants from 30 diverse libraries utilizing a range of strategies, including rational modification of surface residues as well as directed evolution efforts with peptide insertion libraries, chimeric libraries, and libraries based on systematic alteration of variable regions (VR) using different parental capsids. The diversity of approaches increases the likelihood that we will find capsids with novel properties.

The image below illustrates our efforts to achieve diverse heart-tropic AAV capsids.



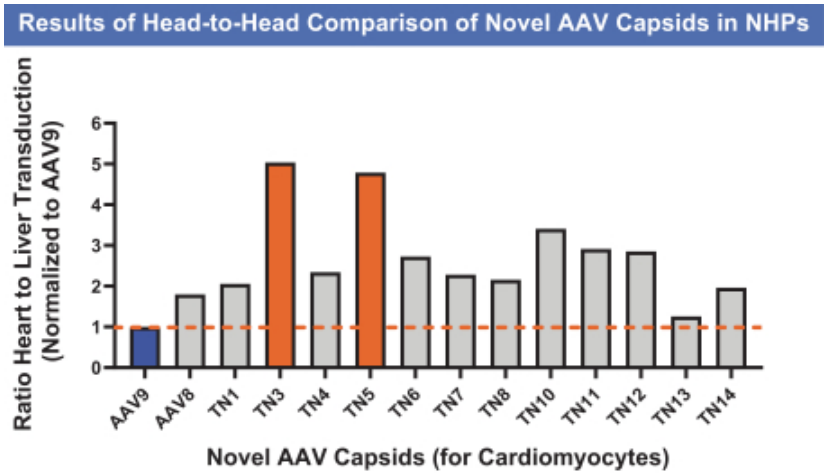
- *Screening models:* We have performed our screens in a variety of *in vitro*, *in vivo*, and *in silico* libraries. Current efforts are focused on direct screening in NHPs, as well as use of machine learning

algorithms. We believe our probability of finding novel variants that will translate to superior attributes in humans is highest in NHPs. We believe our *in silico* approaches can complement these efforts to help predict novel variants.

- *Screening criteria:* We have broad criteria for the selection of novel capsids, including improved tropism for the heart compared to other organs, with a particular interest in de-targeting the liver; improved transduction of specific heart cell types; lower susceptibility to neutralizing antibodies; and comparable manufacturing in both HEK293- and Sf9/rBV-based manufacturing systems. We seek capsids that can outperform the relevant parental capsids, which may vary depending on the intended use and on some or all of these criteria.

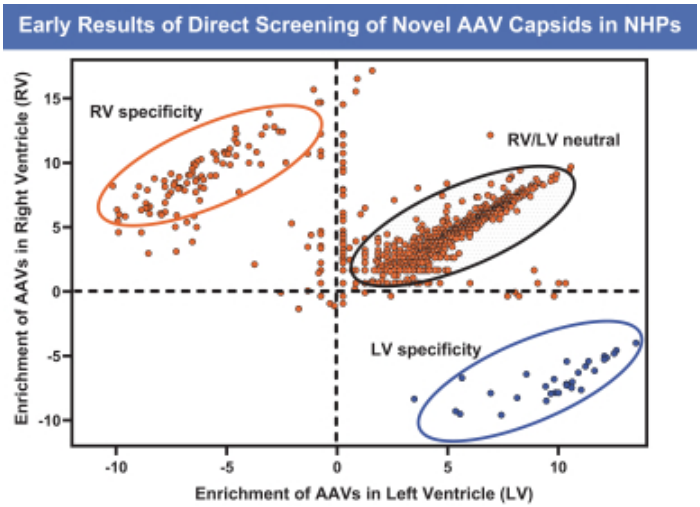
Through these efforts, we have discovered proprietary capsids with superior performance over parental variants in multiple species, including NHPs. These capsids have improved tropism for the heart compared to other organs and even for specific cells within the heart; improved transduction and expression within the heart cells; and lower susceptibility to neutralizing antibodies. We have also developed insights about the performance of novel capsids across different species including mice and NHPs.

The data below are from the results of a head-to-head comparison in NHPs of novel capsids that were first identified via screening efforts in iPSC-CMs and a mouse model. Several capsids identified have superior transduction in the heart and lower transduction of the liver compared to AAV9, leading to an overall better heart-to-liver transduction ratio as validated in an NHP model. As shown below, our TNC-CM3 capsid has a five-fold better heart-to-liver transduction ratio compared to AAV9.



Additionally, we have shown that several capsids we identified through this effort, such as TNC-CM5, have overall better ability to evade human neutralizing antibodies compared to AAV9.

The data below show preliminary results from efforts to identify novel AAV capsids by direct screening in NHPs. These results show it is possible to identify variants that have higher specificity for CMs of the (RV) compared to CMs of the LV. These capsids that are identified to have higher tropism for the RV may enable better targeting of heart tissue for conditions predominantly affecting a specific chamber of the heart such as arrhythmogenic right ventricular cardiomyopathy (ARVC):



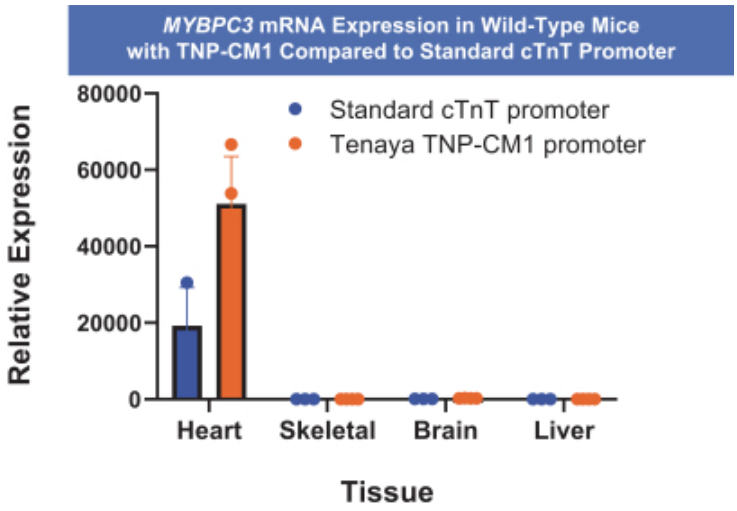
3. Promoters and Regulatory Elements

Enabled by our in-house molecular biology capabilities, we have created novel heart-specific promoters and regulatory elements to support our AAV-based programs and regulatory elements control gene expression within the cells. We are designing promoters and regulatory elements to help ensure a more precise and conditional expression of therapeutic payloads in different cell types in the heart. We believe our innovations in promoters and regulatory elements may further support the successful clinical development of our product candidates.

Illustrative examples of our innovations in this area include:

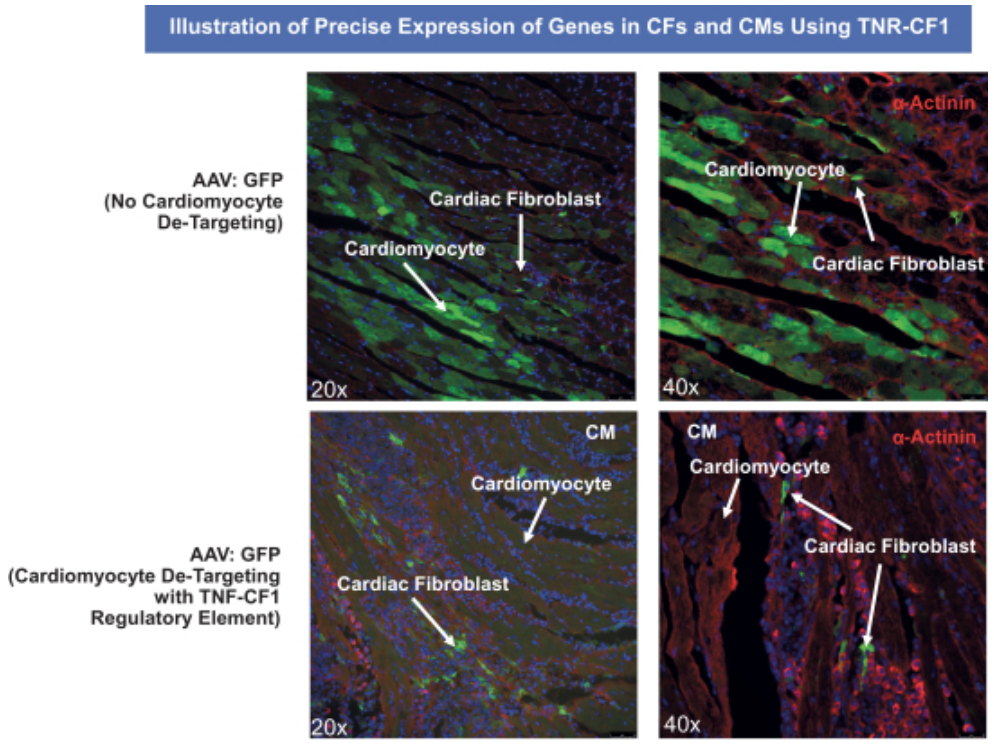
- *Heart specificity:* We have developed cardiac-specific promoters that enable more selective and robust expression in the heart as compared to other organs. During optimization of our MYBPC3 gene therapies, we discovered a CM-specific promoter, TNP-CM1, with improved performance attributes as compared to the standard cTnT promoter. *In vitro* and *in vivo* analyses confirmed that TNP-CM1 significantly increased expression of the *MYBPC3* gene compared to what can be achieved with the standard cTNT promoter. In addition, we observed 1000-fold selectivity of expression in cardiac tissue relative to other tissues.

In the figure below, we show data that demonstrate how our TNP-CM1 promoter outperformed a standard cTnT promoter in terms of robust gene expression in the heart of mice without loss of heart specificity:



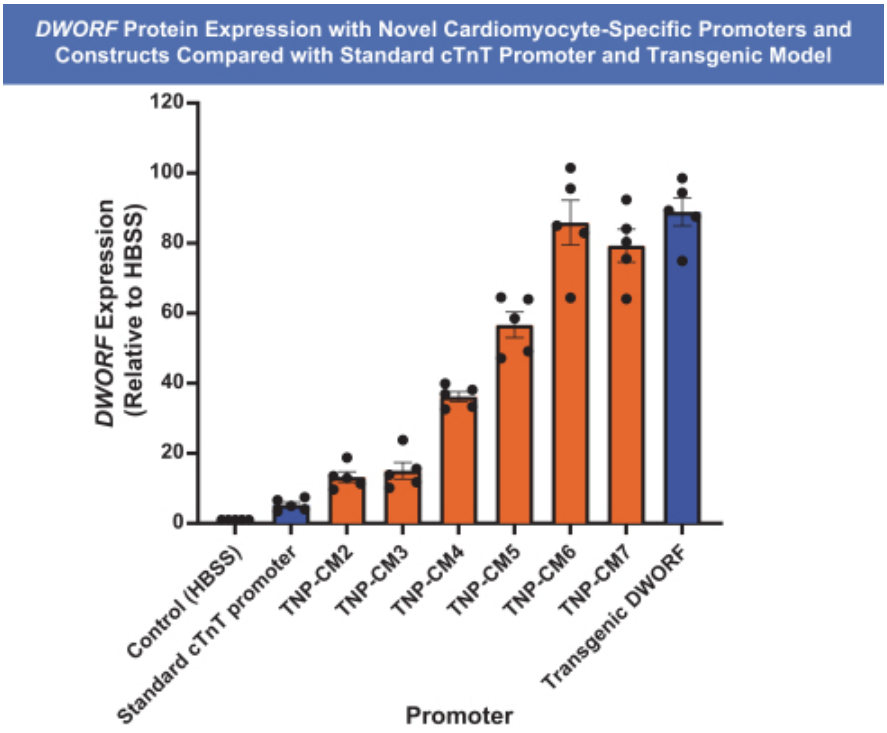
- *Cell specificity:* We have also developed a proprietary combination of regulatory elements that enable more optimal and selective expression in one cell type in the heart compared to others. For our Reprogramming program for cellular regeneration, we discovered ways to optimize the robust co-expression of two protein-coding genes and one miRNA gene delivered within a single AAV in CFs, which we believe supports higher efficacy in preclinical models. We also discovered how to use specific micro-RNA binding sites to silence the translation of those same genes in both existing CMs as well as newly created CMs, which may provide a safety benefit and reduce the chance for off-target effects.

In the figure below, we illustrate how the use of a novel regulatory element, TNR-CF1, helped prevent the expression of a fluorescent protein (GFP) in the CMs of a mouse model and only allowed expression in the CFs. We have used this regulatory element in our Reprogramming program to focus the expression of our proprietary factors in resident CFs for the creation of new CMs, but to prevent the expression of those factors both in resident CMs and in newly created CMs, which we believe will improve the safety profile of our future product candidates:



- *Tunable gene expression:* We have also demonstrated the ability to develop an entire spectrum of novel promoters to titer the expression of genes within CMs. Through data (not shown) generated in our DWORF program, more than ten promoters were designed and tested *in vitro* in hiPSC-CMs, and *in vivo* in murine models to optimize the expression of the *DWORF* gene to be higher than what can be achieved with a standard cTnT promoter.

In the figure below, we show data for six of our promoters and cassette engineering efforts that illustrate how we have been able to create a suite of cardiac-specific constructs that are able to mediate significantly higher expression of the *DWORF* gene than can be achieved with a standard cTnT promoter:

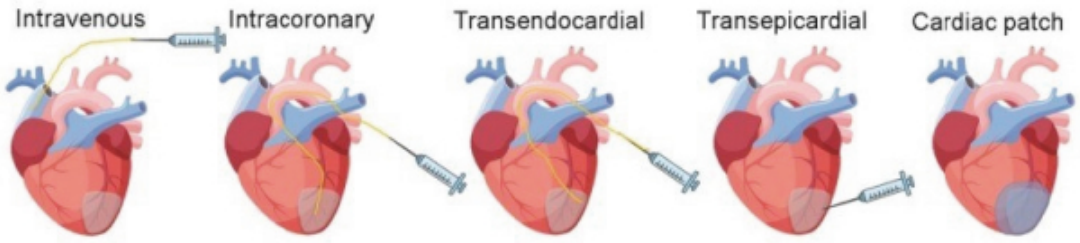


4. Drug Delivery

Delivery of drugs to the heart is widely considered to be an important challenge to successful translation of cardiac gene therapy and regenerative medicines into approved products. The diversity of programs in our current pipeline necessitates the use of different delivery methods. We are actively exploring different ROAs as well as different infusion- or injection-based catheters to support more targeted delivery and more efficient uptake of therapies based on viral vectors. We believe our discoveries in drug delivery can widen the therapeutic index of our product candidates by reducing the dose required for a therapeutic benefit.

Several distinct methods of drug delivery for the heart have been explored by different groups for gene- or cell-based therapies, including infusion-based approaches, such as peripheral IV infusion, intracoronary infusion, and retrograde coronary sinus infusion, and injection-based, such as transendocardial injection and epicardial injection. These delivery methods vary significantly in terms of degree of invasiveness, distribution of therapy around the heart, degree of therapy uptake into the heart, technical difficulty of administration, and clinical relevance and experience. For some approaches, additional methods to improve therapeutic delivery have also been tested to improve perfusion of AAV into the heart. Through these efforts, several groups have demonstrated how different delivery methods can meaningfully affect the relative uptake and biodistribution of therapies in the heart compared to peripheral organs.

Illustrative examples of various delivery methods for the heart are shown below:[1]

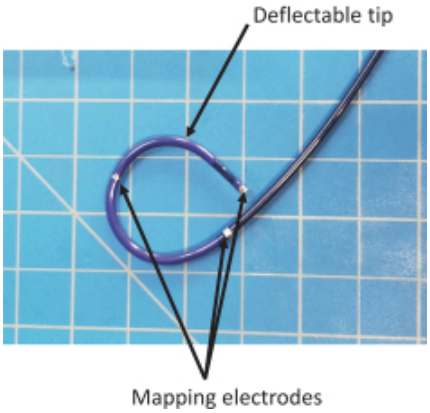


For the initial product candidates emerging from our Gene Therapy platform, including those from our MYBPC3 program, we generally need broad distribution across the heart tissue that is more suited to infusion-based approaches. By contrast, for the initial product candidates emerging from our Cellular Regeneration platform, including those from our Reprogramming program, we need more precise delivery into the heart tissue directly around a scar area of the LV in a way that is more suited to injection-based approaches.

Illustrative examples of our innovations and capabilities in drug delivery include:

- *Catheters*: To support our Reprogramming program for cardiac regeneration, we are developing a novel transendocardial injection catheter for more precise delivery of therapeutic payloads around the scar area that is formed after heart attack, but in a way that is minimally invasive and would not require heart surgery. The prototype of our catheter was designed with the help of interventional cardiologists and is based on similar catheters that have been successfully used in clinical trials. The catheter is designed to be steered into the heart via the femoral artery in the groin area. It has a deflectable tip that can be curved to better access the different parts of the heart. This initial prototype was tested in a large animal model and was able to direct injections to all areas of the LV. We are adding mapping capabilities to the design to allow for more precise delivery during the treatment procedure.

  The figures below include a picture of an initial prototype of our novel injection-based catheter for our Reprogramming program for cardiac regeneration, plus an illustration of how a deflectable tip plus embedded mapping electrodes can allow for more precise delivery:



- *ROAs*: We prioritize head-to-head comparison of different ROAs in large animal models to confirm the optimal method for delivery for each product candidate. For our Reprogramming program, we have conducted experiments in pig models to demonstrate that a less invasive catheter-based

(1) Source: Duan **J Transl Int. Med** 2020.

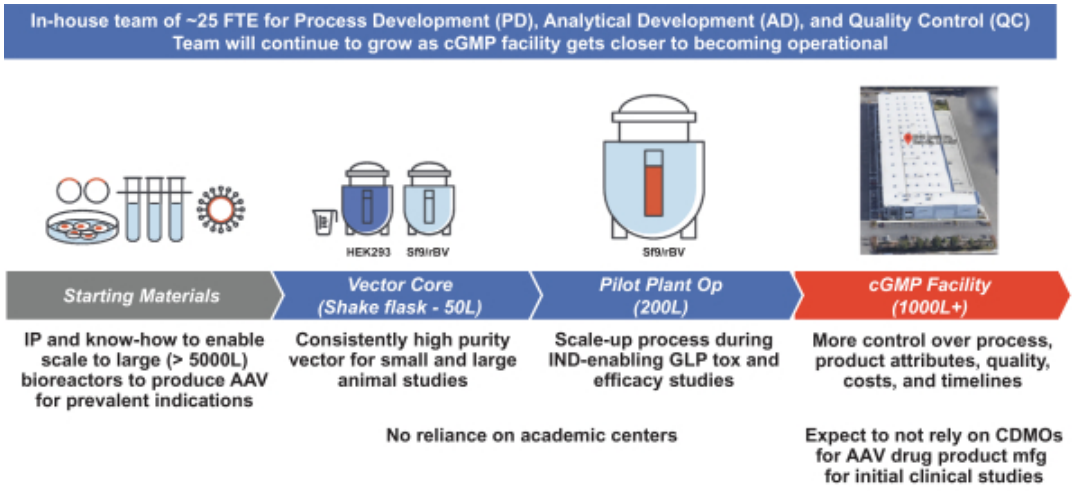
transendocardial injection to the LV inside wall can achieve a similar degree of drug uptake and biodistribution as a more invasive direct epicardial injection to the LV outside wall requiring open-heart surgery. For our MYBPC3 program, we have conducted experiments in NHPs to compare the degree of drug uptake and biodistribution for peripheral IV infusion and infusions delivered directly into the heart.

5. Manufacturing

We are internalizing AAV manufacturing capabilities to support our Gene Therapy and Cellular Regeneration platforms. Our overall strategy is to have total ownership of our PD, AD, and QC so that we have deep insight into the attributes of our drug substance (DS) and drug product (DP). Internalized manufacturing will enable continuous process improvement and innovation that can support manufacturing requirements for clinical development and commercialization not only for rare populations but also for more prevalent indications, and allow us to be a partner of choice in strategic drug development partnerships and with early-stage academic programs.

Overall, the internalization of these efforts provides us with know-how that yields several advantages that allow us to be in a better position to swiftly transfer technology know-how to CDMOs in order to support our future capacity expansion needs or to achieve dual sourcing for product candidates for risk mitigation purposes.

In the figure below, we show the breadth and depth of our current and emerging AAV manufacturing capabilities:



- *Vector core:* We have established vector production to support early research involving both parental and novel AAV capsids at the 50L scale. We have hired key PD, AD and QC personnel to internalize those capabilities. We have also established the necessary PD expertise to support comparable product efficacy in both HEK293-based and Sf9/rBV-based manufacturing systems for both existing AAV serotypes as well as for novel capsids discovered from our capsid engineering efforts.
- *Pilot plant operation:* We have established an in-house Pilot Plant Operation at the 200L scale to support all non-clinical studies including those involving large animal models, such as pigs and NHPs, under Good Laboratory Practice regulations. Our initial production at this scale has been at yields and with full/empty capsid ratios that compare favorably to industry standards.
- *cGMP facility:* We have initiated construction of a dedicated cGMP facility for drug product manufacturing in the San Francisco Bay Area. The facility will initially produce drug product at the

1000L scale to support FIH studies for our MYBPC3 program. The facility will use a modular pod design that will support scale-out and scale-up of manufacturing capacity in response to evolving needs. We expect this facility will be operational in the first half of 2022.

- *Intellectual property:* We have in-licensed certain manufacturing-related intellectual property to support our programs. We have filed a patent application on process improvements that will support scale-up of AAV manufacturing to larger bioreactors necessary for supply of our gene therapy product candidates intended for more prevalent heart disease populations.

Our Programs

MYBPC3 Program for gHCM

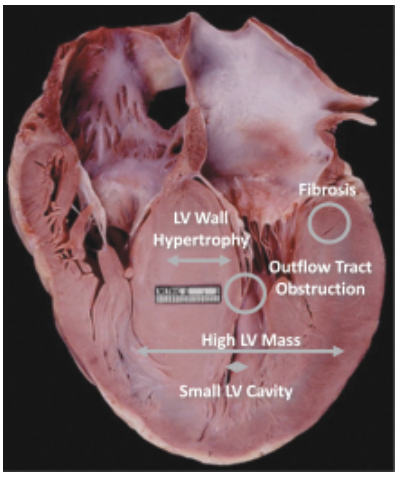
We are developing an AAV-based gene therapy designed to deliver a functional *MYBPC3* gene in adults and children with gHCM due to *MYBPC3* gene mutations, estimated to affect more than 115,000 patients in the United States. These mutations can cause the heart walls of affected individuals to become significantly thickened, leading to fibrosis, abnormal heart rhythms, cardiac dysfunction, HF, and sudden cardiac death in some adults and children. Based on publicly available information to date, we believe there are currently no approved treatments that address the underlying genetic cause of this disease. Our product candidate, TN-201, uses a differentiated approach that enables more robust expression of the *MYBPC3* gene in the heart. We have demonstrated significant and durable disease reversal and survival benefit in a relevant murine model after a single dose, as well as tolerability in mice and non-human primates (NHPs). The program is currently in IND-enabling studies, and we have obtained feedback from multiple regulatory agencies including the FDA, to guide our path to clinical development. TN-201 has also been granted Orphan Drug Designation (ODD) by the FDA. We intend to submit an IND or CTA to the FDA or EMA, respectively, in 2022.

Overview of Hypertrophic Cardiomyopathy

HCM is a condition in which the heart walls become thickened without an obvious cause, resulting in a reduced ability to pump blood effectively. A chronic, progressive disease, HCM is usually caused by the inheritance of mutations in the contractile machinery proteins in the heart muscle cell. Signs and symptoms of HCM may begin in infancy, childhood or adulthood. Mildly and moderately affected patients experience chest pain, have trouble breathing, and have reduced exercise tolerance and fatigue. In certain HCM patients, disease progression results in a substantial limitation in activities and impact on quality of life. The most severely affected patients suffer premature death due to end-stage HF, malignant ventricular arrhythmia, or stroke. HCM with onset in childhood and adolescence is, in particular, associated with significant unmet medical need. When compared with adult-onset HCM, childhood-onset HCM is 36% more likely to develop life-threatening ventricular arrhythmias and twice as likely to require transplant or ventricular assist device.

Patients with HCM can present with either the obstructive form (oHCM) or the non-obstructive form (nHCM) of the disease. Both forms of the disease involve significant LV hypertrophy (LVH); however, in oHCM, the thickening of the LV wall is such that the LV outflow tract (LVOT) narrows and “obstructs” the proper flow of blood out of the LV to the rest of the body. We estimate approximately 50%-65% of HCM patients have oHCM while 35%-50% have nHCM. Both oHCM and nHCM can have equally severe disease presentation involving arrhythmia, HF, reduced quality of life, sudden cardiac death, and overall early mortality.

An example of an actual heart from a patient who had oHCM is shown below, characterized by LVH, high LV mass, LVOT narrowing, an overall small LV heart chamber and fibrosis.

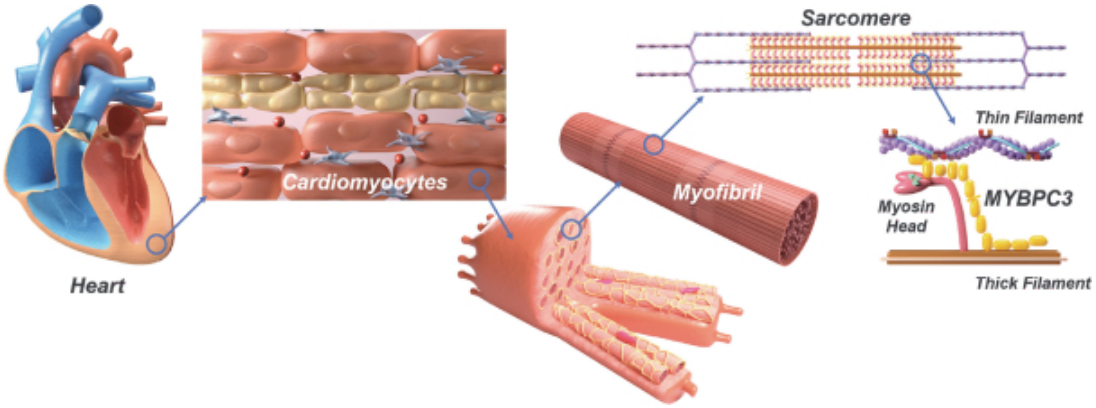


HCM is the most common form of heritable cardiomyopathy and is estimated to affect one in every 500 people, approximating more than 600,000 potential patients in the United States. A majority of HCM patients are currently undiagnosed, with diagnosis typically starting with the onset of symptoms, family screening, or the discovery of an abnormal ECG pattern.

More than 2,000 mutations in eleven or more genes have been linked to HCM. The onset of disease is on average earlier and the disease severity is on average greater for HCM patients with pathogenic mutations in genes involving the sarcomere structure, including the *MYBPC3* gene. Mutations in the *MYBPC3* gene are in fact the most common cause of HCM, estimated to represent approximately 19% of the overall HCM population and to affect approximately 115,000 patients in the United States. Mutations in the *MYBPC3* gene have also been associated with other forms of cardiomyopathy, including DCM, RCM, mixed cardiomyopathy, and ventricular non-compaction,which can lead to poor outcomes, particularly in children.

Disease-causing mutations occur throughout the *MYBPC3* gene, with most mutations being truncating mutations. The phenotype of the patients with these mutations is the same, regardless of the location of the truncation. *MYBPC3* mutations result in both oHCM and nHCM, with one study involving a series of more than 1000 patients finding that 31% of patients with truncating *MYBPC3* mutations presented with LVOT characteristic of oHCM, while 69% of patients had nHCM.

The schematic below illustrates the cellular localization of MYBPC3, within the heart. CMs contain multiple myofibrils, which are comprised of myofilaments containing many sarcomeres. The sarcomeres contain thin filaments containing actin and thick filaments containing myosin; the myosin head binds and pulls actin like a hand on a rope and thus supports normal muscle contraction. MYBPC3 (in yellow) is located between the thin and thick filaments and regulates the folding of the myosin head and its interaction with actin, and in this way, is also a critical element supporting normal muscle contraction. Based on published findings, it has been shown that MYBPC3 is involved in the folding of the myosin head into a state in which the head does not interact with actin or contribute to contraction.



The reduced MYBPC3 protein levels associated with heterozygous mutations in the *MYBPC3* gene result in increased activity of the myosin contractile machinery, which over time leads to LV muscle thickening, known as hypertrophy, excess deposition of extracellular matrix in the cardiac muscle, known as fibrosis, and disorganized muscle cells. As a result, the LV wall stiffens, and the chamber is reduced in size, decreasing the heart's ability to pump. The contractile strength of the muscle declines in some cases, resulting in LV systolic dysfunction, which ultimately can necessitate advanced therapies, such as left ventricular assist devices (LVADs) or transplantation, in the most severely affected patients. Fibrosis and muscle cell disarray may also lead to arrhythmias in some patients, including life-threatening ventricular arrhythmias and atrial fibrillation, which can lead to stroke.

Infants with homozygous *MYBPC3* gene mutations represent a particularly severe patient group with high risk of death within a year after birth without heart transplantation. HCM patients who are heterozygous for *MYBPC3* gene mutations are typically diagnosed earlier in life, have more severe disease associated with increases in arrhythmia, sudden cardiac death and cardiovascular mortality as compared to genotype negative HCM patients.

Analysis of the hearts of patients who carry truncation mutations of the *MYBPC3* gene show on average an approximately 40% reduction in the level of functional MYBPC3 protein. In the most severe cases in which both copies of the gene are affected, there is a complete lack of functional MYBPC3 protein expression. We believe these findings support the idea that mutations of the *MYBPC3* gene cause human disease through haploinsufficiency, and also support the hypothesis that gene replacement may address the underlying cause of disease by increasing the levels of functional MYBPC3 protein.

The current goal of HCM treatment is to relieve symptoms and prevent sudden cardiac death in people at high risk. In current guideline-directed care, patients are typically prescribed one or more symptomatic therapies, including beta-blockers, verapamil, diltiazem, and disopyramide. These therapies do not address the underlying genetic cause of HCM and do not appear to affect disease progression. No randomized clinical trials have assessed these therapies specifically in HCM. The standards of care are slightly different for patients with oHCM versus nHCM, but the unmet need is high in both forms of the disease. Cardioverter-defibrillators may be

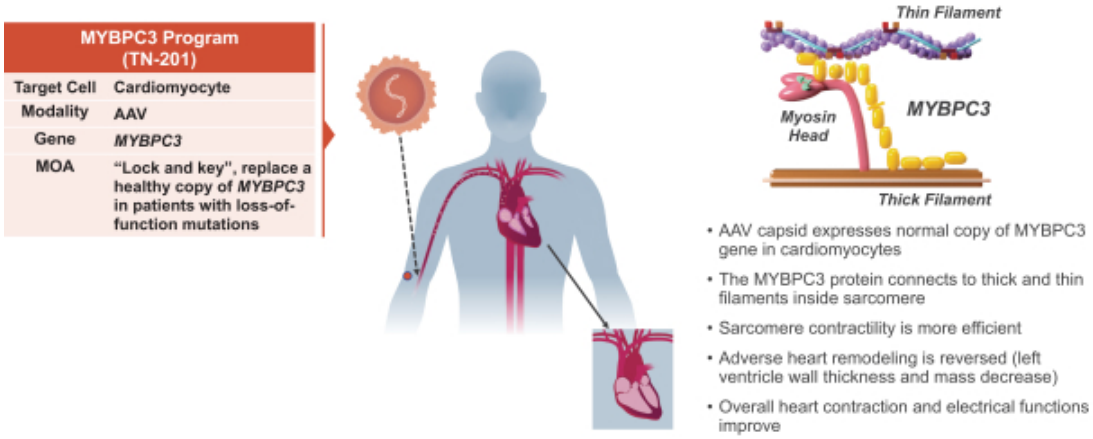
implanted for patients at high risk for malignant arrhythmias and sudden death. For a subset of HCM patients with severe and disabling disease, surgery or other invasive interventions may be appropriate. For patients with oHCM, myectomy is one such option that involves the surgical removal of portions of the septum. Young adult patients with HCM have four-fold higher mortality than the general U.S. population at a similar age; even with a transplant, ten-year survival after transplant for pediatric HCM patients remains less than 50%. Adult HCM patients with LV systolic dysfunction have increased mortality and high rates of cardiac transplantation and LVAD implantation.

Based on publicly available information to date, we believe there are currently no approved therapies specifically for the treatment of HCM and no therapies in clinical development specifically for HCM patients with *MYBPC3* gene mutations.

Our Solution: MYBPC3 Gene Therapy

We are developing an AAV-based gene therapy designed to deliver a fully-functional *MYBPC3* gene driven by our proprietary heart-tropic promoter to restore normal levels of MYBPC3 protein. We believe our product candidate, TN-201, has the potential to address the underlying biological basis of disease in adult and pediatric HCM patients with *MYBPC3* gene mutations.

Based on our preclinical data, we believe that gene replacement, through highly specific and robust expression of *MYBPC3*, has the potential to slow or even reverse the course of gHCM disease in patients with *MYBPC3* mutations, including LV hypertrophy and disease progression leading to outflow tract obstruction, HF, atrial fibrillation, and malignant arrhythmias. By improving upon these aspects of disease, TN-201 may improve heart functional capacity, stabilize or reverse disease symptoms, reduce the need for invasive treatments and improve survival for the most severely impacted patients. As with other AAV-based gene therapies, benefits are expected to be durable and a one-time dose may be sufficient for disease stabilization and potentially reversal. The idea of “lock and key” gene therapy is illustrated in the diagram below.

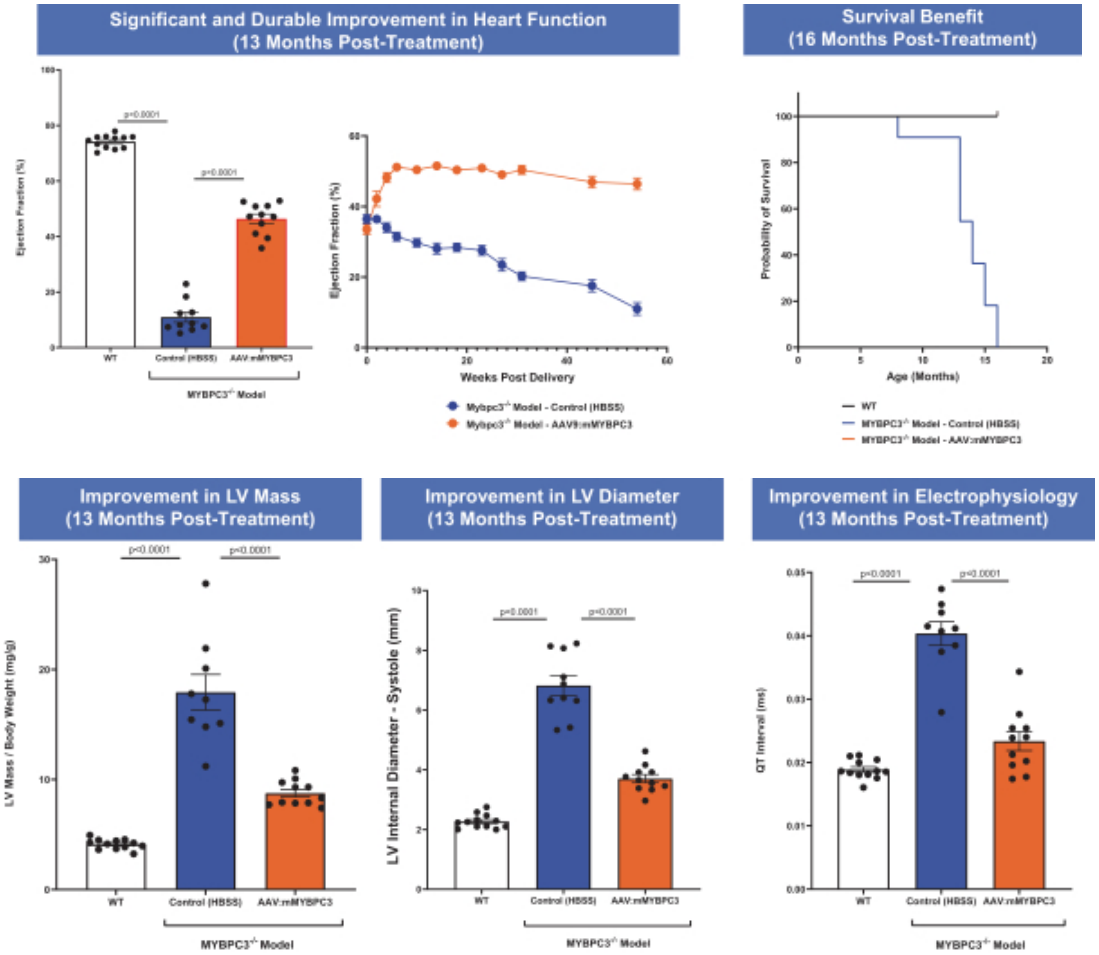


Preclinical Studies

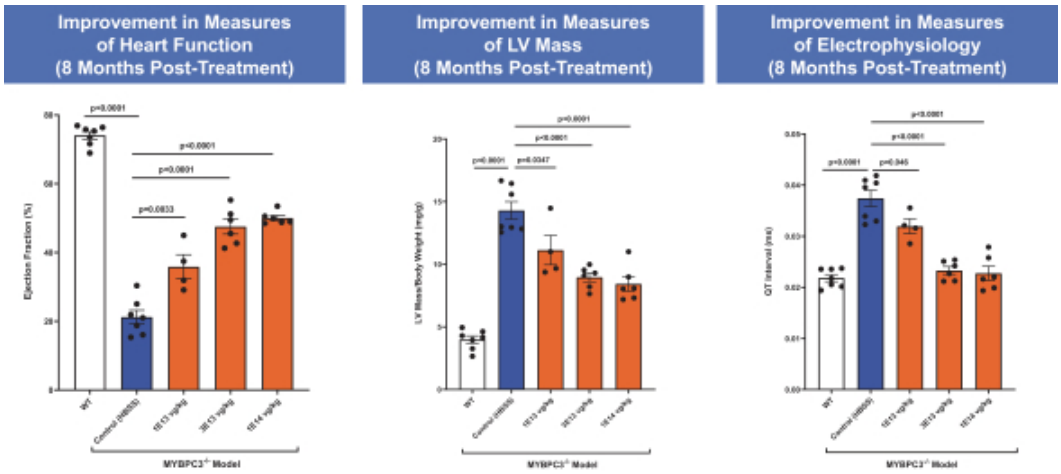
We developed a *MYBPC3* knockout (KO) mouse model that simulates key aspects of the severe gHCM phenotype starting as early as two weeks of age. It is worth noting that this *MYBPC3* KO model is homozygous, i.e., both copies of the gene are missing and so there is no production of the MYBPC3 protein. As expected, the severity of disease and the rate of disease progression are both greater than what is normally observed in most MYBPC3 patients, the majority of whom are heterozygous for *MYBPC3* gene mutations, i.e., they have one normal, healthy copy of the gene that is producing at least some of the necessary MYBPC3 protein, plus one defective copy of the gene that is either producing no MYBPC3 protein at all or that is producing MYBPC3

protein that does not function properly in the sarcomere. The *MYBPC3* KO model is nonetheless useful as it provides important proof of concept for the potentially beneficial *in vivo* effect of the MYBPC3 protein replacement via a gene therapy approach.

In preclinical studies, we systemically administered a version of TN-201 optimized for the mouse (AAV:mMYBPC3) at 1×10^{14} vg/kg in two-week-old *MYBPC3* KO mice. As shown in the figures below, treatment with AAV:mMYBPC3 improved heart function for the KO mice above their pre-treatment baseline levels, indicating partial reversal of the disease with an initial improvement of EF of more than 20% versus untreated controls that eventually increases to more than 30% at 13 months. At more than 13 months post treatment, these measures had not diminished, suggesting that a single systemic dose may be sufficient for a durable reversal of gHCM caused by *MYBPC3* gene mutations. AAV:mMYBPC3 treatment also led to sustained improvements in LV mass normalized to body weight (BW) and EF. There is also a clear survival benefit with 100% survival in the AAV:mMYBPC3 arm and 100% mortality in the untreated control arm out to 16 months following dosing. Additionally, we observed improvements in LV diameter and ECG measurements. A summary of certain pre-clinical data supporting TN-201 was presented at the American Society of Gene and Cell Therapy (ASGCT) conference in 2021. Based on publicly available information, we believe these data are the first known demonstration of significant and durable disease reversal in a severe *MYBPC3* KO model. Similar data have been observed in the *MYBPC3* KO mouse model with our product candidate TN-201, using a human version of the *MYBPC3* gene.



In addition, a dose-response relationship has been demonstrated with AAV:mMYBPC3. As shown below, 1×10^{13} vg/kg, 3×10^{13} vg/kg and 1×10^{14} vg/kg weight-based doses all produced significant improvements in EF, LV mass normalized to body mass (LVM/BM), and measures of electrophysiological function (QT interval) at eight months post-injection in the *MYBPC3* KO HCM mouse model. The 1×10^{13} vg/kg dose had the lowest levels of efficacy, while the 3×10^{13} vg/kg had high improvement in the EF, similar to the 1×10^{14} vg/kg dose, suggesting a plateau in the dose-response curve. A similar dose response has also been observed with TN-201 in the *MYBPC3* KO mouse model.



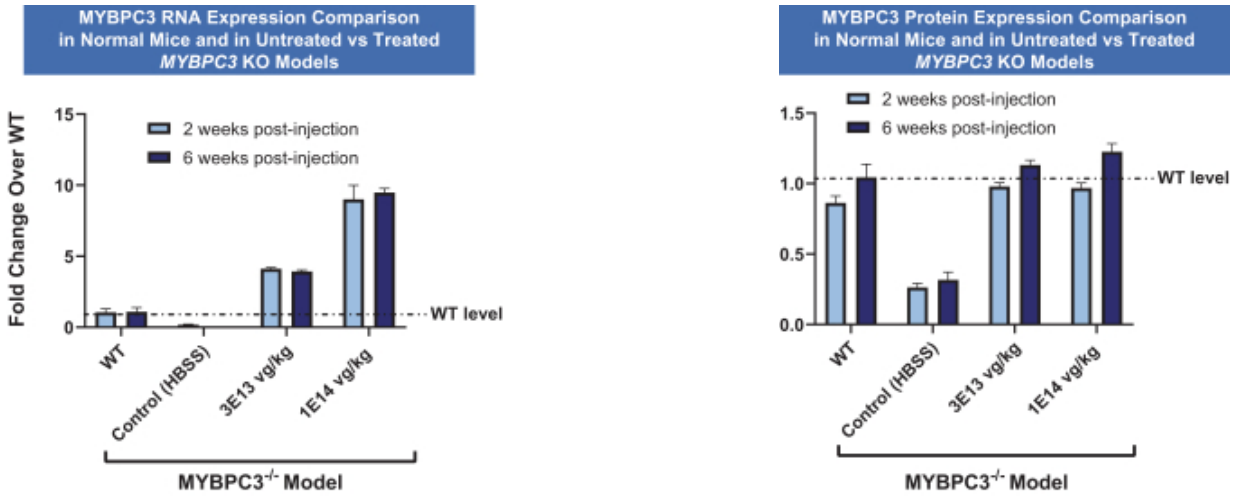
Based on these data, it may be feasible to consider doses for TN-201 in the 3×10^{13} vg/kg to 1×10^{14} vg/kg range during clinical development. This dose range is also within the dose ranges reported by other companies in connection with an FDA-approved product and clinical studies of product candidates using AAV9 for gene therapy, including where the primary intended organ for the product candidate is the heart.

At these doses of AAV9:mMYBPC3, we found that the vector copy number (VCN) from the heart samples of mice and NHPs are equal to or greater than the desired 1 vector genome per diploid genome (vg/dg) threshold. The significance of this threshold is that with a VCN greater than 1, each CM in the heart sample has on average at least 1 functional copy of the *MYBPC3* gene, which we believe may be enough to compensate for the mutated gene. Data in the public domain presented by other companies also demonstrated that AAV9 gene therapies administered at similar doses also resulted in VCN greater than 1 in multiple species including mice and pigs as well as in clinical studies with children and adults.

One-time dosing of AAV:mMYBPC3 at $3x10^{13}$ and $1x10^{14}$ vg/kg achieved normal levels of protein expression in *MYBPC3* KO mouse model hearts within two to six weeks following delivery. As the *MYBPC3* KO model does not produce any functional MYBPC3 protein, these data illustrate that AAV:mMYBPC3 is able to express 100% of the normal level of the protein. By comparison, severe symptomatic patients that are heterozygous for *MYBPC3* truncation mutations on average already produce 60% of the normal level of this protein, we believe suggesting that TN-201 needs to produce no more than 40% of the normal level of MYBPC3 protein in such patients. From our preclinical studies with the *MYBPC3* KO model, we have not observed MYBPC3 protein levels substantially above normal levels, suggesting that protein accumulation does not occur and supporting the potential for a broad therapeutic index with lessened concern of overexpression-related potential toxicities.

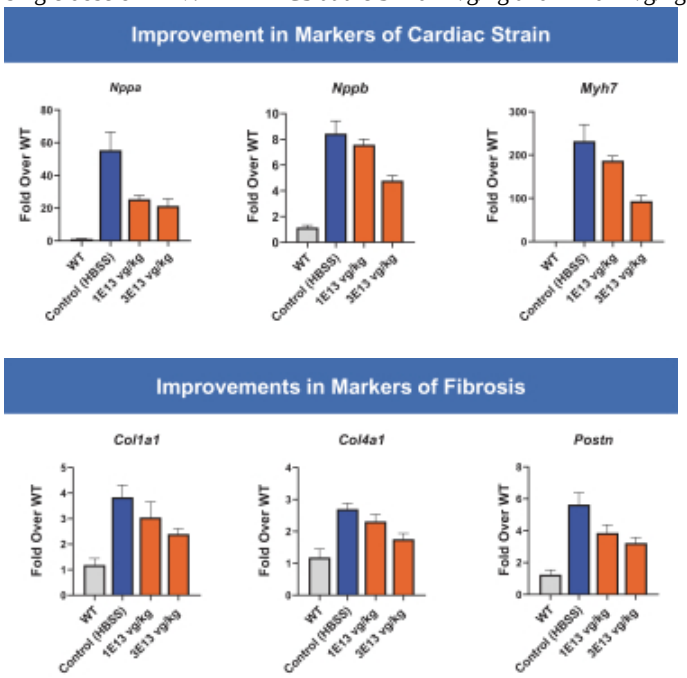
In addition, histological assessments of AAV:mMYBPC3 treated *MYBPC3* KO model murine hearts support the uniform and robust distribution of expression following AAV:mMYBPC3 infusion, suggesting gene therapy may be able to replace the missing *MYBPC3* gene uniformly across the heart and this observation is consistent with heart biopsy samples from patients treated with other AAV9-based gene therapies in development.

The figure below demonstrates a restoration of MYBPC3 protein levels to wildtype levels within two weeks following a single dose of AAV:mMYBPC3 at the 3×10^{13} vg/kg and 1×10^{14} vg/kg dose levels.



Consistent with observed therapeutic benefit, treatment of *MYBPC3* KO mice with AAV:mMYBPC3 is also associated with a substantial reduction of expression of genes associated with fibrosis and B-type natriuretic peptide (BNP), a circulating factor associated with heart damage and heart wall stretch. We intend to evaluate the impact of treatment on BNP as a potential PD biomarker in initial clinical studies.

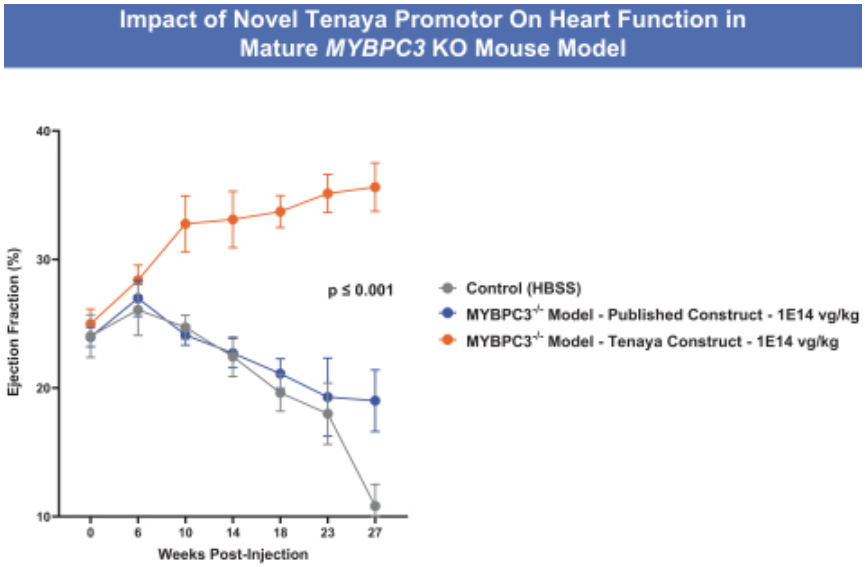
The figures below shows dose-dependent inhibition of expression of genes associated with cardiac strain (Nppa, Nppb, and Myh7) and fibrosis (*Col1a1*, *Col4a1*, *and Postn*) following a single dose of AAV:mMYBPC3 at the 3×10^{13} vg/kg and 1×10^{14} vg/kg dose levels.



Treatment with either TN-201 or AAV:mMYBPC3 in the *MYBPC3* KO model has not been associated with significant BW differences, clinical observations, or differences in histopathological assessments across dose levels. In addition, no impact on BW has been observed at dose levels between 3×10^{13} vg/kg and 6×10^{14} vg/kg in safety studies in wildtype neonatal mice twelve weeks after dosing. The 6×10^{14} vg/kg dose level is estimated to be six to 20 times greater than the approximated target dose, further supporting a broad therapeutic index.

Comparison with Previously Published Results for Our MYBPC3 Gene Therapy

Our approach is differentiated from previously published MYBPC3 gene therapy approaches. During optimization of our MYBPC3 gene therapies, we discovered a CM-specific promoter, TNP-CM1, with improved performance attributes as compared to the standard cTnT promoter. *In vitro* and *in vivo* analyses confirmed that TNP-CM1 significantly increased expression of the *MYBPC3* gene compared to what can be achieved with the standard cTnT promoter. See "Business—Our Approach and Capabilities—3. Promoters and Regulatory Elements." TNP-CM1 has been tested in a hiPSC-CM disease model, in multiple murine models, and in NHPs. As demonstrated below, our proprietary cassette significantly improved heart function in our *MYBPC3* KO mouse model in comparison to a published construct containing a standard cTnT promoter and utilizing the same AAV capsid. These data are also significant as the *MYBPC3* KO models were treated at three months of age (rather than two weeks) suggesting that it is possible to reverse cardiac dysfunction even after significant onset of disease.



Planned Clinical Development

TN-201 was selected as the development candidate for the MYBPC3 gene therapy program. The manufacturing process for TN-201 drug substance has been locked at the 200L scale. We intend to submit an IND or CTA to the FDA or EMA, respectively, in 2022. If our IND or CTA is approved, we plan to initiate global first-in-human studies in patients with *MYBPC3* gene mutations. We have obtained useful feedback from regulatory authorities in multiple countries and the FDA has granted orphan drug designation for TN-201.

As the mechanism of action for TN-201 is relevant for patients with *MYBPC3* gene mutations that present with either oHCM or nHCM, we intend to explore the effect of TN-201 in both populations in clinical studies. During clinical development, we plan to assess clinically relevant PD markers and echo parameters that have been shown to have meaningful changes within a few weeks to months in prior trials of HCM patients.

We also plan to initiate a prospective and retrospective natural history study in patients with *MYBPC3* mutation-associated cardiomyopathy by the end of 2021. The objective of the natural history study, a non-interventional clinical study that follows patients with *MYBPC3* mutations over time, is to characterize the outcomes, burden of illness, risk factors, quality of life, and biomarkers associated with disease progression in patients with cardiomyopathy due to *MYBPC3* mutations as well as treatments, procedures, and patient outcomes.

HDAC6i Program for HFpEF and gDCM

We are developing an HDAC6i small molecule for various forms of HF, including HFpEF. This disease involves systemic inflammation, left ventricular hypertrophy, fibrosis, and diastolic dysfunction resulting in high morbidity and mortality in affected individuals. HFpEF is one of the greatest areas of unmet need in heart disease with more than three million patients in the United States and currently no approved disease-modifying therapies. Our product candidate, TYA-11631, is a differentiated compound with unique chemical structures and high specificity for HDAC6. We have demonstrated *in vivo* activity of our HDAC6 molecules in multiple animal models, including significant disease reversal in two different models of HFpEF as well as tolerability in mice and NHPs. Based on publicly available information to date, we believe, TYA-11631 is the first HDAC6i being developed for heart disease. We have initiated IND-enabling activities and intend to submit an IND to the FDA in 2022.

Overview of HFpEF

HFpEF is generally defined as HF with an EF greater than or equal to 50%. In patients with HFpEF, the LV is stiffened and does not adequately relax, and increased pressure is needed for the ventricle to properly fill. As a result, blood begins to build up inside the left atrium of the heart and eventually swells into the lungs, veins and tissues of the body. HFpEF is progressive in many patients. Symptoms initially include fatigue, shortness of breath, and tissue swelling, resulting in reduced physical activity. Over time, this results in a substantial limitation in activities and impact on quality of life, and patients are at risk of premature death.

At least half of all hospital admissions for HF are related to HFpEF and approximately 24% of the HFpEF population is considered to have New York Heart Association Class III or Class IV disease, representing a disease burden that markedly impacts quality of life and limits physical activity. Among patients hospitalized for HFpEF, readmission for HF and mortality rates over a five-year period are as high as 40% and 75%, respectively.

Patients with HFpEF represent approximately half of HF patients. There are estimated to be over 3,000,000 patients diagnosed with HFpEF in the United States. HFpEF prevalence is rapidly increasing, with prevalence anticipated to increase by more than 45% by 2030. The increase in HFpEF prevalence is at least in part due to the high overlap of this condition with diabetes and obesity which are also on the rise in the United States and globally.

Despite limited data demonstrating efficacy in the HFpEF setting, patients generally receive therapies prescribed for HFrEF, including diuretics, beta-blockers, and ACE inhibitors. Patients with HFpEF are generally not responsive to therapies that have been shown to improve outcomes of patients with HFrEF. Without the development of more effective therapies specifically for HFpEF patients, disease management is mostly directed toward treating associated conditions and symptoms. Despite agreement for the need for therapies that alter the trajectory of HFpEF, clinical trials that have enrolled patients with HFpEF have not led to new therapies that meaningfully improve morbidity or mortality for the HFpEF patient population. We believe that HFpEF remains one of the greatest unmet needs in cardiovascular medicine.

Overview of gDCM

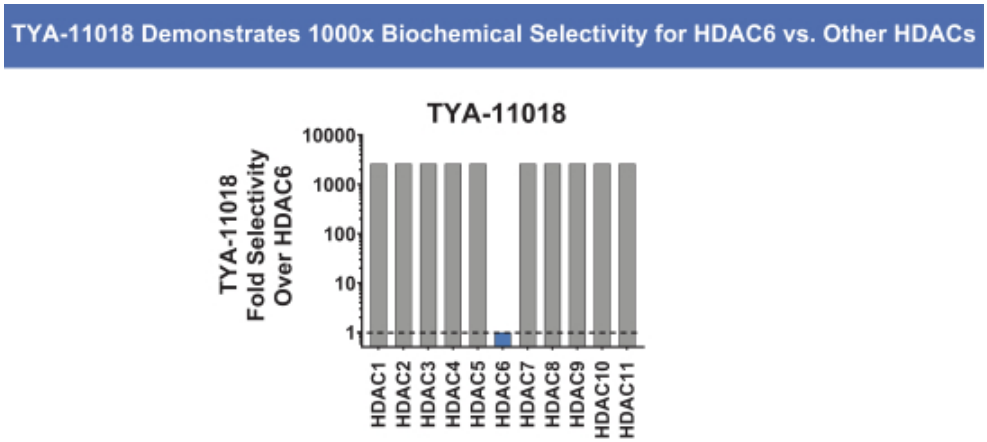
Genetic abnormalities linked to gDCM are estimated to be present in about 30% to 40% of DCM patients. Variants in more than 40 genes have been linked with gDCM with many patients having more than two mutations meeting criteria for causation of DCM. Despite a common disease phenotype, mutations linked to

gDCM are present in proteins with diverse cellular locations within the CM, including localization to the nucleus, cellular membrane, sarcomere, and ion channels. Mutations, deletions, and truncations in one such protein, Bcl2-associated anthanogene 3 (BAG3), have been thought to be causative of DCM in a subset of gDCM patients. Patients with BAG3 DCM represents a particularly high unmet need with an average age of onset of 37 years and an increased rate of heart transplant and LVAD placement. For additional information regarding DCM and gDCM, see the "*DWORF Program for DCM — Overview of DCM*" below.

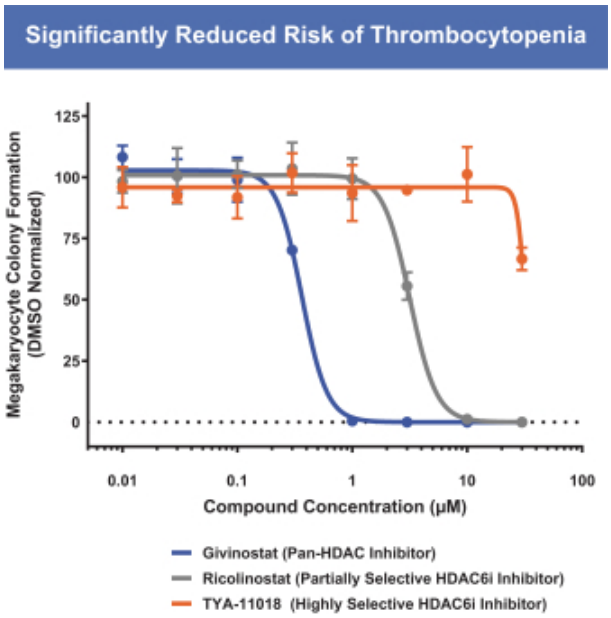
Our Solution: HDAC6 inhibitor (TYA-11631)

We have developed a number of highly selective proprietary HDAC6 small molecule inhibitors (HDAC6i), including TYA-11018 and our product candidate, TYA-11631. HDAC inhibitors have long been considered promising targets for many indications in a range of therapeutic areas, including oncology and other indications. Several partially selective HDAC6i are already in clinical development, but none yet for heart disease. There are currently no other HDAC inhibitors in clinical development for heart disease indications and we intend to be the first to advance a selective HDAC6i into clinical development for the treatment of HF.

Less selective HDAC inhibitors in development in other indications have been associated with dose-limiting toxicities and safety liabilities, such as thrombocytopenia. In contrast, we have identified a number of highly selective and potent HDAC6i with high levels of selectivity for HDAC6. As demonstrated in the figure below, some of our proprietary inhibitors are greater than 1,000 times more selective for HDAC6 than for other HDAC family members.



Internal data indicate that the higher selectivity of our compounds may translate to lower safety risks as compared to other selective compounds. As shown below, in *in vitro* experiments we have observed reduced off-target effects relative to other pan-HDAC inhibitors or partially selective HDAC6 inhibitors in clinical development, as measured by the relative number of megakaryocyte colonies formed in the presence of the compounds tested at different concentrations. No thrombocytopenia has been observed in animal models.

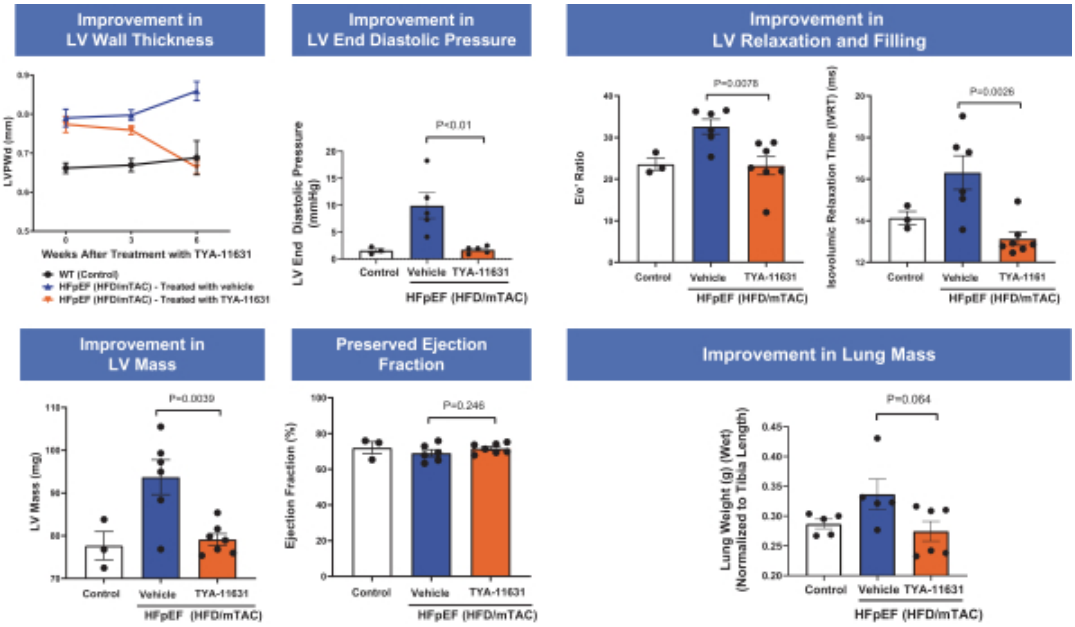


Our product candidate, TYA-11631, has favorable drug-like properties, including pharmacokinetics (PK), oral bioavailability, panel selectivity, protein-binding activity, and cellular toxicity, supporting the potential for once-daily oral dosing in humans. To date, there have been no adverse findings in multiple pilot toxicology studies in rats and NHPs with TYA-11631 and TYA-11018, including no treatment-related mortality, adverse effects in clinical signs, body weight, food consumption, or clinical pathology. We have filed patent applications across multiple chemical series encompassing TYA-11631, TYA-11018, and other potential back-up molecules, as well as patent applications related to methods of use.

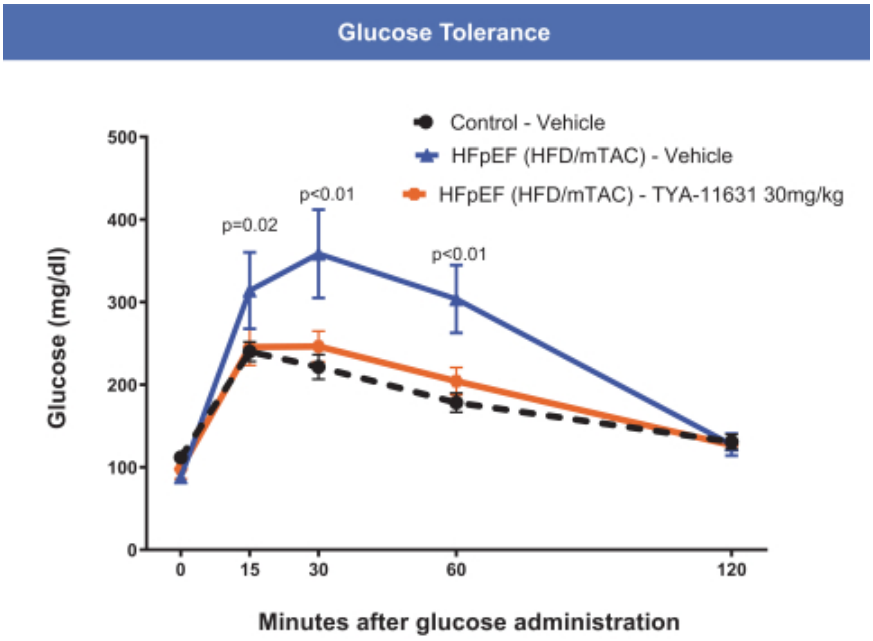
TYA-11631: Preclinical Studies in HFpEF

Treatment with TYA-11631 has reversed measures of HFpEF, including heart filling defects known as diastolic dysfunction, in multiple animal models. In one HFpEF model developed in-house, we surgically applied moderate aortic banding (mTAC) in wild type mice fed a high fat diet (HFD) for eight weeks. These interventions induced a cardio-metabolic HF phenotype that simulated the systemic and cardiovascular features of HFpEF in humans. Aspects of the HFpEF phenotype included increased LV wall thickness, LV hypertrophy, increased diastolic pressure, impaired LV relaxation and filling, and glucose intolerance, all where the EF is greater than or equal to 50%, called preserved EF.

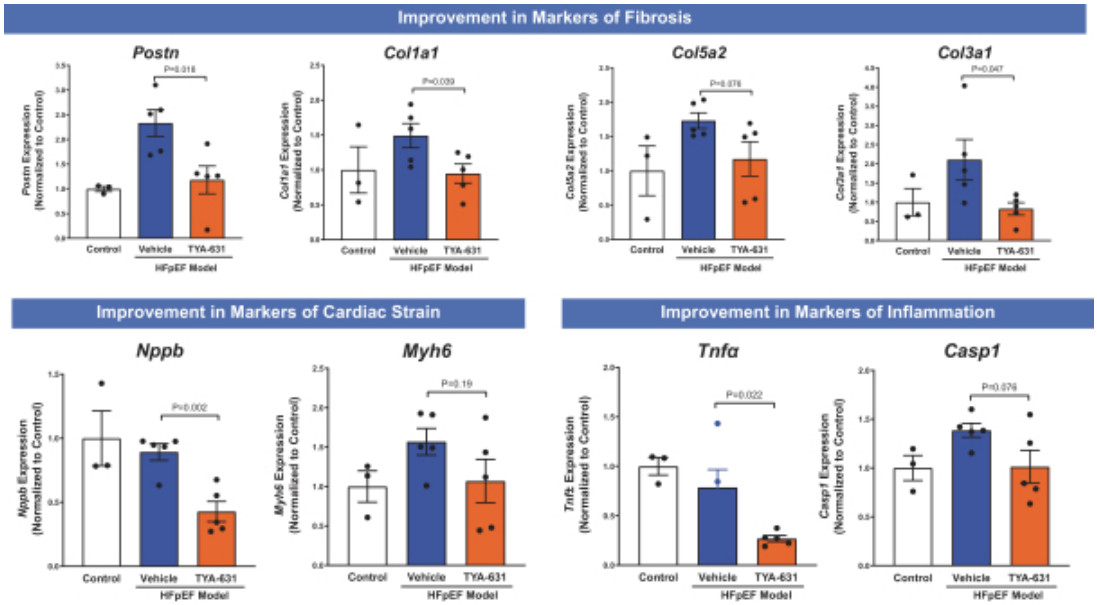
After the HFpEF phenotypes were established, animals were dosed orally with TYA-11631 or vehicle for six weeks. As illustrated below, TYA-11631 treatment reversed HFpEF disease phenotype across all studied parameters, including restoration of LV wall thickness, LV end diastolic pressure, LV relaxation and filling, and LV mass, compared to control. In addition, as shown below, the treated mice exhibited a clear trend of decreased lung weight, indicative of improvement in pulmonary congestion consistent with the reduction of filling pressure.



In addition, as illustrated below, in multiple studies in HFpEF models, we have also observed an improvement in glucose tolerance suggesting that treatment with a selective HDAC6i may have a positive impact on glucose metabolism.

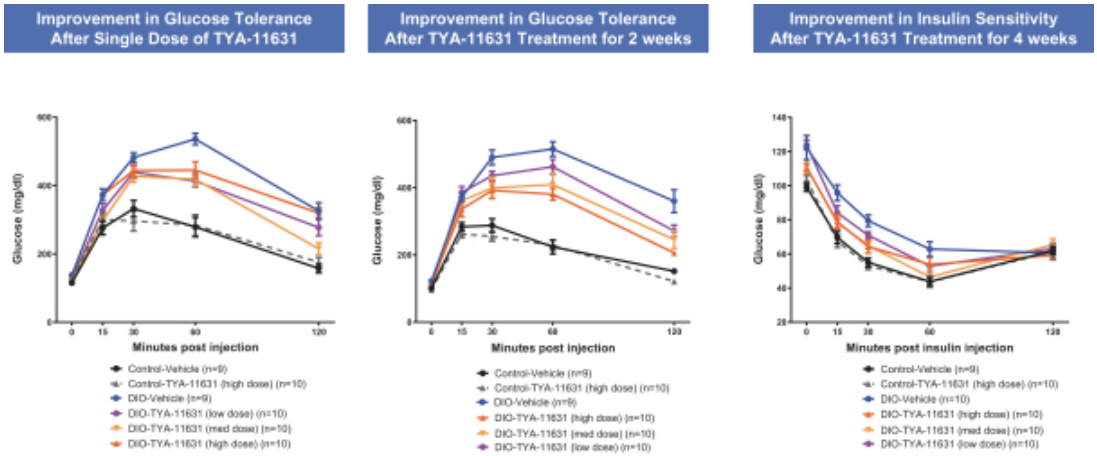


Consistent with the observed improvement in HFpEF phenotype, TYA-11631 treatment in this HFpEF model was also associated with reductions of key biomarkers of fibrosis, hypertrophy and cardiac damage, and inflammation in heart samples compared to levels observed in control animals, as shown in the figure below:

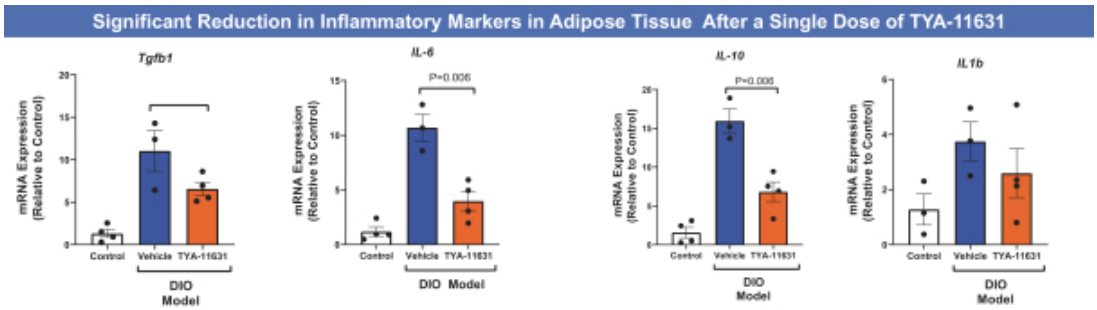


TYA-11631: Preclinical Studies in Models of Metabolic Disease

In addition to improvements in glucose metabolism associated with TYA-11631 treatment in HFpEF mouse models, treatment with TYA-11631 has also lead to improvements in glucose tolerance and insulin sensitivity in a Diet Induced Obesity (DIO) mouse model. As shown below, treatment with a single dose of TYA-11631 improves glucose tolerance in a dose-dependent manner in the DIO model. Furthermore, TYA-11631 treatment improves glucose tolerance in a dose-dependent manner after daily dosing for two weeks and insulin sensitivity in a dose-dependent manner after daily dosing for four weeks.



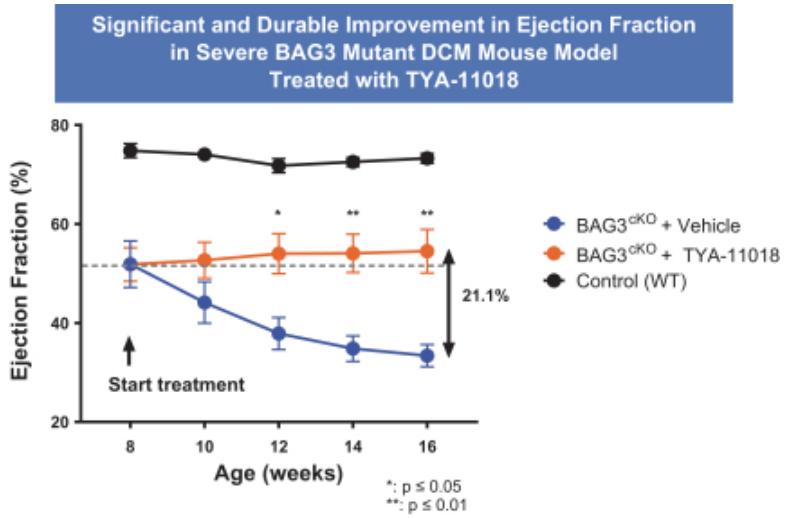
A single dose treatment of TYA-11631 in the DIO model is also associated with a significant reduction in inflammatory markers in adipose tissue relative to controls as shown below. Inflammatory biomarkers in adipose tissue are thought to be linked to glucose tolerance and insulin sensitivity. For example, adipose IL-6 deficiency has been associated with improvements in glucose tolerance. Loss of IL-10 has also been shown to protect mice from DIO and improve glucose tolerance and insulin sensitivity. Collectively, these data are supportive of a role for HDAC6 inhibition on glucose tolerance and insulin resistance with potential applicability to sub-populations of HFpEF patients with obesity, diabetes, or metabolic syndrome.



HDAC6 Inhibitors: Preclinical Studies in DCM

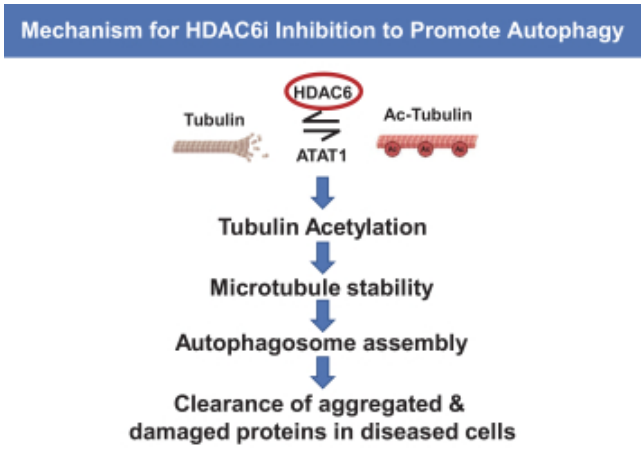
Through our target identification Precision Medicine platform, HDAC6 was initially identified as a target for a genetically defined subset of DCM, BAG3 mutant DCM. We screened a large chemical library to identify compounds able to reverse sarcomere defects in BAG3-deficient iPSC-CMs. Sarcomere defects were rapidly and systemically assessed through our proprietary machine learning algorithms. Whereas a pan-HDAC inhibitor was identified in the initial compound screen as reversing sarcomere defects, we conducted follow-up screens using RNAi knockdowns of HDAC family members to identify HDAC6 as a potential therapeutic target *in vitro*.

We have validated these *in vitro* findings by testing our HDAC6i compounds in BAG3 mutant mice models. As shown in the figure below, treatment of a rapidly worsening mouse model of BAG3 mutant DCM with TYA-11018 resulted in a greater than 20% improvement in EF after eight weeks of treatment compared to a control group treated with vehicle.

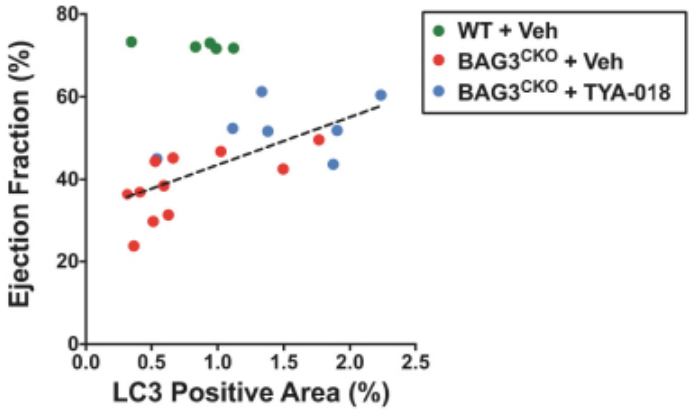


In contrast to other HDAC proteins, HDAC6 is a tubulin deacetylase. When HDAC6 is inhibited, tubulin acetylation is promoted, leading to increased microtubule stability. Increased microtubule stability has been linked to an increase in assembly of vesicles called autophagosomes which are involved in the clearance of aggregated and misfolded proteins in diseased cells. In the diseased heart, one potential mechanism of action for HDAC6 inhibition is promoting autophagy, driving a clearance of aggregated proteins in the heart, and thus restoring normal cellular function and structure. Protein aggregation is characteristic of some forms of DCM and have been linked to CM and cardiac dysfunction. The BAG3 mutant DCM patient population may be particularly sensitive to this mechanism of action for HDAC6 inhibition. BAG3 facilitates autophagy as a co-chaperone protein with heat shock proteins and mutations in the BAG3 gene may lead to potentially defective autophagy in the heart.

The schematic below shows promotion of autophagy as a potential mechanism of action for HDAC6 inhibition in DCM.



The role of HDAC6 inhibition in the promotion of autophagy is supported by biomarker analyses in TYA-11018 *in vivo* efficacy studies in the BAG3 DCM mouse model. As shown in the figure below, one autophagy marker, LC3, increases in correlation with functional measures such as EF in efficacy studies, suggestive of the potential role of autophagy as a mechanism of action for HDAC6 inhibition in DCM.

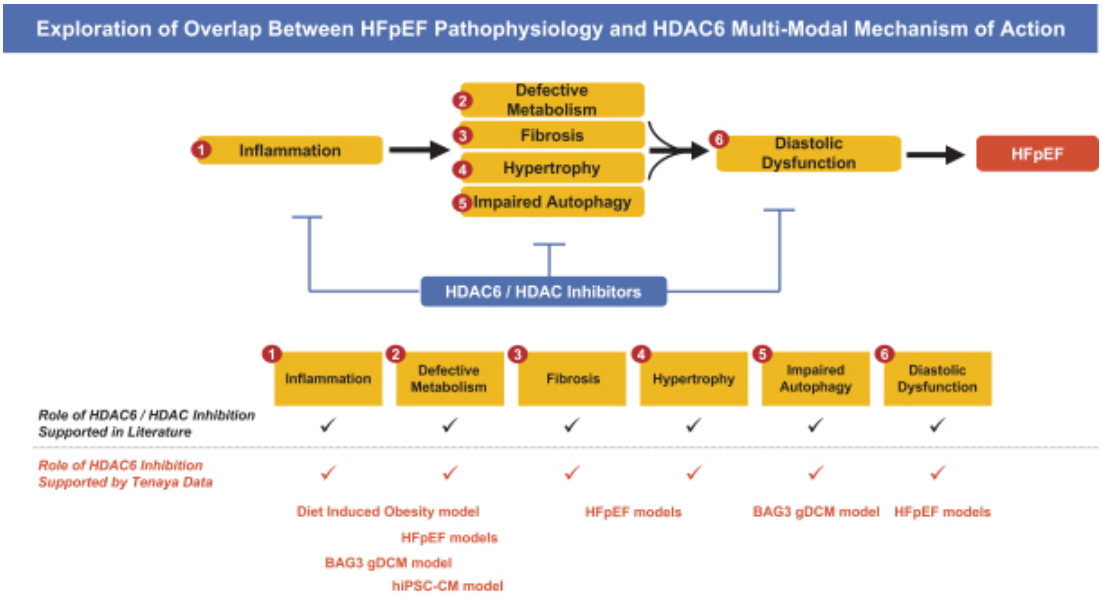


HDAC6 Inhibitors: Potential Mechanism of Action in HFpEF

The pathophysiological mechanisms underlying HFpEF is an active area of scientific research. Key aspects of HFpEF disease biology include oxidative stress and inflammation, cardiac fibrosis, cardiac hypertrophy, cardiac stiffness, which all result in diastolic dysfunction, and decreased ability of the heart to fill its chambers during contraction. Defects in glucose tolerance and insulin sensitivity and overall defective metabolism have also been proposed to play a role in HFpEF onset and progression due to high overlap in the HFpEF population with diabetes and obesity as comorbidities.

HDAC6 has been generally associated with several of these potential HFpEF mechanisms. Our preclinical data generated to date is consistent with what is known in the published literature and is suggestive of a multi-modal mechanism of action that may address multiple aspects of disease.

The schematic below shows a conceptual model of HFpEF disease biology highlighting key aspects (the yellow boxes in the figure below) for which there are external and internal data supporting the potential utility of HDAC6i.



1. *Inflammation / Oxidative stress:* Published studies have linked inhibition of HDAC6 with inflammasome biology and enhancement of regulatory T cell activity. In our preclinical studies, TYA-11631 has shown improvement in inflammatory markers in adipose tissue from the DIO model, while TYA-11018 has shown improvement in inflammatory markers in a BAG3 model of DCM.

2. *Defective metabolism / glucose metabolism:* In a published study, HDAC6 KO mice had a significant improvement in dexamethasone-induced whole-body glucose intolerance and insulin resistance compared to wildtype mice, suggesting that HDAC6 may be an important regulator of gluconeogenesis and glucose metabolism. In our preclinical studies, TYA-11631 has also shown improvement in glucose tolerance in a HFpEF model; dose-dependent improvements in glucose tolerance and insulin resistance in a DIO mouse model; and improvement in glucose uptake in iPSC-CMs. TYA-11018 has also shown improvement in dysregulated metabolic pathways in a BAG model of DCM.

3. *Fibrosis:* In published studies, HDAC6 inhibition by siRNA or partially selective inhibitors attenuates myofibroblast markers and HDAC6 knockdown has been demonstrated to inhibit CF proliferation. In our preclinical studies, TYA-11631 significantly improved markers of cardiac fibrosis in a HFpEF model.

4. *Hypertrophy:* Published studies illustrate that HDAC inhibitors can prevent cardiac hypertrophy in animal models in response to various hypertrophic stimuli. In a published study, HDAC inhibition suppressed cardiac hypertrophy and fibrosis in a model of hypertension through regulation of HDAC6/HDAC8 enzyme activity. In our preclinical studies, TYA-11631 has also shown improved in LV hypertrophy in multiple HFpEF models.

5. *Impaired autophagy:* Published studies illustrate the role of reduced autophagy in HFpEF and in aging hearts. In our preclinical studies, TYA-11018 has shown improvement in autophagy in a BAG model of DCM that was correlated with improvement in heart function.

6. *Diastolic dysfunction:* In a published study, pan-HDAC inhibitors improved diastolic dysfunction in two distinct murine models of HFpEF and HDAC inhibition improved cardiopulmonary function in a feline model of diastolic dysfunction. In our preclinical studies, TYA-11631 has also shown improved diastolic dysfunction in multiple HFpEF models.

TYA-11631: Planned Clinical Development

We plan to submit an IND to the FDA in 2022 and, if approved, initiate first-in-human safety studies in healthy volunteers before initiating proof-of-concept studies and proof-of-activity studies. During clinical development, we plan to examine the role of TYA-11631 in sub-populations of HFpEF patients with obesity, diabetes or metabolic syndrome as well as potentially in sub-populations of gDCM where there is stronger alignment between the multi-modal mechanism of action of TYA-11631 with the pathophysiology of the disease.

PKP2 Program for gARVC

We are developing an AAV-based gene therapy designed to deliver a functional *PKP2* gene in adults with gARVC due to *PKP2* gene mutation, estimated to affect more than 70,000 patients in the United States. These mutations can cause enlargement of the RV in affected individuals, replacement of heart muscle with fibrotic tissue and fatty deposits, and severely abnormal heart rhythms (arrhythmia) that can make it harder for the heart to function properly and result in sudden cardiac death in some adults and children. Based on publicly available information to date, we believe there are currently no approved treatments that address the underlying genetic cause of this disease. We have demonstrated prevention of disease progression and survival benefit in a murine model after a single dose. Based on publicly available information to date, we believe these data are the first known demonstrations of durable disease modification, survival benefit, and prevention of arrhythmia using an AAV:PKP2 gene therapy construct. This program is currently at the candidate selection stage.

Overview of ARVC

ARVC is largely an inherited disease characterized by the progressive loss of muscle cells in the heart's RV and replacement with a composite of fibrotic tissue and fatty deposits. As a result of this structural change, the heart becomes dilated and is prone to ventricular arrhythmia (VA) and particularly ventricular tachychardia (VT) (abnormally high heart rate).

When symptoms are present, they tend to occur around 30 years of age, with the mean age of presentation in patients before the age of 40 years old. Patients with ARVC most commonly present with symptoms related to VA (such as palpitations, lightheadedness, and fainting) or cardiac arrest. ARVC is an important cause of sudden cardiac arrest in young patients, and particularly in athletes. The median age at cardiac arrest in ARVC patients is 25 years old.

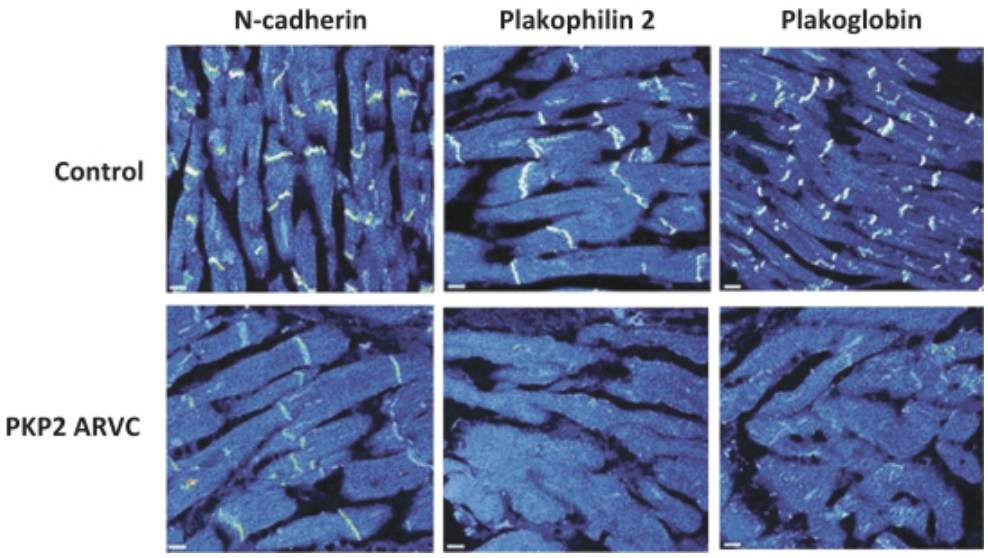
ARVC has an estimated prevalence in the general population of approximately 1:2000. Mutations in the *PKP2* gene are the most common genetic cause of ARVC, with approximately 41% to 46% of ARVC patients carrying pathogenic variants. We therefore estimate more than 70,000 patients in the United States are affected by *PKP2* mutations.

Mutations of the *PKP2* gene are inherited in an autosomal dominant fashion i.e. a mutation in one gene is sufficient to cause the disease. Over 14 mutations have been linked to the *PKP2* gene. Most of these mutations are predicted to result in a truncated protein product, which suggests a disease mechanism due to loss of function, resulting in haploinsufficiency.

As illustrated below, the PKP2 protein is an integral component of cell adhesion protein complexes known as desmosomes which connect adjacent CMs in the heart. Desmosomes are responsible for stabilizing the heart and for maintaining channels called gap junctions that allow for cellular communication among heart cells, which in turn is important to proper synchronization of CM contractions across the myocardium contributing to each heartbeat.

Other components of desmosome include desmoplakin (*DSP* gene), desmoglein 2 (*DSG2* gene), desmocollin 2 (*DSC2* gene), desmin (*DES* gene), and plakoglobin (*JUP* gene). Mutations of the *DSP*, *DSG2*, *DSC2*, *DES*, *JUP* can also cause gARVC, illustrating the importance of the structural integrity of the desmosome complex. Patients with *PKP2* mutations typically present at a younger age than patients carrying other mutations linked to ARVC and are thought to follow a similar disease progression to other ARVC patients.

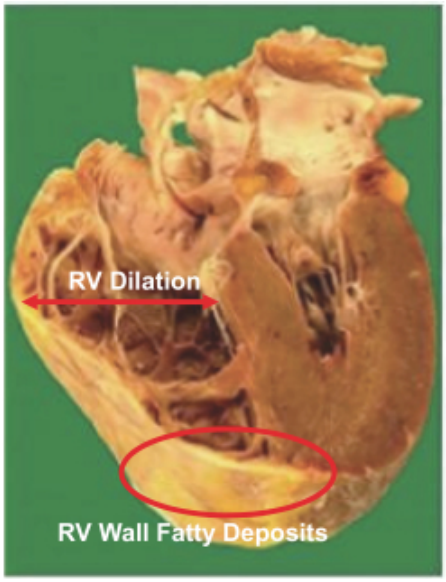
The figure below[2] analyzes heart tissue from an ARVC patient with the *PKP2* mutation and compares it to the heart tissue from a normal individual. The tissue has been stained for desmosome proteins PKP2 and plakoglobin as well as other transmembrane proteins that are not part of the desmosome but that are also present at cell-cell junctions in different body organs (e.g., N-cadherin). As illustrated, N-cadherin, PKP2, and plakoglobin are all correctly localized to the junctions between CMs in the healthy control sample. However, when the *PKP2* gene is mutated, N-cadherin continues to correctly localize but both the PKP2 and plakoglobin proteins are no longer properly localized to the desmosome. Based on publicly available information to date, we believe these data illustrate how PKP2 protein is critical to maintaining the structural integrity of the desmosome, and that mutations in the *PKP2* gene are enough to disrupt this complex in human hearts.



As a result of this impairment, CMs can become detached from each other when placed under the normal mechanical stress of the beating heart, or under the extra mechanical stress in the heart caused by athletic activity. This detachment causes cell death, which in turn causes inflammation, scar formation, and fat deposition.

[2] Source: Asimaki et. al. **NEJM** 2009.

An example of an actual heart from a patient who had ARVC is shown below(3). This illustrates commonly seen abnormalities in ARVC hearts as a result of the improper function of the desmosome, including dilation (enlargement) of the RV chamber and replacement of healthy heart tissue by fibrotic tissue and fatty deposits.

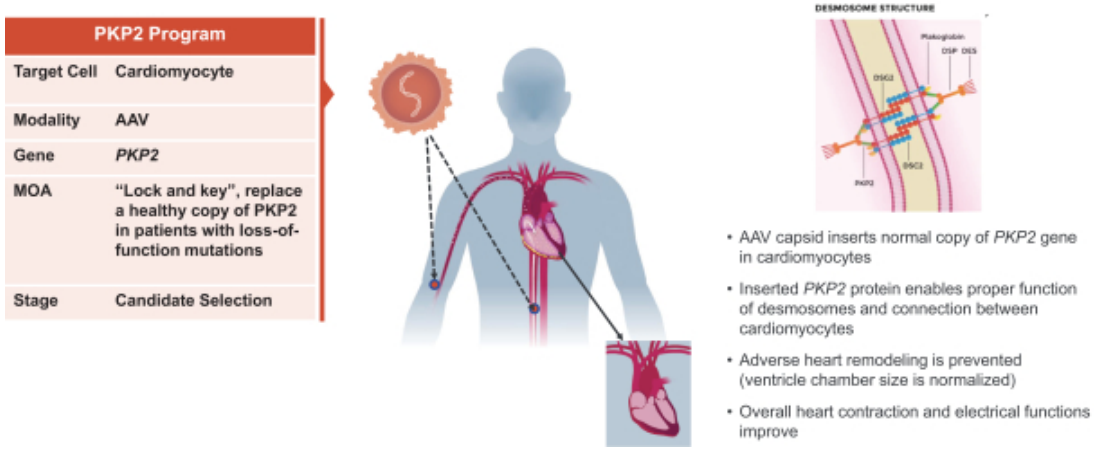


Following a diagnosis, ARVC patients are typically implanted with an Implantable Cardioverter Defibrillator (ICD) placed to control arrhythmias and treated with beta-blockers. ICD implantation may be associated with complications in some patients, including potential for heart perforation and additional surgery. Patients may progress to catheter ablation procedures which have a high rate of recurrence of VA and have not been shown to reduce risk of sudden cardiac death or improve survival. Despite the availability of these treatments, clinical HF has been documented in up to 40% of ARVC patients, and when heart transplantation is required, transplants occur at an average age of 40 and within seven years of the onset of HF symptoms. There are currently no approved therapies that address the underlying genetic causes of ARVC.

(3) Source: Pinamonti et. al **World J Cardiol** 2014.

Our Solution: PKP2 Gene Therapy

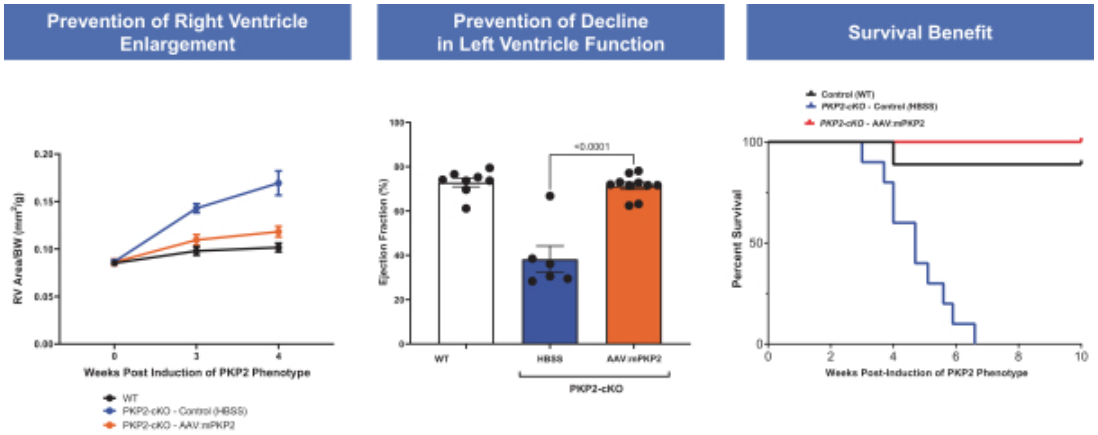
We are developing an AAV-based gene therapy to deliver the fully-functional copy of the *PKP2* gene to deliver a fully functional copy of the human *PKP2* gene to the hearts of gARVC patients carrying *PKP2* mutations. We believe that gene replacement through delivery of the *PKP2* gene to CMs represents a promising "lock and key" treatment that can address the underlying cause of this disease. As the disease is most often caused by haploinsufficiency, expression of a functional *PKP2* gene to replace the missing PKP2 protein in CMs is expected to restore proper structure and function of the desmosome. This in turn can prevent adverse heart remodeling and improve heart contraction and electrical function. The *PKP2* gene will be delivered using AAVs with tropism for the heart and expression of the PKP2 protein will limited to the heart through use of a CM-specific promoter. Our PKP2 gene therapy program, illustrated below, is currently at the candidate selection stage.



Preclinical Studies in PKP2-cKO Model

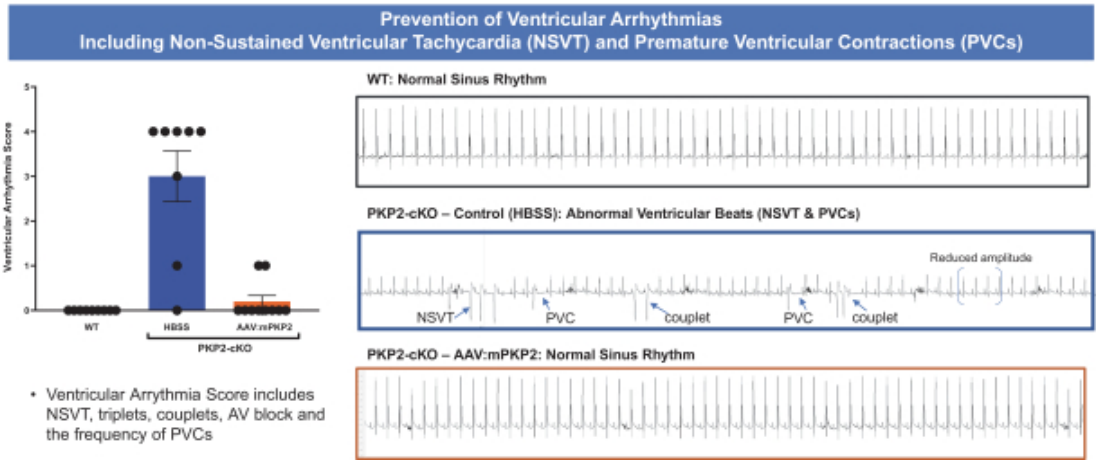
We developed a *PKP2* conditional knockout (*PKP2*-cKO) mouse model that simulates key aspects of gARVC including dilation of the right ventricle, decline in left ventricular heart function, severe arrhythmia, abnormal ECG trace, and early mortality. The onset of symptoms is very rapid and within three weeks after induction of the phenotype. It is worth noting that this *PKP2*-cKO model is homozygous, i.e., both copies of the gene are missing and so there is no production of the PKP2 protein. As expected, the severity of disease and the rate of disease progression in this are both greater than what is normally observed in most *PKP2* patients who are almost all heterozygous for *PKP2* gene mutations, i.e., they have one normal, healthy copy of the gene that is producing at least some of the necessary PKP2 protein, plus one defective copy of the gene that is either producing no PKP2 protein at all or that is producing PKP2 protein that does not function properly in the desmosome. The *PKP2*-cKO model is nonetheless useful as it provides important proof of concept for the potentially beneficial *in vivo* effect of the PKP2 protein replacement via a gene therapy approach.

In preclinical studies, we systematically administered AAV:mPKP2 in *PKP2*-cKO mice in parallel with induction of the ARVC phenotype. As shown in the figures below, AAV:mPKP2 treatment improved several ARVC phenotypes compared to saline-treated controls (HBSS), including preventing right ventricle enlargement, preventing decline of LV function, and improving survival after a single IV dose.

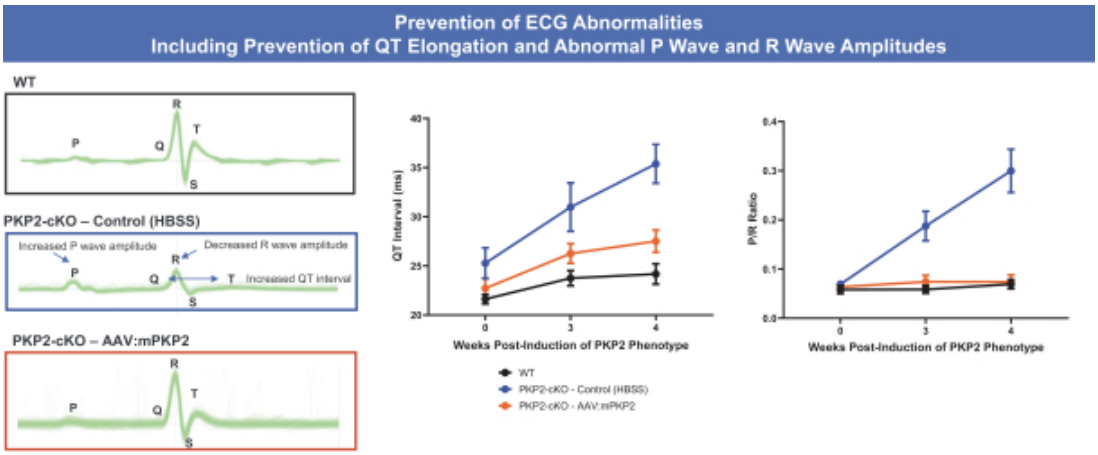


In addition, *PKP2* gene therapy also corrected the hallmark electrophysiological defects associated with ARVC. The graphs below show nearly complete prevention of the arrhythmia in *PKP2*-cKO animals treated with AAV:mPKP2 versus controls, including prevention of nonsustained ventricular tachycardia (NSVT) and premature ventricular contractions (PVCs), which were reduced nearly to wild levels as apparent from the ECG trace and the from the quantification with a Ventricular Arrythmia Score measuring the incidence of spontaneous arrhythmias during 30 minutes of recording.

Ventricular Arrythmia Score	
Description	**Score**
• Sustained Ventricular Tachycardia (S-VT), Ventricular Fibrillation (VT) • Sudden Cardiac Death (SCD)	5
• Non-Sustained Ventricular Tachycardia (NSVT)	4
• > 100 Premature Ventricular Contractions (PVC), Couplets or Triplets	3
• > 50 and < 100 PVCs, Couplets or Triplets	2
• < 50 PVCs, Couplets or Triplets • Premature Junctional Complex (PJC) • Atrioventricular (AV) Block	1
• < 10 PVCs, Couplets or Triplets	0



The graphs below show normalization of the QRS complex in *PKP2*-cKO animals treated with AAV:mPKP2 versus controls, including prevention of QT elongation (as measured by QT interval) and abnormal P wave and R wave amplitudes (as measured by the P/R ratio).



Based on publicly available information to date, we believe these data are the first known demonstration of durable disease modification, survival benefit, and prevention of arrhythmia using an AAV:PKP2 gene therapy construct.

Planned Clinical Development

We intend to submit an IND or CTA to the FDA or EMA, respectively, no earlier than 2023. If our IND or CTA is approved, we plan to initiate global first-in-human studies in patients with truncation mutations of the *PKP2* gene.

DWORF Program for DCM and HFrEF

We are developing an AAV-based gene therapy designed to deliver the *DWORF* gene for patients with DCM, estimated to affect about one million patients in the United States. DCM is a progressive and life-threatening disease that causes left ventricle (LV) enlargement, LV wall thinning, insufficient contraction, reduced blood flow, ventricular arrhythmias, and can result in premature morbidity and need for heart transplant in affected individuals. DWORF is a muscle-specific micro-peptide first discovered by our co-founder Eric Olson, Ph.D. that acts on the sarcoplasmic/endoplasmic reticulum Ca2+ ATPase 2a (SERCA2a) pathway, widely considered to be a promising target in HF. We and our academic collaborators have accumulated significant preclinical *in vivo* proof-of-concept evidence for the therapeutic benefit of over-expression of the *DWORF* gene in multiple murine models, including models of gDCM and HFrEF, as well as tolerability in murine models. Based on publicly available information to date, we believe these are the first demonstrations of the potential benefit of AAV:DWORF. This program is currently at the candidate selection stage.

Overview of DCM

DCM is broadly defined as HF where the EF is below 40% and the LV walls are thin and over-expanded, leading to insufficient contraction, reduced blood flow pumped by the heart, and abnormal heart rhythms. DCM can be caused by a variety of mechanisms, including genetics, coronary artery disease, high blood pressure, heart attack, and viral infection due to a high risk of ventricular arrythmias.

DCM is a life-threatening and progressive disease. Once symptoms appear, a patient's condition typically declines progressively. Typical symptoms of HF due to DCM include shortness of breath, fatigue, swelling in the

extremities, or an irregular heartbeat. As the disease progresses, patients become increasingly debilitated and experience sustained shortness of breath, even at rest. Diastolic function, or the heart's ability to relax and fill with blood, is also impaired because the heart is already expanded and fibrotic. The dilated LV is deprived of an adequate supply of oxygen that may contribute to further fibrosis and the risk of dangerous heart rhythm disturbances. At any stage of the disease, whether or not symptoms have appeared, DCM patients are at risk of sudden cardiac death.

A subset of DCM is caused by genetic mutations in proteins involved in muscle contraction. Mutations in one such protein, phospholamban (PLN), can cause DCM. These mutations are believed to result in abnormal regulation of calcium biology instrumental in muscle contraction, leading to ventricular dilation, fibrosis and HF over time. Some patients with PLN mutations have a high severity of disease, including patients with R9C and R14del mutations.

It is estimated that DCM affects about one million people in the United States, with genetic abnormalities linked to DCM estimated to be present in about 30% to 40% of DCM patients. PLN mutations are rare with an estimated 0.5% of DCM patients carrying PLN mutations.

Current therapy for DCM generally uses therapies developed for HFrEF. While current pharmacologic therapies have improved prognosis and the quality of life of DCM patients, the premature morbidity and mortality rate remains unacceptably high. End-stage DCM is the leading indication for use of last line therapies, including LVADs and heart transplantation. Within five years of diagnosis, 43% of patients with advanced DCM have either died or needed a heart transplant. Thus, there is a large unmet need for novel and more individualized therapeutic options.

Overview of HFrEF

Among patients with HF, the amount of blood that is pumped out of the LV (LV EF), can vary significantly, and is often characterized as reduced if below 40% (HFrEF), mid-range if between 40% to 50% (HFmrEF) or preserved if greater than or equal to 50% of normal LV EF (HFpEF).

Approximately 50% of HF cases are HFrEF, representing a prevalence of nearly four million patients in the United States. In addition, the incidence and prevalence of HFrEF continues to rise. This increase is driven by an aging population, improved survival from MI and other forms of heart disease, and the increasing prevalence of predisposing risk factors such as diabetes and obesity.

HFrEF patients continue to have substantial unmet need despite advances in pharmacological treatments, with up to 30% of treated patients experiencing a significant limitation in physical activity. Development of HF continues to be associated with significant morbidity and mortality, with a one-year mortality rate of 7% and one-year hospitalization rate of 32%. Over a five-year period, readmission for HF and mortality rates are as high as 48% and 75%, respectively, highlighting the significant and increasing burden of illness for patients and healthcare systems.

The standard of care for HFrEF involves multiple different classes of therapies, including ACE inhibitors, beta blockers, vasodilator, aldosterone antagonists, and others. For end-stage HFrEF patients refractory to medical therapy, the treatment options are limited to LVADs and heart transplantation. LVADs have a finite duration of efficacy and are associated with the potential for fatal complications, frequent hospital readmissions, and high treatment cost. Heart transplant availability is restricted by the scarce supply of donor organs, risk of transplant rejection, and lifelong treatment with immunosuppression therapeutic regimes that are associated with organ damage.

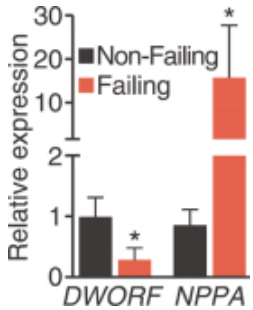
Our Solution: DWORF Gene Therapy

We are developing an AAV-based gene therapy to deliver the *DWORF* gene to CMs for the treatment of DCM and HFrEF. DWORF is a recently discovered small peptide that localizes primarily to the sarcoplasmic

reticulum of the cardiac muscle cell. During muscle cell activation, calcium is released from sarcoplasmic reticulum into the muscle cell's cytosol and into the sarcomere, leading to muscle contraction. Sarcoplasmic/endoplasmic reticulum Ca2+ ATPase 2a (SERCA2a) is a major isoform of SERCA expressed in CMs and plays an essential role in the regulation of cardiac contractility. SERCA2a transports calcium from the cytosol back into the sarcoplasmic reticulum, preserving the calcium gradient required for contraction. DWORF binds to SERCA2a and displaces the inhibitory PLN peptide, resulting in increased SERCA2a activity, increased levels of calcium pumped into the sarcoplasmic reticulum, and increased muscle contraction, ultimately leading to an improvement in heart function.

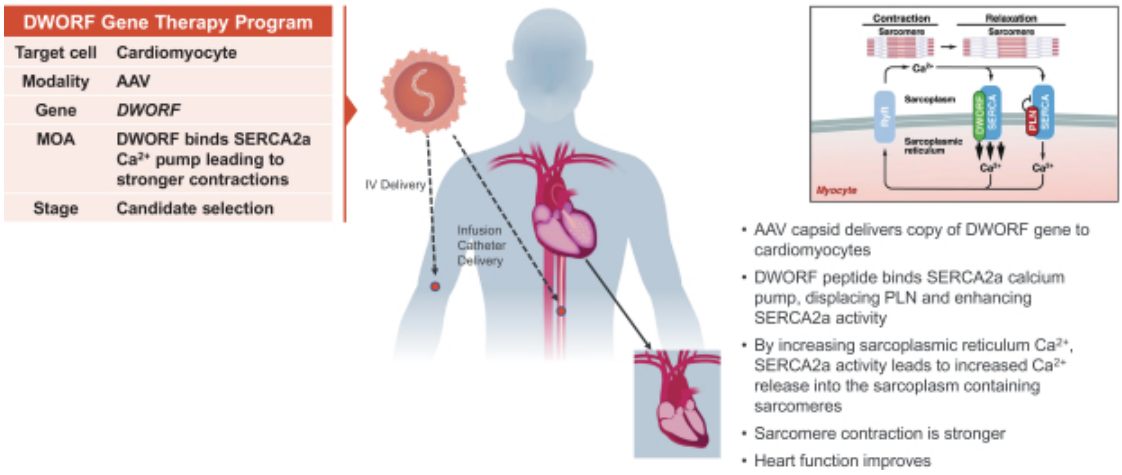
We believe DWORF is an ideal target for the treatment of HFrEF. DWORF is a small peptide that is readily expressed when delivered by AAV. The small size of the *DWORF* gene leaves additional room in the AAV capsid to include optimized combinations or promoters and regulatory elements to tailor *DWORF* gene expression levels. In addition, published studies have shown that *DWORF* gene expression is lower in failing human hearts compared to non-diseased hearts.

The figure below shows expression analyses in human HF tissue. DWORF mRNA is reduced in failing hearts whereas atrial natriuretic peptide (NPPA) mRNA, a marker of congestive HF, is significantly increased in failing hearts.



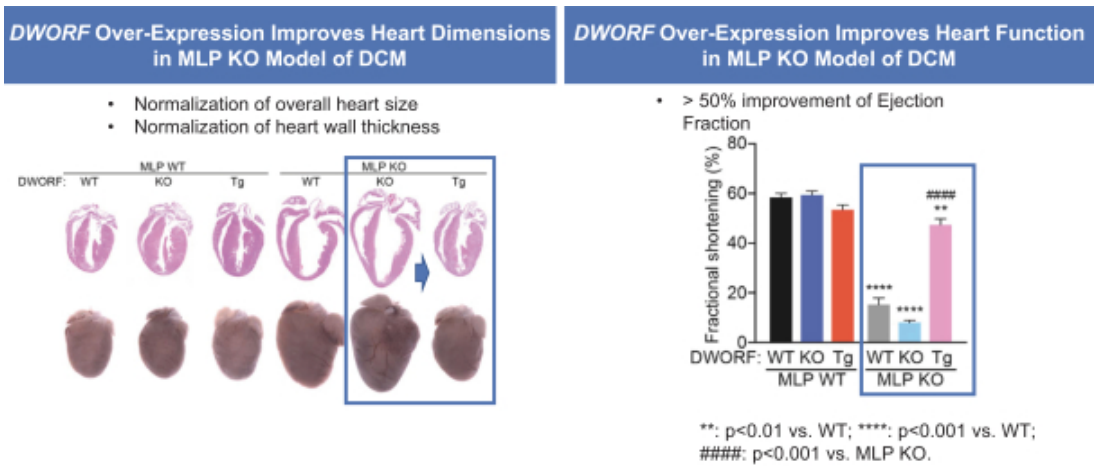
One therapeutic hypothesis is that restoring *DWORF* gene expression to normal levels, through treatment with a *DWORF* gene therapy, may normalize calcium flux in CMs and increase contractile strength in DCM patients as well as the broader HFrEF patient population. In addition, DCM patients carrying PLN mutations have mutant PLN peptides that inhibit SERCA2a and decrease contraction. *DWORF* gene therapy produces DWORF peptides that directly compete with mutant PLN peptides by preferentially binding with SERCA2a, which can increase muscle contraction, potentially resulting in halting or even reversal of disease progression.

Our DWORF program, illustrated below, is currently at the candidate selection stage with multiple constructs under consideration. *DWORF* gene expression is limited to the CM through use of a novel CM-specific promoter. Our intended product candidate will use an AAV capsid with high tropism for the heart, either AAV9 or a novel proprietary capsid developed through our capsid engineering capabilities, to deliver the *DWORF* gene. We are exploring different ROAs including systemic (IV) or delivery directly to the heart through an infusion catheter.

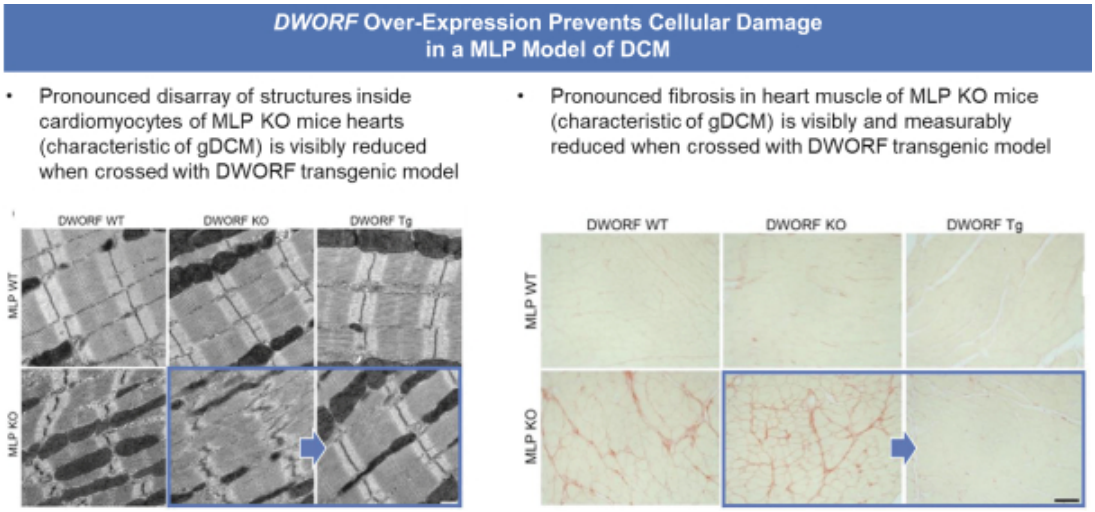


Preclinical Studies

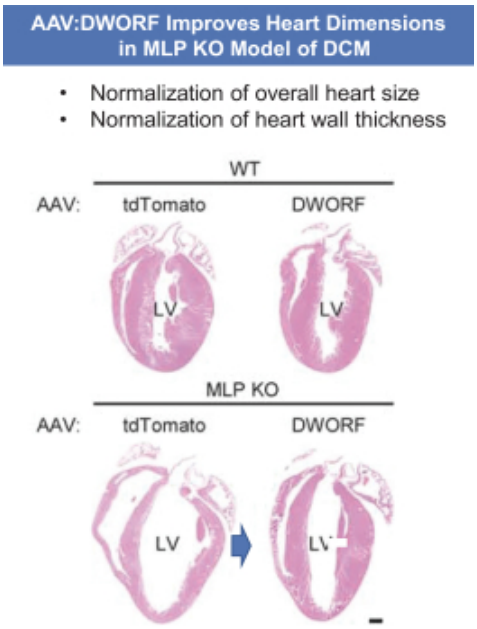
Results in DCM (with MLP KO model): Overexpression of *DWORF* has led to improvements in multiple parameters in mouse models of DCM. Our co-founder Eric Olson, Ph.D. has demonstrated that overexpression of *DWORF* in a transgenic (Tg) model leads to improvements in heart size, normalization of wall thickness and also improvements in EF, as demonstrated in the Muscle Lim Protein (MLP) KO mouse model of DCM, a model considered representative of the broader DCM population.



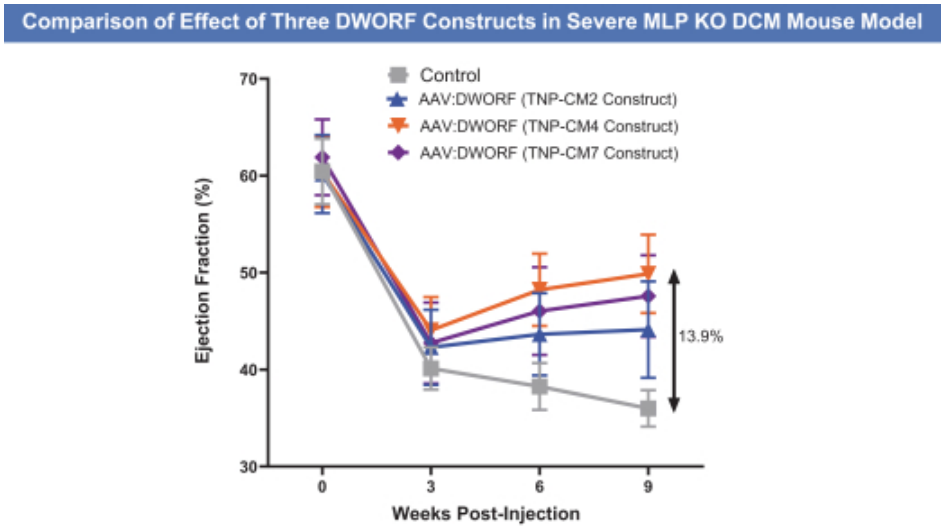
In addition to improvement in heart function, as shown in the figure below, Tg DWORF overexpression also prevents muscle cell disarray and fibrosis in the MLP KO model of DCM.



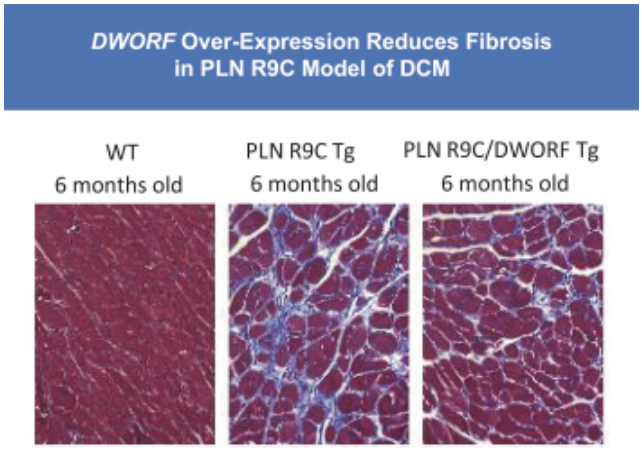
Treatment with AAV:DWORF constructs has shown similar improvements in heart remodeling following treatment. As shown below, experiments conducted in the lab of Eric Olson demonstrated improvements in heart remodeling with an AAV:DWORF construct in the MLP KO mouse model.

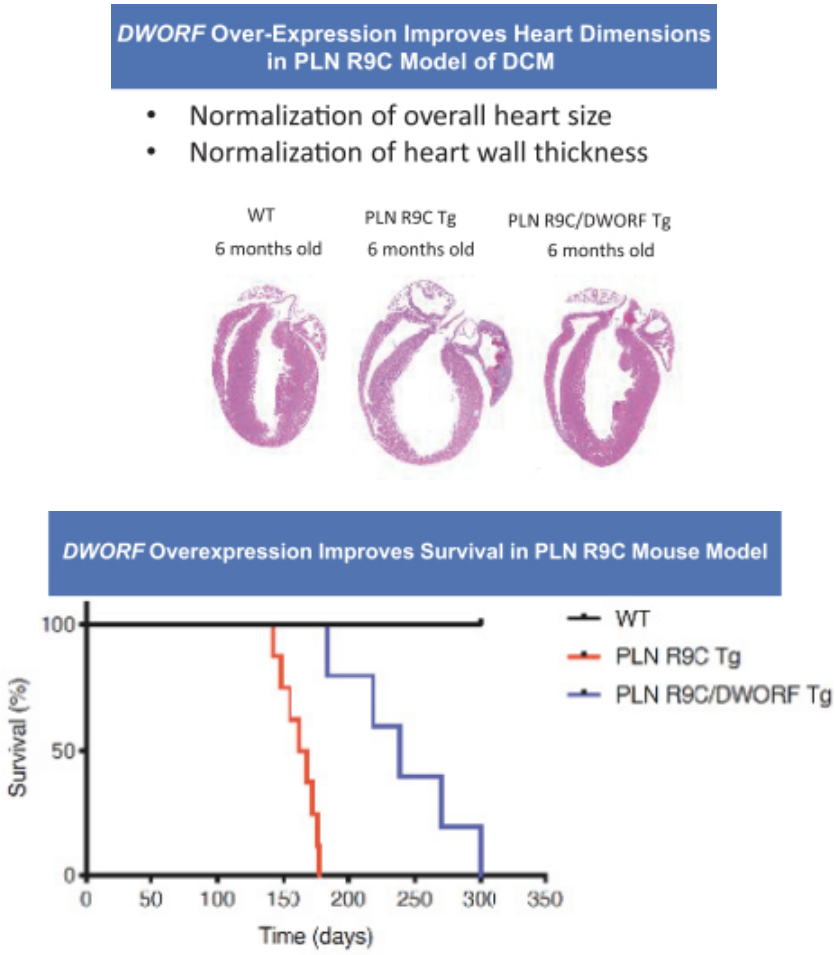


We have also demonstrated improvement in the same MLP KO model using our proprietary AAV:DWORF constructs. We have developed multiple proprietary promoters that drive multiple different levels of expression. As shown below, AAV:DWORF constructs containing these promoters (TNP-CM2, TNP-CM4, and TNP-CM7) improved in EF relative to a saline control in the MLP KO mouse model of DCM, with improvements in EF as high as approximately 14% achieved with constructs containing the TNP-CM4 promoter:



Results in DCM (with PLN Mutant Models): Overexpression of *DWORF* has also demonstrated meaningful improvements in mouse models of PLN mutant DCM. In experiments conducted in the lab of Eric Olson, mice with PLN R9C mutations are characterized by strong PLN inhibition of the SERCA2a calcium pump, resulting in decreased calcium flux, reduced heart muscle contraction, and decreased heart function. Tg overexpression of *DWORF* has been shown, as illustrated below, to improve fibrosis and heart remodeling in animals six months of age and improve survival in this genetic model of HF.





We have tested different AAV:DWORF constructs in both healthy and disease mouse models and have not observed any safety signals at clinically relevant levels of *DWORF* overexpression.

Planned Clinical Development

After selection of our product candidate, we plan to initiate IND-enabling studies. We intend to submit an IND or CTA to the FDA or EMA, respectively, no earlier than 2023. During clinical development, we plan to examine the role of AAV:DWORF in DCM as well as potentially in sub-populations of HFrEF where there is alignment between AAV:DWORF with the pathophysiology of the disease.

Reprogramming Program for HF due to Prior MI

We are developing an AAV-based approach to cellular regeneration that involves converting (or reprogramming) existing CFs within the heart to turn into new CMs and to replace cells permanently lost due to MI. There are estimated to be more than four million patients in the United States living with HF due to prior MI. The loss of CMs in affected individuals permanently impairs heart contraction, leading to HF and potentially fatal arrhythmias, and the death of approximately 5% to 10% of MI survivors within the first year. There are currently no approved treatments that address the underlying loss of heart tissue. The potential utility of our unique approach to creating new CMs was first demonstrated by our co-founder Deepak Srivastava, M.D. We

have discovered a proprietary combination of three genes that can drive robust *in vivo* reprogramming of CFs to CMs when delivered together in a single AAV capsid. Based on publicly available information to date, we believe our results in a pig model of HF due to prior MI represent the first-ever successful demonstration of the potential benefit of this approach in a human-sized heart. This program is currently at the candidate selection stage.

Overview of HF due to prior MI

CAD is the single most common cause of HF. CAD is often associated with an MI, in which blood flow to a section of the heart, usually the LV, becomes limited, causing the cells in that section of the heart, including CMs and CFs, to die. The heart cannot replace the lost CMs while the CFs multiply significantly, resulting in scar tissue formation and stiffening of the LV walls, leading to progressive and irreversible cardiovascular remodeling. As a result, the heart continues to lose its ability to pump as strongly and may fail over time. In addition to HF, these patients also have a persistent risk of arrhythmias and increased likelihood of a second heart attack or sudden death.

In the United States, greater than 800,000 people have a heart attack every year; of these approximately 200,000 already had a prior heart attack. Approximately 20% of patients age 45 and older will have another heart attack within five years of their first one. Despite advances in treatment options, mortality due to heart attack is still high; data from the U.S. National Vital Statistics Reports shows the median life expectancy among individuals aged 65 to 69 who have had a heart attack is just 8.3 years as compared to 18.7 years among those who have not.

There are no known therapies that address the loss of CMs associated with MI and the resulting morbidity and mortality.

Our Solution: Direct In Vivo Reprogramming of Resident CFs to Create CMs

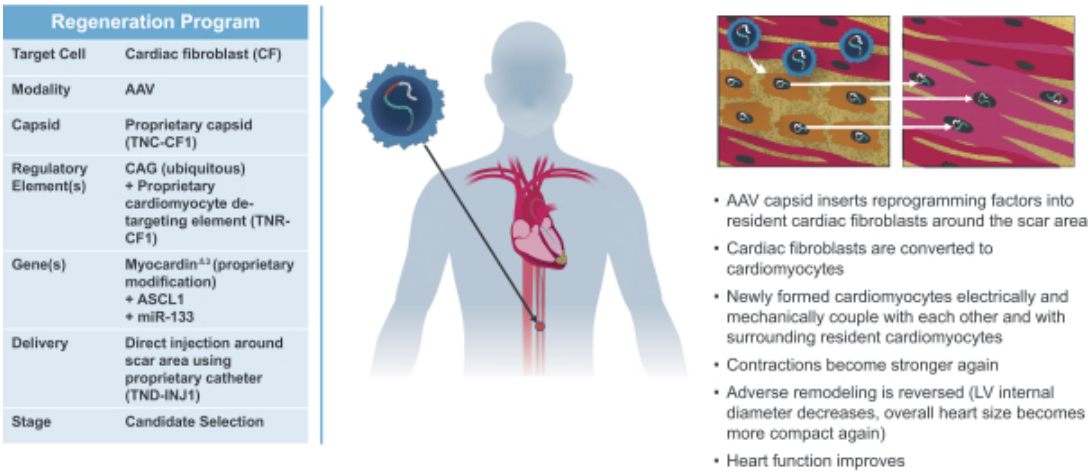
Cellular reprogramming is the process of converting cells of one type into another cell type. Shinya Yamanaka and John Gurdon won the Nobel Prize for their discovery that cells in the body can be reprogrammed to become stem cells, called iPSCs, capable of developing into any other type of cell in the body using a combination of four transcriptional factors. Since then, researchers have also found other combinations of factors capable of directly converting cells from one type to another without first going through the iPSC state. Dr. Srivastava, one of our co-founders and a member of our board of directors, was the first to demonstrate direct reprogramming of CFs into CMs in both *in vitro* and *in vivo* models, creating the potential for a new approach to cardiac regeneration.

Building on this pioneering work, we have developed a novel AAV-based therapy for direct *in vivo* reprogramming of resident CFs into CMs to replace the CMs lost due to an MI. Our goal is to convert the CFs into new CMs to help repair the heart after an MI, and ultimately slow down, stabilize or even potentially reverse the progression to HF. Our approach leverages substantial in-house advances in our reprogramming factors, capsid engineering, regulatory elements, and drug delivery to translate cardiac reprogramming science towards clinically relevant solutions.

- *Reprogramming factors*. Through extensive *in vitro* screening efforts in actual human CFs, we identified a unique combination of three genes encoding Myocardin, ASCL1, and miR-133 that together can drive robust direct *in vivo* reprogramming of CFs to CMs, and that we have designed to fit into a single AAV. We use the term reprogramming factors to refer to such combination of genes and any other combinations of genes that when delivered together in a single AAV into CFs, result in the direct reprogramming of the CFs into CMs.
- *Capsid engineering*. While AAV9 can be used to target CMs, it does not sufficiently transduce CFs. We have discovered a novel capsid, TNC-CF1, which has a higher transduction efficiency for human CFs as compared to currently known AAV serotypes. Initial data suggest this novel capsid may also be less susceptible to neutralizing antibodies compared to known serotypes.

- *Regulatory elements*. We have pursued rigorous, iterative optimization efforts to create proprietary reprogramming products. We have further optimized Myocardin and cassette regulatory elements to both decrease cassette size and improve reprogramming efficiency. After extensive exploration of single and double promoter strategies, we have selected the CAG promoter to drive robust expression of our reprogramming factors. We limit expression of our reprogramming factors in mature CMs by including a miR-208 binding site that decreases reprogramming factor expression in mature CMs after differentiation from fibroblasts.
- *Drug delivery*. We are developing, in conjunction with leaders in interventional cardiology, a proprietary percutaneous endomyocardial injection catheter (TND-INJ1) to inject and deliver our gene therapies around scars in the heart in a non-surgical, minimally-invasive procedure. Many potential sites for future clinical studies have experience with endomyocardial injection catheters through previous and ongoing cell therapy studies.

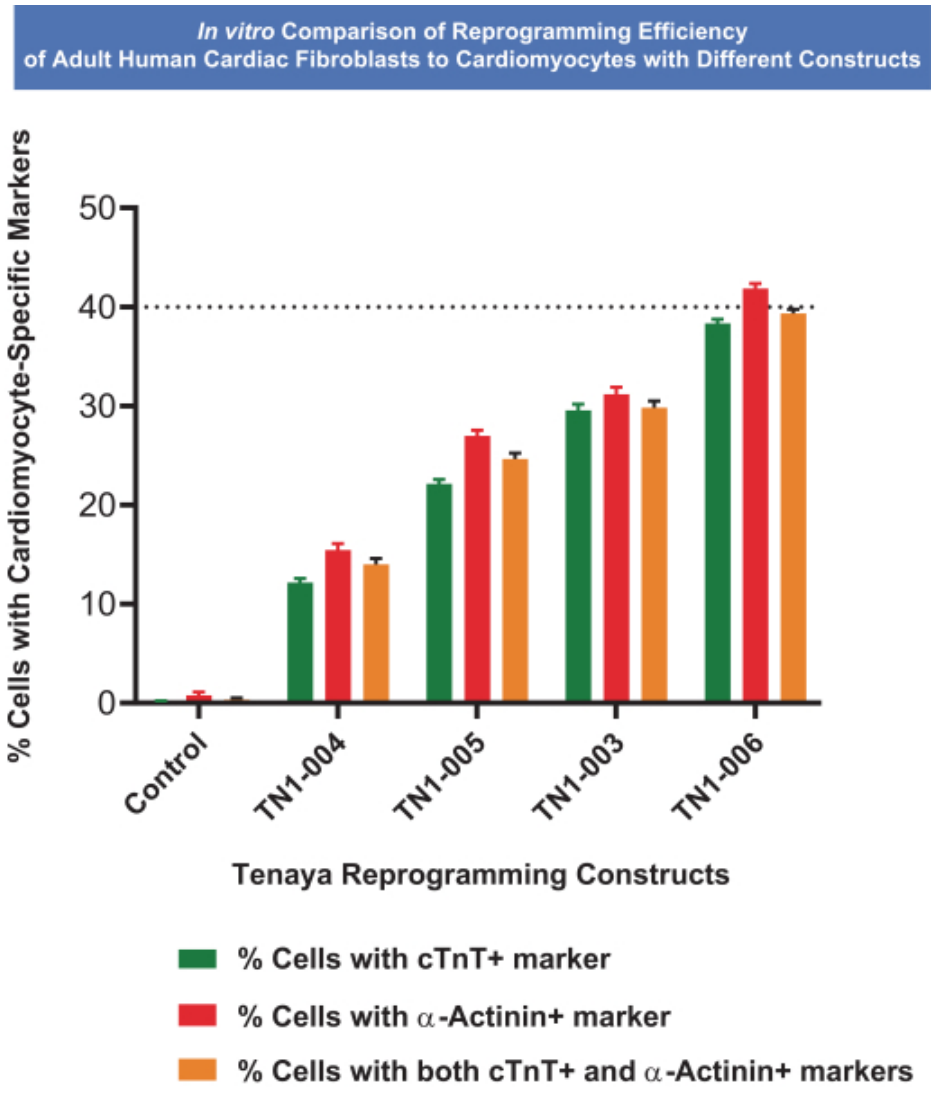
The schematic below summarizes the components of our intended reprogramming gene therapy product candidate and mechanism of action.



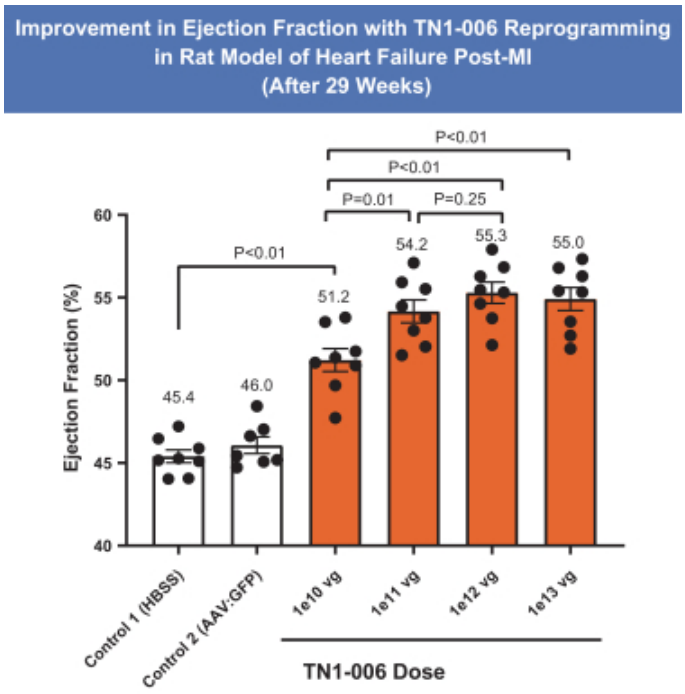
Preclinical Studies

We have conducted *in vitro* and *in vivo* experiments to optimize our direct reprogramming approach. Our most advanced results have been achieved primarily with two different constructs, TN1-002 and TN1-006. A summary of certain preclinical data supporting the Reprogramming program in general and TN1-002 in particular was presented at the ASGCT conference in 2020.

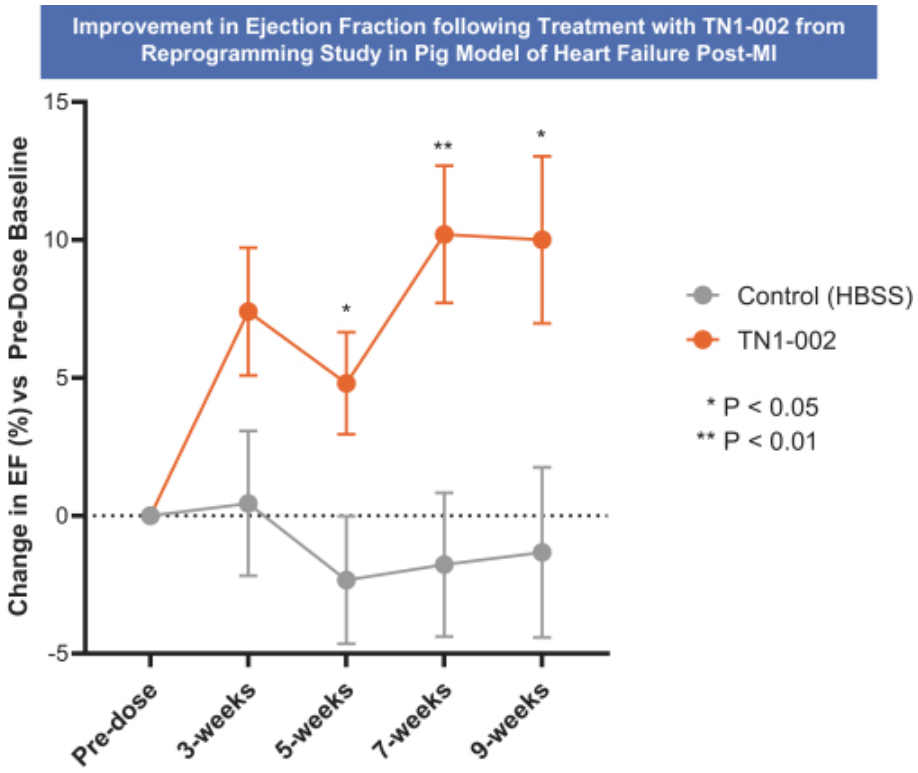
- *Results from in vitro conversion of human CFs*. Our reprogramming approach has been optimized *in vitro* in adult human CFs. We have conducted extensive iterative experiments to compare the relative efficiency of various constructs to convert CFs to CMs. CM-specific markers like cTnT and a-Actinin are measured to determine the proportion of cells that have been converted from CFs to CMs. The figure below illustrates the results from such an experiment, demonstrating how our TN1-006 construct can convert approximately 40% of human CFs to CMs:



- *Results from rodent disease models*. We have demonstrated durable and dose-dependent improvement in EF in both mouse and rat models of HF following an induced MI. In our rat model, TN1-006 was injected directly around the scar area formed two weeks after an induced MI. The figure below demonstrates dose-dependent improvement in EF, with an approximately 10% improvement in EF achieved at the highest dose compared to controls that was sustained up to the end of the experiment at 29 weeks:

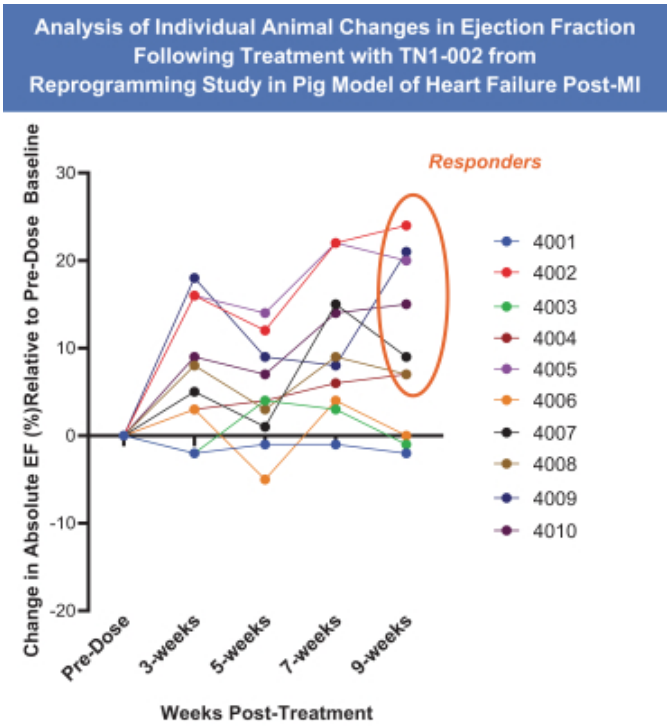


- *Results from pig disease model*. We have demonstrated durable improvement in EF in a pig model of HF following an induced MI. In a pig model, TN1-002 was injected directly around the scar area formed 28 days after an induced MI. The figure below demonstrates approximately 10% improvement in EF compared to each animal's own pre-dose baseline and more than 11% improvement compared to control-treated animals that remained sustained until the end of the experiment at nine weeks:



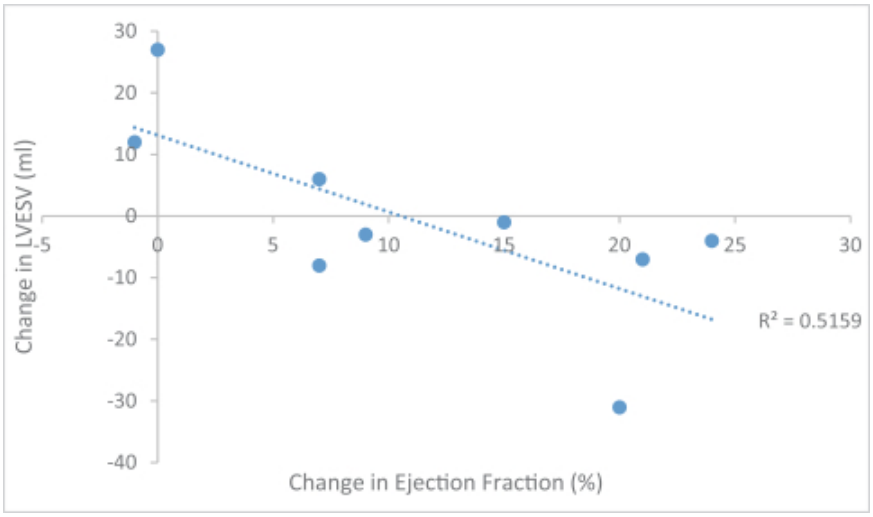
We believe these data compare favorably to published efficacy data for other cell and gene therapy interventions in large animal models. Very few previous therapeutic attempts have achieved meaningful improvement in EF compared to pre-dose baseline in large animal models, with typical improvements, when observed, of less than 5%. From an assessment of the published literature, including a meta-analysis of multiple therapeutics in HFrEF, we believe that each 5% increase in EF is expected to reduce mortality by approximately 15%.

This pig model is known to have high variability in disease progression among individual animals. In order to confirm that the results obtained with TN1-002 reflected true improvements in heart function, we conducted extensive additional analysis of other parameters, including heart size (for example, LV diameter and volume during systole and diastole), measures of cardiac output (for example, stroke volume), measures of heart injury (for example, troponin levels), and final scar size at the level of individual animals. As shown in the figure below, our analysis revealed high heterogeneity in the change in absolute EF% among individual animal responses to TN1-002 from a decline of -2% to improvement of +24%, and that seven out of ten treated animals were considered "responders" (based on EF% increase of greater than 5% over pre-dose baseline) while three out of ten were considered "non-responders".



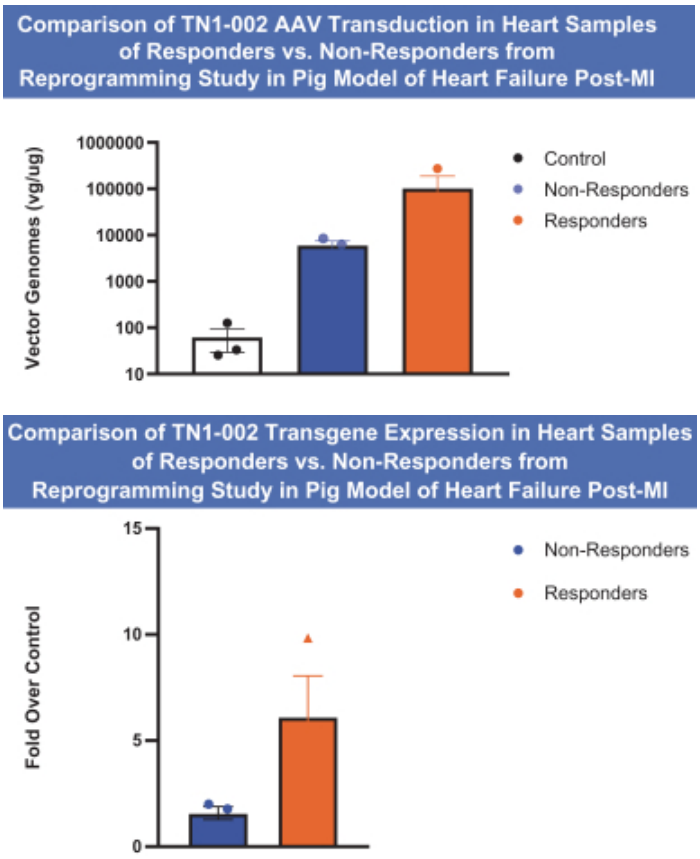
Further analysis of responder animals as compared to non-responder animals demonstrated responders generally had improvement in most parameters that were internally consistent and suggestive of positive heart remodeling. By comparison, the pattern of these additional parameters was not internally consistent among non-responders.

The figure below demonstrates the expected inverse correlation of the degree of EF improvement of responders to the change in heart size, as measured by LV end systolic volume:



Further analysis of heart samples from responder as compared to non-responder animals from this study revealed that responder animals had significantly higher measurable levels of the TN1-002 vector and the reprogramming factors than the non-responder animals. This provides additional support that the improvements in EF results seen in this experiment were a direct result of the delivery and expression of reprogramming factors by our AAV capsid.

The figures below illustrate that the level of AAV transduction and transgene expression was observed to be higher in samples obtained from responders compared to non-responders to TN1-002 in the study of reprogramming in the pig model of HF post-MI:



Our preclinical findings to date provide direction to our ongoing candidate selection efforts. We continue to seek ways to ensure more consistent delivery and expression of our reprogramming factors to CFs, including with the use of novel capsids and novel delivery methods.

- *Safety*. To date, no negative safety findings have been associated with either TN1-002 or TN1-006 in *in vivo* experiments in rat and pig models, including clinical findings, histopathology, assessment of arrhythmia, and other measures.

Planned Clinical Development

We have received feedback from the FDA through an INTERACT (INitial Targeted Engagement for Regulatory Advice on CBER producTs) review to inform the design of our future preclinical studies. After selection of our product candidate, we plan to initiate IND-enabling studies. We intend to submit an IND or CTA to the FDA or EMA, respectively, no earlier than 2023.

Our development plan is anticipated to include patients with advanced HF due to prior MI who meet qualifications for a heart transplant or LVAD as well as a broader patient population with severe ischemic cardiomyopathy. In the future, we also may explore potential for development in other forms of HF caused by a loss of CMs, but not involving a myocardial infarction.

Pipeline Expansion Opportunities

We believe the versatility of our three product platforms and our related differentiated capabilities enables us to rapidly expand our portfolio beyond the initial areas of focus. In addition to the named programs in our current pipeline, there are several programs emerging from each of our platforms that are intended to address rare genetic cardiomyopathies as well as more prevalent forms of heart disease. We continue to research, discover and evaluate new programs arising from our three product platforms. We also continue to explore opportunities to collaborate with leading academic and biopharmaceutical organizations with complementary science and capabilities that share our bold vision for the development of next-generation therapies to benefit individuals and families fighting heart disease.

Third Party Agreements

2020 License Agreement with The Board of Regents of the University of Texas System on behalf of UTSW

We have licensed intellectual property from UTSW in a license agreement effective January 10, 2020 with regard to our DWORF program. We entered into the license agreement with The Board of Regents of the University of Texas System on behalf of UTSW for a worldwide license to develop and commercialize products covered by the UTSW-licensed intellectual property relating to therapeutics overexpressing the peptide named DWORF for all uses. Our license under the license agreement is exclusive with respect to the UTSW patent rights licensed thereunder and non-exclusive with respect to the UTSW tangible materials provided thereunder. All of the DWORF gene therapy product candidates currently in our pipeline rely upon the license granted to us under this agreement. Such license is subject to (a) certain non-commercial rights reserved by UTSW and (b) certain rights retained by the U.S. government, including so called march-in rights.

Under the license agreement, we are obligated to make milestone payments to UTSW aggregating up to $2.75 million upon the achievement of specified development and regulatory approval milestones and up to $12 million upon the achievement of specified sales milestones, in each case, for products covered by the UTSW licensed patent rights. We are also obligated to pay single-digit royalties to UTSW based on net sales by us or our affiliates and sublicensees of products covered by the UTSW licensed patent rights. In addition, in the event we grant a sublicense or an option to obtain a sublicense under the UTSW licensed patent rights, we are obligated to pay UTSW a specified portion of the income we receive therefrom. Further, in the event we undergo a change of control, we may be obligated to make a payment to UTSW of up to $3 million.

Our royalty obligations with respect to each product covered by UTSW licensed patent rights in a country extend until the latest of expiration of the last-to-expire patent claim licensed from UTSW covering the product in the country, the exclusivity term covering the product in the country and a specified number of years after the first commercial sale of the product in the country.

Under the license agreement, we are obligated to use a certain level of effort to develop and commercialize one or more products covered by the UTSW licensed patent rights and to achieve certain development or regulatory approval milestones within set times, subject to certain extensions and required payments for such extensions.

UTSW has the right to terminate the license agreement for our uncured material breach of the license agreement, including if we fail to use a certain level of effort to achieve specified development or regulatory

approval milestones within specified timeframes, or if we unsuccessfully challenge the validity of the UTSW licensed patent rights or for certain events related to our bankruptcy. We have the right to terminate the agreement at any time.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on intellectual property. We believe our three product platforms, scientific know-how, five core internal capabilities, and experience provides us with competitive advantages. However, we face substantial competition from many different sources, including large and specialty pharmaceutical companies and biotechnology companies, academic research institutions and governmental agencies, and public and private research institutions. Any product candidate we develop and commercialize will have to compete with existing therapies as well as therapies currently in development and that may be developed in the future.

Due to the depth and diversity of our pipeline, we may face competition from a variety of companies, including:

- **General cardiovascular drug development:** Companies known to have approved products and active drug development efforts for cardiovascular disease include but are not limited to AstraZeneca, Bayer, Bristol Myers Squibb, Cytokinetics, Eli Lilly, Johnson & Johnson/Janssen, Maze Therapeutics, Merck, Novartis, and Novo Nordisk;
- **Gene Therapy platform:** Companies known to be pursuing gene therapy approaches for the heart include but are not limited to 4D Molecular Therapeutics, Bayer, Bristol Myers Squibb, BioMarin Pharmaceutical, DiNAQOR, Nuevocor, Precigen, Renova Therapeutics, Renovacor, Rocket Pharmaceuticals, Sardicor, Stride Bio, and uniQure;
- **Cellular Regeneration platform:** Companies known to be pursuing approaches to cellular regeneration for the heart include but are not limited to AstraZeneca, Bayer, BioCardia, Cardior Pharmaceuticals, Jaan Biotherapeutics, Khloris Biosciences, Mesoblast, Mogrify, Sana Biotechnologies and Xylocor Therapeutics; and
- **Precision Medicine platform:** Companies known to be pursuing approaches to drug discovery for the heart using disease models based on iPSC-CMs include but are not limited to DiNAQOR and Tara Biosystems.

We cannot predict whether other therapies may be developed that demonstrate greater efficacy, and we may have direct and substantial competition from such therapies in the future. We expect to face increasing competition as new, more effective treatments enter the market and further advancements in technologies are made. We expect market adoption of any treatments that we develop and commercialize to be dependent on, among other things, efficacy, safety, delivery, price and the availability of reimbursement from government and other third-party payors.

Many of our current or potential competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and gene therapy industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These companies also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our product candidates.

Intellectual Property

Our success depends in part on our ability to obtain and maintain intellectual property protection for our product candidates, technology and know-how, to operate without infringing, misappropriating or otherwise violating the intellectual property or other the proprietary rights of others and to prevent others from infringing, misappropriating or otherwise violating our intellectual property or other proprietary rights. To protect our intellectual property rights, we primarily rely on patent and trade secret laws, confidentiality procedures, and employee disclosure and invention assignment agreements. Our policy is to seek to protect our proprietary position by, among other methods, pursuing patent applications in the United States and in certain jurisdictions outside of the United States related to our proprietary technology, inventions, improvements and product candidates that are important to the development and implementation of our business. Our patent portfolio is intended to cover our product candidates and components thereof, their methods of use and processes for their manufacture, our proprietary reagents and assays and any other inventions that are commercially important to our business. The development of our product candidates and technology is at an early stage and consequently, our patent portfolio is also at an early stage. We have in-licensed one issued U.S. patent, own one issued U.S. patent, and own one allowed U.S. patent application relating to our technology and product candidates. Many of our and our licensors' patent applications are either at the provisional stage or at an early stage in prosecution. We cannot be sure that any patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any patents that may be granted to us in the future will be commercially useful in protecting our technology and product candidates.

Our owned and exclusively licensed patent portfolio covers various aspects of our programs and technology, including our small-molecule compounds, gene delivery vectors, and gene therapy programs. Further details on certain segments of our patent portfolio are included below.

Gene Therapy Platform

MYBPC3: With regard to our MYBPC3 program, as of July 1, 2021, we solely own two pending Patent Cooperation Treaty (PCT) patent applications and one pending U.S. patent application which the USPTO has allowed and which we expect to issue as a U.S. patent in due course. Any U.S. or foreign patents issued from national stage filings of the PCT patent applications are expected to expire in 2041, assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees and that national phase entries are timely made based upon the pending PCT applications, and without taking potential patent term extensions or adjustments into account. The pending U.S. provisional patent applications cover various aspects of our MYBPC3 lead products, including *MYBPC3* gene expression vectors, recombinant AAV (rAAV) virions, rAAV viral genomes, expression cassettes, and methods of using such compositions for therapeutic indications.

PKP2: With regard to our PKP2 program, as of July 1, 2021, we solely own three pending U.S. provisional patent applications. Patents claiming priority to these three U.S. provisional patent applications, if issued, are expected to expire between 2041 and 2042, assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees and without taking potential patent term extensions or adjustments into account. These provisional patent applications are related to proprietary *PKP2* gene expression vectors and methods of use.

DWORF: With regard to our DWORF program, as of July 1, 2021, we exclusively license one U.S. patent and one pending U.S. patent application from UTSW (the UT Patents). The U.S. patent is expected to expire, and the pending U.S. patent application, if issued, is expected to expire, in 2037, assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees and without taking potential patent term extensions or adjustments into account. The UT Patents covers methods of enhancing activity of the SERCA pump using the DWORF peptide and using such methods to treat heart disease. Furthermore, we solely own a pending U.S. provisional patent application related to proprietary vectors and methods of use. Patents claiming priority to this U.S. provisional patent application, if issued, are expected to expire in 2041, assuming payment of all appropriate

maintenance, renewal, annuity or other governmental fees, and without taking potential patent term extensions or adjustments into account.

Cellular Regeneration Platform

With respect to our Cellular Regeneration platform, as of July 1, 2021, we solely own three patent families directed to product candidates in our Reprogramming program, including two pending PCT patent applications, one issued U.S. patent, one pending non-provisional U.S. patent application and nine foreign counterparts of these patent applications. Any U.S. or foreign patents issued from national stage filings of the PCT patent applications are expected to expire between 2039 and 2041, assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees and that national phase entries are timely made based upon the pending PCT applications, and without taking potential patent term extensions or adjustments into account. The three patent families cover various aspects of our Reprogramming program, including gene delivery vectors, methods of treating a heart condition, engineered myocardin proteins, vectors encoding engineered myocardins, and methods of use. Additionally, we solely own a fourth patent family that is directed to AAV-based gene vectors for cardiac cell transduction, with one pending international PCT patent application. Any U.S. or foreign patents issued from national stage filings of this PCT patent application are expected to expire in 2040, assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees and that national phase entries are timely made based upon the pending PCT applications, and without taking potential patent term extensions or adjustments into account.

Precision Medicine Platform

With regard to our HDAC6i program, as of July 1, 2021, we solely own two pending PCT patent applications and four pending U.S. provisional patent applications. Any U.S. or foreign patents issued from national stage filings of these PCT patent applications are expected to expire in 2040, assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees and that national phase entries are timely made based upon the pending PCT applications, and without taking potential patent term extensions or adjustments into account. Our patent applications cover our lead HDAC6i compounds and various analogs.

Trade Secrets

In addition to our reliance on patent protection for our technology and product candidates, we also rely on trade secret protection of our confidential information and know-how relating to our proprietary technology, product platforms and product candidates. Through development of internal manufacturing capabilities for AAV-based gene vectors, we have secured proprietary know-how and trade secrets related to our most-advanced programs as well as vector technologies widely applicable to potential AAV therapies. However, trade secrets can be difficult to protect. We seek to protect our trade secrets, proprietary technology and processes, in part, by entering into confidentiality and invention assignment agreements with our employees, consultants, scientific advisors, contractors and other third parties. However, we cannot guarantee that we have entered into such agreements with each party that has or may have had access to our trade secrets or proprietary information or has been involved in the development of intellectual property. Additionally, these agreements may be breached and we may not have adequate remedies for any breach. Furthermore, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. As a result, we may not be able to meaningfully protect our trade secrets. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. However, such security measures may be breached and we may not have adequate remedies for such breaches.

For more information regarding the risks related to our intellectual property, see “Risk Factors—Risks Related to Our Intellectual Property.”

Manufacturing

We intend to rely on our internal manufacturing capabilities for the production of drug substance for initial clinical studies of our MYBPC3 gene therapy program. Over time we intend to rely on a combination of our internal manufacturing capabilities as well as on external CDMOs for our portfolio programs as they progress through various stages of clinical development and eventually to commercialization, if approved.

We plan to fully integrate and internalize AAV manufacturing capabilities to support our initial product candidates from our Gene Therapy and Cellular Regeneration platforms. We have established an in-house Pilot Plant Operation facility that operates at the 200L scale to support all non-clinical studies including IND-enabling efficacy, pharmacology and toxicology studies. This facility is compliant with Good Laboratory Practice (GLP) regulations and can produce materials sufficient for large animal studies including pigs and NHPs. Our initial production at this scale has been at yields and with full to empty capsid ratios that compare favorably to industry standards.

We have initiated construction of a dedicated cGMP facility for drug product manufacturing in the San Francisco Bay Area that we expect will be operational in the first half of 2022. The facility will initially produce drug product at the 1000L scale to support first-in-human studies for our MYBPC3 program. The facility will use a modular pod design that will support scale-out and scale-up of manufacturing capacity in response to evolving needs.

In addition to our internal cGMP manufacturing capabilities, we have also negotiated and entered into master service agreements with two CDMOs for additional capacity and risk mitigation. Additionally, we will rely on third parties for certain manufacturing related release assays, for which we intend to secure dual-sourced capacity for risk mitigation.

To optimize our use of resources and utilize extensive experience in small molecule manufacturing, we intend to work with CDMOs for our small molecule programs. We intend to initiate cGMP manufacturing for our HDAC6 inhibitor program, TYA-11631, before the end of 2021.

Government Regulation

Government authorities in the United States at the federal, state and local level and in other countries regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of biologic and small molecule therapeutic products. Generally, before a new therapeutic product can be marketed, considerable data demonstrating a biologic candidate's quality, safety, purity and potency, or a small molecule candidate's quality, safety and efficacy, must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority. For biologic candidates, potency is similar to efficacy and is interpreted to mean the specific ability or capacity of the product, as indicated by appropriate laboratory tests or by adequately controlled clinical data obtained through the administration of the product in the manner intended, to effect a given result.

U.S. Biologic and Small Molecule Drug Product Development

In the United States, the FDA regulates small molecule and biologic therapeutic products under the Food, Drug and Cosmetic Act (FDCA) and the Public Health Service Act (PHSA). Biopharmaceuticals, including both small molecule and biologic products, also are subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or post-market may subject an applicant to administrative or judicial sanctions. These sanctions

could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, untitled or warning letters, product recalls or market withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement and civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Biologics must be licensed by the FDA through a biologics license application (BLA), and small molecule products must be approved by the FDA through a new drug application (NDA), before they may be legally marketed in the United States. The process generally involves the following:

- Completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with GLP requirements;
- Submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- Approval by an independent institutional review board (IRB), or ethics committee at each clinical trial site before each trial may be initiated;
- Performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, GCP requirements and other clinical trial-related regulations to establish the safety and potency or efficacy of the investigational product for each proposed indication;
- Submission to the FDA of a BLA or NDA;
- A determination by the FDA within 60 days of its receipt of a BLA or NDA to accept the filing for review;
- Satisfactory completion of a FDA pre-approval inspection of the manufacturing facility or facilities where biologic or small molecule product will be produced to assess compliance with cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the biologic's identity, strength, purity, potency, and quality controls, or the small molecule product's identity, chemistry, and quality controls;
- Potential FDA audit of the preclinical study and/or clinical trial sites that generated the data in support of the BLA or NDA;
- Satisfactory completion of other studies required by the FDA, including immunogenicity, carcinogenicity, genotoxicity, and stability studies;
- FDA review and approval of the BLA or NDA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the biologic or small molecular therapeutic in the United States; and
- Compliance with any post-approval requirements, including the potential requirement to implement a REMS, and the potential requirement to conduct post-approval studies.

The data required to support a BLA or NDA are generated in two distinct developmental stages: preclinical and clinical. The preclinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for any future product candidates will be granted on a timely basis, or at all.

Preclinical Studies and IND

Preclinical studies include laboratory evaluation of product biochemistry, formulation and stability, as well as *in vitro* and animal studies to assess the potential for toxicity and to establish a rationale for therapeutic use for supporting subsequent clinical testing. The conduct of preclinical studies is subject to federal regulations and

requirements, including GLP regulations for safety/toxicology studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, among other things, to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational product to humans and must become effective before human clinical trials may begin. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical Trials

The clinical stage of development involves the administration of the investigational product to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Furthermore, each clinical trial must be reviewed and approved by an IRB for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

A sponsor who wishes to conduct a clinical trial outside of the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of a BLA or NDA. The FDA will accept a well-designed and well-conducted foreign clinical trial not conducted under an IND if the trial was conducted in accordance with GCP requirements and the FDA is able to validate the data through an onsite inspection if deemed necessary.

Clinical trials in the United States generally are conducted in three sequential phases, known as Phase 1, Phase 2 and Phase 3, and may overlap.

- Phase 1 clinical trials generally involve a small number of healthy volunteers or disease-affected patients who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, tolerability and safety of the drug.
- Phase 2 clinical trials involve studies in disease-affected patients to determine the dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, possible adverse effects and safety risks are identified and a preliminary evaluation of efficacy is conducted.
- Phase 3 clinical trials generally involve a large number of patients at multiple sites and are designed to provide the data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. These trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of a BLA or NDA.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the investigational product, findings from animal or *in vitro* testing that suggest a significant risk for human subjects and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure.

Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk or non-compliance with GCP requirements. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the investigational product has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether a trial may move forward at designated check-points based on access to certain data from the trial. Concurrent with clinical trials, companies usually complete additional animal studies and also must develop additional information about the biochemical and physical characteristics of the investigational product as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product and, among other things, companies must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidates do not undergo unacceptable deterioration over their shelf life.

Further, as a result of the COVID-19 pandemic, the extent and length of which are uncertain, we will be required to develop and implement additional clinical trial policies and procedures designed to help protect trial participants from the COVID-19 virus, which may include using telemedicine visits and remote monitoring of patients and clinical sites. We will also need to ensure data from our clinical studies that may be disrupted as a result of the pandemic is collected pursuant to the trial protocol and is consistent with GCPs, with any material protocol deviation reviewed and approved by the site IRB. Patients who may miss scheduled appoints, any interruption in trial drug supply, or other consequence that may result in incomplete data being generated during a trial as a result of the pandemic must be adequately documented and justified. For example, on March 18, 2020, the FDA issued a guidance, as updated subsequently by the FDA, on conducting clinical trials during the pandemic. The guidance describes a number of considerations for sponsors of clinical trials impacted by the pandemic, including the requirement to include in the clinical trial report (or as a separate document) contingency measures implemented to manage the trial and any disruption of the trial as a result of COVID-19, among others. Other industry guidance issued by the FDA during the COVID-19 pandemic includes manufacturing, supply chain, and drug and biological product inspections during the COVID-19 public health emergency; GMP considerations for responding to COVID-19 infection in employees in biopharmaceutical manufacturing; and remote interactive evaluations of drug manufacturing and bioresearch monitoring facilities, among others. If new guidance and policies are promulgated by the FDA that require changes in our clinical protocol or clinical development plans, our anticipated timelines and regulatory approval may be delayed or materially impacted.

NDA and BLA Review Process

Following completion of the clinical trials, data is analyzed to assess whether the investigational product is safe and effective for the proposed indicated use or uses. The results of preclinical studies and clinical trials are then submitted to the FDA as part of a BLA for a biologic product or an NDA for a small molecule drug product,

along with proposed labeling, biochemistry and manufacturing information to ensure product quality, identity, purity and other relevant data. In short, the BLA or NDA is a request for approval to market the biologic or drug product for one or more specified indications and must contain proof of safety, purity and potency for a biologic, or safety and efficacy for a small molecule drug product. The application may include both negative and ambiguous results of preclinical studies and clinical trials, as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of the FDA. FDA approval of a BLA or NDA must be obtained before the product may be marketed in the United States.

Under the Prescription Drug User Fee Act (PDUFA), as amended, each BLA or NDA must be accompanied by a user fee. FDA adjusts the PDUFA user fees on an annual basis. According to the FDA's FY 2021 fee schedule, effective through September 30, 2021, the user fee for an application requiring clinical data, such as a BLA or NDA, is approximately $2.9 million. PDUFA also imposes an annual program fee for each marketed human prescription drug product ($336,432 in 2021) and an annual establishment fee on facilities used to manufacture prescription biologics or small molecular drug products. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on BLAs or NDA for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA reviews all submitted BLAs and NDAs before it accepts them for filing and may request additional information rather than accepting the BLA or NDA for filing. The FDA must make a decision on accepting a BLA or NDA for filing within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth review of the BLA or NDA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has ten months, from the filing date, in which to complete its initial review of an original BLA or NDA and respond to the applicant, and six months from the filing date of an original BLA or NDA designated for priority review. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs or NDAs, and the review process is often extended by FDA requests for additional information or clarification.

Before approving a BLA or NDA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMP requirements. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The FDA also may audit data from clinical trials to ensure compliance with GCP requirements. Additionally, the FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes physicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions, if any. The FDA is not bound by recommendations of an advisory committee, but it considers such recommendations when making decisions on approval. The FDA likely will reanalyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process. After the FDA evaluates a BLA or NDA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug product with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the BLA or NDA identified by the FDA. The Complete Response Letter may require additional clinical data, additional pivotal Phase 3 clinical trial(s) and/ or other significant and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the BLA or NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the BLA or NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data.

Orphan Drugs

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product available in the United States for this type of disease or condition will be recovered from sales of the product.

For biologic or small molecule drug products, an orphan drug designation must be requested before submitting a BLA or NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years from the date of such approval, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity by means of greater effectiveness, greater safety or providing a major contribution to patient care or in instances of drug supply issues. However, competitors may receive approval of either a different product for the same indication or the same product for a different indication but that could be used off-label in the orphan indication. Orphan drug exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval before we do for the same product, as defined by the FDA, for the same indication we are seeking approval, or if a product candidate is determined to be contained within the scope of the competitor's product for the same indication or disease. If one of our products designated as an orphan drug receives marketing approval for an indication broader than the indication for which it is designated, it may not be entitled to orphan drug exclusivity. Orphan drug status in the European Union has similar, but not identical, requirements and benefits.

Expedited Development and Review Programs

The FDA has a fast-track program that is intended to expedite or facilitate the process for reviewing new drug products that meet certain criteria. Specifically, new drug products are eligible for fast-track designation if they are intended to treat a serious or life-threatening condition and preclinical or clinical data demonstrate the potential to address unmet medical needs for the condition. Fast track designation applies to both the product and the specific indication for which it is being studied. The sponsor can request the FDA to designate the product for fast-track status any time before receiving a BLA or NDA approval, but ideally no later than the pre-BLA or pre-NDA meeting.

Any product submitted to the FDA for marketing, including under a fast-track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it treats a serious or life-threatening condition and, if approved, would provide a significant improvement in safety and effectiveness compared to available therapies.

A product may also be eligible for accelerated approval, if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, it must demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality (IMM), which is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of approval, the FDA may require that a sponsor of a drug product receiving accelerated approval to perform adequate and well-controlled post-marketing clinical trials. If the FDA concludes that a biologic or small molecule drug product shown to be potent or effective for the proposed indication can be safely used only if distribution or use is restricted, it may require such post-marketing

restrictions as it deems necessary to assure safe use of the product. In some cases, FDA may limit the scope of the indication. Such restrictions could have a materially adverse effect on our business and our ability to obtain profitability.

Additionally, a drug product may be eligible for designation as a breakthrough therapy if the product is intended, alone or in combination with one or more other drug products, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints. The benefits of breakthrough therapy designation include the same benefits as fast-track designation, plus intensive guidance from the FDA to ensure an efficient drug development program. Fast track designation, priority review, accelerated approval and breakthrough therapy designation do not change the standards for approval, but may expedite the development or approval process. Depending on other factors that impact clinical trial timelines and development, such as our ability to identify and onboard clinical sites and rates of study participant enrollment and drop-out, we may not realize all the benefits of these expedited or accelerated review programs.

Abbreviated Licensure Pathway of Biological Products as Biosimilars or Interchangeable Biosimilars

The Patient Protection and Affordable Care Act (Affordable Care Act or ACA), signed into law in 2010, includes the Biologics Price Competition and Innovation Act of 2009 (BPCIA), which created an abbreviated approval pathway for biological products shown to be highly similar to an FDA-licensed reference biological product. The BPCIA attempts to minimize duplicative testing, and thereby lower development costs and increase patient access to affordable treatments. An application for licensure of a biosimilar product must include information demonstrating biosimilarity based upon the following, unless the FDA determines otherwise:

- Analytical studies demonstrating that the proposed biosimilar product is highly similar to the approved product notwithstanding minor differences in clinically inactive components;
- Animal studies (including the assessment of toxicity); and
- A clinical trial or trials (including the assessment of immunogenicity and pharmacokinetic or pharmacodynamic) sufficient to demonstrate safety, purity and potency in one or more conditions for which the reference product is licensed and intended to be used.

In addition, an application must include information demonstrating that:

- The proposed biosimilar product and reference product utilize the same mechanism of action for the condition(s) of use prescribed, recommended or suggested in the proposed labeling, but only to the extent the mechanism(s) of action are known for the reference product;
- The condition or conditions of use prescribed, recommended or suggested in the labeling for the proposed biosimilar product have been previously approved for the reference product;
- The route of administration, the dosage form and the strength of the proposed biosimilar product are the same as those for the reference product; and
- The facility in which the biological product is manufactured, processed, packed or held meets standards designed to assure that the biological product continues to be safe, pure and potent.

Biosimilarity means that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components, and that there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity and potency of the product. In addition, the law provides for a designation of “interchangeability” between the reference and biosimilar products, whereby the biosimilar may be substituted for the reference product without the intervention of the healthcare provider who prescribed the reference product. The higher standard of interchangeability must be demonstrated by information sufficient to show that:

- The proposed product is biosimilar to the reference product;

- The proposed product is expected to produce the same clinical result as the reference product in any given patient; and
- For a product that is administered more than once to an individual, the risk to the patient in terms of safety or diminished efficacy of alternating or switching between the biosimilar and the reference product is no greater than the risk of using the reference product without such alternation or switch.

FDA approval is required before a biosimilar may be marketed in the United States. However, complexities associated with the large and intricate structures of biological products and the process by which such products are manufactured pose significant hurdles to the FDA's implementation of the law that are still being worked out by the FDA. For example, the FDA has discretion over the kind and amount of scientific evidence—laboratory, preclinical and/or clinical—required to demonstrate biosimilarity to a licensed biological product.

The FDA intends to consider the totality of the evidence provided by a sponsor to support a demonstration of biosimilarity and recommends that sponsors use a stepwise approach in the development of their biosimilar products. Biosimilar product applications thus may not be required to duplicate the entirety of preclinical and clinical testing used to establish the underlying safety and effectiveness of the reference product. However, the FDA may refuse to approve a biosimilar application if there is insufficient information to show that the active ingredients are the same or to demonstrate that any impurities or differences in active ingredients do not affect the safety, purity or potency of the biosimilar product. In addition, as with BLAs, biosimilar product applications will not be approved unless the product is manufactured in facilities designed to assure and preserve the biological product's safety, purity and potency.

The submission of a biosimilar application does not guarantee that the FDA will accept the application for filing and review, as the FDA may refuse to accept applications that it finds are insufficiently complete. The FDA will treat a biosimilar application or supplement as incomplete if, among other reasons, any applicable user fees assessed under the Biosimilar User Fee Act of 2012 have not been paid. In addition, the FDA may accept an application for filing but deny approval on the basis that the sponsor has not demonstrated biosimilarity, in which case the sponsor may choose to conduct further analytical, preclinical or clinical studies and submit a BLA for licensure as a new biological product.

The timing of final FDA approval of a biosimilar for commercial distribution depends on a variety of factors, including whether the manufacturer of the branded product is entitled to one or more statutory exclusivity periods, during which time the FDA is prohibited from approving any products that are biosimilar to the branded product. The FDA cannot approve a biosimilar application for twelve years from the date of first licensure of the reference product.

Additionally, a biosimilar product sponsor may not submit an application for four years from the date of first licensure of the reference product. A reference product may also be entitled to exclusivity under other statutory provisions. For example, a reference product designated for a rare disease or condition (an orphan drug) may be entitled to seven years of exclusivity, in which case no product that is biosimilar to the reference product may be approved until either the end of the twelve-year period provided under the biosimilarity statute or the end of the seven-year orphan drug exclusivity period, whichever occurs later. In certain circumstances, a regulatory exclusivity period can extend beyond the life of a patent, and thus block biosimilarity applications from being approved on or after the patent expiration date. In addition, the FDA may under certain circumstances extend the exclusivity period for the reference product by an additional six months if the FDA requests, and the manufacturer undertakes, studies on the effect of its product in children, a so-called pediatric extension.

The first biological product determined to be interchangeable with a branded product for any condition of use is also entitled to a period of exclusivity, during which time the FDA may not determine that another product is interchangeable with the reference product for any condition of use. This exclusivity period extends until the earlier of: one year after the first commercial marketing of the first interchangeable product; 18 months after

resolution of a patent infringement suit against the applicant that submitted the application for the first interchangeable product, based on a final court decision regarding all of the patents in the litigation or dismissal of the litigation with or without prejudice; 42 months after approval of the first interchangeable product, if a patent infringement suit against the applicant that submitted the application for the first interchangeable product is still ongoing; or 18 months after approval of the first interchangeable product if the applicant that submitted the application for the first interchangeable product has not been sued.

Abbreviated NDA Pathway for Generic Drug Products

The Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as "the Hatch-Waxman Act," established abbreviated FDA approval procedures for drugs that are shown to be bioequivalent to drugs previously approved by the FDA through its NDA process, which are commonly referred to as the "innovator" or "reference" drugs. Approval to market and to distribute these bioequivalent drugs is obtained by filing an abbreviated NDA (ANDA) with the FDA. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the API, drug product formulation, specifications, stability, analytical methods, manufacturing process validation data, quality control procedures and bioequivalence. Rather than demonstrating safety and effectiveness, an ANDA applicant must demonstrate that its product is bioequivalent to an approved reference drug. In certain situations, an applicant may submit an ANDA for a product with a strength or dosage form that differs from a reference drug based upon FDA approval of an ANDA Suitability Petition. The FDA will approve an ANDA Suitability Petition if it finds that the product does not raise questions of safety and efficacy requiring new clinical data. ANDAs generally cannot be submitted for products that are not bioequivalent to the referenced drug or that are labeled for a use that is not approved for the reference drug. Applicants seeking to market such products can submit an NDA under Section 505(b)(2) of the FDCA with supportive data from clinical trials.

Post-Approval Requirements

Following approval of a new product, the manufacturer and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and record-keeping requirements, requirements to report adverse experiences and comply with promotion and advertising requirements, which include restrictions on promoting drugs for unapproved uses or patient populations, known as "off-label use," and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such uses. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. Further, if there are any modifications to the drug product, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new application or supplement, which may require the development of additional data or preclinical studies and clinical trials.

The FDA may also place other conditions on approvals including the requirement for REMS, to assure the safe use of the product. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- Restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market, or product recalls;

- Warning letters, or holds on post-approval clinical studies;
- Refusal of the FDA to approve pending applications or supplements to approved applications;
- Applications, or suspension or revocation of product license approvals;
- Product seizure or detention, or refusal to permit the import or export of products; or
- Injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs and biologics may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

FDA Regulation of Combination Biologic-Medical Device Products

Certain products may be comprised of components, such as biologic components and device components, that would normally be regulated under different types of regulatory authorities and frequently by different Centers at the FDA. These products are known as combination products. Under the FDCA and its implementing regulations, the FDA is charged with assigning a Center with primary jurisdiction, or a lead Center, for review of a combination product. The designation of a lead Center generally eliminates the need to receive approvals from more than one FDA component for combination products, although it does not preclude consultations by the lead Center with other components of the FDA. The determination of which Center will be the lead Center is based on the "primary mode of action" of the combination product. Thus, if the primary mode of action of a biologic-device combination product candidate is attributable to the biologic product candidate, the FDA Center responsible for premarket review of the drug product would have primary jurisdiction for the combination product. The FDA has also established an Office of Combination Products to address issues surrounding combination products and provide more certainty to the regulatory review process. That Office serves as a focal point for combination product issues for agency reviewers and industry. It is also responsible for developing guidance and regulations to clarify the regulation of combination products, and for assignment of the FDA Center that has primary jurisdiction for review of combination products where the jurisdiction is unclear or in dispute.

A combination product with a biologic product candidate as the primary mode of action generally would be reviewed and approved pursuant to the biologic approval processes under the FDCA. In reviewing the BLA application for such a product, however, FDA reviewers in the Center for Biologics Evaluation and Research could consult with their counterparts in the device center to ensure that the device component of the combination product meet applicable requirements regarding safety, effectiveness, durability and performance. In addition, under FDA regulations, combination products are subject to cGMP requirements applicable to both biologics and devices, including the Quality System (QS), regulations applicable to medical devices.

We may develop one or more of our biologic product candidates in combination with a novel delivery medical device, such as an injection catheter device for more precise delivery of a biologic product candidate. Regulatory review of such combination product candidate will increase the timing, cost, and the complexity of the FDA review and approval process, and subject us to additional regulations and exposure to liability. Pending discussion with the FDA, if the medical device is considered a significant risk device under the FDA's Investigational Device Exemption (IDE) regulations, then we may be required to comply with the IDE regulations for clinical studies in addition to the IND regulations and may be required to submit both an IDE and an IND before commencing clinical testing of the combination product. We cannot provide any assurance regarding how FDA will regulate our combination product, or if we will be successful in obtaining approval for any combination product.

510(k) clearance process

To obtain 510(k) clearance, a pre-market notification is submitted to the FDA demonstrating that the proposed device is substantially equivalent to a previously cleared 510(k) device or a device that was in commercial distribution before May 28, 1976 for which the FDA has not yet required the submission of a PMA application. The FDA's 510(k) clearance process may take three to twelve months from the date the application is submitted and filed with the FDA, but may take longer if FDA requests additional information, among other reasons. In some cases, the FDA may require clinical data to support substantial equivalence. In reviewing a pre-market notification submission, the FDA may request additional information, which may significantly prolong the review process. Notwithstanding compliance with all these requirements, clearance is never assured.

After a device receives 510(k) clearance, any subsequent modification of the device that could significantly affect its safety or effectiveness, or that would constitute a major change in its intended use, will require a new 510(k) clearance or require a PMA. In addition, the FDA may make substantial changes to industry requirements, including which devices are eligible for 510(k) clearance, which may significantly affect the process.

De novo classification process

If a new medical device does not qualify for the 510(k) premarket notification process because no predicate device to which it is substantially equivalent can be identified, the device is automatically classified into Class III. The Food and Drug Administration Modernization Act of 1997 established a different route to market for low to moderate risk medical devices that are automatically placed into Class III due to the absence of a predicate device, called the "Request for Evaluation of Automatic Class III Designation," or the de novo classification process. This process allows a manufacturer whose novel device is automatically classified into Class III to request down-classification of its medical device into Class I or Class II on the basis that the device presents low or moderate risk, rather than requiring the submission and approval of a PMA. If the manufacturer seeks reclassification into Class II, the manufacturer must include a draft proposal for special controls that are necessary to provide a reasonable assurance of the safety and effectiveness of the medical device. The FDA may reject the reclassification petition if it identifies a legally marketed predicate device that would be appropriate for a 510(k) or determines that the device is not low to moderate risk and requires PMA or that general controls would be inadequate to control the risks and special controls cannot be developed. Obtaining FDA marketing authorization, de novo down-classification, or approval for medical devices is expensive and uncertain, and may take several years, and generally requires significant scientific and clinical data.

PMA approval process

The PMA process, including the gathering of clinical and nonclinical data and the submission to and review by the FDA, can take several years or longer. The applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness, including information about the device and its components regarding, among other things, device design, manufacturing, and labeling. PMA applications are subject to an application fee. In addition, PMAs for medical devices must generally include the results from extensive preclinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with the Quality System Regulation (QSR), which imposes extensive testing, control, documentation, and other QA and GMP requirements.

Other U.S. Regulatory Matters

Manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in the United States in addition to the FDA, including the Centers for Medicare & Medicaid Services (CMS), other divisions of the Department of Health and Human Services, the Department of Justice, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency, and state and local governments.

For example, in the United States, sales, marketing and scientific and educational programs must also comply with state and federal fraud and abuse laws. These laws include the federal Anti-Kickback Statute, which makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer or pay any remuneration that is intended to induce or reward referrals, including the purchase, recommendation, order or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. Violations of this law are punishable by up to five years in prison, criminal fines, administrative civil money penalties and exclusion from participation in federal healthcare programs. Moreover, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

Pricing and rebate programs must comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the ACA. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities also are potentially subject to federal and state consumer protection and unfair competition laws.

The distribution of biologic and pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with any of these laws or regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, requests for recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals or refusal to allow a firm to enter into supply contracts, including government contracts. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: changes to our manufacturing arrangements; additions or modifications to product labeling; the recall or discontinuation of our products; or additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

U.S. Data Privacy and Security Laws

In the United States, there are a broad variety of laws, rules, regulations and standards relating to privacy, data protection and information security that may apply to our activities, such as state data breach notification laws, state personal data privacy laws (for example, the California Consumer Privacy Act of 2018 (CCPA)), state health information privacy laws, and federal and state consumer protection laws (for example, Section 5(c) of the Federal Trade Commission Act). A range of enforcement agencies exist at both the state and federal levels that can enforce these laws, rules, regulations and standards. For example, the CCPA, which took effect on January 1, 2020, requires covered businesses that process personal information of California residents to disclose their data collection, use, and sharing practices. Further, the CCPA provides California residents with new data privacy rights (including the ability to opt out of certain disclosures of personal information), imposes new operational requirements for covered businesses, provides for significant civil penalties for violations as well as a private right of action for certain data breaches and statutory damages (that is expected to increase data breach class action litigation and result in significant exposure to costly legal judgements and settlements). Aspects of the CCPA and its interpretation and enforcement remain uncertain. In addition, California voters passed the California Privacy Rights Act of 2020 (CPRA) in November 2020, which becomes effective in most material

respects on January 1, 2023. The CPRA will, among other things, give California residents the ability to limit use of certain sensitive personal information, further restrict the use of cross-contextual advertising, establish restrictions on the retention of personal information, expand the types of data breaches subject to the CCPA's private right of action, provide for increased penalties for CPRA violations concerning California residents under the age of 16, and establish a new California Privacy Protection Agency to implement and enforce the new CCPA and CPRA. Although there are limited exemptions for clinical trial data under the CCPA, the CCPA and other similar laws could impact our business activities, depending on their interpretation. Further, laws in all 50 states require businesses to provide notice to customers whose personal data has been disclosed as a result of a data breach. We will continue to monitor and assess the impact of these state laws, which may impose substantial penalties for violations, impose significant costs for investigation and compliance, allow private class-action litigation and carry significant potential liability for our business. For more information, see "Risk Factors— Risks Related to Regulatory Approval and Other Legal Compliance Matters—We are subject to stringent laws, rules, regulations, policies, industry standards and contractual obligations regarding data privacy and security and may be subject to additional laws and regulations in jurisdictions into which we expand. Many of these laws and regulations are subject to change and reinterpretation and could result in claims, changes to our business practices, monetary penalties, increased cost of operations or other harm to our business."

U.S. Patent-Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of any future product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Act. The Hatch-Waxman Act permits restoration of the patent term of up to five years as compensation for patent term lost during product development and FDA regulatory review process. Patent-term restoration, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent-term restoration period is generally one-half the time between the effective date of an IND and the submission date of a BLA or NDA plus the time between the submission date of a BLA or NDA and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant BLA or NDA. However, there can be no assurance that our pending patent applications will issue or that we will benefit from any patent term extension or favorable adjustments to the terms of any patents we may own or in-license in the future.

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. A reference biological product is granted twelve years of data exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. "First licensure" typically means the initial date the particular product at issue was licensed in the United States. Date of first licensure does not include the date of licensure of (and a new period of exclusivity is not available for) a biological product if the licensure is for a supplement for the biological product or for a subsequent application by the same sponsor or manufacturer of the biological product (or licensor, predecessor in interest or other related entity) for a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength or for a modification to the structure of the biological product that does not result in a change in safety, purity or potency. Therefore, one must determine whether a new product includes a modification to the structure of a previously licensed product that results in a change in safety, purity or potency to assess whether the licensure of the new product is a first licensure that triggers its own period of exclusivity. Whether a subsequent application, if approved, warrants exclusivity as the "first licensure" of a biological product is determined on a case-by-case basis with data submitted by the sponsor.

The FDCA provides a five-year period of non-patent marketing exclusivity in the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an ANDA, or a 505(b)(2) NDA submitted by another company for a generic version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement with respect to one or more patents listed for the drug in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations publication. The FDCA also provides three years of marketing exclusivity for a NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness or generate such data themselves.

European Union Drug Development

Similar to the United States, the various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the European Union, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the member state regimes. Under the current regime, before a clinical trial can be initiated, it must be approved in each of the EU countries where the trial is to be conducted by two distinct bodies: the National Competent Authority (NCA) and one or more Ethics Committees (ECs). Under the current regime, all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

The EU clinical trials legislation currently is undergoing a transition process mainly aimed at harmonizing and streamlining clinical-trial authorization, simplifying adverse-event reporting procedures, improving the supervision of clinical trials and increasing their transparency. Recently enacted Clinical Trials Regulation EU No 536/2014 ensures that the rules for conducting clinical trials in the European Union will be identical. In the meantime, Clinical Trials Directive 2001/20/EC continues to govern all clinical trials performed in the European Union.

EU Drug Review and Approval

In the European Economic Area (EEA), which is comprised of the 27 Member States of the European Union (including Norway and excluding Croatia), Iceland and Liechtenstein, medicinal products can only be commercialized after obtaining a Marketing Authorization (MA). There are two types of Marketing Authorizations:

- The Community MA is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use (CHMP), of the EMA, and is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced-therapy medicines such as gene-therapy, somatic cell-therapy or tissue-engineered medicines and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral

diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or for products that are in the interest of public health in the European Union.

- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State (RMS). The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics (SPC) and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SPC, labeling or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e., in the RMS and the Member States Concerned).

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the member states of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Foreign Data Privacy and Security Laws

Outside of the United States, legal requirements relating to the collection, storage, processing, and transfer of personal data continue to evolve. For example, in the EU, the GDPR requires data controllers to implement more stringent operational requirements for processors and controllers of personal data, including transparent and expanded disclosure to data subjects about how their personal data is to be used, limitations on retention of information, mandatory data breach notification requirements, and higher standards for data controllers to demonstrate that they have obtained valid consent for certain data processing activities. Failure to comply with the GDPR may result in fines up to €20,000,000 or 4% of the total worldwide annual turnover of the preceding financial year, whichever is higher, and other administrative penalties. The GDPR may increase our responsibility and liability in relation to personal data that we may process, and we may be required to implement additional measures in an effort to comply with the GDPR and with other laws, rules and regulations in the EU, including those of EU member states, relating to privacy and data protection. We are also subject to the UK GDPR, a version of the GDPR as implemented into UK law. If our efforts to comply with GDPR or other applicable foreign laws, rules and regulations are not successful, or are perceived to be unsuccessful, it could adversely affect our business. For more information, see “Risk Factors—Risks Related to Regulatory Approval and Other Legal Compliance Matters—We are subject to stringent laws, rules, regulations, policies, industry standards and contractual obligations regarding data privacy and security and may be subject to additional laws and regulations in jurisdictions into which we expand. Many of these laws and regulations are subject to change and reinterpretation and could result in claims, changes to our business practices, monetary penalties, increased cost of operations or other harm to our business.”

Coverage and Reimbursement

Sales of our products will depend, in part, on the extent to which our products will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. In the United States, no uniform policy of coverage and reimbursement for drug products exists. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products will be

made on a payor-by-payor basis. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

The U.S. government, state legislatures, and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid healthcare costs, including price-controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. For example, the ACA contains provisions that may reduce the profitability of drug products through increased rebates for drugs reimbursed by Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Adoption of general controls and measures, coupled with the tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceutical drugs.

The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. The ACA made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers' rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs from 15.1% of average manufacturer price (AMP), to 23.1% of AMP and adding a new rebate calculation for "line extensions" (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP. The ACA also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization and by enlarging the population potentially eligible for Medicaid drug benefits. The CMS has proposed to expand Medicaid rebate liability to the territories of the United States as well.

The Medicare Prescription Drug, Improvement and Modernization Act of 2003 (MMA), established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Unlike Medicare Part A and B, Part D coverage is not standardized. While all Medicare drug plans must give at least a standard level of coverage set by Medicare, Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan likely will be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

For a drug product to receive federal reimbursement under the Medicaid or Medicare Part B programs, or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the AMP and Medicaid rebate amounts reported by the manufacturer.

As noted above, the marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. An increasing emphasis on cost containment measures in the United States has increased and we expect it will

continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

In addition, in most foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement, in order to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product in the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the United States and generally, prices tend to be significantly lower.

We are unable to predict the future course of federal or state healthcare legislation in U.S. or foreign legislation directed at containing or lowering the cost of healthcare and prescription drug prices. These and any further changes in the law or regulatory framework that reduce our revenue or increase our costs could have a material and adverse effect on our business, financial condition and results of operations. It is also possible that additional governmental action will be taken to address the COVID-19 pandemic. The continuing efforts of the government, insurance companies, managed care organizations, and other payors of healthcare services and medical products to contain or reduce costs of healthcare and/or impose price controls may adversely affect the demand for our product candidates, if approved, and our ability to achieve or maintain profitability.

Employees and Human Capital Resources

As of June 30, 2021, we had more than 85 full-time employees, with approximately 47 engaged in research and development activities and approximately 25 engaged in manufacturing activities. None of our employees are represented by a labor union or covered under a collective bargaining agreement. We consider our relationship with our employees to be good, in part as measured by relatively high scores from employees surveys and our relatively low turnover.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and new employees, advisors and consultants. The principal purposes of our equity and cash incentive plans are to attract, retain and reward personnel through the granting of stock-based and cash-based compensation awards, in order to increase stockholder value and the success of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives.

Facilities

Our corporate headquarters are in South San Francisco, where we lease a facility containing approximately 32,370 square feet of office and laboratory space located at 171 Oyster Point Blvd., 5th Floor, South San Francisco, CA 94080. The lease expires on May 31, 2025, unless earlier terminated in accordance with the lease, and we may renew the lease term for two additional five-year periods.

We also have subleased space at another facility in South San Francisco containing approximately 24,000 square feet of additional office and laboratory space located at 131 Oyster Point Blvd, 4th Floor, South San Francisco, CA 94080. The sublease expires on November 30, 2021, unless earlier terminated in accordance with the sublease.

We also have a leased space at a facility in Union City containing additional manufacturing and office space located at 33498 Central Avenue, Union City, CA 94587. The lease expires ten years and three months following

the date the premises is delivered by the landlord in the required condition, unless earlier terminated in accordance with the lease. We may renew the lease term for one additional five-year period.

We believe that these existing facilities are adequate for our current needs and that suitable additional or alternative space will be available in the future on commercially reasonable terms, if required.

Legal Proceedings

From time to time, we may become involved in litigation or other legal proceedings. We are not currently a party to any litigation or legal proceedings that, in the opinion of our management, are likely to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources, and other factors.

MANAGEMENT

Executive Officers, Key Employees, and Directors

The following table sets forth the names and positions of our executive officers, key employees, and directors and their ages as of June 30, 2021:

Name	Age	Position
Executive Officers:		
Faraz Ali, M.B.A.	48	Chief Executive Officer, Secretary and Director
Timothy Hoey, Ph.D.	63	Chief Scientific Officer
Leone D. Patterson, M.B.A.	58	Chief Financial and Business Officer
Whittemore (Whit) Tingley, M.D., Ph.D.	54	Chief Medical Officer
Key Employees:		
Kee-Hong Kim, Ph.D.	56	Senior Vice President, Manufacturing/Technical Operations
Matthew Pollman, M.D.	59	Vice President of Clinical Development
Jay Vora, Ph.D., M.B.A.	55	Senior Vice President, Portfolio and Program Management
Non-Employee Directors:		
Eli Casdin, M.B.A.(1)	48	Director
Jin-Long Chen, Ph.D.(3)	58	Director
David V. Goeddel, Ph.D.(3)	70	Director
JeenJoo (JJ) Kang, Ph.D.(1)	37	Director
Deepak Srivastava, M.D.(3)	55	Director
Catherine Stehman-Breen, M.D.(2)	58	Director
Jeffrey T. Walsh, M.B.A.(1)(2)	55	Director
R. Sanders (Sandy) Williams, M.D.(2)	72	Director

(1) Member of the audit committee.
(2) Member of the compensation committee.
(3) Member of the corporate governance and nominating committee.

Executive Officers

Faraz Ali, M.B.A. has served as our Chief Executive Officer and Secretary since June 2018 and as a member of our board of directors since September 2018. Prior to joining us, Mr. Ali was Chief Business Officer at REGENXBIO, a public biotechnology company, from February 2016 to January 2018. From May 2011 to February 2016, Mr. Ali was Vice President, Global Commercial Development and External Affairs at bluebird bio, a public biotechnology company. From August 2001 to November 2010, Mr. Ali held various roles at Genzyme, including Head of U.S. Marketing and Strategic Planning for the rare disease business unit. Prior to Genzyme, Mr. Ali served in leadership roles at GE Corporate and GE Healthcare. Mr. Ali holds a B.S. in Electrical Engineering from Stanford University and an M.B.A. with distinction from Harvard Business School.

We believe Mr. Ali is qualified to serve on our board of directors because of the perspective and experience he brings as our Chief Executive Officer, his experience in leadership and corporate development positions in the biotechnology industry and with companies focused on gene therapies and therapies for rare and orphan diseases, and his educational background.

Timothy Hoey, Ph.D. has served as our Chief Scientific Officer since August 2017. From 2005 to June 2017, he held various roles at OncoMed Pharmaceuticals, a public biotechnology company, including as the Senior Vice-President, Cancer Biology and co-Chief Scientific Officer from January 2016 to June 2017. From 1993 to 2005, Dr. Hoey served in various roles at Tularik, a public biopharmaceutical company acquired by Amgen in 2004, including as Director, Biology Department at both Tularik and Amgen. Dr. Hoey received a B.S. in Biology from the University of Michigan and a Ph.D. in Biological Sciences from Columbia University.

Leone D. Patterson, M.B.A. began serving as our Chief Financial and Business Officer in June 2021. Prior to joining us, Ms. Patterson served as the President and Chief Financial Officer of Adverum Biotechnologies, a public biotechnology company, from February 2021 to June 2021, and as its President from December 2019 to June 2021. She also served as Adverum's Chief Financial Officer from June 2016 to April 2019, as its Chief Executive Officer from May 2018 to June 2020, and as a member of its board of directors from October 2018 to June 2020. From March 2015 to June 2016, Ms. Patterson served as the Chief Financial Officer of Diadexus, a public diagnostics company. Diadexus voluntarily filed for Chapter 7 bankruptcy in June 2016 while Ms. Patterson was its Chief Financial Officer. Before that, she was Vice President and Chief Financial Officer of Transcept Pharmaceuticals, a private biopharmaceutical company, from June 2012 until it was acquired by Paratek Pharmaceuticals in October 2014. From November 2010 to June 2012, Ms. Patterson served as Vice President and Global Corporate Controller of NetApp. From July 2007 to November 2010, Ms. Patterson was Vice President of Finance at Exelixis. Before Exelixis, Ms. Patterson served as Vice President of Global Business Planning and Analysis of the Vaccines and Diagnostics Division of Novartis AG, from April 2006 to July 2007. From 1999 to 2006, she held various positions, including Vice President, Corporate Controller, at Chiron (now part of Novartis). From 1989 to 1999, Ms. Patterson worked in the audit practice of accounting firm KPMG, where she held various positions including Senior Manager. Ms. Patterson currently serves on the board of directors and as the Chair of the audit committee of Nkarta, a public biotechnology company, and Eliem Therapeutics, a private biotechnology company. Ms. Patterson holds a B.S. in Business Administration and Accounting from Chapman University and an Executive M.B.A. from St. Mary's College. Ms. Patterson is also a Certified Public Accountant (inactive status).

Whittemore (Whit) Tingley, M.D., Ph.D. has served as our Chief Medical Officer since December 2018. Before joining us, he served as the Vice President of Clinical Research, Cardiology, at Cytokinetics, a public biotechnology company, from September 2017 to December 2018. From 2009 to September 2017, Dr. Tingley held various medical director and group medical director roles at Genentech. Before that, Dr. Tingley was adjunct assistant professor of medicine in the cardiology division at the University of California, San Francisco, and was an attending cardiologist in the UCSF Cardiology Faculty Practice. Dr. Tingley earned a B.A. degree from Brown University and an M.D. and a Ph.D. from the Johns Hopkins University School of Medicine. He completed internship and residency programs at the Johns Hopkins Hospital, a cardiology fellowship at University of California, San Francisco and post-doctoral research at Gladstone Institutes.

Key Employees

Kee-Hong Kim, Ph.D. has served as our Senior Vice President, Manufacturing/Technical Operations since October 2018. Before joining us, he served as the Senior Vice President, Technical Operations of Agilis Biotherapeutics, a private biotechnology company, from September 2017 to August 2018. From February 2016 to August 2017, Dr. Kim was a Director at Shire, a public biopharmaceutical company, first as the head of gene therapy process development then as the global CMC lead of gene therapy. From April 2015 to January 2016, Dr. Kim ran his own biopharmaceutical consulting firm. Before that, he served as the Director of Process Development at Avalanche Biotechnologies from March 2013 to April 2015. Earlier in his career, Dr. Kim also served as a Senior Process Development Engineer at Dendreon Corp and held various leadership roles at several technical organizations including Aeras TB Foundation and Walter Reed Army Medical Center. He received a Ph.D. in biochemical engineering from Colorado State University and completed his post-doctoral training at Cornell University.

Matthew Pollman, M.D. has served as our Senior Vice President, Clinical Development since June 2021, and previously he was as a consultant for our company from October 2018 to June 2021. Dr. Pollman currently serves as a member of the board of directors of NaviGate Cardiac Structures, a private medical device company, and Perfusion Solutions, a private medical supply company. He has also served on the External Selection Committee of NIH Center for Accelerated Innovations at Cleveland Clinic since September 2013. Prior to joining us, he served as the Executive Vice President of NaviGate Cardiac Structures, a private medical device company, from June 2016 to June 2021. In addition, he served as the Chief Medical Officer of Juventas

Therapeutics, a private biotechnology company, from June 2016 to January 2019, and as a member of the board of directors of Juventas Therapeutics from June 2008 to January 2019. Prior to that, Dr. Pollman was the Chairman of Guided Interventions, a private medical device company from August 2013 to May 2017. From July 2008 to July 2013, he served as a Founder, President, and Chief Scientific Officer of CV Ingenuity, a private medical device company. Earlier in his career, he served on the faculty at Harvard Medical School and Morehouse School of Medicine, as the Medical Director, Research and Development at Abbott, a public medical device company, and as Director of the New Ventures Group at Guidant Corporation, a public medical device company, until its acquisition by Abbott. Dr. Pollman earned a B.S from Southwestern Adventist University, and an M.S. and M.D. from Loma Linda University, and completed his medical training at University of California San Francisco, Stanford University, and Brigham and Women's Hospital.

Jay Vora, Ph.D., M.B.A. has served as our Senior Vice President, Portfolio and Program Management since November 2020. From November 2017 to October 2020, Dr. Vora served as Head of Alliance Management at Sangamo Therapeutics, a public biotechnology company, and program leader on one of Sangamo's gene therapy programs. Before then, he was the Vice President of Program and Alliance Management at REGENXBIO from November 2015 to May 2017, where he supported multiple AAV-based gene therapy programs. Prior to that, Dr. Vora held roles in product development and program management at BioMarin and Chiron Corporation and worked in management consulting at PRTM. Dr. Vora earned a B.S. in pharmacy from University of Mumbai, an M.S. in medicinal chemistry from the University of Cincinnati, an M.B.A. from the Haas School of Business at the University of California, Berkeley, and a Ph.D. in Pharmaceutical Sciences from Northeastern University.

Non-Employee Directors

Eli Casdin, M.B.A. has served as a member of our board of directors since August 2019 and as a member of our audit committee since September 2019. Since founding Casdin Capital LLC in 2011, Mr. Casdin has served as its Chief Investment Officer. Mr. Casdin has served as Chief Executive Officer and a director of CM Life Sciences, Inc., CM Life Sciences II Inc., and CM Life Sciences III Inc., respectively, since July 2020, December 2020, and January 2021, all blank check companies. Mr. Casdin also served as a director of Exact Science, a public biotechnology company, from October 2017 to September 2020. From 2007 to July 2011, Mr. Casdin served as a Vice President and Analyst at Alliance Bernstein, with a focus on the life science and healthcare industries. Mr. Casdin was an Associate at Bear Stearns in 2007, and an Analyst at Cooper Hill Partners, one of the earliest biotechnology-focused investment firms, from 2003 to 2006. Mr. Casdin earned a B.S. from Columbia University and an M.B.A. from Columbia Business School and he currently serves on the Columbia University School of General Studies Board of Directors.

We believe Mr. Casdin is qualified to serve on our board because his extensive expertise and experience analyzing and investing in the life sciences industry.

Jin-Long Chen, Ph.D. has served as member of our board of directors since October 2016. Dr. Chen is the founder of NGM Biopharmaceuticals and has served as a member of the NGM board of directors and as Chief Scientific Officer since January 2008. He was also NGM's President until November 2014. Previously, Dr. Chen held various positions at Amgen, most recently as Vice President, Metabolic Disorders. Prior to joining Amgen when Amgen acquired Tularik in 2004, Dr. Chen served as Vice President of Biology at Tularik. Dr. Chen received a B.S. in nutrition and food science from Fu-Jen Catholic University and a Ph.D. in molecular and cell biology from the University of California, Berkeley.

We believe Dr. Chen is qualified to serve on our board because of his extensive medical research experience, and his experience as a founder, executive, and director of a public biopharmaceutical company.

David V. Goeddel, Ph.D. has served as a member of our board of directors since August 2016 and as a member of our compensation committee since December 2018. Dr. Goeddel has served as a Managing Partner of The Column Group, a venture capital firm, since 2007. Dr. Goeddel is a member of the board of directors at NGM Biopharmaceuticals, a public biopharmaceutical company. Additionally, Dr. Goeddel serves on the board

of directors for A2 Biotherapeutics (Chairman), Surrozen and Hexagon Bio (Chairman), all privately held biopharmaceutical companies. Dr. Goeddel co-founded Tularik in November 1991, was Vice President of Research until 1996, and served as Chief Executive Officer from 1996 until 2004. He then served as Amgen's first Senior Vice President until May 2006. Prior to Tularik, he was the first scientist hired by Genentech, and from 1978 to 1993 served in various positions, including Fellow, Staff Scientist and Director of Molecular Biology. His pioneering work in the fields of gene cloning and expression of human proteins was the basis for five marketed therapeutics developed by Genentech, including human insulin, human growth hormone, interferon-alpha, interferon-gamma and tissue plasminogen activator. Dr. Goeddel has received numerous scientific awards including the Scheele Medal, the Eli Lilly Award in Biological Chemistry, the Inventor of the Year Award, the Jacob Heskel Gabbay Award, the Howley Prize for Arthritis Research and the Warren Alpert Foundation Prize. He is a member of the National Academy of Sciences and the American Academy of Arts and Sciences. He holds a B.A. in chemistry from the University of California, San Diego and a Ph.D. in biochemistry from the University of Colorado.

We believe Dr. Goeddel is qualified to serve on our board of directors because of his experience serving as a board member of public and private life sciences companies, his experience as a founder and Chief Executive Officer of a public biopharmaceutical company, his depth of knowledge and substantial experience as a research scientist, his extensive experience in investing in diverse biotechnology companies and his experience as a public company board member, including within the biotechnology industry.

JeenJoo (JJ) Kang, Ph.D. has served as a member of our board of directors since August 2016. Dr. Kang has also served as a member of our compensation committee since December 2018, as a member of our audit committee since September 2019, and as our President, Treasurer and Secretary from August 2016 to June 2018. Dr. Kang has served as a Venture Partner at The Column Group since 2020, and prior to that served as an Associate beginning in 2015, then as a Partner from 2019 to 2020. She has served as the Chief Executive Officer of Appia Bio, a private biotechnology company, since July 2020. Previously, she worked at FibroGen in project management and corporate strategy from 2005 to 2009. Dr. Kang earned a B.A. in Chemistry from Harvard University and a Ph.D. in chemical biology at the California Institute of Technology.

We believe Dr. Kang is qualified to serve on our board of directors due to her educational background and her experience in investing in the life sciences industry.

Deepak Srivastava, M.D. has served as a member of our board of directors since October 2016. Dr. Srivastava has been a consultant for our company since September 2016 and Chairman of our Scientific Advisory Board since October 2016. Dr. Srivastava has been President of Gladstone Institutes since January 2018. He is currently the Younger Family Professor and a senior investigator at the Gladstone Institute of Cardiovascular Disease and director of the Roddenberry Stem Cell Center. Since 2005, Dr. Srivastava has been a professor in the Departments of Pediatrics and Biochemistry and Biophysics at UC San Francisco, and he is the Wilma and Adeline Pirag Distinguished Professor in pediatric developmental cardiology. He is the immediate past-president of the International Society for Stem Cell Research. Dr. Srivastava is a member of the American Academy of Arts and Sciences and the National Academy of Medicine. He received a B.S. from Rice University and an M.D. from the University of Texas. He trained in pediatrics at the University of California, San Francisco, and in pediatric cardiology at Harvard Medical School.

We believe Dr. Srivastava is qualified to serve on our board because of his scientific and educational background and his extensive expertise in the cardiovascular field and as a co-Founder of the company with specific expertise in the science of using direct *in vivo* reprogramming approach to cellular regeneration.

Catherine Stehman-Breen, M.D. has served as a member of our board of directors since June 2020. Beginning in December 2020, Dr. Stehman-Breen has served as the Chief Executive Officer and a member of the board of directors of Chroma Medicine, a private biotechnology company. From July 2019 to December 2020, Dr. Stehman-Breen served as Chief Development Officer of Obsidian Therapeutics, a private biotechnology company. Since March 2018, she has served as an entrepreneur-in-residence at Atlas Ventures, a venture capital

firm. Dr. Stehman-Brown serves as a director of Generation Bio, a public biotechnology company. Dr. Stehman-Breen also serves a member of the board of directors of Dyne Therapeutics, a public biotechnology company. She also previously served as Dyne's Chief Medical Officer from March 2018 to July 2019. From April 2018 to July 2019, Dr. Stehman-Breen served as Chief Medical Officer Disarm Therapeutics, a private biotechnology company. From March 2017 to December 2017, she served as Chief Medical Officer of Sarepta Therapeutics, a public biopharmaceutical company. Before that, she served as Vice President, Clinical Development and Regulatory Affairs at Regeneron Pharmaceuticals, a public biotechnology company, from January 2015 to March 2017. From 2003 to 2015, she held senior leadership roles at Amgen including Vice President, Global Development, leading the neuroscience, nephrology and bone therapeutic areas. Dr. Stehman-Breen earned a B.A. in biology and psychology from Colby College, an M.S. in epidemiology from the University of Washington, where she also completed her residency and fellowship training, and an M.D. from the University of Chicago in 1990. Dr. Stehman-Breen spent six years as a faculty member in the Division of Nephrology at the University of Washington.

We believe Dr. Stehman-Breen is qualified to serve on our board based on her medical expertise, her experience with clinical development and regulatory affairs in many therapeutics areas, her expertise as an executive in the biotechnology industry and her experience as a public company board member, including within the biotechnology industry.

Jeffrey T. Walsh, M.B.A. has served as a member of our board of directors since March 2020 and as a member of our audit committee since September 2020. Since 2011, Mr. Walsh has served in various roles at bluebird bio, including most recently as Strategic Advisor from January 2020 to April 2021, and previously as Chief Operating Officer, Chief Financial Officer, and Chief Strategy Officer. From 2008 to 2011, Mr. Walsh served as Chief Business Officer of Taligen Therapeutics, Inc. until it was acquired by Alexion Pharmaceuticals, Inc. Mr. Walsh started his career at SmithKline Beecham Corporation in finance and worldwide business development roles from 1987 to 1995. He subsequently held senior business development, finance, sales and operations roles at Allscripts Healthcare Solutions Inc. from 1995 to 1998, PathoGenesis Corp. from 1998 to 2000, EXACT Sciences Corporation from 2000 to 2004, and Inotek Pharmaceuticals Corp. from 2004 to 2008. He received a B.A. in sociology and economics from Yale University and an M.B.A. from the Kellogg Graduate School of Management at Northwestern University.

We believe that Mr. Walsh's qualifications to serve on our board of directors include his leadership and management experience in the biotechnology industry and his experience in finance and business development and strategic planning as an executive officer at multiple healthcare companies.

R. Sanders (Sandy) Williams, M.D. has served as a member of our board of directors since October 2016 and as a member of our compensation committee since December 2018. Dr. Williams has served as the President Emeritus of Gladstone Institutes, a non-profit biomedical research enterprise since January 2018 and previously served as its President from November 2009 to December 2017. Dr. Williams also served as the Chief Executive Officer of Gladstone Foundation, a not-for-profit organization supporting Gladstone Institutes from January 2016 to December 2018. Since January 2018, Dr. Williams has served as Professor of Medicine and Senior Advisor for International Strategy at Duke University and, beginning in February 2021, is acting as its Interim Vice President for Research and Innovation. Dr. Williams has also served as a Professor of Medicine at the University of California, San Francisco since 2010. From 2010 to 2017, Dr. Williams was the President and the Robert W. and Linda L. Mahley Distinguished Professor of Medicine of Gladstone Institutes. Prior to this, Dr. Williams served in various roles, including as Dean and Senior Vice Chancellor of the Duke University School of Medicine, from 2001 to 2010. He was the founding Dean of the Duke-NUS Graduate Medical School, Singapore, from 2003 to 2008 and served on its Governing Board from 2003 to 2010. From 1990 to 2001, Dr. Williams was Chief of Cardiology and Director of the Ryburn Center for Molecular Cardiology at the University of Texas, Southwestern Medical Center. Dr. Williams is a member of the board of directors of the Laboratory Corporation of America Holdings, a public diagnostic technologies company, serving on the audit committee and chairing the quality and compliance committee. Dr. Williams also serves as a member of the board of directors of Amgen,

Inc., a biotechnology company, serving as a member of the governance and nominating and corporate responsibility and compliance committees. Dr. Williams was elected to the National Academy of Medicine in 2002. Dr. Williams received an A.B. from Princeton University and an M.D. from Duke University.

We believe Dr. Williams is qualified to serve on our board because of his scientific and educational background, his extensive expertise in the cardiovascular field, and his experience as a public company board member, including within the biotechnology industry.

Family Relationships

There are no family relationships among any of our executive officers or directors.

Legal Proceedings and Bankruptcy

There are no material legal proceedings to which any of our directors is a party adverse to us or in which any such person has a material interest adverse to us.

Board Composition

Our board of directors currently consists of nine members. After the completion of this offering, the number of directors will be fixed from time to time by our board of directors, subject to the terms of our amended and restated certificate of incorporation and amended and restated bylaws. Each of our current directors will continue to serve as a director until the election and qualification of his or her successor, or until his or her earlier death, resignation or removal.

Our amended and restated certificate of incorporation will provide that our board of directors will be divided into three classes with staggered three-year terms. Only one class of directors will be elected at each annual meeting of stockholders, with the other classes continuing for the remainder of their respective three-year terms. Our current directors will be divided among the three classes as follows:

- the Class I directors will be David V. Goeddel, Jeffrey T. Walsh, and R. Sanders (Sandy) Williams, and their terms will expire at the annual meeting of stockholders to be held in 2022;
- the Class II directors will be Eli Casdin, Jin-Long Chen, and Catherine Stehman-Brown, and their terms will expire at the annual meeting of stockholders to be held in 2023; and
- the Class III directors will be Faraz Ali, JeenJoo (JJ) Kang, and Deepak Srivastava, and their terms will expire at the annual meeting of stockholders to be held in 2024.

At each annual meeting of stockholders, upon the expiration of the term of a class of directors, the successor to each such director in the class will be elected to serve from the time of election and qualification until the third annual meeting following his or her election and until his or her successor is duly elected and qualified, in accordance with our amended and restated certificate of incorporation. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one third of our directors.

This classification of our board of directors may have the effect of delaying or preventing changes in control of our company.

Director Independence

Upon the completion of this offering, our common stock will be listed on Nasdaq Global Select Market. Under the rules of Nasdaq Stock Market LLC (Nasdaq), independent directors must comprise a majority of a listed company’s board of directors within one year of the completion of this offering. In addition, the rules of Nasdaq require that, subject to specified exceptions, each member of a listed company’s audit, compensation and corporate governance and nominating committees be independent. Audit committee members and

compensation committee members must also satisfy the independence criteria set forth in Rule 10A-3 and Rule 10C-1, respectively, under the Securities Exchange Act of 1934, as amended (the Exchange Act). Under the rules of Nasdaq, a director will only qualify as an "independent director" if, in the opinion of that company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.

To be considered to be independent for purposes of Rule 10A-3 and under the rules of Nasdaq, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors or any other board committee: (i) accept, directly or indirectly, any consulting, advisory or other compensatory fee from the listed company or any of its subsidiaries or (ii) be an affiliated person of the listed company or any of its subsidiaries.

To be considered independent for purposes of Rule 10C-1 and under the rules of Nasdaq, the board of directors must affirmatively determine that each member of the compensation committee is independent, including a consideration of all factors specifically relevant to determining whether the director has a relationship to the company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including: (i) the source of compensation of such director, including any consulting, advisory or other compensatory fee paid by the company to such director and (ii) whether such director is affiliated with the company, a subsidiary of the company or an affiliate of a subsidiary of the company.

Our board of directors undertook a review of its composition, the composition of its committees and the independence of our directors and considered whether any director has a material relationship with us that could compromise his or her ability to exercise independent judgment in carrying out his or her responsibilities. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that Eli Casdin, Jin-Long Chen, David V. Goeddel, JeenJoo (JJ) Kang, Deepak Srivastava, Catherine Stehman-Breen, Jeffrey T. Walsh, and R. Sanders (Sandy) Williams representing eight of our nine directors, do not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is "independent" as that term is defined under the rules of .

In making these determinations, our board of directors considered the current and prior relationships that each non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director, and the transactions involving them described in the section titled "Certain Relationships and Related Party Transactions."

Board Leadership Structure

Our board of directors is currently chaired by David V. Goeddel. As a general policy, our board of directors believes that separation of the positions of Chair of our board of directors and Chief Executive Officer reinforces the independence of our board of directors from management, creates an environment that encourages objective oversight of management's performance and enhances the effectiveness of our board of directors as a whole. As such, Mr. Ali serves as our Chief Executive Officer while Dr. Goeddel serves as the Chair of our board of directors but is not an officer. We currently expect and intend the positions of Chair of our board of directors and Chief Executive Officer to continue to be held by two individuals in the future.

Role of the Board in Risk Oversight

Our board of directors has an active role, as a whole and also at the committee level, in overseeing the management of our risks. Our board of directors is responsible for general oversight of risks and regular review of information regarding our risks, including credit risks, liquidity risks and operational risks. The compensation committee is responsible for overseeing the management of risks relating to our executive compensation plans and arrangements. The audit committee is responsible for overseeing the management of risks relating to

accounting matters and financial reporting. The corporate governance and nominating committee is responsible for overseeing the management of risks associated with the independence of our board of directors and potential conflicts of interest. Although each committee is responsible for evaluating certain risks and overseeing the management of such risks, our entire board of directors is regularly informed through discussions from committee members about such risks.

Board Committees

Our board of directors has an audit committee, a compensation committee and a corporate governance and nominating committee, each of which has the composition and the responsibilities described below.

Audit Committee

The members of our audit committee are Eli Casdin, JeenJoo (JJ) Kang, and Jeffrey T. Walsh. Mr. Walsh is the chair of our audit committee and is an audit committee financial expert, as that term is defined under the SEC rules implementing Section 407 of the Sarbanes-Oxley Act of 2002, and possesses financial sophistication, as defined under the rules of Nasdaq. Our audit committee will oversee our corporate accounting and financial reporting process and assist our board of directors in monitoring our financial systems. Our audit committee will also:

- select and hire the independent registered public accounting firm to audit our financial statements;
- help to ensure the independence and performance of the independent registered public accounting firm;
- approve audit and non-audit services and fees;
- review financial statements and discuss with management and the independent registered public accounting firm our annual audited and quarterly financial statements, the results of the independent audit and the quarterly reviews and the reports and certifications regarding internal controls over financial reporting and disclosure controls;
- prepare the audit committee report that the SEC requires to be included in our annual proxy statement;
- review reports and communications from the independent registered public accounting firm;
- review the adequacy and effectiveness of our internal controls and disclosure controls and procedure;
- review our policies on risk assessment and risk management;
- review and monitor conflicts of interest situations, and approve or prohibit any involvement in matters that may involve a conflict of interest or taking of a corporate opportunity;
- review related party transactions; and
- establish and oversee procedures for the receipt, retention and treatment of accounting related complaints and the confidential submission by our employees of concerns regarding questionable accounting or auditing matters.

Our audit committee operates under a written charter, which satisfies the applicable rules of the SEC and the listing standards of the Nasdaq Stock Market LLC.

Compensation Committee

The members of our compensation committee are Catherine Stehman-Brown, Jeffrey T. Walsh, and R. Sanders (Sandy) Williams. Dr. Williams is the chair of our compensation committee. Our compensation committee will oversee our compensation policies, plans and benefits programs. The compensation committee will also:

- oversee our overall compensation philosophy and compensation policies, plans and benefit programs;

- review and approve compensation for our executive officers and directors;
- prepare the compensation committee report that the SEC will require to be included in our annual proxy statement; and
- administer our equity compensation plans.

Our compensation committee operates under a written charter, which satisfies the applicable rules of the SEC and the listing standards of the Nasdaq Stock Market LLC.

Corporate Governance and Nominating Committee

The members of our corporate governance and nominating committee are Jin-Long Chen, David V. Goeddel, and Deepak Srivastava. Dr. Srivastava is the chair of our corporate governance and nominating committee. Our corporate governance and nominating committee will oversee and assist our board of directors in reviewing and recommending nominees for election as directors. Specifically, the corporate governance and nominating committee will:

- identify, evaluate and make recommendations to our board of directors regarding nominees for election to our board of directors and its committees;
- consider and make recommendations to our board of directors regarding the composition of our board of directors and its committees;
- review developments in corporate governance practices;
- evaluate the adequacy of our corporate governance practices and reporting; and
- evaluate the performance of our board of directors and of individual directors.

Our corporate governance and nominating committee operates under a written charter, which satisfies the applicable rules of the SEC and the listing standards of the Nasdaq Stock Market LLC.

Director Compensation

Prior to this offering, we had not implemented a formal policy with respect to compensation payable to our non-employee directors. We reimburse our directors for expenses associated with attending meetings of our board of directors and its committees.

The following table presents the total compensation each of our non-employee directors received during the year ended December 31, 2020. In addition, in June 2021, Mr. Walsh was awarded an option to purchase 10,000 shares of our common stock.

Name	Option Awards($)(1)	All Other Compensation ($)	Total ($)
Eli Casdin, M.B.A.	—	—	—
Jin-Long Chen, Ph.D.	—	—	—
David V. Goeddel, Ph.D.	—	—	—
JeenJoo (JJ) Kang, Ph.D.	—	—	—
Deepak Srivastava, M.D.	—	75,000(2)	75,000
Catherine Stehman-Breen, M.D.	151,983	—	151,983
Jeffrey T. Walsh, M.B.A.	142,713	—	142,713
R. Sanders (Sandy) Williams, M.D.	—	—	—

(1) The amounts disclosed represent the aggregate grant date fair value of the award as calculated in accordance with ASC 718. The assumptions used in calculating the grant date fair value of the award disclosed in this column are set forth in Note 2 to our audited financial statements included elsewhere in this prospectus.

These amounts do not correspond to the actual value that may be recognized by the named executive officers upon vesting of the applicable awards.

(2) The amount disclosed relates to compensation paid under the Company's consulting agreement with Dr. Srivastava.

Non-Employee Director Compensation Policy

In June 2021, our board of directors adopted, and in July 2021 our stockholders approved, a new compensation policy for our non-employee directors that became effective as of the date of the effectiveness of the registration statement of which this prospectus forms a part. This policy was developed with input from our compensation committee's independent compensation consultant, Compensia, regarding practices and compensation levels at comparable companies. It is designed to attract, retain and reward our non-employee directors.

Under this director compensation policy, each non-employee director will receive cash and equity compensation for his or her services as a member of our board of directors, as described below. We also will reimburse our non-employee directors for reasonable, customary and documented travel expenses to meetings of our board of directors or its committees.

The director compensation policy includes a maximum annual limit of $500,000 of cash compensation and equity awards that may be paid, issued or granted to a non-employee director in any fiscal year. For purposes of these limitations, the value of an equity award is based on its grant date fair value. Any cash compensation paid or equity awards granted to a person for his or her services as an employee, for his or her services as a consultant (other than as a non-employee director), or prior to the date of the effectiveness of the registration statement of which this prospectus forms a part will not count for purposes of the limitation. The maximum limit does not reflect the intended size of any potential compensation or equity awards to our non-employee directors.

Cash Compensation

Following the completion of this offering, each non-employee director will be paid an annual cash retainer of $35,000. In addition, each non-employee director who serves as chair or chair or member of a committee will be entitled to receive the following cash compensation under the policy for his or her services:

Board Chair:	$30,000
Lead Independent Director:	$20,000
Audit Committee Chair:	$15,000
Audit Committee Member:	$ 7,500
Compensation Committee Chair:	$10,000
Compensation Committee Member:	$ 5,000
Nominating and Corporate Governance Committee Chair:	$ 8,000
Nominating and Corporate Governance Committee Member:	$ 4,000

The above-listed fees for service as chair or members of committees are payable in addition to the non-employee director retainer. Each non-employee director who serves as a committee chair will receive only the additional annual cash fee as the chair of the committee, and not the additional annual fee as a member of the committee. All cash payments to non-employee directors are paid quarterly in arrears on a prorated basis.

Equity Compensation

Initial Award. Each person who first becomes a non-employee director after the effective date of the director compensation policy will receive, on the first trading day on or after the date that the person first becomes a non-employee director, an initial award (the Initial Award) of stock options to purchase shares of our common stock with grant date fair value equal to $320,000. The Initial Award will be scheduled to vest in equal installments as to one thirty-sixth (1/36th) of the shares of our common stock subject to the Initial Award on a monthly basis following the Initial Award's grant date, on the same day of the month as the grant date, subject to continued services to us through the applicable vesting dates. If the person was a member of our board of

directors and also an employee, then becoming a non-employee director due to termination of employment will not entitle the person to an Initial Award.

Annual Award. Each non-employee director who has served continuously as a non-employee director for no less than 6 months as of the date of an annual meeting of our stockholders occurring following the effective date of our non-employee director compensation policy will receive, on the first trading day immediately after the date of each annual meeting, an annual award (the Annual Award) of stock options to purchase shares of our common stock with grant date fair value equal to $160,000. Each Annual Award will be scheduled to vest in full upon the first anniversary of the date of grant or, if earlier, the day immediately before the date of the next annual meeting of the Company that occurs after the Annual Award's grant date, subject to continued services to us through the applicable vesting date.

Change in Control. In the event of our change in control, as defined in our 2021 Plan (or its successor plan, as applicable), each non-employee director's then outstanding equity awards covering shares of our common stock will accelerate vesting in full, provided that he or she remains a non-employee director through the date of our change in control.

Other Award Terms. Each Initial Award and Annual Award will be granted under our 2021 Equity Incentive Plan (or its successor plan, as applicable) and form of award agreement under such plan. These awards will have a maximum term to expiration of 10 years from their grant and a per share exercise price equal to 100% of the fair market value of a share of our common stock on the award's grant date.

2021 Non-Employee Director Equity Awards

In June 2021, our board of directors approved an option grant to Jeffrey T. Walsh to provide him additional incentives to remain with us and to promote further alignment between his interests and those of our stockholders. The number of shares subject to the option grant is 10,000 and the exercise price per share is $9.36. The grant is subject to the terms and conditions of the 2016 Plan and form of option agreement thereunder, and will vest as to 1/12th of the total shares subject to the grant each month following the vesting commencement date, subject to Mr. Walsh's continued service with us, and further subject to vesting acceleration under certain circumstances as described under "—Non-Employee Director Compensation Policy."

Compensation Committee Interlocks and Inside Participation

None of the members of our board of directors who serve on our compensation committee is or has been an officer or employee of our company.

None of our executive officers currently serves, or in the past fiscal year has served, as a member of the board of directors or compensation committee (or other board committee performing equivalent functions or, in the absence of any such committee, the entire board of directors) of any entity that has one or more executive officers serving on our board of directors or compensation committee.

Code of Business Conduct and Ethics

In June 2021, our board of directors adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions. Following this offering, the code of business conduct and ethics will be available on our website at www.tenayatherapeutics.com. We intend to disclose future amendments to such code, or any waivers of its requirements, applicable to any principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions or our directors on our website identified above or in a current report on Form 8-K. Information contained on, or accessible through, our website is not incorporated by reference into this prospectus and should not be considered to be part of this prospectus. The inclusion of our website address in this prospectus is an inactive textual reference only.

EXECUTIVE COMPENSATION

Our named executive officers for 2020, which consist of our principal executive officer and the next two most highly compensated executive officers during 2020, are:

- Faraz Ali, M.B.A., Chief Executive Officer;
- Timothy Hoey, Ph.D., Chief Scientific Officer; and
- Whittemore (Whit) Tingley, M.D., Ph.D., Chief Medical Officer.

Summary Compensation Table

The following table sets forth information regarding the compensation of our named executive officers for the year ended December 31, 2020.

Name and Principal Position	Year	Salary ($)	Bonus ($)	Option Awards ($)(1)	All Other Compensation ($)	Total ($)
Faraz Ali, M.B.A. *Chief Executive Officer*	2020	425,000	126,500	197,500	1,300	750,300
Timothy Hoey, Ph.D. *Chief Scientific Officer*	2020	375,000	95,000	46,800	3,557	520,357
Whittemore (Whit) Tingley, M.D., Ph.D. *Chief Medical Officer*	2020	371,000	95,000	—	1,520	467,520

(1) The amounts disclosed represent the aggregate grant date fair value of the award as calculated in accordance with ASC 718. The assumptions used in calculating the grant date fair value of the award disclosed in this column are set forth in Note 2 to our audited financial statements included elsewhere in this prospectus. These amounts do not correspond to the actual value that may be recognized by the named executive officers upon vesting of the applicable awards.

Outstanding Equity Awards at Fiscal Year End

The following table sets forth information concerning outstanding equity awards held by each of our named executive officers as of December 31, 2020:

		Option Awards				Stock Awards	
Name	Grant Date(1)	Number of Securities Underlying Unexercised Options Exercisable (#)	Number of Securities Underlying Unexercised Options Unexercisable (#)	Option Exercise Price ($)(2)	Option Expiration Date	Number of Shares of Stock that Have Not Vested (#)	Market Value of Shares of Stock that Have Not Vested ($)(3)
Faraz Ali, M.B.A.	9/6/2018	425,000(4)	—	0.66	9/5/2028	—	—
	3/10/2020	7,812	33,854(5)	2.70	3/9/2030	—	—
Timothy Hoey, Ph.D.	9/17/2017	—	—	0.42	9/16/2027	27,778(6)	156,668
	2/6/2019	33,333(7)	—	0.78	2/5/2029	—	—
	2/7/2020	2,291	7,708(5)	2.70	2/6/2030	—	—
Whittemore (Whit) Tingley, M.D., Ph.D.	12/10/2018	75,000(8)	—	0.78	12/9/2028	—	—

(1) Each of the outstanding equity awards was granted pursuant to our Amended and Restated 2016 Equity Incentive Plan (the 2016 Plan).
(2) This column represents the fair market value of a share of our common stock on the date of grant, as determined by our board of directors.

(3) This column represents the fair market value of a share of our common stock as of December 31, 2020, the market value has been calculated based on an estimated per-share common stock value of $5.64 per share as of December 31, 2020.
(4) 1/5th of the shares subject to this option vested on the first anniversary of the vesting commencement date and 1/60th of the shares vest monthly thereafter, subject to the optionee's continued status as a service provider through each vest date. All of the shares underlying this option are subject to an early exercise provision.
(5) 1/48th of the shares subject to this option vest monthly after the grant date, subject to the optionee's continued status as a service provider through each vest date.
(6) The shares were acquired pursuant to an early exercise provision and remain subject to our repurchase right in accordance with the vesting schedule of the exercised option. 1/4th of the total number of shares subject to the option vested on August 14, 2018 and 1/48th of the total number of shares subject to the option vest monthly thereafter, subject to the optionee's continued status as a service provider through each vest date.
(7) 1/48th of the shares subject to this option vest monthly after the grant date, subject to the optionee's continued status as a service provider through each vest date. All of the shares underlying this option are subject to an early exercise provision.
(8) 1/4th of the shares subject to this option vested on the first anniversary of the vesting commencement date and 1/48th of the shares vest monthly thereafter, subject to the optionee's continued status as a service provider through each vest date. All of the shares underlying this option are subject to an early exercise provision.

2021 Executive Officer Equity Awards

In January 2021, our compensation committee approved option grants to Dr. Hoey covering 16,666 shares and to Dr. Tingley covering 25,000 shares, in each case, at an exercise price per share of $5.64. In February 2021, our board of directors approved an option grant to Mr. Ali covering 416,666 shares at an exercise price per share of $5.64. In June 2021, our board of directors approved option grants to Mr. Ali covering 166,666 shares and to Dr. Tingley covering 108,333 shares, in each case, at an exercise price per share of $9.36. These grants were made to provide them additional incentives to remain with us and to promote further alignment between their interests and those of our stockholders. In July 2021, our board of directors approved a new hire option grant to Ms. Patterson covering 354,166 shares at an exercise price per share of $10.56.

These grants are subject to the terms and conditions of the 2016 Plan and form of option agreement thereunder, and the grants to Mr. Ali, Dr. Hoey, and Dr. Tingley vest as to 1/48th of the total shares subject to the grant each month following the vesting commencement date, and the grant to Ms. Patterson vests as to 25% on the one-year anniversary of Ms. Patterson's start date and as to 1/48th of the total shares subject to the grant each month following such anniversary date, in each case subject to the executive officer's continued service with us, and further subject to vesting acceleration under certain circumstances as described under "—Potential payments upon termination or change in control."

Executive Employment Arrangements

Each of our current executive officers has executed our standard form of confidential information, invention assignment and arbitration agreement.

We have entered into an employment offer letter agreement with each of our named executive officers in connection with his or her employment with us. These offer letters provide for "at will" employment.

Faraz Ali, M.B.A.

We have entered into a confirmatory employment letter with Mr. Ali, our Chief Executive Officer. The confirmatory employment letter has no specific term and provides for at-will employment. Mr. Ali's current annual base salary is $475,000 and his annual target bonus is 35% of his annual base salary.

Timothy Hoey, Ph.D.

We have entered into a confirmatory employment letter with Dr. Hoey, our Chief Scientific Officer. The confirmatory employment letter has no specific term and provides for at-will employment. Dr. Hoey's current annual base salary is $385,000 and his annual target bonus is 30% of his annual base salary.

Leone D. Patterson, M.B.A.

We have entered into an employment letter with Ms. Patterson, our Chief Financial and Business Officer. Ms. Patterson began employment in June 2021. The employment letter has no specific term and provides for at-will employment. Ms. Patterson's current annual base salary is $400,000 and her annual target bonus is 30% of her annual base salary.

Whittemore (Whit) Tingley, M.D., Ph.D.

We have entered into a confirmatory employment letter with Dr. Tingley, our Chief Medical Officer. The confirmatory employment letter has no specific term and provides for at-will employment. Dr. Tingley's current annual base salary is $402,000 and his annual target bonus is 30% of his annual base salary.

Potential Payments Upon Termination or Change in Control

Executive Change in Control and Severance Plan

In June 2021, our board of directors adopted an Executive Change in Control and Severance Plan, or the Executive Severance Plan, pursuant to which our named executive officers and certain other key employees are eligible to receive severance benefits, as specified in and subject to the employee signing a participation agreement under our Executive Severance Plan. This Executive Severance Plan was developed with input from Compensia regarding severance practices at comparable companies. It is designed to attract, retain and reward senior level employees. The Executive Severance Plan will be in lieu of any other severance payments and benefits to which such key employee was entitled prior to signing the participation agreement.

Each of our named executive officers has signed a participation agreement under our Executive Severance Plan providing for the rights to the applicable payments and benefits described below.

In the event of a "qualifying termination" of the employment of a named executive officer, which generally includes a termination of employment by us for a reason other than "cause" or the named executive officer's death or "disability" (as such terms are defined in our Executive Severance Plan), but in the case of Mr. Ali includes a termination of employment by him for "good reason" or by us for a reason other than "cause" or his death or disability, in all cases, that occurs outside the change in control period (as described below), then the named executive officer will be entitled to the following payments and benefits:

- a lump sum payment equal to nine months of the named executive officer's annual base salary as in effect immediately prior to his or her qualifying termination of employment, or twelve months in the case of Mr. Ali; and
- continued health coverage under COBRA or a lump sum payment equal to the premium cost of continued health coverage under the Consolidated Omnibus Reconciliation Act of 1985 as amended, or COBRA, for a period of twelve months.

In the event of a termination of employment by the named executive officer for "good reason" or by us for a reason other than "cause" or the named executive officer's death or disability, in each case, within a period beginning upon and ending twelve months following a "change in control" (as defined in our Executive Severance Plan), or in the case of Mr. Ali beginning three months prior to and ending 18 months following a

"change in control" (such period, in either case, the "change in control period"), then the named executive officer will be entitled to the following payments and benefits:

- a lump sum payment equal to 12 months of the named executive officer's annual base salary as in effect immediately prior to his or her qualifying termination of employment;
- continued health coverage under COBRA or a lump sum payment equal to the cost of continued health coverage under COBRA for a period of 12 months;
- 100% accelerated vesting of all outstanding equity awards, and, with respect to equity awards with performance-based vesting, all performance goals or other vesting criteria will be deemed achieved at 100% of target levels for the relevant performance period(s); and
- in the case of Mr. Ali, a lump sum payment equal to 100% of his target annual bonus for the year in which the qualifying termination occurs.

The receipt of the payments and benefits provided for under the Executive Severance Plan described above is conditioned on the named executive officer signing and not revoking a separation and release of claims agreement and such release becoming effective and irrevocable no later than the 60th day following the named executive officer's involuntary termination of employment, as well as continued compliance with the invention assignment and confidentiality agreement applicable to the named executive officer.

In addition, if any of the payments or benefits provided for under the Executive Severance Plan or otherwise payable to a named executive officer would constitute "parachute payments" within the meaning of Section 280G of the Code and could be subject to the related excise tax, the named executive officer will receive either full payment of such payments and benefits or such lesser amount that would result in no portion of the payments and benefits being subject to the excise tax, whichever results in the greater amount of after-tax benefits to them. The Executive Severance Plan does not require us to provide any tax gross-up payments to the named executive officers.

Employee Benefit and Stock Plans

2021 Equity Incentive Plan

In June 2021, our board of directors adopted, and in July 2021 our stockholders approved, our 2021 Equity Incentive Plan (2021 Plan). The 2021 Plan became effective on the business day immediately prior to the effective date of the registration statement of which this prospectus forms a part. Our 2021 Plan provides for the grant of incentive stock options, within the meaning of Section 422 of the Internal Revenue Code (the Code), to our employees and any of our parent and subsidiary corporations' employees, and for the grant of nonstatutory stock options, restricted stock, restricted stock units, stock appreciation rights, performance units, and performance shares to our employees, directors, and consultants and our subsidiary corporations' employees and consultants.

Authorized shares. A total of 4,000,000 shares of our common stock are reserved for issuance pursuant to our 2021 Plan. In addition, the shares reserved for issuance under our 2021 Plan will also include shares of our common stock subject to or issued pursuant to awards granted under our 2016 Plan that, after the effective date of the registration statement of which this prospectus forms a part, expire or otherwise terminate without having been exercised in full, are tendered to or withheld by us for payment of an exercise price or for tax withholding obligations, or are forfeited to or repurchased by us due to failure to vest (provided that the maximum number of shares that may be added to the 2021 Plan is 2,430,000 shares). The number of shares available for issuance under our 2021 Plan will also include an annual increase on the first day of each fiscal year beginning with our 2022 fiscal year, equal to the least of: 4,000,000 shares; four percent (4%) of the outstanding shares of our common stock as of the last day of the immediately preceding fiscal year; or such other amount as our board of directors may determine. This annual increase will operate only until the ten year anniversary of our board's approval of the 2021 Plan.

If an award expires or becomes unexercisable without having been exercised in full, is surrendered pursuant to an exchange program, or, with respect to restricted stock, restricted stock units, performance units or performance shares, is forfeited to or repurchased by us due to failure to vest, the unpurchased shares (or for awards other than stock options or stock appreciation rights, the forfeited or repurchased shares) will become available for future grant or sale under the 2021 Plan (unless the 2021 Plan has terminated). With respect to stock appreciation rights, only the net shares actually issued will cease to be available under the 2021 Plan and all remaining shares under stock appreciation rights will remain available for future grant or sale under the 2021 Plan (unless the 2021 Plan has terminated). Shares that have actually been issued under the 2021 Plan will not be returned to the 2021 Plan except if shares issued pursuant to awards of restricted stock, restricted stock units, performance shares, or performance units are repurchased by or forfeited to us due to failure to vest, such shares will become available for future grant under the 2021 Plan. Shares used to pay the exercise price of an award or satisfy the tax withholding obligations related to an award will become available for future grant or sale under the 2021 Plan. To the extent an award is paid out in cash rather than shares, such cash payment will not result in a reduction in the number of shares available for issuance under the 2021 Plan.

Plan administration. Our board of directors or one or more committees appointed by our board of directors will administer our 2021 Plan. The compensation committee of our board of directors will initially administer our 2021 Plan. In addition, if we determine it is desirable to qualify transactions under our 2021 Plan as exempt under Rule 16b-3 of the Exchange Act, such transactions will be structured to satisfy the requirements for exemption under Rule 16b-3. Subject to the provisions of our 2021 Plan, the administrator has the power to administer our 2021 Plan and make all determinations deemed necessary or advisable for administering the 2021 Plan, including but not limited to, the power to determine the fair market value of our common stock, select the service providers to whom awards may be granted, determine the number of shares covered by each award, approve forms of award agreements for use under the 2021 Plan, determine the terms and conditions of awards (including, but not limited to, the exercise price, the time or times at which awards may be exercised, any vesting acceleration or waiver or forfeiture restrictions and any restriction or limitation regarding any award or the shares relating thereto), construe and interpret the terms of our 2021 Plan and awards granted under it, prescribe, amend and rescind rules relating to our 2021 Plan, including creating sub-plans, modify or amend each award, including but not limited to the discretionary authority to extend the post-termination exercisability period of awards, and allow a participant to defer the receipt of payment of cash or the delivery of shares that would otherwise be due to such participant under an award. The administrator also has the authority to allow participants the opportunity to transfer outstanding awards to a financial institution or other person or entity selected by the administrator and to institute an exchange program by which outstanding awards may be surrendered or cancelled in exchange for awards of the same type, which may have a higher or lower exercise price and/or different terms, awards of a different type, and/or cash or by which the exercise price of an outstanding award is increased or reduced. The administrator’s decisions, interpretations, and other actions are final and binding on all participants.

Stock options. Stock options may be granted under our 2021 Plan. The exercise price of options granted under our 2021 Plan must at least be equal to the fair market value of our common stock on the date of grant. The term of an option may not exceed ten years. With respect to any participant who owns more than 10% of the voting power of all classes of our (or any parent or subsidiary of ours) outstanding stock, the term of an incentive stock option granted to such participant must not exceed five years and the exercise price must equal at least 110% of the fair market value on the grant date. The administrator will determine the methods of payment of the exercise price of an option, which may include cash, shares or other property acceptable to the administrator, as well as other types of consideration permitted by applicable law. After the termination of service of an employee, director, or consultant, he or she may exercise his or her option for the period of time stated in his or her option agreement. In the absence of a specified time in an award agreement, if termination is due to death or disability, the option will remain exercisable for twelve months following the termination of service. In all other cases, in the absence of a specified time in an award agreement, the option will remain exercisable for three months following the termination of service. An option, however, may not be exercised later than the expiration of its term. Subject to the provisions of our 2021 Plan, the administrator determines the other terms of options.

Stock appreciation rights. Stock appreciation rights may be granted under our 2021 Plan. Stock appreciation rights allow the recipient to receive the appreciation in the fair market value of our common stock between the exercise date and the date of grant. Stock appreciation rights may not have a term exceeding ten years. After the termination of service of an employee, director, or consultant, he or she may exercise his or her stock appreciation right for the period of time stated in his or her stock appreciation rights agreement. In the absence of a specified time in an award agreement, if termination is due to death or disability, the stock appreciation rights will remain exercisable for twelve months following the termination of service. In all other cases, in the absence of a specified time in an award agreement, the stock appreciation rights will remain exercisable for three months following the termination of service. However, in no event may a stock appreciation right be exercised later than the expiration of its term. Subject to the provisions of our 2021 Plan, the administrator determines the other terms of stock appreciation rights, including when such rights become exercisable and whether to pay any increased appreciation in cash or with shares of our common stock, or a combination thereof, except that the per share exercise price for the shares to be issued pursuant to the exercise of a stock appreciation right will be no less than 100% of the fair market value per share on the date of grant.

Restricted stock. Restricted stock may be granted under our 2021 Plan. Restricted stock awards are grants of shares of our common stock that vest in accordance with terms and conditions established by the administrator. The administrator will determine the number of shares of restricted stock granted to any employee, director, or consultant and, subject to the provisions of our 2021 Plan, will determine the terms and conditions of such awards. The administrator may impose whatever vesting conditions it determines to be appropriate (for example, the administrator may set restrictions based on the achievement of specific performance goals or continued service to us), except the administrator, in its sole discretion, may accelerate the time at which any restrictions will lapse or be removed. Recipients of restricted stock awards generally will have voting and dividend rights with respect to such shares upon grant without regard to vesting, unless the administrator provides otherwise. Shares of restricted stock that do not vest are subject to our right of repurchase or forfeiture.

Restricted stock units. Restricted stock units may be granted under our 2021 Plan. Restricted stock units are bookkeeping entries representing an amount equal to the fair market value of one share of our common stock. Subject to the provisions of our 2021 Plan, the administrator determines the terms and conditions of RSUs, including the vesting criteria and the form and timing of payment. The administrator may set vesting criteria based upon the achievement of company-wide, divisional, business unit or individual goals (including, but not limited to, continued employment or service), applicable federal or state securities laws or any other basis determined by the administrator in its discretion. The administrator, in its sole discretion, may pay earned restricted stock units in the form of cash, in shares or in some combination thereof. In addition, the administrator, in its sole discretion, may accelerate the time at which any restrictions will lapse or be removed.

Performance units and performance shares. Performance units and performance shares may be granted under our 2021 Plan. Performance units and performance shares are awards that will result in a payment to a participant only if performance objectives established by the administrator are achieved or the awards otherwise vest. The administrator will establish performance objectives or other vesting criteria in its discretion, which, depending on the extent to which they are met, will determine the number or the value of performance units and performance shares to be paid out to participants. The administrator may set performance objectives based on the achievement of company-wide, divisional, business unit, or individual goals (including, but not limited to, continued employment or service), applicable federal or state securities laws or any other basis determined by the administrator in its discretion. After the grant of a performance unit or performance share, the administrator, in its sole discretion, may reduce or waive any performance objectives or other vesting provisions for such performance units or performance shares. Performance units will have an initial value established by the administrator on or prior to the grant date. Performance shares will have an initial value equal to the fair market value of our common stock on the grant date. The administrator, in its sole discretion, may pay out earned performance units or performance shares in cash, shares, or in some combination thereof.

Non-transferability of awards. Unless the administrator provides otherwise, our 2021 Plan generally does not allow for the transfer of awards and only the recipient of an award may exercise an award during his or her

lifetime. If the administrator makes an award transferrable, such award will contain such additional terms and conditions as the administrator deems appropriate.

Certain adjustments. In the event of certain changes in our capitalization, to prevent diminution or enlargement of the benefits or potential benefits available under our 2021 Plan, the administrator will adjust the number and class of shares that may be delivered under our 2021 Plan and/or the number, class, and price of shares covered by each outstanding award and the numerical share limits set forth in our 2021 Plan.

Dissolution or liquidation. In the event of our proposed liquidation or dissolution, the administrator will notify participants as soon as practicable and, to the extent not exercised, all awards will terminate immediately prior to the consummation of such proposed transaction.

Merger or change in control. Our 2021 Plan provides that in the event of a merger or change in control, as defined under our 2021 Plan, each outstanding award will be treated as the administrator determines, without a participant's consent. The administrator is not required to treat all awards, all awards held by a participant or all awards of the same type similarly.

If a successor corporation does not assume or substitute for any outstanding award, then the participant will fully vest in and have the right to exercise all of his or her outstanding options and stock appreciation rights, all restrictions on restricted stock and restricted stock units will lapse, and for awards with performance-based vesting, unless specifically provided for otherwise under the applicable award agreement or other agreement or policy applicable to the participant, all performance goals or other vesting criteria will be deemed achieved at 100% of target levels and all other terms and conditions met. If an option or stock appreciation right is not assumed or substituted in the event of a change in control, the administrator will notify the participant in writing or electronically that such option or stock appreciation right will be exercisable for a period of time determined by the administrator in its sole discretion and the option or stock appreciation right will terminate upon the expiration of such period.

For awards granted to an outside director, in the event of a change in control, the outside director will fully vest in and have the right to exercise all of his or her outstanding options and stock appreciation rights, all restrictions on restricted stock and restricted stock units will lapse and, for awards with performance-based vesting, unless specifically provided for otherwise under the applicable award agreement or other agreement or policy applicable to the participant, all performance goals or other vesting criteria will be deemed achieved at 100% of target levels and all other terms and conditions met.

Clawback. Awards will be subject to any clawback policy of ours, and the administrator also may specify in an award agreement that the participant's rights, payments, and/or benefits with respect to an award will be subject to reduction, cancellation, forfeiture, and/or recoupment upon the occurrence of certain specified events. Our board of directors may require a participant to forfeit, return, or reimburse us all or a portion of the award and/or shares issued under the award, any amounts paid under the award, and any payments or proceeds paid or provided upon disposition of the shares issued under the award in order to comply with such clawback policy or applicable laws.

Amendment; termination. The administrator has the authority to amend, alter, suspend or terminate our 2021 Plan, provided such action does not materially impair the rights of any participant.

2021 Employee Stock Purchase Plan

In June 2021, our board of directors adopted, and in July 2021 our stockholders approved, our 2021 Employee Stock Purchase Plan (ESPP). Our ESPP became effective on the business day immediately prior to the effective date of the registration statement of which this prospectus forms a part. However, no offering period or purchase period under the ESPP will begin unless and until otherwise determined by our board of directors.

Authorized shares. A total of 800,000 shares of our common stock will be available for sale under our ESPP. The number of shares of our common stock that will be available for sale under our ESPP also includes an annual increase on the first day of each fiscal year following the fiscal year in which the first offering period under the ESPP commences, equal to the least of: 800,000 shares; one percent (1%) of the outstanding shares of our common stock as of the last day of the immediately preceding fiscal year; or such other amount as our board of directors may determine. This annual increase will operate only until the ten year anniversary of our board's approval of our ESPP.

ESPP administration. We expect that the compensation committee of our board of directors will administer our ESPP and will have full and exclusive discretionary authority to construe, interpret, and apply the terms of the ESPP, delegate ministerial duties to any of our employees, designate separate offerings under the ESPP, designate our subsidiaries and affiliates as participating in the ESPP, determine eligibility, adjudicate all disputed claims filed under the ESPP, and establish procedures that it deems necessary for the administration of the ESPP, including, but not limited to, adopting such procedures and sub-plans as are necessary or appropriate to permit participation in the ESPP by employees who are foreign nationals or employed outside the United States. The administrator's findings, decisions and determinations are final and binding on all participants to the full extent permitted by law.

Eligibility. Subject to the administrator implementing an offering period, generally, all of our employees will be eligible to participate if they are customarily employed by us, or any participating subsidiary or affiliate, for at least 20 hours per week and more than five months in any calendar year. The administrator, in its discretion, may, prior to an enrollment date, for all options to be granted on such enrollment date in an offering, determine that an employee who (1) has not completed at least two years of service (or a lesser period of time determined by the administrator) since his or her last hire date, (2) customarily works not more than 20 hours per week (or a lesser period of time determined by the administrator), (3) customarily works not more than five months per calendar year (or a lesser period of time determined by the administrator), (4) is a highly compensated employee within the meaning of Section 414(q) of the Code, or (5) is a highly compensated employee within the meaning of Section 414(q) of the Code with compensation above a certain level or is an officer or subject to disclosure requirements under Section 16(a) of the Exchange Act, is or is not eligible to participate in such offering period.

However, an employee may not be granted rights to purchase shares of our common stock under our ESPP if such employee: immediately after the grant would own capital stock and/or hold outstanding options to purchase such stock possessing five percent (5%) or more of the total combined voting power or value of all classes of capital stock of ours or of any parent or subsidiary of ours; or holds rights to purchase shares of our common stock under all employee stock purchase plans of ours or any parent or subsidiary of ours that accrue at a rate that exceeds $25,000 worth of shares of our common stock for each calendar year in which such rights are outstanding at any time.

Offering and Purchase Periods

The ESPP will include a component that allows us to make offerings intended to qualify under Section 423 of the Code and a component that allows us to make offerings not intended to qualify under Section 423 of the Code to designated companies, as described in the ESPP. Offering periods will begin and end on such dates as may be determined by the administrator in its discretion, in each case on a uniform and nondiscriminatory basis, and may contain one or more purchase periods. The administrator may change the duration of offering periods (including commencement dates) with respect to future offerings so long as such change is announced prior to the scheduled beginning of the first offering period affected. No offering period may last more than 27 months.

Contributions. Subject to the administrator implementing an offering period, ESPP will permit participants to purchase shares of our common stock through contributions (in the form of payroll deductions or otherwise to the extent permitted by the administrator) in an amount determined by the administrator, but not exceeding 15% of their eligible compensation.

Exercise of purchase right. Subject to the administrator implementing an offering period, amounts contributed and accumulated by the participant during any offering period will be used to purchase shares of our common stock at the end of each purchase period. The purchase price of the shares will be determined by the administrator, but will be no less than 85% of the lower of the fair market value of our common stock on the first trading day of the offering period or on the exercise date. Participants may end their participation at any time during an offering period and will be paid their accrued contributions that have not yet been used to purchase shares of our common stock. Participation ends automatically upon termination of employment with us.

Non-transferability. A participant may not transfer rights granted under our ESPP (other than by will, the laws of descent and distribution or as otherwise provided under our ESPP).

Merger or change in control. Our ESPP will provide that in the event of a merger or change in control, as defined under our ESPP, a successor corporation may assume or substitute each outstanding purchase right. If the successor corporation refuses to assume or substitute for the outstanding purchase right, the offering period then in progress will be shortened, and a new exercise date will be set that will be before the date of the proposed merger or change in control. The administrator will notify each participant that the exercise date has been changed and that the participant's option will be exercised automatically on the new exercise date unless prior to such date the participant has withdrawn from the offering period.

Amendment; termination. The board will have the authority suspend or terminate our ESPP and the administrator will have the authority to amend the ESPP, except that, subject to certain exceptions described in our ESPP, no such action may adversely affect any outstanding rights to purchase shares of our common stock under our ESPP. Our ESPP automatically will terminate in 2041, unless we terminate it sooner.

Amended and Restated 2016 Equity Incentive Plan

Our Amended and Restated 2016 Equity Incentive Plan (2016 Plan) allows us to provide incentive stock options, within the meaning of Section 422 of the Code, nonstatutory stock options, stock appreciation rights, restricted stock awards and restricted stock units (each, an "award" and the recipient of such award, a participant) to eligible employees, directors and consultants, including employees and consultants of any of our parent or subsidiary companies. One business day prior to the effectiveness of the registration statement of which this prospectus forms a part, our 2016 Plan terminated and we will not grant any additional awards under our 2016 Plan. However, our 2016 Plan will continue to govern the terms and conditions of the outstanding awards previously granted under our 2016 Plan.

As of March 31, 2021, stock options covering 1,727,968 shares of our common stock were outstanding under our 2016 Plan and there were no stock appreciation rights, restricted stock awards or restricted stock units outstanding under our 2016 Plan.

Plan administration. Our compensation committee has the authority, concurrent with our board of directors to administer our 2016 Plan. Different committees may administer our 2016 Plan with respect to different service providers. The administrator has all authority and discretion necessary or appropriate to administer our 2016 Plan and to control its operation, including the authority to construe and interpret the terms of our 2016 Plan and the awards granted under our 2016 Plan. The administrator's decisions are final and binding on all participants and any other persons holding awards.

The administrator's powers include the power to institute an exchange program (without stockholder approval) under which (1) outstanding awards are surrendered or cancelled in exchange for awards of the same type (which may have higher or lower exercise prices and different terms), awards of a different type and/or cash, (2) participants would have the opportunity to transfer any outstanding awards to a financial institution or other person or entity selected by the administrator and/or (3) the exercise price of an outstanding award is increased or reduced. The administrator's powers also include the power to prescribe, amend and rescind rules and regulations

relating to our 2016 Plan, to modify or amend each award and to make all other determinations deemed necessary or advisable for administering our 2016 Plan.

Eligibility. Employees, directors and consultants, including employees and consultants of any of our parent or subsidiary companies, are eligible to receive awards, provided such consultants render bona fide services not in connection with the offer or sale of securities in a capital-raising transaction and do not directly promote or maintain a market for our securities. Only our employees or employees of our parent or subsidiary companies are eligible to receive incentive stock options.

Stock options. Stock options have been granted under our 2016 Plan. Subject to the provisions of our 2016 Plan, the administrator determines the term of an option, the number of shares subject to an option, and the time period in which an option may be exercised.

The term of an option is stated in the applicable award agreement, but the term of an option may not exceed 10 years from the grant date. The administrator determines the exercise price of options, which generally may not be less than 100% of the fair market value of our common stock on the grant date, except as provided for in the 2016 Plan. However, an incentive stock option granted to an individual who directly or by attribution owns more than 10% of the total combined voting power of all of our classes of stock or of any our parent or subsidiary companies will have a term of no longer than five years from the grant date and will have an exercise price of at least 110% of the fair market value of our common stock on the grant date. In addition, to the extent that the aggregate fair market value of the shares with respect to which incentive stock options are exercisable for the first time by an employee during any calendar year (under all plans of ours and any of our parent or subsidiary companies) exceeds $100,000, such options will be treated as nonstatutory stock options.

The administrator determines how a participant may pay the exercise price of an option, and the permissible methods are generally set forth in the applicable award agreement. If a participant's status as a "service provider" (as defined in our 2016 Plan) terminates, that participant may exercise the vested portion of his or her option for the period of time stated in the applicable award agreement. Vested options generally will remain exercisable for 30 days or such longer period of time as set forth in the applicable award agreement if a participant's status as a service provider terminates for a reason other than death or disability. If a participant's status as a service provider terminates due to death or disability, vested options generally will remain exercisable for six months from the date of termination (or such other longer period as set forth in the applicable award agreement). In no event will an option remain exercisable beyond its original term. If a participant does not exercise his or her option within the time specified in the award agreement, the option will terminate. Except as described above, the administrator has the discretion to determine the post-termination exercisability periods for an option.

Non-transferability of awards. Unless determined otherwise by the administrator, awards may not be sold, transferred, pledged, assigned or otherwise alienated or hypothecated in any manner other than by will or by the laws of descent and distribution. In addition, during an applicable participant's lifetime, only that participant may exercise their award. If the administrator makes an award transferable, such award may only be transferred (1) by will, (2) by the laws of descent and distribution or (3) as permitted by Rule 701 of the Securities Act of 1933, as amended (the Securities Act).

Certain adjustments. If there is a dividend or other distribution (whether in the form of cash, shares, other securities or other property), recapitalization, stock split, reverse stock split, reorganization, merger, consolidation, split-up, spin-off, combination, repurchase, exchange of shares or our other securities or other change in our corporate structure affecting the shares, the administrator will make proportionate adjustments to the number and class of shares that may be delivered under our 2016 Plan or the number, class and price of shares covered by each outstanding award. The administrator's determination regarding such adjustments will be final, binding and conclusive.

Dissolution or liquidation. In the event of our proposed dissolution or liquidation, the administrator will notify each participant as soon as practicable prior to the effective date of such proposed transaction. To the

extent it has not been previously exercised, an award will terminate immediately prior to the consummation of such proposed action.

Merger and change in control. In the event of our merger with or into another corporation or entity or a "change in control" (as defined in our 2016 Plan), each outstanding award will be treated as the administrator determines, including, without limitation, that (1) awards will be assumed, or substantially equivalent awards will be substituted, by the acquiring or succeeding corporation (or an affiliate thereof) with appropriate adjustments as to the number and kind of shares and prices; (2) upon written notice to a participant, the participant's awards will terminate upon or immediately prior to the consummation of such merger or change in control; (3) outstanding awards will vest and become exercisable, realizable or payable, or restrictions applicable to an award will lapse, in whole or in part, prior to or upon consummation of such merger or change in control, and, to the extent the administrator determines, terminate upon or immediately prior to the effectiveness of such merger or change in control; (4) (a) the termination of an award in exchange for an amount of cash or property, if any, equal to the amount that would have been attained upon the exercise of such award or realization of the participant's rights as of the date of the occurrence of the transaction (and, for the avoidance of doubt, if as of the date of the occurrence of the transaction the administrator determines in good faith that no amount would have been attained upon the exercise of such award or realization of the participant's rights, then such award may be terminated by us without payment) or (b) the replacement of such award with other rights or property selected by the administrator in its sole discretion; or (5) any combination of the foregoing. The administrator will not be obligated to treat all awards, all awards a participant holds or all awards of the same type, similarly.

In the event that the successor corporation does not assume or substitute for an award (or portion thereof), the participant will fully vest in and have the right to exercise all of his or her outstanding options and stock appreciation rights, including shares as to which such awards would not otherwise be vested or exercisable, all restrictions on restricted stock and restricted stock units will lapse, and, with respect to awards with performance-based vesting, all performance goals or other vesting criteria will be deemed achieved at 100% of target levels and all other terms and conditions met. In addition, if an option or stock appreciation right is not assumed or substituted in the event of a merger or change in control, the administrator will notify the participant in writing or electronically that the option or stock appreciation right will be exercisable for a period of time determined by the administrator in its sole discretion, and the option or stock appreciation right will terminate upon the expiration of such period.

Amendment and termination. Our board of directors may, at any time, amend, alter, suspend or terminate our 2016 Plan in any respect, including, without limitation, amendment of any form of award agreement or instrument to be executed pursuant to our 2016 Plan. To the extent necessary and desirable to comply with applicable laws, we will obtain stockholder approval of any amendment to our 2016 Plan. No amendment, alteration, suspension or termination of our 2016 Plan will impair the rights of a participant, unless mutually agreed otherwise between the participant and the administrator in writing. As noted above, one business day prior to the effectiveness of the registration statement of which this prospectus forms a part, our 2016 Plan terminated, and we will not grant any additional awards under our 2016 Plan thereafter.

Executive Incentive Compensation Plan

In June 2021, our board of directors adopted the Executive Incentive Compensation Plan (Incentive Compensation Plan). Our Incentive Compensation Plan allows our compensation committee to grant incentive awards, generally payable in cash, to employees selected by our compensation committee, including our executive officers, based upon performance goals established by our compensation committee.

Under our Incentive Compensation Plan, our compensation committee will determine the performance goals applicable to any award, which goals may include, without limitation, goals related to research and development, regulatory milestones or regulatory-related goals, gross margin, financial milestones, new product or business development, operating margin, product release timelines or other product release milestones, publications, cash

flow, procurement, savings, internal structure, leadership development, project, function or portfolio-specific milestones, license or research collaboration agreements, capital raising, initial public offering preparations, patentability and individual objectives such as peer reviews or other subjective or objective criteria. The performance goals may differ from participant to participant and from award to award.

The compensation committee of our board of directors will administer our Incentive Compensation Plan and will, in its sole discretion and at any time, increase, reduce or eliminate a participant's actual award, and/or increase, reduce or eliminate the amount allocated to the bonus pool for a particular performance period. The actual award may be below, at or above a participant's target award, in the discretion of the administrator. The administrator may determine the amount of any increase, reduction or elimination on the basis of such factors as it deems relevant, and it will not be required to establish any allocation or weighting with respect to the factors it considers.

Actual awards generally will be paid in cash (or its equivalent) only after they are earned, and, unless otherwise determined by the administrator, to earn an actual award a participant must be employed by us through the date the actual award is paid. The compensation committee may reserve the right to settle an actual award with a grant of an equity award under our then-current equity compensation plan, which equity award may have such terms and conditions, including vesting, as the compensation committee determines. Payment of awards will occur as soon as practicable after they are earned, but no later than the dates set forth in our Incentive Compensation Plan.

Our board of directors and our compensation committee have the authority to amend, suspend or terminate our Incentive Compensation Plan, provided such action does not impair the existing rights of any participant with respect to any earned awards.

Limitation of Liability and Indemnification

Our amended and restated certificate of incorporation and amended and restated bylaws, each to be effective upon the completion of this offering, will provide that we will indemnify our directors and officers, and may indemnify our employees and other agents, to the fullest extent permitted by Delaware law. Delaware law prohibits our amended and restated certificate of incorporation from limiting the liability of our directors for the following:

- any breach of the director's duty of loyalty to us or to our stockholders;
- acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- unlawful payment of dividends or unlawful stock repurchases or redemptions; and
- any transaction from which the director derived an improper personal benefit.

If Delaware law is amended to authorize corporate action further eliminating or limiting the personal liability of a director, then the liability of our directors will be eliminated or limited to the fullest extent permitted by Delaware law, as so amended. Our amended and restated certificate of incorporation does not eliminate a director's duty of care and, in appropriate circumstances, equitable remedies, such as injunctive or other forms of non-monetary relief, remain available under Delaware law. This provision also does not affect a director's responsibilities under any other laws, such as the federal securities laws or other state or federal laws. Under our amended and restated bylaws, we will also be empowered to purchase insurance on behalf of any person whom we are required or permitted to indemnify.

In addition to the indemnification required in our amended and restated certificate of incorporation and amended and restated bylaws, we have entered into an indemnification agreement with each member of our board of directors and each of our officers. These agreements provide for the indemnification of our directors and

officers for certain expenses and liabilities incurred in connection with any action, suit, proceeding or alternative dispute resolution mechanism or hearing, inquiry or investigation that may lead to the foregoing, to which they are a party, or are threatened to be made a party, by reason of the fact that they are or were a director, officer, employee, agent or fiduciary of our company, or any of our subsidiaries, by reason of any action or inaction by them while serving as an officer, director, agent or fiduciary, or by reason of the fact that they were serving at our request as a director, officer, employee, agent or fiduciary of another entity. In the case of an action or proceeding by or in the right of our company or any of our subsidiaries, no indemnification will be provided for any claim where a court determines that the indemnified party is prohibited from receiving indemnification. We believe that these charter and bylaw provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duties. They may also reduce the likelihood of derivative litigation against directors and officers, even though an action, if successful, might benefit us and our stockholders. Moreover, a stockholder's investment may be harmed to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions. Insofar as indemnification for liabilities arising under the Securities Act, may be permitted to our directors, officers and controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act, and is, therefore, unenforceable. There is no pending litigation or proceeding naming any of our directors or officers as to which indemnification is being sought, nor are we aware of any pending or threatened litigation that may result in claims for indemnification by any director or officer.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

Other than compensation arrangements, including employment, termination of employment and change in control arrangements, with our directors and executive officers, including those discussed in the sections titled "Management" and "Executive Compensation" and the registration rights described in the section titled "Description of Capital Stock—Registration Rights," the following is a description of each transaction since January 1, 2018 and each currently proposed transaction in which:

- we have been or are to be a participant;
- the amount involved exceeded or exceeds $120,000; and
- any of our directors, executive officers or holders of more than 5% of our outstanding capital stock, or any immediate family member of, or person sharing the household with, any of these individuals or entities, had or will have a direct or indirect material interest.

Convertible Preferred Stock Issuances

In August 2019, March 2020 and August 2020, we issued and sold an aggregate of 9,259,245 shares of our Series B convertible preferred stock at a purchase price of $9.936 per share for an aggregate purchase price of approximately $92.0 million.

Purchasers of our Series B convertible preferred stock include venture capital funds that beneficially own more than 5% of our outstanding capital stock and/or are represented on our board of directors. The following table presents the number of shares and total purchase price paid by these entities.

Investor	Shares of Series B Convertible Preferred Stock	Total Purchase Price
Casdin Partners Master Fund, L.P.(1)	2,012,880	$ 19,999,995.55
SymBiosis II, LLC	1,509,660	$ 14,999,996.66
Funds affiliated with The Column Group(2)	1,006,440	$ 9,999,997.78

(1) Eli Casdin, a member of our board of directors is the Chief Investment Officer of Casdin Capital LLC and the managing member of Casdin Partners GP, LLC.

(2) Entities affiliated with The Column Group holding our securities are aggregated for reporting ownership information include The Column Group III, LP and The Column Group III-A, LP. David V. Goeddel, a member of our board of directors, is the Managing Partner of The Column Group, and JeenJoo (JJ) Kang, a member of our board of directors, is a Venture Partner of The Column Group.

In December 2020 and January 2021, we issued and sold an aggregate of 8,526,371 shares of our Series C convertible preferred stock at a purchase price of $12.432 per share for an aggregate purchase price of approximately $106.0 million.

Purchasers of our Series C convertible preferred stock include venture capital funds that beneficially own more than 5% of our outstanding capital stock and/or are represented on our board of directors. The following table presents the number of shares and total purchase price paid by these entities.

Investor	Shares of Series C Convertible Preferred Stock	Total Purchase Price
Funds affiliated with Casdin Capital LLC(1)	723,938	$ 8,999,999.29
Funds affiliated with FMR LLC(2)	1,608,750	$ 19,999,998.65
Funds affiliated with RTW Investments, LP(3)	1,608,750	$ 19,999,998.65
SymBiosis II, LLC	482,625	$ 5,999,998.14

(1) Entities affiliated with Casdin Capital LLC holding our securities are aggregated for reporting ownership information include Casdin Partners Master Fund, L.P. and Casdin Private Growth Equity Fund, L.P. Eli Casdin, a member of our board of directors is the Chief Investment Officer of Casdin Capital LLC and the managing member of Casdin Partners GP, LLC.
(2) Entities affiliated with Fidelity holding our securities are aggregate for reporting ownership information include Fidelity Advisor Series VII: Fidelity Advisor Biotechnology Fund and Fidelity Select Portfolios: Biotechnology Portfolio.
(3) Entities affiliated with RTW Investments, LP holding our securities are aggregate for reporting ownership information include RTW Innovation Master Fund, Ltd., RTW Master Fund, Ltd., and RTW Venture Fund Limited.

Promissory Note

On September 13, 2017, we entered into a full recourse note (the Note) with Timothy Hoey, Ph.D., our Chief Scientific Officer, pursuant to which we loaned $70,000 to cover the aggregate exercise price of Dr. Hoey's early exercise stock option for 166,666 shares of our common stock. On June 30, 2021, the full amount of the Note was repaid.

Investors' Rights Agreement

We are party to an investors' rights agreement, as amended, with certain holders of our capital stock, including entities affiliated with The Column Group III, LP, The Column Group III-A, LP, Casdin Partners Master Fund, L.P., Casdin Private Growth Equity Fund, L.P., Fidelity Advisor Series VII: Fidelity Advisor Biotechnology Fund, Fidelity Select Portfolios: Biotechnology Portfolio, RTW Master Fund, Ltd., RTW Innovation Master Fund, Ltd. and RTW Venture Fund Limited, and SymBiosis II, LLC,. Under our investors' rights agreement, among other things, certain holders of our capital stock have the right to demand that we file a registration statement or request that their shares of our capital stock be covered by a registration statement that we are otherwise filing. See the section titled "Description of Capital Stock—Registration Rights" for additional information regarding these registration rights.

Voting Agreement

We are party to a voting agreement, as amended, with certain holders of our capital stock, including entities affiliated with The Column Group III, LP, The Column Group III-A, LP, Casdin Partners Master Fund, L.P., Casdin Private Growth Equity Fund, L.P., Fidelity Advisor Series VII: Fidelity Advisor Biotechnology Fund, Fidelity Select Portfolios: Biotechnology Portfolio, RTW Master Fund, Ltd., RTW Innovation Master Fund, Ltd. and RTW Venture Fund Limited, SymBiosis II, LLC, JeenJoo (JJ) Kang, a member of our board directors, and Deepak Srivastava, a member of our board of directors. The parties to the voting agreement have agreed, among other things and subject to certain conditions, to vote the shares of our capital stock held by them so as to elect the following individuals as directors: (1) two individuals designated by The Column Group III, LP and/or The Column Group III-A, LP, currently JeenJoo (JJ) Kang and David V. Goeddel, (2) one individual designated by Casdin Master Fund L.P., currently Eli Casdin, (3) our chief executive officer, currently Faraz Ali, and (4) five individuals designated by the holders of a majority the outstanding shares of common stock and preferred stock (voting together as a single class on an as-converted basis), currently Deepak Srivastava, R. Sanders (Sandy) Williams, Jin-Long Chen, Jeffrey T. Walsh, and Catherine Stehman-Breen. Upon the consummation of this offering, the obligations of the parties to the voting agreement to vote their shares so as to elect these nominees, as well as the other rights and obligations under the voting agreement, will terminate, and none of our stockholders will have any special rights regarding the nomination, election or designation of members of our board of directors. Our existing certificate of incorporation contains provisions regarding election of members of the board of directors that correspond to the voting agreement; however, such provisions will be removed in the amended and restated certificate of incorporation that will be effective at the closing of this offering.

Indemnification Agreements

We have entered into separate indemnification agreements with each of our directors and executive officers, in addition to the indemnification provided for in our amended and restated certificate of incorporation and bylaws. The indemnification agreements and our amended restated certificate of incorporation and bylaws that will be in effect upon the closing of this offering require us to indemnify our directors, executive officers and certain controlling persons to the fullest extent permitted by Delaware law. See the section titled "Executive Compensation—Limitation of Liability and Indemnification" for additional information.

Related Party Transaction Policy

Our audit committee will have the primary responsibility for reviewing and approving or disapproving "related party transactions," which are transactions between us and related persons in which the aggregate amount involved exceeds or may be expected to exceed $120,000 and in which a related person has or will have a direct or indirect material interest. The charter of our audit committee provides that our audit committee shall review and approve in advance any related party transaction.

In June 2021, our board of directors adopted a formal written policy providing that we are not permitted to enter into any transaction that exceeds $120,000 and in which any related person has a direct or indirect material interest without the consent of our audit committee. In approving or rejecting any such transaction, our audit committee is to consider the relevant facts and circumstances available and deemed relevant to our audit committee, including whether the transaction is on terms no less favorable than terms generally available to an unaffiliated third party under the same or similar circumstances and the extent of the related person's interest in the transaction.

PRINCIPAL STOCKHOLDERS

The following table sets forth the beneficial ownership of our common stock as of June 30, 2021 by:

- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock;
- each of the named executive officers;
- each of our directors; and
- all of our current executive officers and directors as a group.

We have determined beneficial ownership in accordance with the rules of the SEC, and thus it represents sole or shared voting or investment power with respect to our securities. Unless otherwise indicated below, to our knowledge, the persons and entities named in the table have sole voting and sole investment power with respect to all shares that they beneficially owned, subject to community property laws where applicable. The information does not necessarily indicate beneficial ownership for any other purpose, including for purposes of Sections 13(d) and 13(g) of the Exchange Act.

We have based our calculation of the percentage of beneficial ownership prior to this offering on 27,324,920 shares of our common stock outstanding as of June 30, 2021, after giving effect to the automatic conversion of all outstanding shares of our convertible preferred stock into 26,102,278 shares of our common stock immediately prior to the completion of this offering. We have based our calculation of the percentage of beneficial ownership after this offering on 39,324,920 shares of our common stock outstanding immediately after the completion of this offering, assuming no exercise by the underwriters of their option to purchase additional shares. We have deemed shares of our common stock subject to stock options that are currently exercisable or exercisable within 60 days of June 30, 2021, to be outstanding and to be beneficially owned by the person holding the stock option for the purpose of computing the percentage ownership of that person. We did not deem these shares outstanding, however, for the purpose of computing the percentage ownership of any other person.

The following table does not reflect any potential purchases by our executive officers, directors, their affiliated entities or holders of more than 5% of our common stock in this offering. If any shares are purchased by these persons or entities, the number and percentage of shares of our common stock beneficially owned by them after this offering will differ from the amounts set forth in the following table.

Unless otherwise indicated, the address of each beneficial owner listed in the table below is c/o Tenaya Therapeutics, Inc., 171 Oyster Point Boulevard, 5th Floor, South San Francisco, CA 94080.

Name of Beneficial Owner	Shares Beneficially Owned Prior to this Offering		Shares Beneficially Owned After this Offering	
	Shares	Percentage	Shares	Percentage
5% or Greater Stockholders:				
Entities affiliated with The Column Group(1)	9,400,290	34.4%	9,400,290	23.9%
Entities affiliated with Casdin Group(2)	2,736,818	10.0	2,736,818	7.0
SymBiosis II, LLC(3)	1,992,285	7.3	1,992,285	5.1
Entities affiliated with FMR LLC(4)	1,608,750	5.9	1,608,750	4.1
Entities affiliated with RTW(5)	1,608,750	5.9	1,608,750	4.1
Named Executive Officers and Directors:				
Faraz Ali, M.B.A.(6)	507,462	1.8	507,462	1.3
Timothy Hoey, Ph.D.(7)	206,178	*	206,178	*
Whittemore (Whit) Tingley, M.D., Ph.D.(8)	83,263	*	83,263	*
Eli Casdin, M.B.A.(2)	2,736,818	10.0	2,736,818	7.0
Jin-Long Chen, Ph.D.(9)	30,000	*	30,000	*
David V. Goeddel, Ph.D.(1)	9,400,290	34.4	9,400,290	23.9
JeenJoo (JJ) Kang, Ph.D.(10)	25,000	*	25,000	*
Catherine Stehman-Breen, M.D.(11)	8,750	*	8,750	*
Deepak Srivastava, M.D.(12)	334,721	1.2	334,721	*
Jeffrey T. Walsh, M.B.A.(13)	12,291	*	12,291	*
R. Sanders (Sandy) Williams, M.D.(14)	29,999	*	29,999	*
All executive officers and directors as a group (12 persons)(15)	13,374,772	47.7%	13,374,772	33.4%

* Represents beneficial ownership of less than 1% of the outstanding shares of our common stock.

(1) Consists of 4,414,720 shares held directly by The Column Group III, LP and 4,985,570 shares held directly by The Column Group III-A, LP (Column Group Funds). The Column Group III GP, LP (TCG III GP) is the general partner of each of the Column Group Funds. The managing partners of TCG III GP are David V. Goeddel, Peter Svennilson and Tim Kutzkey who may be deemed to share voting and investment power with respect to the shares, and each of whom disclaim beneficial ownership of the shares held by the Column Group Funds except to the extent of their pecuniary interests therein, if any. Dr. Goeddel is a member of our board of directors. The address of the Column Group Funds is 1 Letterman Drive, Building D, Suite DM-900, San Francisco, CA 94129.

(2) Consists of 2,374,849 shares held directly by Casdin Partners Master Fund, L.P. (CPMF) and 361,969 shares held directly by Casdin Private Growth Equity Fund, L.P. (CPGEF). Casdin Capital, LLC is the investment advisor to CPMF and CPGEF. Casdin Partners GP, LLC is the general partner of CPMF. Casdin Private Growth Equity Fund GP, LLC is the general partner of CPGEF. Eli Casdin, a member of our board of directors, is the managing member of Casdin Capital, LLC, Casdin Partners GP, LLC and Casdin Private Growth Equity Fund GP, LLC and may be deemed to have voting and investment power with respect to the shares and who disclaims beneficial ownership of the shares except to the extent of his pecuniary interests therein, if any. The address of these entities and individuals is 1350 Avenue of the Americas, Suite 2600, New York, NY 10019.

(3) These shares are beneficially owned by Thomas Layton Walton. The shares are directly held by SymBiosis II, LLC over which Mr. Walton exercises sole investment power. The address of Mr. Walton is PO Box 1860, Bentonville, AR 72712.

(4) Consists of 402,187 shares held by Fidelity Advisor Series VII: Advisor Biotechnology Fund (Advisor Series VII) and 1,206,563 shares held directly by Fidelity Select Portfolios: Biotechnology Portfolio (Select Portfolios). These accounts are managed by direct or indirect subsidiaries of FMR LLC. Abigail P. Johnson is a director, the chairman, the chief executive officer and president of FMR LLC. Members of the Johnson

family, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940 to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Abigail P. Johnson has the sole power to vote or direct the voting of the shares owned directly by the various investment companies registered under the Investment Company Act (the Fidelity Funds) advised by Fidelity Management & Research Company (FMR Co.), a wholly owned subsidiary of FMR LLC, which power resides with the Fidelity Funds' Board of Trustees. FMR Co. carries out the voting of the shares under written guidelines established by the Fidelity Funds' Board of Trustees. The address of FMR LLC is 245 Summer Street, Boston, MA 02210.

(5) Consists of 1,608,750 shares in the aggregate held by RTW Innovation Master Fund, Ltd., RTW Master Fund, Ltd. and RTW Venture Fund Limited. Roderick Wong is the managing partner and chief investment officer of RTW Investments, LP and as such has sole voting and investment control over the shares. Dr. Wong disclaims beneficial ownership of the shares except to the extent of his pecuniary interest therein, if any. The address of the RTW funds is 40 10th Avenue, Floor 7, New York, NY 10014.

(6) Consists of 507,462 shares subject to outstanding options that are exercisable within 60 days of June 30, 2021, of which 155,833 shares may be repurchased by us, if exercised, at the original exercise price per share.

(7) Consists of 166,666 shares held directly by Dr. Hoey and 39,512 shares subject to outstanding options that are exercisable within 60 days of June 30, 2021, of which 11,805 shares may be repurchased by us, if exercised, at the original exercise price per share.

(8) Consists of 83,263 shares subject to outstanding options that are exercisable within 60 days of June 30, 2021, of which 25,000 shares may be repurchased by us, if exercised, at the original exercise price per share.

(9) Includes 5,000 shares subject to outstanding options that are exercisable within 60 days of June 30, 2021.

(10) Consists of 25,000 shares held directly by Dr. Kang. Excludes 9,400,290 shares held by The Column Group funds as set forth in footnote (1) above for which Dr. Kang has no voting or investment control.

(11) Consists of 8,750 shares subject to outstanding options that are exercisable within 60 days of June 30, 2021.

(12) Consists of 162,500 shares held directly by Dr. Srivastava and 141,666 shares held directly by Gladstone Institutes for which Dr. Srivastava serves as President and may be deemed to have voting and investment control over the shares. Dr. Srivastava disclaims beneficial ownership of the shares held by Gladstone Institutes. Also includes 30,555 shares subject to outstanding options that are exercisable within 60 days of June 30, 2021.

(13) Includes 12,291 shares subject to outstanding options that are exercisable within 60 days of June 30, 2021.

(14) Consists of 29,999 shares held directly by Dr. Williams.

(15) Includes 686,833 shares subject to outstanding options that are exercisable within 60 days of June 30, 2021, of which 192,638 shares may be repurchased by us, if exercised, at the original exercise price per share.

DESCRIPTION OF CAPITAL STOCK

The following descriptions of our capital stock and certain provisions of our amended and restated certificate of incorporation and amended and restated bylaws are summaries and are qualified by reference to the amended and restated certificate of incorporation and the amended and restated bylaws that will be in effect upon completion of this offering. Copies of these documents will be filed with the SEC as exhibits to our registration statement of which this prospectus forms a part. The descriptions of the common stock and preferred stock reflect changes to our capital structure that will occur upon the completion of this offering.

Immediately prior to the completion of this offering, upon the filing of our amended and restated certificate of incorporation to be effective upon completion of this offering, our authorized capital stock will consist of 1,000,000,000 shares of common stock, par value $0.0001 per share, and 200,000,000 shares of preferred stock, par value $0.0001 per share.

Immediately prior to the completion of this offering, all the outstanding shares of our convertible preferred stock will automatically convert into an aggregate of 26,102,278 shares of our common stock.

Based on 27,324,727 shares of common stock outstanding as of March 31, 2021, and after giving effect to the automatic conversion of all of our outstanding convertible preferred stock into an aggregate of 26,102,278 shares of common stock immediately prior to the completion of this offering and the issuance of 12,000,000 shares of common stock in this offering, there will be 39,324,727 shares of common stock outstanding upon the completion of this offering. As of March 31, 2021, we had 82 stockholders of record.

Common Stock

Voting Rights

Each holder of common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. Our amended and restated certificate of incorporation and amended and restated bylaws to be in effect upon the completion of this offering do not provide for cumulative voting rights. Because of this, the holders of a plurality of the shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they should so choose. With respect to matters other than the election of directors, at any meeting of the stockholders at which a quorum is present or represented, the affirmative vote of a majority of the voting power of the shares present in person or represented by proxy at such meeting and entitled to vote on the subject matter shall be the act of the stockholders, except as otherwise required by law. The holders of a majority of the stock issued and outstanding and entitled to vote, present in person or represented by proxy, shall constitute a quorum for the transaction of business at all meetings of the stockholders.

Dividends

Subject to preferences that may be applicable to any then-outstanding preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then-outstanding shares of preferred stock.

Rights, Preferences and Privileges

Holders of our common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our preferred stock that we may designate in the future.

Fully Paid and Nonassessable

All of our outstanding shares of common stock are, and the shares of common stock to be issued in this offering, upon payment and delivery in accordance with the underwriting agreement, will be fully paid and nonassessable.

Preferred Stock

Upon the completion of this offering, our board of directors will have the authority, without further action by the stockholders, to issue up to 200,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, redemption rights, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of common stock. The issuance of preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in our control or other corporate action. Upon the completion of this offering, no shares of preferred stock will be outstanding, and we have no present plan to issue any shares of preferred stock.

Options

As of March 31, 2021, we had outstanding options to purchase an aggregate of 1,727,968 shares of our common stock, with a weighted-average exercise price of $3.06 per share, under our 2016 Plan.

Registration Rights

After the completion of this offering, under our investors' rights agreement, as amended, the holders of up to 26,102,278 shares of common stock or their transferees, will have the right to require us to register the offer and sale of their shares or to include their shares in any registration statement we file, in each case as described below.

Demand Registration Rights

After the completion of this offering, the holders of up to 26,102,278 shares of our common stock will be entitled to certain demand registration rights. At any time beginning after 180 days following the date hereof, the holders of at least 50% of the shares having registration rights then outstanding can request that we file a registration statement to register the offer and sale of their shares. We are only obligated to effect up to two such registrations. Each such request for registration must cover securities of which the anticipated aggregate gross proceeds, before deducting underwriting discounts and expenses, is at least $10.0 million. These demand registration rights are subject to specified conditions and limitations, including the right of the underwriters to limit the number of shares included in any such registration under certain circumstances. If we determine that it would be materially detrimental to us and our stockholders to effect such a demand registration, we have the right to defer such registration, not more than twice in any twelve-month period, for a period of up to 90 days.

Form S-3 Registration Rights

After the completion of this offering, the holders of up to 26,102,278 shares of our common stock will be entitled to certain Form S-3 registration rights. At any time after the completion of this offering when we are

eligible to file a registration statement on Form S-3, any holders having these rights then outstanding can request that we register the offer and sale of their shares of our common stock on a registration statement on Form S-3 so long as the request covers securities the anticipated aggregate public offering price of which is at least $1.0 million. These stockholders may make an unlimited number of requests for registration on a registration statement on Form S-3. However, we will not be required to effect a registration on Form S-3 if we have effected two such registrations within the twelve month period preceding the date of the request. These Form S-3 registration rights are subject to specified conditions and limitations, including the right of the underwriters to limit the number of shares included in any such registration under certain circumstances. Additionally, if we determine that it would be seriously detrimental to us and our stockholders to effect such a demand registration, we have the right to defer such registration, not more than twice in any twelve month period, for a period of up to 90 days.

Piggyback Registration Rights

After the completion of this offering, the holders of up to 26,102,278 shares of our common stock will be entitled to certain "piggyback" registration rights. If we propose to register the offer and sale of shares of our common stock under the Securities Act, the holders of these shares can request that we include their shares in such registration, subject to certain marketing and other limitations, including the right of the underwriters to limit the number of shares included in any such registration statement under certain circumstances. As a result, whenever we propose to file a registration statement under the Securities Act, other than with respect to (i) a registration solely to employee benefit plans; (ii) a registration relating to the offer and sale of debt securities; (iii) a registration relating to a corporate reorganization or other transaction covered by Rule 145 promulgated under the Securities Act; (iv) a registration on any registration form that does not permit secondary sales; or (v) a registration pursuant to the demand or Form S-3 registration rights described in the preceding two paragraphs above, the holders of these shares are entitled to notice of the registration and have the right, subject to certain limitations, to include their shares in the registration.

Expenses of Registration

We will pay all expenses relating to any demand registrations, Form S-3 registrations and piggyback registrations, subject to specified exceptions.

Termination

The registration rights terminate upon the earliest of (i) the date that is four years after the closing of this offering; (ii) immediately prior to the closing of certain liquidation events; and (iii) as to a given holder of registration rights, the date after the closing of this offering when such holder of registration rights can sell all of such holder's registrable securities during any 90-day period pursuant to Rule 144 promulgated under the Securities Act.

Anti-Takeover Effects of Certain Provisions of Delaware Law, Our Amended and Restated Certificate of Incorporation and Our Amended and Restated Bylaws

Certain provisions of Delaware law and certain provisions that will be included in our amended and restated certificate of incorporation and amended and restated bylaws summarized below may be deemed to have an anti-takeover effect and may delay, deter or prevent a tender offer or takeover attempt that a stockholder might consider to be in its best interests, including attempts that might result in a premium being paid over the market price for the shares held by stockholders.

Preferred Stock

Our amended and restated certificate of incorporation will contain provisions that permit our board of directors to issue, without any further vote or action by the stockholders, shares of preferred stock in one or more

series and, with respect to each such series, to fix the number of shares constituting the series and the designation of the series, the voting rights (if any) of the shares of the series and the powers, preferences or relative, participation, optional and other special rights, if any, and any qualifications, limitations or restrictions, of the shares of such series.

Classified Board

Our amended and restated certificate of incorporation will provide that our board of directors is divided into three classes, designated Class I, Class II and Class III. Each class will be an equal number of directors, as nearly as possible, consisting of one third of the total number of directors constituting the entire board of directors. The term of initial Class I directors shall terminate on the date of the 2022 annual meeting, the term of the initial Class II directors shall terminate on the date of the 2023 annual meeting, and the term of the initial Class III directors shall terminate on the date of the 2024 annual meeting. At each annual meeting of stockholders beginning in 2022, the class of directors whose term expires at that annual meeting will be subject to reelection for a three-year term.

Removal of Directors

Our amended and restated certificate of incorporation will provide that stockholders may only remove a director for cause by a vote of no less than a majority of the shares present in person or by proxy at the meeting and entitled to vote.

Director Vacancies

Our amended and restated certificate of incorporation will authorize only our board of directors to fill vacant directorships.

No Cumulative Voting

Our amended and restated certificate of incorporation will provide that stockholders do not have the right to cumulate votes in the election of directors.

Special Meetings of Stockholders

Our amended and restated certificate of incorporation and amended and restated bylaws will provide that, except as otherwise required by law, special meetings of the stockholders may be called only by an officer at the request of a majority of our board of directors, by the Chair of our board of directors or by our Chief Executive Officer.

Advance Notice Procedures for Director Nominations

Our amended and restated bylaws will provide that stockholders seeking to nominate candidates for election as directors at an annual or special meeting of stockholders must provide timely notice thereof in writing. To be timely, a stockholder’s notice generally will have to be delivered to and received at our principal executive offices before notice of the meeting is issued by the secretary of the company, with such notice being served not less than 90 nor more than 120 days before the meeting. Although the amended and restated bylaws will not give the board of directors the power to approve or disapprove stockholder nominations of candidates to be elected at an annual meeting, the amended and restated bylaws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed or may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of the company.

Action by Written Consent

Our amended and restated certificate of incorporation and amended and restated bylaws will provide that any action to be taken by the stockholders must be effected at a duly called annual or special meeting of stockholders and may not be effected by written consent.

Amending Our Certificate of Incorporation and Bylaws

Our amended and restated certificate of incorporation may be amended or altered in any manner provided by the Delaware General Corporation Law (DGCL). Our amended and restated bylaws may be adopted, amended, altered or repealed by stockholders only upon approval of at least majority of the voting power of all the then outstanding shares of the common stock, except for any amendment of the above provisions, which would require the approval of a two-thirds majority of our then outstanding common stock. Additionally, our amended and restated certificate of incorporation will provide that our bylaws may be amended, altered or repealed by the board of directors.

Authorized but Unissued Shares

Our authorized but unissued shares of common stock and preferred stock will be available for future issuances without stockholder approval, except as required by the listing standards of the Nasdaq Stock Market LLC, and could be utilized for a variety of corporate purposes, including future offerings to raise additional capital, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could render more difficult or discourage an attempt to obtain control of the company by means of a proxy contest, tender offer, merger or otherwise.

Exclusive Jurisdiction

Our amended and restated bylaws will provide that, unless we consent to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of fiduciary duty, any action asserting a claim arising pursuant to the DGCL, any action regarding our amended and restated certificate of incorporation or amended and restated bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine. This provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act or any other claim for which the U.S. federal courts have exclusive jurisdiction. Our amended and restated bylaws further provide that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. Any person or entity purchasing or otherwise acquiring any interest in our securities shall be deemed to have notice of and consented to these provisions. Although we believe these provisions benefit us by providing increased consistency in the application of law for the specified types of actions and proceedings, the provisions may have the effect of discouraging lawsuits against us or our directors and officers. There is uncertainty as to whether a court would enforce such provisions, and the enforceability of similar choice of forum provisions in other companies' charter documents has been challenged in legal proceedings. We also note that stockholders cannot waive compliance (or consent to noncompliance) with the federal securities laws and the rules and regulations thereunder. See the section titled "Risk factors—Our amended and restated bylaws that will become effective upon the closing of this offering provide that the Court of Chancery of the State of Delaware and the federal district courts of the United States of America will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees."

Business Combinations with Interested Stockholders

We are governed by Section 203 of the DGCL. Subject to certain exceptions, Section 203 of the DGCL prohibits a public Delaware corporation from engaging in a business combination (as defined in such section)

with an "interested stockholder" (defined generally as any person who beneficially owns 15% or more of the outstanding voting stock of such corporation or any person affiliated with such person) for a period of three years following the time that such stockholder became an interested stockholder, unless (i) prior to such time the board of directors of such corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder; (ii) upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of such corporation at the time the transaction commenced (excluding for purposes of determining the voting stock of such corporation outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned (1) by persons who are directors and also officers of such corporation and (2) by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or (iii) at or subsequent to such time the business combination is approved by the board of directors of such corporation and authorized at a meeting of stockholders (and not by written consent) by the affirmative vote of at least 66 2/3% of the outstanding voting stock of such corporation not owned by the interested stockholder.

Our amended and restated certificate of incorporation and our amended and restated bylaws will provide that we must indemnify our directors and officers to the fullest extent authorized by the DGCL. We are expressly authorized to, and do, carry directors' and officers' insurance providing coverage for our directors, officers and certain employees for some liabilities. We believe that these indemnification provisions and insurance are useful to attract and retain qualified directors and executive officers.

The limitation on liability and indemnification provisions in our certificate of incorporation and bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duty. These provisions may also have the effect of reducing the likelihood of derivative litigation against directors and officers, even though such an action, if successful, might otherwise benefit us and our stockholders. In addition, each investor's investment may be adversely affected to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions.

Listing

Our common stock has been approved for listing on the Nasdaq Global Select Market under the symbol "TNYA."

Transfer Agent and Registrar

Upon completion of this offering, the transfer agent and registrar for our common stock will be Computershare Trust Company, N.A. The transfer agent and registrar's address is 150 Royall Street, Canton, Massachusetts 02021.

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock, and although our common stock has been approved for listing on the Nasdaq Global Select Market, we cannot assure investors that there will be an active public market for our common stock following this offering. We cannot predict what effect, if any, sales of our shares in the public market or the availability of shares for sale will have on the market price of our common stock. Future sales of substantial amounts of common stock in the public market, including shares issued upon exercise of outstanding options, or the perception that such sales may occur, however, could adversely affect the market price of our common stock and also could adversely affect our future ability to raise capital through the sale of our common stock or other equity-related securities of ours at times and prices we believe appropriate.

Upon completion of this offering, based on our shares outstanding as of March 31, 2021, and after giving effect to the conversion of all outstanding shares of our convertible preferred stock, 39,324,727 shares of our common stock will be outstanding, or 41,124,727 shares of common stock if the underwriters exercise their option to purchase additional shares in full. All of the shares of common stock expected to be sold in this offering will be freely tradable without restriction or further registration under the Securities Act unless held by our "affiliates," as that term is defined in Rule 144 under the Securities Act. The remaining outstanding shares of our common stock will be deemed "restricted securities" as that term is defined under Rule 144. Restricted securities may be sold in the public market only if their offer and sale is registered under the Securities Act or if the offer and sale of those securities qualify for an exemption from registration, including exemptions provided by Rules 144 and 701 under the Securities Act, which are summarized below.

As a result of the lock-up agreements and market stand-off provisions described below and the provisions of Rules 144 or 701, the shares of our common stock that will be deemed "restricted securities" will be available for sale in the public market following the completion of this offering as follows:

- no shares will be eligible for sale on the date of this prospectus; and
- 27,324,727 shares will be eligible for sale upon expiration of the lock-up agreements and market stand-off provisions described below, following the date that is 180 days after the date of this prospectus.

Lock-up Agreements and Market Stand-Off Agreements

Our officers, directors and substantially all of our securityholders have entered into market stand-off agreements with us. We, our officers, directors and substantially all of our securityholders have also entered into lock-up agreements with the underwriters, subject to certain exceptions, not to dispose of or hedge any common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of this prospectus continuing through the date 180 days after the date of this prospectus, except with the prior consent of Morgan Stanley & Co. LLC, Cowen and Company LLC, and Piper Sandler & Co. See the section titled "Underwriters" for additional information.

Rule 144

Rule 144, as currently in effect, generally provides that, once we have been subject to the public company reporting requirements of Section 13 or Section 15(d) of the Exchange Act for at least 90 days, a stockholder who is not deemed to have been one of our affiliates at any time during the preceding 90 days and who has beneficially owned the shares of our capital stock proposed to be sold for at least six months is entitled to sell such shares in reliance upon Rule 144 without complying with the volume limitation, manner of sale or notice conditions of Rule 144. If such stockholder has beneficially owned the shares of our capital stock proposed to be sold for at least one year, then such person is entitled to sell such shares in reliance upon Rule 144 without complying with any of the other conditions of Rule 144. Rule 144 also provides that a stockholder who is

deemed to have been one of our affiliates at any time during the preceding 90 days and who has beneficially owned the shares of our common stock proposed to be sold for at least six months is entitled to sell such shares in reliance upon Rule 144 within any three month period beginning 90 days after the date of this prospectus a number of such shares that does not exceed the greater of the following:

- 1% of the number of shares of our capital stock then outstanding, which will equal 393,247 shares immediately after the completion of this offering, assuming no exercise by the underwriters of their option to purchase additional shares; or
- the average weekly trading volume of our common stock during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Sales of our capital stock made in reliance upon Rule 144 by a stockholder who is deemed to have been one of our affiliates at any time during the preceding 90 days are also subject to the current public information, manner of sale and notice conditions of Rule 144.

Rule 701

Rule 701 generally provides that, once we have been subject to the public company reporting requirements of Section 13 or Section 15(d) of the Exchange Act for at least 90 days, a stockholder who purchased shares of our common stock pursuant to a written compensatory benefit plan or contract and who is not deemed to have been one of our affiliates at any time during the preceding 90 days may sell such shares in reliance upon Rule 144 without complying with the current public information or holding period conditions of Rule 144. Rule 701 also provides that a stockholder who purchased shares of our common stock pursuant to a written compensatory benefit plan or contract and who is deemed to have been one of our affiliates during the preceding 90 days may sell such shares under Rule 144 without complying with the holding period condition of Rule 144. However, all stockholders who purchased shares of our common stock pursuant to a written compensatory benefit plan or contract are required to wait until 90 days after the date of this prospectus before selling such shares pursuant to Rule 701.

Registration Rights

After the completion of this offering, the holders of up to 26,102,278 shares of our common stock will be entitled to certain rights with respect to the registration of such shares under the Securities Act. The registration of these shares of our common stock under the Securities Act would result in these shares becoming eligible for sale in the public market without restriction under the Securities Act immediately upon the effectiveness of such registration. See the section titled “Description of Capital Stock—Registration Rights” for a description of these registration rights.

Registration Statement

After the completion of this offering, we intend to file a registration statement on Form S-8 under the Securities Act to register all of the shares of our common stock subject to equity awards outstanding or reserved for issuance under our equity compensation plans. The shares of our common stock covered by such registration statement will be eligible for sale in the public market without restriction under the Securities Act immediately upon the effectiveness of such registration statement, subject to vesting restrictions, the conditions of Rule 144 applicable to affiliates, and any applicable market stand-off agreements and lock-up agreements. See the section titled “Executive Compensation—Employee Benefit and Stock Plans” for a description of our equity compensation plans.

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS

The following is a summary of the material U.S. federal income tax considerations of the ownership and disposition of our common stock acquired in this offering by a "non-U.S. holder" (as defined below), but does not purport to be a complete analysis of all the potential tax considerations relating thereto. This summary is based upon the provisions of the Internal Revenue Code of 1986, as amended (the Code), Treasury Regulations promulgated thereunder, administrative rulings and judicial decisions, all as of the date hereof. These authorities may be changed, possibly retroactively, so as to result in U.S. federal income tax consequences different from those set forth below. We have not sought, and do not intend to seek, any ruling from the Internal Revenue Service (IRS), with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS or a court will agree with such statements and conclusions.

This summary also does not address the tax considerations arising under the laws of any non-U.S., state or local jurisdiction or under U.S. federal gift and estate tax rules, and does not address tax considerations applicable to an investor's particular circumstances or to investors that may be subject to special tax rules, including, without limitation:

- banks, insurance companies, regulated investment companies, real estate investment trusts or other financial institutions;
- tax-exempt organizations;
- pension plans and tax-qualified retirement plans;
- controlled foreign corporations, passive foreign investment companies and corporations that accumulate earnings to avoid U.S. federal income tax;
- brokers or dealers in securities or currencies;
- traders in securities that elect to use a mark-to-market method of accounting for their securities holdings;
- persons that own, or are deemed to own, more than 5% of our capital stock (except to the extent specifically set forth below);
- certain former citizens or long-term residents of the United States;
- partnerships (or entities or arrangements classified as such for U.S. federal income tax purposes), other pass-through entities, and investors therein;
- persons who hold our common stock as a position in a hedging transaction, "straddle," "conversion transaction" or other risk reduction transaction;
- persons who hold or receive our common stock pursuant to the exercise of any option or otherwise as compensation;
- persons subject to special tax accounting rules as a result of any item of gross income with respect to our common stock being taken into account in an "applicable financial statement" as defined in Section 451(b) of the Code;
- persons who do not hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, property held for investment); or
- persons deemed to sell our common stock under the constructive sale provisions of the Code.

In addition, if a partnership (or an entity or arrangement classified as a partnership for U.S. federal income tax purposes) holds our common stock, the tax treatment of a partner in such partnership or other entity generally will depend on the status of the partner and upon the activities of the partnership or other entity. A partner in a partnership or other such entity that will hold our common stock should consult his, her or its own tax advisor regarding the tax consequences of the ownership and disposition of our common stock through a partnership or other such entity, as applicable.

You are urged to consult your tax advisor with respect to the application of the U.S. federal income tax laws to your particular situation, as well as any tax consequences of the purchase, ownership and disposition of our common stock arising under the U.S. federal gift or estate tax rules or under the laws of any state or local, non-U.S. or other taxing jurisdiction or under any applicable tax treaty.

Non-U.S. Holder Defined

For purposes of this discussion, you are a "non-U.S. holder" if you are a beneficial owner of our common stock that, for U.S. federal income tax purposes, is not a partnership (including any entity or arrangement treated as a partnership and the equity holders therein) or:

- an individual who is a citizen or resident of the United States;
- a corporation or other entity taxable as a corporation created or organized in the United States or under the laws of the United States or any political subdivision thereof, or otherwise treated as such for U.S. federal income tax purposes;
- an estate whose income is subject to U.S. federal income tax regardless of its source; or
- a trust (i) whose administration is subject to the primary supervision of a U.S. court and that has one or more U.S. persons who have the authority to control all substantial decisions of the trust or (ii) that has made a valid election under applicable Treasury Regulations to be treated as a U.S. person.

Distributions

As described in the section titled "Dividend Policy," we have never declared or paid cash dividends on our capital stock, and we do not anticipate paying any cash dividends in the foreseeable future. However, if we do make distributions on our common stock, those payments will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those distributions exceed both our current and our accumulated earnings and profits, the excess will constitute a return of capital and will first reduce your basis in our common stock, but not below zero, and then will be treated as gain from the sale of stock.

Subject to the discussions below on effectively connected income and in the subsections titled "—Backup Withholding and Information Reporting" and "—Foreign Account Tax Compliance Act (FATCA)," any dividend paid to you generally will be subject to U.S. federal withholding tax either at a rate of 30% of the gross amount of the dividend or such lower rate as may be specified by an applicable income tax treaty between the United States and your country of residence. In order to receive a reduced treaty rate, you must provide us with a properly executed IRS Form W-8BEN or W-8BEN-E or other appropriate version of IRS Form W-8 certifying qualification for the reduced rate. If you are eligible for a reduced rate of U.S. federal withholding tax pursuant to an income tax treaty, you may obtain a refund of any excess amounts withheld by filing an appropriate claim for refund with the IRS. If you hold our common stock through a financial institution or other agent acting on your behalf, you will be required to provide appropriate documentation to the agent, which then will be required to provide certification to us or our paying agent, either directly or through other intermediaries.

Dividends received by you that are treated as effectively connected with your conduct of a U.S. trade or business (and, if required by an applicable income tax treaty, are attributable to a permanent establishment or fixed base maintained by you in the United States) are generally exempt from the 30% U.S. federal withholding tax, subject to the discussion below in the subsections titled "—Backup Withholding and Information Reporting" and "—Foreign Account Tax Compliance Act (FATCA)." In order to obtain this exemption, you must provide us with a properly executed IRS Form W-8ECI or applicable successor form properly certifying such exemption. Such effectively connected dividends, although not subject to U.S. federal withholding tax, are taxed at the same rates applicable to U.S. persons, net of certain deductions and credits, subject to an applicable income tax treaty providing otherwise. In addition, if you are a corporate non-U.S. holder, dividends you receive that are

effectively connected with your conduct of a U.S. trade or business may also be subject to a branch profits tax at a rate of 30% or such lower rate as may be specified by an applicable income tax treaty between the United States and your country of residence. You should consult your tax advisor regarding the tax consequences of the ownership and disposition of our common stock, including any applicable tax treaties that may provide for different rules.

Gain on Disposition of Common Stock

Subject to the discussion in the subsections titled "—Backup Withholding and Information Reporting," and "—Foreign Account Tax Compliance Act (FATCA)," you generally will not be required to pay U.S. federal income tax on any gain realized upon the sale or other disposition of our common stock unless:

- the gain is effectively connected with your conduct of a U.S. trade or business (and, if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by you in the United States);
- you are an individual who is present in the United States for a period or periods aggregating 183 days or more during the calendar year in which the sale or disposition occurs and certain other conditions are met; or
- our common stock constitutes a U.S. real property interest by reason of our status as a "U.S. real property holding corporation" (USRPHC), for U.S. federal income tax purposes at any time within the shorter of the five-year period preceding your disposition of, or your holding period for, our common stock, unless our common stock is regularly traded on an established securities market and you hold no more than 5% of our outstanding common stock, directly, indirectly and constructively, at all times, during the shorter of the five-year period ending on the date of the taxable disposition or your holding period for our common stock.

We believe that we are not currently and will not become a USRPHC for U.S. federal income tax purposes, and the remainder of this discussion so assumes. However, because the determination of whether we are a USRPHC depends on the fair market value of our U.S. real property interests relative to the fair market value of our U.S. and worldwide real property interests plus our other assets used or held for use in a trade or business, there can be no assurance that we will not become a USRPHC in the future. If we are a USRPHC and either our common stock is not regularly traded on an established securities market or you hold, or are treated as holding, more than 5% of our outstanding common stock, directly or indirectly, during the applicable testing period, you will generally be taxed on any gain in the same manner as gain that is effectively connected with the conduct of a U.S. trade or business, except that the branch profits tax generally will not apply. If we are a USRPHC and our common stock is not regularly traded on an established securities market, your proceeds received on the disposition of shares will also generally be subject to withholding at a rate of 15%. You are encouraged to consult your own tax advisors regarding the possible consequences to you if we are, or were to become, a USRPHC.

If you are a non-U.S. holder described in the first bullet above, you will be required to pay tax on the gain derived from the sale (net of certain deductions and credits) under the same U.S. federal income tax rates applicable to U.S. persons, and a corporate non-U.S. holder described in the first bullet above also may be subject to the branch profits tax at a 30% rate, or such lower rate as may be specified by an applicable income tax treaty. If you are an individual non-U.S. holder described in the second bullet above, you will be subject to tax on such gain at 30% (or such lower rate specified by an applicable income tax treaty) on the gain derived from the sale, which gain may be offset by U.S. source capital losses for the year, provided you have timely filed U.S. federal income tax returns with respect to such losses. You should consult your tax advisor regarding any applicable income tax treaties or other agreements that may provide for different rules.

Backup Withholding and Information Reporting

Generally, we must report annually to the IRS the amount of dividends paid to you, your name and address and the amount of tax withheld, if any. A similar report will be sent to you. Pursuant to applicable income tax treaties or other agreements, the IRS may make these reports available to tax authorities in your country of residence.

Payments of dividends on or of proceeds from the disposition of our common stock made to you may also be subject to backup withholding at a current rate of 24% unless you establish an exemption, for example, by properly certifying your non-U.S. status on a properly completed IRS Form W-8BEN or W-8BEN-E or another appropriate version of IRS Form W-8. Notwithstanding the foregoing, backup withholding may apply if either we or our paying agent has actual knowledge, or reason to know, that you are a U.S. person.

Backup withholding is not an additional tax; rather, the U.S. federal income tax liability of persons subject to backup withholding will be reduced by the amount of tax withheld. If withholding results in an overpayment of taxes, a refund or credit may generally be obtained from the IRS, provided that the required information is furnished to the IRS in a timely manner.

Foreign Account Tax Compliance Act (FATCA)

The Foreign Account Tax Compliance Act, Treasury Regulations issued thereunder and official IRS guidance (collectively FATCA), generally impose a U.S. federal withholding tax of 30% on dividends on, and, subject to the discussion of certain proposed Treasury Regulations below, the gross proceeds from a sale or other disposition of our common stock, paid to a "foreign financial institution" (as specially defined under these rules), unless such institution enters into an agreement with the U.S. government to, among other things, withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding the U.S. account holders of such institution (which includes certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with U.S. owners) or otherwise establishes an exemption. FATCA also generally imposes a U.S. federal withholding tax of 30% on dividends on and, subject to the discussion of certain proposed Treasury Regulations below, the gross proceeds from a sale or other disposition of our common stock paid to a "non-financial foreign entity" (as specially defined under these rules) unless such entity provides the withholding agent with a certification identifying the substantial direct and indirect U.S. owners of the entity, certifies that it does not have any substantial U.S. owners, or otherwise establishes an exemption. The withholding tax will apply regardless of whether the payment otherwise would be exempt from withholding tax, including under the exemptions described above. Under certain circumstances, you might be eligible for refunds or credits of such taxes. An intergovernmental agreement between the United States and your country of residence may modify the requirements described in this section. Prospective investors should consult with their own tax advisors regarding the application of FATCA withholding to their investment in, and ownership and disposition of, our common stock.

The Treasury Secretary has issued proposed Treasury Regulations, which, if finalized in their present form, would eliminate withholding under FATCA with respect to payment of gross proceeds from a sale or other disposition of our common stock. In its preamble to such proposed Treasury Regulations, the U.S. Treasury stated that taxpayers may generally rely on the proposed Treasury Regulations until final regulations are issued.

The preceding discussion of U.S. federal tax considerations is for general information only. It is not tax advice to investors in their particular circumstances. Each prospective investor should consult its own tax advisor regarding the particular U.S. federal, state and local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed change in applicable laws.

UNDERWRITERS

Under the terms and subject to the conditions in an underwriting agreement dated the date of this prospectus, the underwriters named below, for whom Morgan Stanley & Co. LLC, Cowen and Company, LLC and Piper Sandler & Co. are acting as representatives, have severally agreed to purchase, and we have agreed to sell to them, severally, the number of shares indicated below:

Name	Number of Shares
Morgan Stanley & Co. LLC	4,980,000
Cowen and Company, LLC	3,600,000
Piper Sandler & Co.	2,700,000
Chardan Capital Markets LLC	720,000
Total:	12,000,000

We currently expect that Pavilion Global Markets Ltd. will participate as a selling group member in this offering, in order to facilitate offers and sales of our common stock to one or more investors.

The underwriters and the representatives are collectively referred to as the “underwriters” and the “representatives,” respectively. The underwriters are offering the shares of common stock subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the several underwriters to pay for and accept delivery of the shares of common stock offered by this prospectus are subject to the approval of certain legal matters by their counsel and to certain other conditions. The underwriters are obligated to take and pay for all of the shares of common stock offered by this prospectus if any such shares are taken. However, the underwriters are not required to take or pay for the shares covered by the underwriters’ over-allotment option described below.

The underwriters initially propose to offer part of the shares of common stock directly to the public at the offering price listed on the cover page of this prospectus and part to certain dealers at a price that represents a concession not in excess of $0.63 per share under the public offering price. After the initial offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the representatives. The offering of the shares by the underwriters is subject to the receipt and acceptance and subject to the underwriters’ right to reject any order in whole or in part.

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to 1,800,000 additional shares of common stock at the public offering price listed on the cover page of this prospectus, less underwriting discounts and commissions. The underwriters may exercise this option solely for the purpose of covering over-allotments, if any, made in connection with the offering of the shares of common stock offered by this prospectus. To the extent the option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase about the same percentage of the additional shares of common stock as the number listed next to the underwriter’s name in the preceding table bears to the total number of shares of common stock listed next to the names of all underwriters in the preceding table.

The following table shows the per share and total public offering price, underwriting discounts and commissions, and proceeds before expenses to us. These amounts are shown assuming both no exercise and full exercise of the underwriters’ option to purchase up to an additional 1,800,000 shares of common stock.

	Per Share	Total	
		No Exercise	Full Exercise
Public offering price	$ 15.00	$ 180,000,000	$ 207,000,000
Underwriting discounts and commissions	1.05	12,600,000	14,490,000
Proceeds, before expenses, to us	13.95	167,400,000	192,510,000

The estimated offering expenses payable by us, exclusive of the underwriting discounts and commissions, are approximately $3.7 million. We have agreed to reimburse the underwriters for expense relating to clearance of this offering with the Financial Industry Regulatory Authority, Inc. (FINRA) and compliance with state securities or "blue sky" laws up to $40,000.

The underwriters have informed us that they do not intend sales to discretionary accounts to exceed 5% of the total number of shares of common stock offered by them.

Our common stock has been approved for listing on the Nasdaq Global Select Market under the trading symbol "TNYA".

In connection with this offering, we have agreed that we will not, and will not publicly disclose and intention, to (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, or file with the Securities and Exchange Commission a registration statement under the Securities Act relating to the offering of any shares of our common stock or securities convertible into or exercisable or exchangeable for any shares of our common stock, or (ii) enter into any swap or other arrangement that transfers all or a portion of the economic consequences of ownership of any shares of common stock or any such other securities, in each case regardless of whether any of these transactions are to be settled by the delivery of shares of common stock or such other securities, in cash or otherwise, and in each case without the prior written consent of Morgan Stanley & Co. LLC, Cowen and Company, LLC and Piper Sandler & Co. on behalf of the underwriters for a period of 180 days after the date of this prospectus, other than the shares of our common stock to be sold in this offering; the issuance by us of shares of common stock upon the exercise of an option or warrant, vesting or settlement of restricted stock or restricted stock units or the conversion of a security outstanding on the date hereof; the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act provided that there is no transfer of common stock during the restricted period and any public announcement or filing under the Exchange Act indicates that no transfer of common stock is permitted during the restricted period; the issuance of shares or options to purchase shares of common stock or securities convertible into or exercisable for common stock to our employees, officers, directors, advisors, or consultants pursuant to an existing equity compensation plan, provided that any such recipient enter into a lockup agreement with the underwriters; the filing of a registration statement on Form S-8 with respect to an existing employee benefit plan; and the sale or issuance of or entry into an agreement to sell or issue shares of common stock in connection with our acquisition of one or more businesses, products or technologies (whether by means of merger, stock purchase, asset purchase or otherwise) or in connection with joint ventures, commercial relationships or other strategic transactions, provided, that, the aggregate number of shares of common stock so sold or issued does not exceed 5% of the total number of shares of common stock and provided further that any recipient of such shares enter into a lockup agreement with the underwriters.

In connection with this offering, all of our directors and officers and substantially all of our securityholders have agreed that, without the prior written consent of Morgan Stanley & Co. LLC, Cowen and Company, LLC and Piper Sandler & Co. on behalf of the underwriters, they will not, and will not publicly disclose an intention to, during the period from the date of this prospectus continuing through the date 180 days after the date of this prospectus (the Restricted Period):

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any shares of common stock or any securities convertible into or exercisable or exchangeable for shares of common stock; or
- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the common stock

whether any such transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise. In addition, each such person agrees that, without the prior written consent of

Morgan Stanley & Co. LLC, Cowen and Company, LLC and Piper Sandler & Co. on behalf of the underwriters, such other person will not, during the Restricted Period:

- make any demand for, or exercise any right with respect to, the registration of any shares of common stock or any security convertible into or exercisable or exchangeable for common stock; or
- engage in any hedging or other transaction designed or intended, or which could reasonably be expected to lead to or result in, a sale or disposition of any shares of common stock, or any securities convertible into or exercisable or exchangeable for common stock.

The restrictions described in the immediately preceding paragraph are subject to specified exceptions, including, without limitation:

- transactions related to shares of our common stock or other securities acquired in this offering or in open market transactions after the completion of this offering, provided that any required filing under Section 16 of the Exchange Act includes footnote disclosure and no other public announcement or filing, with limited exceptions, be required or voluntarily made in connection with subsequent sales of the common stock or other securities acquired in such open market transactions;
- transfers of shares of our common stock or any security convertible into or exercisable or exchangeable for common stock as a bona fide gift or charitable contribution, by will or intestate succession, or to an immediate family member or to certain trusts, provided that no filing under Section 16 of the Exchange Act shall be required or voluntarily made;
- transfers or distributions of shares of common stock or any other securities by a stockholder that is a trust to a trustor or beneficiary of the trust or to the estate of a beneficiary of such trust provided that no filing under Section 16 of the Exchange Act shall be required or voluntarily made;
- distributions of our common stock or any security convertible into or exercisable or exchangeable for common stock to limited partners, members, stockholders or holders of similar equity interests, or transfers of shares of common stock or any security convertible into or exercisable or exchangeable for common stock to another corporation, partnership, limited liability company, trust or other business entity that is an affiliate, or to any investment fund or other entity controlled or managed by an affiliate, provided that no filing under Section 16 of the Exchange Act shall be required or voluntarily made;
- transfers of our common stock or any security convertible into or exercisable or exchangeable for common stock pursuant to a domestic order or divorce, provided that any filing required by Section 16 of the Exchange Act shall clearly indicate in the footnotes thereto that such transfer is being made pursuant to these circumstances and that no other public announcement or filing shall be required or shall be voluntarily made;
- the exercise, vesting or settlement of options, restricted stock units or other equity awards granted under a stock incentive plan or other equity award plan as described in the prospectus, or transfers or disposition of shares of our common stock or any security convertible into or exercisable or exchangeable for common stock to us upon a vesting or settlement event of our restricted stock units or other securities or the exercise of warrants or options to purchase our securities on a “cashless” or “net exercise” basis to cover estimated taxes, withholding tax and remittance obligations in connection with such vesting, settlement or exercise, insofar as such vesting, settlement or exercise is effected solely by the surrender of outstanding options (or the common stock issuable upon the exercise thereof) or shares of common stock to the Company and our cancellation of all or a portion thereof, provided that no filing under Section 16 of the Exchange Act shall be required or voluntarily made within 90 days after the date of the prospectus and after such 90 days and during the Restricted Period any filing under Section 16 of the Exchange Act will include a statement that such transaction reflects these circumstances;
- transfers or dispositions of shares of common stock or any security convertible into or exercisable or exchangeable for common stock pursuant to any contractual arrangement in effect on the date of the

underwriting agreement and disclosed to the underwriters in writing that provides for the repurchase by us of common stock or any security convertible into or exercisable or exchangeable for common stock pursuant to a repurchase right arising in connection with the termination of employment with or service to the Company; provided that any filing under Section 16 of the Exchange Act reporting a reduction in beneficial ownership of common stock indicates by footnote disclosure or otherwise the nature of the transfer or disposition pursuant to these circumstances and that no other public announcement or filing shall be required or shall be voluntarily made;

- transfers of our common stock or any security convertible into or exercisable or exchangeable for common stock in connection with a bona fide third-party tender offer, merger, consolidation or other similar transaction made to all holders of our common stock involving a change of control of our Company that has been approved by our board of directors and is open to all holders of our common stock, provided that in the event that such tender offer, merger, consolidation or other such transaction is not completed, the securities shall continue to be subject to the restrictions on transfer set forth in the lock-up agreement, and provided that no filing under Section 16 of the Exchange Act shall be required or voluntarily made;
- facilitating the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock, provided that (i) such plan does not provide for the transfer of common stock during the Restricted Period and (ii) to the extent a public announcement or filing under the Exchange Act, if any, is required of or voluntarily made by the Company regarding the establishment of such plan during the Restricted Period, such announcement or filing shall include a statement to the effect that no transfer of common stock may be made under such plan during the Restricted Period; and
- the conversion of outstanding preferred stock into shares of common stock in connection with the consummation of the offering or any conversion or reclassification of common stock as described in the prospectus, provided that such shares of common stock received upon conversion remain subject to the terms of the lock-up agreement and provided that any filing required by Section 16 of the Exchange Act related to any conversion or reclassification of common stock clearly indicate in the footnotes thereto the nature and conditions of such conversion or reclassification; and
- if an entity advised by an investment adviser, transfers pursuant to a merger or reorganization with or into another institutional client that shares the same investment advisor registered pursuant to the requirements of the Investment Advisors Act of 1940, as amended.

Certain of the exceptions described above are subject to a requirement that the donee, trustee, transferee or distributee enter into a lock-up agreement with the underwriters containing similar restrictions. Certain of the exceptions described above are subject to a requirement that the transfer or distribution does not involve a disposition for value.

Morgan Stanley & Co. LLC, Cowen and Company, LLC and Piper Sandler & Co. in their sole discretion, may release the common stock and other securities subject to the lock-up agreements described above in whole or in part at any time. The lock-up agreements of certain significant holders are subject to a pro rata release.

In order to facilitate the offering of the common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting agreement, creating a short position. A short sale is covered if the short position is no greater than the number of shares available for purchase by the underwriters under the over-allotment option. The underwriters can close out a covered short sale by exercising the over-allotment option or purchasing shares in the open market. In determining the source of shares to close out a covered short sale, the underwriters will consider, among other things, the open market price of shares compared to the price available under the over-allotment option. The underwriters may also sell shares in excess of the over-allotment option, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could

adversely affect investors who purchase in this offering. As an additional means of facilitating this offering, the underwriters may bid for, and purchase, shares of common stock in the open market to stabilize the price of the common stock. These activities may raise or maintain the market price of the common stock above independent market levels or prevent or retard a decline in the market price of the common stock. The underwriters are not required to engage in these activities and may end any of these activities at any time.

We and the underwriters have agreed to indemnify each other against certain liabilities, including liabilities under the Securities Act.

A prospectus in electronic format may be made available on websites maintained by one or more underwriters, or selling group members, if any, participating in this offering. The representatives may agree to allocate a number of shares of common stock to underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters that may make Internet distributions on the same basis as other allocations.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their respective affiliates have, from time to time, performed, and may in the future perform, various financial advisory and investment banking services for us, for which they received or will receive customary fees and expenses.

In addition, in the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investment and securities activities may involve our securities and instruments. The underwriters and their respective affiliates may also make investment recommendations or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long or short positions in such securities and instruments.

Pricing of the Offering

Prior to this offering, there has been no public market for our common stock. The initial public offering price was determined by negotiations between us and the representatives. Among the factors considered in determining the initial public offering price were our future prospects and those of our industry in general, our sales, earnings and certain other financial and operating information in recent periods, and the price-earnings ratios, price-sales ratios, market prices of securities, and certain financial and operating information of companies engaged in activities similar to ours.

Selling Restrictions

Canada

The shares of our common stock may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares of our common stock must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation,

provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable restrictions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

European Economic Area

In relation to each Member State of the European Economic Area (each, a Relevant State), no shares have been offered or will be offered pursuant to the offering to the public in that Relevant State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation, except that offers of shares may be made to the public in that Relevant State at any time under the following exemptions under the Prospectus Regulation:

(a) to any legal entity which is a qualified investor as defined the Prospectus Regulation;

(b) to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Regulation), subject to obtaining the prior consent of the underwriters; or

(c) in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of shares shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation and each person who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with each of the underwriters and us that it is a "qualified investor" within the meaning of Article 2(e) of the Prospectus Regulation.

In the case of any shares being offered to a financial intermediary as that term is used in the Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares to the public other than their offer or resale in a Relevant State to qualified investors as so defined or in circumstances in which the prior consent of the underwriters have been obtained to each such proposed offer or resale.

For the purposes of this provision, the expression an "offer to the public" in relation to any shares in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase shares or subscribe for any shares, and the expression "Prospectus Regulation" means Regulation (EU) 2017/1129.

We have not authorized and do not authorize the making of any offer of shares through any financial intermediary on their behalf, other than offers made by the underwriters with a view to the final placement of the shares in this document. Accordingly, no purchaser of the shares, other than the underwriters, is authorized to make any further offer of the shares on behalf of us or the underwriters.

United Kingdom

In relation to the United Kingdom, no shares of common stock will be offered pursuant to this offering to the public in the United Kingdom prior to publication of a prospectus in relation to the shares that either (i) has

been approved by the Financial Conduct Authority, or (ii) is to be treated as if it had been approved by the Financial Conduct Authority in accordance with the transitional provision in Regulation 74 of the Prospectus (Amendment etc.) (EU Exit) Regulations 2019, except that offers of shares may be made to the public in the United Kingdom at any time under the following exemptions under the UK Prospectus Regulation:

(a) to any legal entity which is a qualified investor as defined in Article 2 of the UK Prospectus Regulation;

(b) to fewer than 150 natural or legal persons (other than qualified investors as defined in Article 2 of the UK Prospectus Regulation); or

(c) in any other circumstances falling within section 86 of the Financial Services and Markets Act 2000 (FSMA).

For the purposes of this provision, the expression an "offer to the public" in relation to any shares in any relevant state means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase or subscribe for any shares, and the expression "UK Prospectus Regulation" means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018.

We have not authorized and do not authorize the making of any offer of shares through any financial intermediary on their behalf, other than offers made by the underwriters with a view to the final placement of the shares as contemplated in this document. Accordingly, no purchaser of the shares, other than the underwriters, is authorized to make any further offer of the shares on behalf of us or the underwriters.

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are "qualified investors" (as defined in Article 2 of the UK Prospectus Regulation) (i) who have professional experience in matters relating to investments falling within Article 19(5) of the FSMA (Financial Promotion) Order 2005, as amended, or the Order, and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as relevant persons) or otherwise in circumstances which have not resulted and will not result in an offer to the public of the shares in the United Kingdom within the meaning of the FSMA. In the United Kingdom, any investment or investment activity to which this document relates is only available to, and will be engaged in with, relevant persons.

Any person in the United Kingdom who is not a relevant person must not act upon this document or any of its contents or use it as the basis for taking any action. In the United Kingdom, any investment or investment activity that this document relates to may be made or taken exclusively by relevant persons.

Switzerland

The shares of common stock may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland. Neither this document nor any other offering or marketing material relating to the offering, us, or the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, or FINMA, and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Dubai International Financial Center

This prospectus relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority, or DFSA. This prospectus is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus nor taken steps to verify the information set forth herein and has no responsibility for the prospectus. The shares to which this prospectus relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the shares offered should conduct their own due diligence on the shares. If you do not understand the contents of this prospectus you should consult an authorized financial advisor.

Australia

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission, or ASIC, in relation to the offering. This prospectus does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001, or the Corporations Act, and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the shares may only be made to persons, or the Exempt Investors, who are "sophisticated investors" (within the meaning of section 708(8) of the Corporations Act), "professional investors" (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the shares without disclosure to investors under Chapter 6D of the Corporations Act.

The shares applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of twelve months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring shares must observe such Australian on-sale restrictions.

This prospectus contains general information only and does not take into account the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus is appropriate for their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

Hong Kong

The shares of common stock have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the shares of common stock has been or may be issued or has been or may be in the possession of any person for the purposes of issuance, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares of common stock which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Japan

No registration pursuant to Article 4, paragraph 1 of the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended), or the FIEL, has been made or will be made with respect to the solicitation of the application for the acquisition of the shares of common stock.

Accordingly, the shares of common stock have not been, directly or indirectly, offered or sold and will not be, directly or indirectly, offered or sold in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan) or to others for re-offering or re-sale, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan except pursuant to an exemption from the registration requirements, and otherwise in compliance with, the FIEL and the other applicable laws and regulations of Japan.

For Qualified Institutional Investors, or QII

Please note that the solicitation for newly-issued or secondary securities (each as described in Paragraph 2, Article 4 of the FIEL) in relation to the shares of common stock constitutes either a “QII only private placement” or a “QII only secondary distribution” (each as described in Paragraph 1, Article 23-13 of the FIEL). Disclosure regarding any such solicitation, as is otherwise prescribed in Paragraph 1, Article 4 of the FIEL, has not been made in relation to the shares of common stock. The shares of common stock may only be transferred to QIIs.

For Non-QII Investors

Please note that the solicitation for newly-issued or secondary securities (each as described in Paragraph 2, Article 4 of the FIEL) in relation to the shares of common stock constitutes either a “small number private placement” or a “small number private secondary distribution” (each as is described in Paragraph 4, Article 23-13 of the FIEL). Disclosure regarding any such solicitation, as is otherwise prescribed in Paragraph 1, Article 4 of the FIEL, has not been made in relation to the shares of common stock. The shares of common stock may only be transferred en bloc without subdivision to a single investor.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares of common stock may not be circulated or distributed, nor may the shares of common stock be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares of common stock are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

(a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

(b) a trust (where the trustee is not an accredited investor) the sole purpose of which is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares of common stock pursuant to an offer made under Section 275 of the SFA except:

(a) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

(b) where no consideration is or will be given for the transfer;

(c) where the transfer is by operation of law;

(d) as specified in Section 276(7) of the SFA; or

(e) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

United Arab Emirates

The shares have not been, and are not being, publicly offered, sold, promoted or advertised in the United Arab Emirates (including the Dubai International Financial Centre) other than in compliance with the laws of the United Arab Emirates (and the Dubai International Financial Centre) governing the issue, offering and sale of securities. Further, this prospectus does not constitute a public offer of securities in the United Arab Emirates (including the Dubai International Financial Centre) and is not intended to be a public offer. This prospectus has not been approved by or filed with the Central Bank of the United Arab Emirates, the Securities and Commodities Authority or the Dubai Financial Services Authority.

China

This prospectus does not constitute a public offer of shares, whether by sale or subscription, in the People's Republic of China, or the PRC. The shares are not being offered or sold directly or indirectly in the PRC to or for the benefit of, legal or natural persons of the PRC.

Further, no legal or natural persons of the PRC may directly or indirectly purchase any of the shares or any beneficial interest therein without obtaining all prior PRC's governmental approvals that are required, whether statutorily or otherwise. Persons who come into possession of this document are required by the issuer and its representatives to observe these restrictions.

Korea

The shares have not been and will not be registered under the Financial Investments Services and Capital Markets Act of Korea and the decrees and regulations thereunder, or the FSCMA, and the shares have been and will be offered in Korea as a private placement under the FSCMA. None of the shares may be offered, sold or delivered directly or indirectly, or offered or sold to any person for re-offering or resale, directly or indirectly, in Korea or to any resident of Korea except pursuant to the applicable laws and regulations of Korea, including the FSCMA and the Foreign Exchange Transaction Law of Korea and the decrees and regulations thereunder, or the FETL. Furthermore, the purchaser of the shares shall comply with all applicable regulatory requirements (including but not limited to requirements under the FETL) in connection with the purchase of the shares. By the purchase of the shares, the relevant holder thereof will be deemed to represent and warrant that if it is in Korea or is a resident of Korea, it purchased the shares pursuant to the applicable laws and regulations of Korea.

Taiwan

The shares have not been and will not be registered with the Financial Supervisory Commission of Taiwan pursuant to relevant securities laws and regulations and may not be sold, issued or offered within Taiwan through

a public offering or in circumstances which constitutes an offer within the meaning of the Securities and Exchange Act of Taiwan that requires a registration or approval of the Financial Supervisory Commission of Taiwan. No person or entity in Taiwan has been authorized to offer, sell, give advice regarding or otherwise intermediate the offering and sale of the shares in Taiwan.

South Africa

Due to restrictions under the securities laws of South Africa, the shares are not offered, and the offer shall not be transferred, sold, renounced or delivered, in South Africa or to a person with an address in South Africa, unless one or other of the following exemptions applies:

i. the offer, transfer, sale, renunciation or delivery is to:

(a) persons whose ordinary business is to deal in securities, as principal or agent;

(b) the South African Public Investment Corporation;

(c) persons or entities regulated by the Reserve Bank of South Africa;

(d) authorized financial service providers under South African law;

(e) financial institutions recognized as such under South African law;

(f) a wholly-owned subsidiary of any person or entity contemplated in (c), (d) or (e), acting as agent in the capacity of an authorized portfolio manager for a pension fund or collective investment scheme (in each case duly registered as such under South African law); or

(g) any combination of the person in (a) to (f); or

ii. the total contemplated acquisition cost of the securities, for any single addressee acting as principal is equal to or greater than ZAR1,000,000.

No “offer to the public” (as such term is defined in the South African Companies Act, No. 71 of 2008 (as amended or re-enacted), or the South African Companies Act) in South Africa is being made in connection with the issue of the shares. Accordingly, this document does not, nor is it intended to, constitute a “registered prospectus” (as that term is defined in the South African Companies Act) prepared and registered under the South African Companies Act and has not been approved by, and/or filed with, the South African Companies and Intellectual Property Commission or any other regulatory authority in South Africa. Any issue or offering of the shares in South Africa constitutes an offer of the shares in South Africa for subscription or sale in South Africa only to persons who fall within the exemption from “offers to the public” set out in section 96(1)(a) of the South African Companies Act. Accordingly, this document must not be acted on or relied on by persons in South Africa who do not fall within section 96(1)(a) of the South African Companies Act (such persons being referred to as SA Relevant Persons). Any investment or investment activity to which this document relates is available in South Africa only to SA Relevant Persons and will be engaged in South Africa only with SA Relevant Persons.

Israel

This document does not constitute a prospectus under the Israeli Securities Law, 5728-1968, (Israeli Securities Law), and has not been filed with or approved by the Israel Securities Authority. In Israel, this prospectus is being distributed only to, and is directed only at, and any offer of the shares of common stock is directed only at, (i) a limited number of persons in accordance with the Israeli Securities Law and (ii) investors listed in the first addendum (the Addendum), to the Israeli Securities Law, consisting primarily of joint

investment in trust funds, provident funds, insurance companies, banks, portfolio managers, investment advisors, members of the Tel Aviv Stock Exchange, underwriters, venture capital funds, entities with equity in excess of NIS 50 million and "qualified individuals," each as defined in the Addendum (as it may be amended from time to time), collectively referred to as qualified investors (in each case, purchasing for their own account or, where permitted under the Addendum, for the accounts of their clients who are investors listed in the Addendum). Qualified investors are required to submit written confirmation that they fall within the scope of the Addendum, are aware of the meaning of same and agree to it.

LEGAL MATTERS

The validity of the issuance of our common stock offered in this prospectus will be passed upon for us by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California. Davis Polk & Wardwell LLP, Menlo Park, California, is acting as counsel for the underwriters.

EXPERTS

The financial statements as of December 31, 2019 and 2020, and for each of the two years in the period ended December 31, 2020, included in this prospectus have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report appearing herein. Such financial statements have been so included in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of our common stock offered by this prospectus. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement, as permitted by the rules and regulations of the SEC. For further information with respect to us and our common stock, we refer you to the registration statement, including the exhibits filed as a part of the registration statement. Statements contained in this prospectus concerning the contents of any contract or any other document is not necessarily complete. If a contract or document has been filed as an exhibit to the registration statement, please see the copy of the contract or document that has been filed. Each statement in this prospectus relating to a contract or document filed as an exhibit is qualified in all respects by the filed exhibit. The SEC also maintains an Internet website that contains the registration statement of which this prospectus forms a part, as well as the exhibits thereto. These documents, along with future reports, proxy statements and other information about us, are available at the SEC's website, www.sec.gov.

As a result of this offering, we will become subject to the information and reporting requirements of the Exchange Act and, in accordance with this law, will file periodic reports, proxy statements and other information with the SEC. These periodic reports, proxy statements and other information will be available for inspection and copying at the SEC's public reference facilities and the website of the SEC referred to above. We also maintain a website at www.tenayatherapeutics.com where these materials are available. Upon the completion of this offering, you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. Information contained on, or accessible through, our website is not incorporated by reference into this prospectus and should not be considered to be part of this prospectus. The inclusion of our website address in this prospectus is an inactive textual reference only.

TENAYA THERAPEUTICS, INC.

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and Board of Directors of Tenaya Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Tenaya Therapeutics, Inc. (the Company) as of December 31, 2019 and 2020, the related statements of operations and comprehensive loss, convertible preferred stock and stockholders' deficit, and cash flows, for each of the two years in the period ended December 31, 2020, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2019 and 2020, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2020, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Deloitte and Touche LLP

San Francisco, California
May 7, 2021 (July 26, 2021, as to the effects of the reverse stock split described in Note 13)

We have served as the Company's auditor since 2019.

TENAYA THERAPEUTICS, INC.

Balance Sheets
(in thousands, except share and per share data)

	December 31, 2019	December 31, 2020
ASSETS		
Current assets:		
Cash and cash equivalents	$ 23,872	$ 128,535
Investments in marketable securities	2,753	—
Prepaid expenses and other current assets	1,117	1,429
Total current assets	27,742	129,964
Property and equipment, net	9,575	17,185
Restricted cash, non-current	399	547
Other non-current assets	285	465
Total assets	$ 38,001	$ 148,161
LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' DEFICIT		
Current liabilities:		
Accounts payable	$ 600	$ 1,017
Accrued expenses and other current liabilities	1,959	3,161
Convertible preferred stock tranche liability	786	—
Deferred rent and other lease liabilities, current	775	863
Total current liabilities	4,120	5,041
Deferred rent and other lease liabilities, non-current	4,525	3,662
Other non-current liabilities	53	19
Total liabilities	8,698	8,722
Commitments and contingencies (Note 6)		
Convertible preferred stock, $0.0001 par value; 17,816,666 and 26,102,301 shares authorized as of December 31, 2019 and 2020; 11,403,077 and 24,493,528 shares issued and outstanding as of December 31, 2019 and 2020; aggregate liquidation preference of $227,900 as of December 31, 2020	73,042	220,754
Stockholders' deficit:		
Common stock, $0.0001 par value; 21,408,000 and 30,330,000 shares authorized as of December 31, 2019 and 2020; 1,193,488 and 1,210,306 shares issued and outstanding as of December 31, 2019 and 2020	—	—
Additional paid-in capital	764	1,584
Notes receivable from stockholders	(86)	(87)
Accumulated deficit	(44,417)	(82,812)
Total stockholders' deficit	(43,739)	(81,315)
Total liabilities, convertible preferred stock and stockholders' deficit	$ 38,001	$ 148,161

The accompanying notes are an integral part of these financial statements.

TENAYA THERAPEUTICS, INC.

Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)

	Year Ended December 31,	
	2019	2020
Operating expenses:		
Research and development	$ 23,148	$ 31,099
General and administrative	4,564	7,813
Total operating expenses	27,712	38,912
Loss from operations	(27,712)	(38,912)
Other income:		
Interest income	453	87
Change in fair value of convertible preferred stock tranche liability	11	75
Other income (expense), net	1,017	355
Total other income	1,481	517
Loss before income tax expense	(26,231)	(38,395)
Income tax expense	—	—
Net loss and comprehensive loss	$ (26,231)	$ (38,395)
Net loss per share, basic and diluted	$ (34.71)	$ (39.50)
Weighted-average shares used in computing net loss per share, basic and diluted	755,779	972,091

The accompanying notes are an integral part of these financial statements.

TENAYA THERAPEUTICS, INC.

Statements of Convertible Preferred Stock and Stockholders' Deficit
(in thousands, except share data)

	Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Notes Receivable from Stockholders	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount	Shares	Amount				
Balance as of January 1, 2019	8,316,662	$ 43,393	1,093,159	$ —	$ 230	$ (84)	$ (18,186)	$ (18,040)
Issuance of Series B convertible preferred stock, net of issuance costs of $221 and recognition of convertible preferred stock liability upon issuance of Series B convertible preferred stock of $797	3,086,415	29,649	—	—	—	—	—	—
Issuance of common stock to a related party for the grant of rights and licenses	—	—	16,666	—	75	—	—	75
Issuance of common stock upon exercise of stock options	—	—	89,746	—	5	—	—	5
Repurchase of common stock related to early exercise of options	—	—	(6,083)	—	—	—	—	—
Vesting of early exercised stock options	—	—	—	—	40	—	—	40
Notes receivable from stockholders	—	—	—	—	—	(2)	—	(2)
Stock-based compensation	—	—	—	—	414	—	—	414
Net loss and other comprehensive loss	—	—	—	—	—	—	(26,231)	(26,231)
Balance as of December 31, 2019	11,403,077	73,042	1,193,488	—	764	(86)	(44,417)	(43,739)
Issuance of Series B convertible preferred stock, net of issuance costs of $49 and settlement of convertible preferred stock tranche liability of $711	6,172,830	61,995	—	—	—	—	—	—
Issuance of Series C convertible preferred stock, net of issuance costs of $283	6,917,621	85,717	—	—	—	—	—	—
Issuance of common stock upon exercise of stock options	—	—	17,846	—	34	—	—	34
Repurchase of common stock related to early exercise of options	—	—	(1,028)	—	—	—	—	—
Vesting of early exercised stock options	—	—	—	—	45	—	—	45
Notes receivable from stockholders	—	—	—	—	—	(1)	—	(1)
Stock-based compensation	—	—	—	—	741	—	—	741
Net loss and other comprehensive loss	—	—	—	—	—	—	(38,395)	(38,395)
Balance as of December 31, 2020	24,493,528	$ 220,754	1,210,306	$ —	$ 1,584	$ (87)	$ (82,812)	$ (81,315)

The accompanying notes are an integral part of these financial statements.

TENAYA THERAPEUTICS, INC.

Statements of Cash Flows
(in thousands)

	Year Ended December 31, 2019	2020
Cash flows from operating activities:		
Net loss	$ (26,231)	$ (38,395)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	1,989	2,483
Stock-based compensation	414	741
Accretion of discount on marketable securities	(96)	—
Loss on disposal of property and equipment	14	33
Non-cash stock expense related to the grant of rights and licenses from a related party	75	—
Change in fair value of convertible preferred stock tranche liability	(11)	(75)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(378)	(312)
Other non-current assets	(15)	(180)
Accounts payable	397	142
Accrued expenses and other current liabilities	514	925
Deferred rent and other lease liabilities	(691)	(775)
Other non-current liabilities	(77)	(34)
Net cash used in operating activities	(24,096)	(35,447)
Cash flows from investing activities:		
Purchases of property and equipment	(2,926)	(9,763)
Purchases of marketable securities	(12,657)	—
Proceeds from maturities of marketable securities	10,000	2,753
Net cash used in investing activities	(5,583)	(7,010)
Cash flows from financing activities:		
Proceeds from issuance of Series B convertible preferred stock, net of issuance costs	30,446	61,284
Proceeds from issuance of Series C convertible preferred stock, net of issuance costs	—	85,951
Proceeds from exercise of stock options	68	34
Repurchases of common stock	(3)	(1)
Net cash provided by financing activities	30,511	147,268
Net increase in cash, cash equivalents and restricted cash	832	104,811
Cash, cash equivalents and restricted cash at beginning of period	23,439	24,271
Cash, cash equivalents and restricted cash at end of period	$ 24,271	$ 129,082
Components of cash, cash equivalents and restricted cash:		
Cash and cash equivalents	$ 23,872	$ 128,535
Restricted cash, non-current	399	547
Cash, cash equivalents and restricted cash	$ 24,271	$ 129,082
Supplemental disclosure of non-cash investing and financing activities:		
Property and equipment included in accounts payable and accrued expenses and other current liabilities	$ 110	$ 364
Settlement of convertible preferred stock tranche liability in connection with the issuance of Series B convertible preferred stock	$ —	$ 711
Deferred offering costs related to Series C convertible preferred stock included in accounts payable and accrued expenses and other current liabilities	$ —	$ 234

The accompanying notes are an integral part of these financial statements.

1. Organization and Description of Business

Description of the Business

Tenaya Therapeutics, Inc. (the Company) was incorporated in the state of Delaware in August 2016 and is headquartered in South San Francisco, California. The Company is a preclinical stage biotechnology company focused on discovering, developing and delivering curative therapies that address the underlying drivers of heart disease. The Company is advancing product candidates from three distinct but interrelated product platforms: gene therapy, cellular regeneration and precision medicine.

Liquidity

The Company has incurred net losses since inception and expects such losses to continue in the future as it conducts research and development activities. As of December 31, 2020, the Company had an accumulated deficit of $82.8 million. The Company incurred a net loss of $26.2 million and $38.4 million during the years ended December 31, 2019 and 2020. The Company had $128.5 million of cash and cash equivalents as of December 31, 2020. In addition, in January 2021, the Company raised $20.0 million in gross proceeds from the issuance and sale of shares of its Series C convertible preferred stock (see Note 13).

Management recognizes the need to raise capital to fully implement its business plan. The Company has historically financed its operations primarily with proceeds from the issuance of its convertible preferred stock and may seek to raise capital through equity financings, debt financings, license agreements, collaborative agreements or other sources of financing. Management believes that its existing cash and cash equivalents as of December 31, 2020, together with the funds raised in January 2021 from the sale of Series C convertible preferred stock, are sufficient to fund the Company's operations for at least the next twelve months following the issuance date of these financial statements.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (GAAP).

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, and the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. Significant estimates and assumptions made in the accompanying financial statements include, but are not limited to, the fair value of common stock, the valuation of equity-based awards, the useful lives of property and equipment, the fair value of the convertible preferred stock tranche liability, accrued expenses related to research and development activities and the valuation allowance for deferred tax assets. Management bases its estimates on historical experience, the current economic environment, and on various other assumptions that are believed to be reasonable under the circumstances. Actual results may differ from those estimates or assumptions.

Fair Value Measurements

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability, or an exit price, in the principal or most advantageous market for that asset or liability in an orderly transaction
between market participants on the measurement date. Fair value measurement establishes a three-level fair value

hierarchy that requires an entity to maximize the use of observable inputs, where available, and minimize the use of unobservable inputs when measuring fair value. The three-level hierarchy of inputs is as follows:

Level 1—Observable inputs such as unadjusted quoted prices in active markets for identical assets or liabilities as of the measurement date;

Level 2—Inputs (other than quoted prices included within Level 1) that are directly observable for the asset or liability or indirectly observable for similar assets or liabilities;

Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The Company's cash and cash equivalents, prepaid expenses and other current assets, accounts payable and accrued expenses and other current liabilities approximate their fair value due to their short-term nature.

Concentrations of Credit Risk

Financial instruments, which potentially subject the Company to concentration of risk, consist principally of cash, cash equivalents and marketable securities. All of the Company's cash, cash equivalents and marketable securities are invested through banks and other accredited financial institutions in the United States. Such amounts may exceed federally insured limits. The Company has not experienced any losses on its deposits of cash and cash equivalents.

Risks and Uncertainties

The Company is subject to certain risks similar to that of other early-stage biopharmaceutical companies, including, but not limited to, the ability to obtain future financing, possible failure of future clinical trials, the need to obtain regulatory approvals for its product candidates, the need to successfully commercialize and gain market acceptance of the Company's product candidates, competitive developments, protection of the proprietary technology, the ability to make milestone, royalty or other payments due under licensing agreements, and the Company's ability to attract and retain employees necessary to support its growth.

The ongoing COVID-19 pandemic has disrupted and may continue to disrupt the Company's business and delay its programs and timelines. The Company does not yet know the full extent of potential delays to its preclinical trials, which could prevent or delay the Company from initiating clinical trials and obtaining approval for its product candidates. The extent to which the COVID-19 pandemic may impact the Company's future operating results and financial condition is uncertain.

Segment Information and Geographical Information

The Company has one operating segment and one reportable segment, which is the business of developing treatments that address heart failure. The Company's chief operating decision maker, its Chief Executive Officer, reviews financial information on an aggregate basis for the purpose of allocating resources and evaluating financial performance. All of the Company's assets are located in the United States.

Cash and Cash Equivalents

The Company considers all highly liquid investments purchased with an original maturity of three months or less on the date of purchase to be cash equivalents. Cash equivalents primarily consist of money market funds, commercial paper and U.S. government agencies bonds that are stated at fair value.

Restricted Cash

As of December 31, 2019 and 2020, the Company's restricted cash of $0.4 million and $0.5 million represent security deposits for the Company's operating leases in South San Francisco, California. The security deposits are in the form of a letter of credit secured by restricted cash.

Marketable Securities

The Company invests in marketable securities, primarily securities issued by the U.S. government and its agencies as well as commercial paper. All marketable securities have been classified as available-for-sale and are carried at estimated fair value as determined based upon quoted market prices or pricing models for similar securities. Management determines the appropriate classification of its marketable debt securities at the time of purchase and reevaluates such designation at each balance sheet date. Unrealized gains and losses are excluded from earnings and are reported as a component of other comprehensive loss. Realized gains and losses and declines in fair value judged to be other than temporary, if any, on available-for-sale securities are included in other income (expense), net. There are no material realized gains or losses on marketable securities for all periods presented. The cost of securities sold is based on the specific-identification method. Interest earned on marketable securities is included in interest income.

Property and Equipment, Net

Property and equipment are stated at cost, less accumulated depreciation. Depreciation is computed using the straight-line method over the estimated useful lives of the assets, generally three to five years. Leasehold improvements are amortized over the shorter of the assets' expected lives or the remaining lease term. Costs for capital assets not yet placed into service are capitalized as construction in progress and are not depreciated until the asset is placed in service.

Upon retirement or sale, the cost of disposed assets and their related accumulated depreciation are removed from the balance sheets. Any resulting gains or losses on dispositions of property and equipment are included as a component of other income (expense), net, within the Company's statements of operations and comprehensive loss. Repair and maintenance costs, which are not considered improvements and do not extend the useful life of property and equipment, are expensed as incurred.

Impairment for Long-Lived Assets

Long-lived assets, including construction in progress, are reviewed for impairment annually or whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability of assets to be held and used is measured by comparing the carrying amount of an asset to the estimated undiscounted future net cash flows expected to be generated by the asset. If the carrying amount of the asset exceeds its estimated future cash flows, an impairment charge is recognized in the amount by which the carrying amount of the asset exceeds the fair value of the asset. Fair value is determined through various valuation techniques including discounted cash flow models, quoted market values and third-party independent appraisals, as considered necessary. There was no impairment of long-lived assets for any of the periods presented.

Convertible Preferred Stock Tranche Liability

The obligation to issue additional shares of the Company's Series B convertible preferred stock at a fixed price on future dates was determined to be a freestanding financial instrument that is accounted for as a liability. On issuance, the Company recorded the convertible preferred stock tranche liability on the balance sheet at its estimated fair value. The liability is subject to remeasurement at each balance sheet date, with changes in fair value recognized as a gain or loss on remeasurement as a component of other income (expense), net in the

statements of operations and comprehensive loss until settlement or extinguishment. The convertible preferred stock tranche liability was settled upon the second and third closings of the Company's Series B convertible preferred stock in March and August 2020, respectively.

Leases

The Company records rent expense on a straight-line basis over the life of the lease from the date that it obtains the legal right to use and control the leased space. In cases where there is a free rent period or future fixed rent escalations, the Company records a deferred rent liability. Deferred rent consists of the difference between cash payments and the rent expense recognized.

As part of its lease agreements, the Company receives tenant improvement allowances from landlords. The Company recognizes these allowances as a leasehold incentive obligation, included in deferred rent and other lease liabilities, and amortizes allowances on a straight-line basis over the life of the lease. Allowances which contractually are not required to be paid back to the landlord, are amortized as a reduction to rent expense. Allowances which contractually are required to be paid back to the landlord are amortized over the life of the lease with a portion of the payment decreasing the allowance balance and recorded as an increase to rent expense.

Research and Development Expenses

Research and development (R&D) costs are expensed as incurred. Research and development costs include, among others, consulting fees, salaries, benefits, travel, stock-based compensation, laboratory supplies and other non-capital equipment utilized for in-house research, allocated facilities and overhead costs, amounts owed under licensing agreements, amounts paid to contract research organizations (CRO) that conduct research and development activities on the Company's behalf and costs related to compliance with regulatory requirements.

Goods or services incurred for research and development activities that have not yet been invoiced are recorded as liabilities within accrued expenses and other current liabilities on the Company's balance sheets. Amounts recorded for unbilled services often represent estimates, which are typically based on contracted amounts for the proportion of work performed and determined through analysis with internal personnel and external service providers as to the progress or stage of completion of the associated services. The Company makes judgments and estimates in determining the accrued and other current liabilities balance. If the actual timing of the performance of services or the level of effort varies from the estimate, the Company adjusts accrued expenses or prepaid expenses accordingly, which impact research and development expenses. The Company has not experienced any material differences between accrued costs and actual costs incurred. Changes in these estimates that result in material changes to the Company's accrued costs could materially affect the Company's results of operations.

The Company has and may continue to acquire the rights to licensed technology that represents in-process research and development to use and develop in the commercialization of new product candidates. The upfront payments made to acquire licenses, product or rights, or payments made related to future milestone payments are recognized as research and development expenses provided that there is no alternative future use of the rights in other research and development projects, up to the point of regulatory approval. Milestone payments are expensed when the specific milestone has been achieved.

Non-refundable advance payments for goods or services to be rendered as part of future research and development activities are capitalized on the Company's balance sheets until the goods or services are received.

Classification between prepaid expenses and other current assets and other non-current assets is based on an evaluation of when the goods will be delivered and/or services will be performed, with such amounts subsequently amortized to expense once incurred.

Stock-Based Compensation

The Company measures and records expense related to all equity awards granted to employees and non-employees in the statements of operations and comprehensive loss based on their grant date fair values, including stock options and restricted stock awards. For stock-based awards that vest subject to the satisfaction of a service requirement, the expense is recognized using the straight-line method over the requisite service period, which is generally the vesting period. Forfeitures are recognized as they occur.

For purposes of determining the estimated fair value of options granted to employees and nonemployees, the Company uses the Black-Scholes option pricing model.

The fair value of restricted stock awards is determined on the date of grant based on the estimated fair value of the Company's common stock on that date.

Income Taxes

The Company accounts for income taxes using the asset and liability method. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse.

A valuation allowance is recorded for deferred tax assets if it is more likely than not that some portion or all of the deferred tax assets will not be realized. In evaluating the ability to recover its deferred income tax assets, the Company considers all available positive and negative evidence, including its operating results, ongoing tax planning and forecasts of future taxable income on a jurisdiction-by-jurisdiction basis. In the event the Company determines that it would be able to realize its deferred income tax assets in the future in excess of their net recorded amount, it would make an adjustment to the valuation allowance that would reduce the provision for income taxes. Conversely, in the event that all or part of the net deferred tax assets are determined not to be realizable in the future, an adjustment to the valuation allowance would be charged to earnings in the period when such determination is made. As of December 31, 2019 and 2020, the Company has recorded a full valuation allowance on its net deferred tax assets.

Tax benefits related to uncertain tax positions are recognized when it is more likely than not that a tax position will be sustained during an audit. Interest and penalties, if any, related to unrecognized tax benefits are included within the provision for income tax.

Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss by the weighted-average number of shares of the Company's common stock outstanding for the period, without consideration for potential dilutive shares of common stock. As the Company is in a loss position for the periods presented, diluted net loss per share is the same as basic net loss per share, since the effects of potentially dilutive securities are antidilutive. Shares related to early exercised stock options and restricted stock that are subject to repurchase are excluded from the basic and diluted net loss per share calculation until the Company's repurchase right lapses.

Comprehensive Loss

Comprehensive loss includes net loss and certain changes in stockholders' deficit that are excluded from net loss. The Company's comprehensive loss is comprised of unrealized gains and losses on the Company's marketable securities, which were immaterial for all periods presented. Accordingly, comprehensive loss is the same as net loss.

Emerging Growth Company Status

The Company is an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012 (JOBS Act). Under the JOBS Act, emerging growth companies can delay adopting new or revised

accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. The Company has elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date that it (a) is no longer an emerging growth company or (b) affirmatively and irrevocably opts out of the extended transition period provided in the JOBS Act. As a result, these financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

Recently Adopted Accounting Standards

On January 1, 2019, the Company adopted Financial Accounting Standards Board (FASB) Accounting Standards Update (ASU) No. 2016-18, *Statement of Cash Flows* (Topic 230)—Restricted Cash (ASU 2016-18). This standard requires amounts generally described as restricted cash and restricted cash equivalents to be included with cash and cash equivalents when reconciling beginning-of-period and end-of-period total amounts shown on the statements of cash flows. The provisions of ASU 2016-18 are applied retrospectively. The adoption of this standard did not have a material impact on the Company's financial statements.

On January 1, 2019, the Company early adopted FASB ASU No. 2018-07, *Compensation-Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting*. This standard simplifies several aspects of the accounting for nonemployee share-based payment transactions resulting from expanding the scope of Topic 718 to include share-based payment transactions for acquiring goods and services from nonemployees. The adoption of this standard did not have a material impact on the Company's financial statements.

On January 1, 2020, the Company adopted FASB ASU No. 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement*. This standard eliminates, modifies and adds disclosure requirements for fair value measurements. The Company adopted the removed and modified disclosures on a retrospective basis and the new disclosures on a prospective basis. The adoption of this standard did not have a material impact on the Company's financial statements.

Recently Issued Accounting Pronouncements Not Yet Adopted

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*, as amended, which requires lessees to recognize operating and financing lease liabilities and corresponding right-of-use assets on the balance sheet for all leases with lease terms of more than twelve months. In July 2018, the FASB issued ASU No. 2018-11, *Leases, Targeted Improvements (Topic 842)*, an update which provides an alternative transition method, in addition to the existing modified retrospective transition method, by allowing entities to initially apply the new lease standard at the adoption date and recognize a cumulative-effect adjustment to the opening balance of retained earnings in the period of adoption. As an emerging growth company, these new lease standards are effective for the Company for fiscal year beginning January 1, 2022, with early adoption permitted. The Company is evaluating the impact of this standard on its financial statements.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* (ASU 2016-13), which replaces the existing incurred loss impairment model with an expected credit loss model. This standard will require companies to recognize an allowance for credit losses on available-for-sale debt securities rather than the current approach of recording a reduction to the carrying value of the asset. As an emerging growth company, ASU 2016-13 is effective for the Company for fiscal year beginning January 1, 2023. The Company is evaluating the impact of this standard on its financial statements.

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* (ASU 2019-12), which is intended to simplify the accounting for income taxes.

This standard eliminates certain exceptions to the approach for intra period tax allocation, the methodology for calculating income taxes in an interim period and the recognition of deferred tax liabilities for outside basis differences. As an emerging growth company, ASU 2019-12 is effective for the Company for fiscal year beginning January 1, 2022. The Company is evaluating the impact of this standard on its financial statements.

3. Fair Value Measurements

Financial assets and liabilities are recognized at fair value on a recurring basis. The following table summarize the Company's financial assets and liabilities measured at fair value on a recurring basis by level within the fair value hierarchy:

		December 31, 2019			
	Valuation Hierarchy	Amortized Cost	Unrealized Gain	Unrealized Loss	Fair Value
		(in thousands)			
Assets:					
Cash equivalents:					
Money market funds	Level 1	$ 19,373	$ —	$ —	$ 19,373
Commercial paper	Level 2	2,499	—	—	2,499
Government agencies bonds	Level 2	1,001	—	—	1,001
Marketable securities:					
U.S. treasuries	Level 1	2,753	—	—	2,753
Total financial assets		$ 25,626	$ —	$ —	$ 25,626
Liabilities:					
Convertible preferred stock tranche liability	Level 3	$ 786	$ —	$ —	$ 786
Total financial liabilities		$ 786	$ —	$ —	$ 786

		December 31, 2020			
	Valuation Hierarchy	Amortized Cost	Unrealized Gain	Unrealized Loss	Fair Value
		(in thousands)			
Assets:					
Cash equivalents:					
Money market funds	Level 1	$ 127,535	$ —	$ —	$ 127,535
Total financial assets		$ 127,535	$ —	$ —	$ 127,535

Money market funds and U.S. treasuries are classified as Level 1 because they are valued using quoted market prices in active markets for identical assets. Financial instruments classified within Level 2 of the fair value hierarchy are valued based on the observable inputs or can be derived from non-binding quotes from its investment managers, which are based on proprietary valuation models of independent pricing services. These models generally use inputs such as observable market data, quoted market prices for similar instruments, or historical pricing trends of a security relative to its peers.

There were no unrealized losses as of December 31, 2019 and 2020. All available-for-sale marketable securities held as of December 31, 2019 had contractual maturities of less than one year. There were no available-for-sale marketable securities as of December 31, 2020.

Convertible Preferred Stock Tranche Liability

The Company's convertible preferred stock tranche liability (see Note 7) was determined based on significant inputs not observable in the market, which represents a Level 3 measurement within the fair value

hierarchy. Fair value was calculated using an option pricing model that required significant unobservable inputs supported by little or no market activity. The convertible preferred stock tranche liability is considered a non-contingent forward and the standard forward pricing (SFP) model was used with the following key assumptions: (a) calculation of an expected term and (b) a risk-free interest rate. On the second and third closings of the Company's Series B convertible preferred stock financings in March and August 2020, the convertible preferred stock tranche liability was settled and reclassified to Series B convertible preferred stock. Accordingly, there is no convertible preferred stock tranche liability as of December 31, 2020.

The following table summarizes the significant unobservable assumptions used to value the convertible preferred stock tranche liability as of December 31, 2019 and August 24, 2020, the date immediately before the settlement of the tranche liability:

	December 31, 2019	August 24, 2020
Term to Valuation Date (in years)	0.25 – 0.75	0.00
Discount Rate	5.00%	5.00%

The following table summarizes the changes in the estimated fair value of the Company's convertible preferred stock tranche liability measured on a recurring basis using significant Level 3 inputs:

	December 31,	
	2019	2020
	(in thousands)	
Beginning balance	$ —	$ 786
Recognition of convertible preferred stock tranche liability upon the issuance of Series B convertible preferred stock	797	—
Change in fair value upon remeasurement	(11)	(75)
Settlement of convertible preferred stock tranche liability on second and third closings of the Series B convertible preferred stock	—	(711)
Ending balance	$ 786	$ —

4. Balance Sheet Components

Property and Equipment, Net

Property and equipment, net, consists of the following:

	December 31,	
	2019	2020
	(in thousands)	
Leasehold improvements	$ 7,206	$ 7,237
Laboratory equipment	5,846	8,182
Furniture and fixtures	519	534
Computer equipment and software	237	257
Construction in progress	—	7,678
Total property and equipment	13,808	23,888
Less: accumulated depreciation and amortization	(4,233)	(6,703)
Total property and equipment, net	$ 9,575	$ 17,185

Depreciation and amortization expense for the years ended December 31, 2019 and 2020 was approximately $2.0 million and $2.5 million. Construction in progress relates to the Company's manufacturing and office space located in Union City, California (see Note 13), and consists primarily of capitalized machinery and equipment as the Company builds-out its manufacturing facility.

Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consist of the following:

	December 31,	
	2019	2020
	(in thousands)	
Accrued compensation and related expenses	$ 1,121	$ 2,090
Accrued research and development expenses	296	391
Accrued professional services	168	328
Accrued property and equipment	59	231
Other current liabilities	315	121
Total accrued liabilities	$ 1,959	$ 3,161

5. Collaboration and License Agreements

Gladstone Master Collaboration Agreement

In October 2016, the Company entered into a Master Collaboration Agreement (MCA) with a related party, Gladstone Institutes (Gladstone), to collaborate on discovering therapies for the treatment of congestive heart failure and other diseases and conditions as mutually agreed. Under the MCA, the Company was required to provide minimum collaboration funding of $3.6 million during the first two years. During the year ended December 31, 2019, Gladstone completed the collaboration under the MCA and the Company satisfied the minimum collaboration funding requirement of $3.6 million. In addition, on the third-year anniversary of the MCA's effective date in October 2019, pursuant to the MCA, the Company issued 16,666 shares of the Company's common stock to Gladstone in consideration for certain patent rights and technology created in the course of performance of the collaboration being licensed to the Company under the Gladstone License Agreement (as defined below). The related cost was recognized as research and development expenses since the technology acquired had no alternative future use.

During the year ended December 31, 2019, the Company recorded research and development expenses of $0.4 million pursuant to the MCA. There was no expense recognized during the year ended December 31, 2020 pursuant to the MCA.

Gladstone License Agreement

In connection and concurrent with the execution of the MCA, the Company entered into a license agreement with Gladstone (Gladstone License Agreement), pursuant to which Gladstone granted the Company a worldwide, royalty-bearing exclusive patent license and a non-exclusive technology license to develop and commercialize certain products for certain diseases. Upon the execution of the Gladstone License Agreement, the Company paid a non-refundable upfront license fee of $0.1 million and issued 125,000 shares of the Company's common stock to Gladstone. Pursuant to the Gladstone License Agreement, the Company is obligated, among other things, to pay Gladstone (i) annual license maintenance fees ranging from $25,000 to $0.1 million per year, which will be creditable against royalties paid in the following twelve month period, (ii) milestone payments up to $4.1 million for royalty-bearing products directed to a particular target, which are contingent upon achieving specific clinical and commercialization milestone events, and (iii) tiered low-single digit royalties on future net sales of each royalty-bearing product. Under the agreement, the Company is subject to diligence requirements to develop and

commercialize at least one royalty-bearing product. The Company may pay $50,000 to $100,000 to extend the deadline for its diligence milestone obligations for up to four additional one-year terms. As of December 31, 2020, the Company has not recognized any milestone and royalty payments under the Gladstone License Agreement.

During the years ended December 31, 2019 and 2020, the amounts recorded as research and development expenses related to annual license fees payable pursuant to the Gladstone License Agreement were not material.

University of Texas Southwestern License Agreement

In January 2020, the Company entered into a license agreement with the University of Texas Southwestern (UTSW License), pursuant to which UTSW granted the Company a royalty-bearing exclusive and sublicensable patent license and a non-exclusive, non-sublicensable license for mutually agreed upon development activities. Under the UTSW License, the Company is obligated to pay UTSW (i) a non-refundable upfront license fee of $0.1 million, (ii) milestone payments up to a total of $14.8 million in aggregate, which are contingent upon achieving specific development and commercialization milestone events, and (iii) royalties on future net sales of each royalty-bearing product ranging in the low-single digits. As of December 31, 2020, the Company has not recognized any milestone and royalty payments under the UTSW License.

During the year ended December 31, 2020, the Company recorded research and development expenses of $0.1 million related to the upfront license fee payable pursuant to the UTSW License.

Other License Agreements

In addition to the agreements described above, the Company has also entered into other license agreements with various institutions and business entities, none of which are material individually or in the aggregate.

6. Commitments and Contingencies

Facility Leases

In December 2016, the Company entered into a lease agreement (Lease Agreement or Lease) for office and laboratory space in South San Francisco, California. The Lease expires in May 2025 and the Company may renew the lease term for two additional five-year periods. In connection with the execution of the Lease, the Company provided the landlord with a security deposit of $0.4 million in the form of a letter of credit, which is collateralized by a restricted cash deposit and recorded as restricted cash, non-current on the balance sheets as of December 31, 2019 and 2020.

Pursuant to the Lease Agreement, the Company received a tenant improvement allowance (TIA) of $5.8 million in aggregate for leasehold improvements to the facility. As of December 31, 2020, the remaining balance of the TIA that is recorded as a component of deferred rent on the balance sheet is $3.2 million.

In December 2020, the Company entered into a sublease agreement for additional office and laboratory space in South San Francisco, California with a lease term that expires on November 30, 2021. The Company provided the landlord a security deposit of $0.1 million in the form of a letter of credit, which is collateralized by a restricted cash deposit and recorded as restricted cash, non-current on the balance sheet as of December 31, 2020.

During the years ended December 31, 2019 and 2020, the Company recognized rent expense of $2.1 million and $2.4 million.

The following table summarizes the future minimum lease payments for the Company's office space and laboratory facilities as of December 31, 2020:

	Amount
Year ending December 31,	
2021	$ 3,752
2022	2,206
2023	2,283
2024	2,363
2025	999
Total future minimum lease payments	$ 11,603

The Company has previously entered into agreements to sublease portions of the Company's facilities in South San Francisco to two different subtenants, both of which have expired as of December 31, 2020. Pursuant to the sublease agreements, the Company received sublease income of $1.0 million and $0.4 million during the years ended December 31, 2019 and 2020, which are recognized as a component of other income (expense), net within the Company's statements of operations and comprehensive loss.

Purchase Commitments

The Company also entered into contractual agreements with various suppliers in the normal course of its business, including vendors that provide machinery and equipment. All contracts are terminable, with varying provisions regarding termination. If a contract with a specific vendor were to be terminated, the Company would only be obligated for the products or services that the Company had received through the time of termination.

Indemnification

In the normal course of business, the Company enters into agreements that may include indemnification provisions. Pursuant to such agreements, the Company may indemnify, hold harmless and defend an indemnified party for losses suffered or incurred by the indemnified party. In some cases, the indemnification will continue after the termination of the agreement. The maximum potential amounts of future payments the Company could be required to make under these provisions is not determinable. In addition, the Company has entered into indemnification agreements with its directors and certain officers that may require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. As of December 31, 2019 and 2020, the Company does not have any material indemnification claims that were probable or reasonably possible and, consequently, has not recorded any related liabilities.

7. Convertible Preferred Stock

Series B Convertible Preferred Stock Financing

In August 2019, the Company entered into a Series B preferred stock purchase agreement (Series B SPA) for the issuance of up to 9,259,254 shares of the Company's Series B convertible preferred stock at a purchase price of $9.936 per share in multiple closings. The Company completed the initial closing in August 2019, whereby 3,086,415 shares of Series B convertible preferred stock were issued for gross proceeds of $30.7 million. Pursuant to the Series B SPA, the Company was permitted to sell additional shares in subsequent closings contingent upon the approval of the Company's board of directors.

On issuance, the Company determined that its obligation to issue additional shares of Series B convertible preferred stock in future closings was a freestanding instrument that should be classified as a liability on the Company's balance sheets. The freestanding financial instrument, or convertible preferred stock tranche liability,

was recorded at fair value on issuance of $0.8 million with the remaining proceeds being allocated to the Series B convertible preferred stock. Any changes in fair value of convertible preferred stock tranche liability in subsequent reporting periods are recognized as a component of other income (expense), net in the statements of operations and comprehensive loss (see Note 3).

In March 2020, the Company completed its second closing of Series B convertible preferred stock financing and issued 3,086,415 shares of Series B convertible preferred stock at the fixed purchase price of $9.936 per share for gross proceeds of $30.7 million, thereby settling a portion of the convertible preferred stock tranche liability. Immediately prior to the second closing, the Company measured the convertible preferred stock tranche liability to its then fair value. Upon the closing of the second tranche, the convertible preferred stock tranche liability was partially settled and the related balance of the liability of $27,000 was reclassified to Series B convertible preferred stock.

In August 2020, the Company completed its third closing of Series B convertible preferred stock financing and issued 3,086,415 shares of Series B convertible preferred stock at the purchase price of $9.936 per share for gross proceeds of $30.7 million, thereby settling the remainder of the convertible preferred stock tranche liability. Immediately prior to the third closing, the Company measured the convertible preferred stock tranche liability to its then fair value. Upon the closing of the third tranche, the remaining convertible preferred stock tranche liability was settled and the balance of the liability of $0.7 million was reclassified to Series B convertible preferred stock.

Series C Convertible Preferred Stock Financing

In December 2020, the Company entered into a Series C preferred stock purchase agreement (Series C SPA) for the issuance of up to 8,526,381 shares of the Company's Series C convertible preferred stock at a purchase price of $12.432 per share in two closings. The Company completed the initial closing in December 2020, whereby 6,917,621 shares of Series C convertible preferred stock were issued for gross proceeds of $86.0 million.

The Company's convertible preferred stock consists of the following:

	December 31, 2019			
	Shares Authorized	Shares Issued and Outstanding	Net Carrying Value	Liquidation Preference
	(in thousands, except shares and original issue price)			
Convertible Preferred Stock				
Series A	8,316,666	8,316,662	$ 43,393	$ 49,900
Series B	9,500,000	3,086,415	29,649	30,667
Total	17,816,666	11,403,077	$ 73,042	$ 80,567

	December 31, 2020			
	Shares Authorized	Shares Issued and Outstanding	Net Carrying Value	Liquidation Preference
	(in thousands, except shares and original issue price)			
Convertible Preferred Stock				
Series A	8,316,666	8,316,662	$ 43,393	$ 49,900
Series B	9,259,254	9,259,245	91,644	92,000
Series C	8,526,381	6,917,621	85,717	86,000
Total	26,102,301	24,493,528	$ 220,754	$ 227,900

The Company classifies its convertible preferred stock outside of total stockholders' deficit because, in the event of certain change of control events that are not solely within the control of the Company (including liquidation, sale or transfer of the Company), the shares would become redeemable at the option of the holders. As a result, the Company has classified its convertible preferred stock as mezzanine equity on the balance sheets as the preferred stock is contingently redeemable. The Company did not adjust the carrying values of the convertible preferred stock to the deemed liquidation values of such shares since a liquidation event was not probable as of each reporting date. Subsequent adjustments to increase or decrease the carrying values to the ultimate liquidation values will be made only if and when it becomes probable that such liquidation event will occur.

The holders of the Company's Series A, Series B and Series C convertible preferred stock (together, convertible preferred stock) have various rights, preferences and privileges as follows:

Voting Rights

Each holder of shares of convertible preferred stock is entitled to the number of votes equal to the number of shares of common stock into which such shares of convertible preferred stock could be converted. The holders of convertible preferred stock vote together with the holders of common stock as a single class on an as-converted basis on all matters as to which holders of common stock have the right to vote.

The holders of convertible preferred stock, voting as a separate class, are entitled to elect three members of the Company's board of directors. The holders of common stock, voting as a separate class, are entitled to elect one member of the Company's board of directors. Any additional members of the Company's board of directors are elected by the holders of common stock and convertible preferred stock, voting together as a single class on an as-converted basis.

Dividends

Each holder of convertible preferred stock is entitled to receive dividends when and if declared by the board of directors at an annual rate of $0.480 per share for the Series A preferred stock, $0.792 per share for the Series B preferred stock, and $0.996 per share for the Series C preferred stock. Dividends are noncumulative. No dividends have been declared or paid as of December 31, 2020.

Conversion

Each share of convertible preferred stock is convertible, at the option of the holder any time after the issuance date, into shares of common stock determined by dividing the original issue price by the conversion price in effect on the date of conversion. The conversion price of each series of convertible preferred stock is $6.00 for Series A convertible preferred stock, $9.936 for Series B convertible preferred stock, and $12.432 for Series C convertible preferred stock, subject to adjustment for anti-dilution provisions and stock dividend, stock split, combination of shares, reorganization, recapitalization, reclassification or other similar event.

Each share of convertible preferred stock is automatically convertible into common stock immediately upon the earlier of (i) the closing of a firm commitment underwritten initial public offering pursuant to an effective registration statement filed under the Securities Act of 1933, as amended, resulting in aggregate gross proceeds not less than $75.0 million (a "Qualified IPO") or (ii) the Company's receipt of a written request for such conversion from a majority of the holders of convertible preferred stock then outstanding, voting together as a single class on an as-converted basis. With respect to a Qualified IPO at which the price per share is less than $15.54 (subject to adjustment for stock dividend, stock split, combination of shares, reorganization, recapitalization, reclassification or other similar event), each share of convertible preferred stock is convertible into common stock with the written consent of a majority of the holders of the Series C convertible preferred stock then outstanding, voting as a separate class.

Liquidation Preference

In the event of any liquidation, dissolution or winding up of the Company, either voluntary or involuntary, the holders of the preferred stock shall be entitled to receive, prior and in preference to any distribution of any of the assets of the Company to the holders of common stock, an amount per share equal to $6.00 per share for Series A convertible preferred stock, $9.936 per share for Series B convertible preferred stock and $12.432 per share for Series C convertible preferred stock (subject to adjustment for stock dividend, stock split, combination of shares, reorganization, recapitalization, reclassification or other similar event) plus all declared but unpaid dividends. After the distributions described above have been paid in full, the remaining assets of the Company shall be distributed among the holders of common stock in proportion to the numbers of shares of common stock. If the assets of the Company are insufficient to permit the payments to holders of convertible preferred stock of the full amount described above, all assets and funds legally available shall be distributed ratably among holders of convertible preferred stock.

8. Common Stock

The holders of the common stock are entitled to one vote per share on all matters to be voted on by the stockholders of the Company and are entitled to dividends, if and when declared by the board of directors, subject to the prior rights of the preferred stockholders. Common stock issued and outstanding on the balance sheets and statements of convertible preferred stock and stockholders' deficit includes shares related to early exercised options and restricted stock that are subject to repurchase. Common stock issued and outstanding is reduced for any repurchases of early exercised stock options and restricted stock. As of December 31, 2019 and 2020, outstanding common stock included 331,089 and 138,127 shares, respectively, related to early exercised stock options and restricted stock that are unvested and subject to repurchase.

The Company has reserved the following shares of common stock for issuance, on an as-if converted basis:

	December 31, 2020
Conversion of outstanding shares of convertible preferred stock	24,493,528
Options outstanding under the 2016 Plan	1,160,808
Options available for future grant	412,170
Total	26,066,506

9. Stock-Based Compensation

Amended and Restated 2016 Equity Incentive Plan

In October 2016, the Company adopted the 2016 Equity Incentive Plan, which was later amended and restated (the 2016 Plan), which provides for the granting of incentive and non-statutory stock options, stock appreciation rights, restricted stock and restricted stock units and other forms of stock awards to its employees, directors and non-employee service providers.

Under the 2016 Plan, the Company's board of directors has the authority to select the service provider to whom options will be granted and the type of award that will be granted, to determine when awards are to be granted, the number of shares, the term, and the exercise price. Options have a term of ten years and generally vest over a four-year period. As of December 31, 2020, 412,170 shares of common stock were authorized and available for grant under the 2016 Plan.

Stock Option Activity

The following table summarizes stock option activity under the 2016 Plan:

	Number of Options Outstanding	Weighted-Average Exercise Price Per Share	Weighted-Average Remaining Contractual Life (years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2019	880,816	$ 1.14	9.05	$ 2,952
Options granted	312,696	3.42		
Options exercised	(17,846)	1.86		
Options cancelled	(14,858)	2.40		
Outstanding as of December 31, 2020	1,160,808	$ 1.74	8.40	$ 6,060
Exercisable as of December 31, 2020	440,291	$ 1.14	8.05	$ 2,298

The total intrinsic value of options exercised during the years ended December 31, 2019 and 2020 was approximately $0.3 million and $37,000. The aggregate intrinsic is the difference between the fair value of the Company's common stock, as approved by the Company's board of directors, and exercise price of the option.

The weighted average grant-date fair value of options granted during the years ended December 31, 2019 and 2020 was $3.42 and $4.98 per share.

Stock-Based Compensation

The following table summarizes stock-based compensation recognized in the Company's statements of operations and comprehensive loss:

	Year Ended December 31,	
	2019	2020
	(in thousands)	
Research and development	$ 118	$ 378
General and administrative	296	363
Total stock-based compensation	$ 414	$ 741

As of December 31, 2020, there was approximately $2.3 million of unrecognized stock-based compensation, which the Company expects to recognize over a weighted-average period of 3.0 years.

Stock Option Valuation

The fair value of the Company's stock option awards is estimated on the date of grant using the Black-Scholes option pricing model using the following assumptions:

	Year Ended December 31,	
	2019	2020
Expected term (in years)	5.0 – 6.1	5.9 – 6.1
Expected volatility	105% – 192%	178% – 183%
Risk-free interest rate	1.7% – 2.5%	0.4% – 1.5%
Expected dividend yield	—%	—%

The assumptions used to determine the fair value of options granted were as follows. Each of these inputs is subjective and generally requires significant judgement.

Expected Term—The Company determines the expected term, which represents the period that stock-based awards are expected to be outstanding, in accordance with the simplified method due to its limited operating history, which is presumed to be the mid-point between the contractual term and the vesting period.

Expected Volatility—As there is no trading history for the Company's common stock, the Company determines its computation of expected volatility on the historical volatility of a representative group of public companies with similar characteristics to the Company, including stage of product development and life science industry focus. The historical volatility is calculated based on a period of time commensurate with the expected term assumption.

Risk-Free Interest Rate—The Company bases the risk-free interest rate on U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term assumption.

Expected Dividend Yield—The expected dividend yield is assumed to be zero as the Company has never paid and has no plans to pay any dividends on its common stock.

Restricted Stock

The 2016 Plan allows the Company to grant stock options that may be exercised by option holders prior to vesting, subject to certain limitations. The Company has also issued restricted stock awards to certain employees and non-employee founders under its 2016 Plan. The shares related to early exercised stock options and restricted stock are subject to the Company's lapsing repurchase right upon termination at the original purchase price. In order to vest, the holders are required to provide continued service to the Company.

The proceeds from early exercises are initially recorded in accrued expenses and other current liabilities and other non-current liabilities and are reclassified to common stock and additional paid-in capital the vesting conditions are met and the repurchase right lapses. As of December 31, 2019 and 2020, $0.1 million and $53,000 was recorded as liabilities on the balance sheets.

A summary of restricted stock activity is as follows:

	Number of Shares	Weighted Average Fair Value at Date of Grant per Share
Unvested as of December 31, 2019	331,089	$ 0.72
Vested	(191,934)	0.60
Repurchased	(1,028)	0.48
Unvested as of December 31, 2020	138,127	$ 0.90

Employee Recourse Notes

In 2017 and 2018, the Company entered into full recourse notes with certain employees, including one of its officers, upon the exercise of stock options that are treated as substantive exercises for accounting purposes. The Company has the right to repurchase unvested shares up to 90 days after employment is terminated. As of December 31, 2020, the principal and accrued interest amount of the notes was $87,000. The notes are presented in the statements of convertible preferred stock and stockholders' deficit.

10. Income Taxes

No provision for, or benefit from, income taxes was recorded during the years ended December 31, 2019 and 2020. The Company has established a full valuation allowance against its net deferred tax assets due to the uncertainty regarding the realization of such assets. All losses to date have been incurred in the United States. Deferred income taxes reflect the net tax effects of (a) temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes, and (b) operating losses and tax credit carryforwards.

Effective Tax Rate Reconciliation

The effective tax rate of the Company's provision for income taxes differs from the federal statutory rate and the effective tax rate reconciliation is as follows:

	December 31,	
	2019	2020
U.S. federal taxes at statutory rate	21.0%	21.0%
State taxes (net of federal benefit)	9.3	8.1
Credits	0.7	3.6
Stock-based compensation	(0.2)	(0.3)
Section 382 limitation on tax attribute carryforwards	—	(9.0)
Change in valuation allowance	(30.7)	(23.1)
Other	(0.1)	(0.3)
Total	0.0%	0.0%

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows:

	December 31,	
	2019	2020
	(in thousands)	
Balance at beginning of year	$ —	$ 744
Additions based on tax positions related to current year	473	293
Additions based on tax positions related to prior years	271	—
Reductions for tax positions related to prior years	—	(466)
Balance at end of year	$ 744	$ 571

The Company does not expect that its uncertain tax positions will materially change in the next twelve months. The reversal of the uncertain tax benefits would not impact the Company's effective tax rate as the Company continues to maintain a full valuation allowance against its deferred tax assets.

The Company files tax returns in U.S. federal and state with varying statutes of limitations. Due to net operating loss and credit carryforwards, all of the tax years since inception through the 2020 tax year remain subject to examination by the U.S. federal and state authorities. The Company is currently not subject to any income tax audits by federal or state taxing authorities.

Deferred Income Taxes

The tax effects of significant items comprising the Company's deferred income taxes are as follows:

	December 31,	
	2019	2020
	(in thousands)	
Deferred tax assets:		
Net operating losses	$ 11,820	$ 20,917
Tax credits	1,684	1,346
Accrued expenses and other	696	918
Tenant improvements	1,085	896
Property and equipment	93	120
Stock-based compensation	39	79
Other	1	11
Total deferred tax assets	15,418	24,287
Valuation allowance	(15,418)	(24,287)
Net deferred tax assets	$ —	$ —

The tax benefit of net operating losses, temporary differences and credit carryforwards are recorded as an asset to the extent that the Company assesses that realization is more likely than not. Realization of the future tax benefits is dependent on the Company's ability to generate sufficient taxable income within the carryforward period. As a result of the Company's recent history of operating losses, the Company believes that recognition of deferred tax assets arising from the above-mentioned future tax benefits is currently not likely to be realized and, accordingly, has provided a full valuation allowance. The valuation allowance increased by $7.4 million and $8.9 million during the years ended December 31, 2019 and 2020. The increase in the valuation allowance during the year ended December 31, 2020 would have been larger but for the reduction in net operating loss and tax credit carryforwards limited under Section 382. The impact of the Section 382 limitation resulted in the reduction of deferred tax assets for federal research credits and state net operating loss carryforwards, with an offsetting reduction of the valuation allowance.

Net Operating Loss and Tax Credit Carryforwards

As of December 31, 2020, the Company's net operating loss and tax carryforwards are summarized as follows:

	Amount	Expiration in years
Net operating losses, federal (post-December 31, 2017)	$ 75,431	Do Not Expire
Net operating losses, federal (pre-January 1, 2018)	3,093	Begins to Expire 2036
Net operating losses, state	62,508	Begins to Expire 2036
Tax credits, federal	244	Begins to Expire 2036
Tax credits, state	2,068	Do Not Expire

Under Section 382 of the Internal Revenue Code of 1986, as amended, the ability to utilize net operating loss carryforwards or other tax attributes, such as research tax credits, in any taxable year may be limited if the Company has experienced an "ownership change". This annual limitation may result in the expiration of net operating losses and credits before utilization. As of December 31, 2020, a formal study was conducted and concluded that the Company has experienced an ownership change in 2020. As a result, the Company has removed $3.1 million of deferred tax assets related to net operating loss carryforwards and research tax credit carryforwards due to Section 382 limitations. The Company's ability to use its remaining net operating loss carryforwards may be further limited if the Company experiences a Section 382 ownership change as a result of future changes in its stock ownership.

The Company recognizes interest and penalties related to taxes and uncertain tax positions as a component of income tax expense. During the years ended December 31, 2019 and 2020, no interest and penalties were accrued by the Company.

11. Net Loss Per Share

The following potentially dilutive securities were not included in the calculation of diluted net loss per share for the periods presented because the effect would have been anti-dilutive:

	Year Ended December 31,	
	2019	2020
Convertible preferred stock	11,403,077	24,493,528
Outstanding stock options	880,816	1,160,808
Restricted stock subject to future vesting	331,089	138,127
Total	12,614,982	25,792,463

12. Related Party Transactions

Gladstone Institutes

Under the MCA, Gladstone performed specific research activities for the Company in accordance with the mutually agreed-upon annual project plans (see Note 5). During the year ended December 31, 2019, the Company recognized $0.4 million in research and development expenses in relation to the services provided by Gladstone. No such research services were provided during the year ended December 31, 2020. In addition, during the year ended December 31, 2019, the Company recognized $0.2 million in aggregate lab, license and patent fees and $75,000 in stock. During the year ended December 31, 2020, the Company recognized $0.1 million in aggregate lab, license and patent fees. As of December 31, 2019 and 2020, the related party balance included within accounts payable and accrued expenses was $10,000 and $nil.

Scientific Founders

During the years ended December 31, 2019 and 2020, the Company recognized a total of $0.2 million in each period in consulting expense paid to five of its scientific founders.

13. Subsequent Events

The Company evaluated subsequent events from December 31, 2020, the date of these financial statements, through May 7, 2021, the date the financial statements were available for issuance, for events requiring recognition or disclosure in the financial statements for the year ended December 31, 2020, except for the 1-for-6 reverse stock split discussed below, which was evaluated through July 26, 2021.

Series C Convertible Preferred Stock Issuance

In January 2021, the Company sold an additional 1,608,750 shares of Series C convertible preferred stock at the price of $12.432 per share for aggregate gross proceeds of $20.0 million.

Manufacturing and Office Space Lease Agreement

In February 2021, the Company entered into a lease agreement for manufacturing and office space located in Union City, California. The lease has a ten-year term with one five-year renewal option. Upon the execution of the lease agreement, the Company provided the landlord with a security deposit of $3.3 million. Total lease payments during the lease term are expected to be $13.9 million.

2021 Stock Options Grants

In January 2021, the Company granted 129,698 options to employees, each with an exercise price of $5.64 per share and a four-year vesting schedule. In February 2021, the Company granted 416,666 options to its chief executive officer, with an exercise price of $5.64 per share and a four-year vesting schedule.

Reverse Stock Split

In July 2021, the Company's board of directors and stockholders approved an amendment to the Company's amended and restated certificate of incorporation to effect a reverse split of shares of the Company's common stock, convertible preferred stock and authorized shares on a 1-for-6 basis (the Reverse Stock Split) effective on July 23, 2021. The par value of the common stock and preferred stock was not adjusted as a result of the Reverse Stock Split. Accordingly, all share data and per share data amounts for all periods presented in the accompanying financial statements and notes thereto have been retrospectively adjusted to reflect the effect of the Reverse Stock Split.

TENAYA THERAPEUTICS, INC.

Condensed Balance Sheets
(in thousands, except share and per share data)
(unaudited)

	December 31, 2020	March 31, 2021
ASSETS		
Current assets:		
Cash and cash equivalents	$ 128,535	$ 128,439
Prepaid expenses and other current assets	1,429	1,311
Total current assets	129,964	129,750
Property and equipment, net	17,185	21,267
Operating lease right-of-use asset	—	4,415
Restricted cash, non-current	547	547
Other non-current assets	465	3,778
Total assets	$ 148,161	$ 159,757
LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' DEFICIT		
Current liabilities:		
Accounts payable	$ 1,017	$ 2,092
Accrued expenses and other current liabilities	3,161	2,128
Deferred rent and other lease liabilities, current	863	—
Operating lease liabilities, current	—	1,690
Total current liabilities	5,041	5,910
Deferred rent and other lease liabilities, non-current	3,662	—
Operating lease liabilities, non-current	—	7,036
Other non-current liabilities	19	19
Total liabilities	8,722	12,965
Commitments and contingencies (Note 6)		
Convertible preferred stock, $0.0001 par value; 26,102,301 shares authorized as of December 31, 2020 and March 31, 2021; 24,493,528 and 26,102,278 shares issued and outstanding as of December 31, 2020 and March 31, 2021; aggregate liquidation preference of $247,900 as of March 31, 2021	220,754	240,735
Stockholders' deficit:		
Common stock, $0.0001 par value; 30,330,000 shares authorized as of December 31, 2020 and March 31, 2021; 1,210,306 and 1,222,449 shares issued and outstanding as of December 31, 2020 and March 31, 2021	—	—
Additional paid-in capital	1,584	2,054
Notes receivable from stockholders	(87)	(87)
Accumulated deficit	(82,812)	(95,910)
Total stockholders' deficit	(81,315)	(93,943)
Total liabilities, convertible preferred stock and stockholders' deficit	$ 148,161	$ 159,757

The accompanying notes are an integral part of these unaudited condensed financial statements.

TENAYA THERAPEUTICS, INC.

Condensed Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)
(unaudited)

	Three Months Ended March 31,	
	2020	**2021**
Operating expenses:		
Research and development	$ 7,297	$ 9,590
General and administrative	1,969	3,515
Total operating expenses	9,266	13,105
Loss from operations	(9,266)	(13,105)
Other income (expense), net:		
Interest income	57	9
Change in fair value of convertible preferred stock tranche liability	(19)	—
Other income (expense), net	177	(2)
Total other income (expense), net	215	7
Loss before income tax expense	(9,051)	(13,098)
Income tax expense	—	—
Net loss and comprehensive loss	$ (9,051)	$ (13,098)
Net loss per share, basic and diluted	$ (10.15)	$ (11.93)
Weighted-average shares used in computing net loss per share, basic and diluted	891,990	1,097,805

The accompanying notes are an integral part of these unaudited condensed financial statements.

TENAYA THERAPEUTICS, INC.

Condensed Statements of Convertible Preferred Stock and Stockholders' Deficit
(in thousands, except share data)
(unaudited)

	Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Notes Receivable from Stockholders	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount	Shares	Amount				
Balance as of December 31, 2019	11,403,077	$ 73,042	1,193,488	$ —	$ 764	$ (86)	$ (44,417)	$ (43,739)
Issuance of Series B convertible preferred stock, net of issuance costs of $23 and partial settlement of convertible preferred stock tranche liability of $27	3,086,415	30,671	—	—	—	—	—	—
Issuance of common stock upon exercise of stock options	—	—	3,333	—	3	—	—	3
Repurchase of common stock related to early exercise of options	—	—	(612)	—	—	—	—	—
Vesting of early exercised stock options	—	—	—	—	11	—	—	11
Notes receivable from stockholders	—	—	—	—	—	1	—	1
Stock-based compensation	—	—	—	—	154	—	—	154
Net loss and other comprehensive loss	—	—	—	—	—	—	(9,051)	(9,051)
Balance as of March 31, 2020	14,489,492	$103,713	1,196,209	$ —	$ 932	$ (85)	$ (53,468)	$ (52,621)

The accompanying notes are an integral part of these unaudited condensed financial statements.

TENAYA THERAPEUTICS, INC.

Condensed Statements of Convertible Preferred Stock and Stockholders' Deficit
(in thousands, except share data)
(unaudited)

	Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Notes Receivable from Stockholders	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount	Shares	Amount				
Balance as of December 31, 2020	24,493,528	$220,754	1,210,306	$ —	$ 1,584	$ (87)	$ (82,812)	$ (81,315)
Issuance of Series C convertible preferred stock, net of issuance costs of $20	1,608,750	19,981	—	—	—	—	—	—
Issuance of common stock upon exercise of stock options	—	—	12,508	—	29	—	—	29
Repurchase of common stock related to early exercise of options	—	—	(365)	—	—	—	—	—
Vesting of early exercised stock options	—	—	—	—	9	—	—	9
Stock-based compensation	—	—	—	—	432	—	—	432
Net loss and other comprehensive loss	—	—	—	—	—	—	(13,098)	(13,098)
Balance as of March 31, 2021	26,102,278	$240,735	1,222,449	$ —	$ 2,054	$ (87)	$ (95,910)	$ (93,943)

The accompanying notes are an integral part of these unaudited condensed financial statements.

TENAYA THERAPEUTICS, INC.

Condensed Statements of Cash Flows
(in thousands)
(unaudited)

	Three Months Ended March 31,	
	2020	**2021**
Cash flows from operating activities:		
Net loss	$ (9,051)	$ (13,098)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	584	689
Stock-based compensation	154	432
Loss on disposal of property and equipment	35	—
Non-cash operating lease expense	—	171
Change in fair value of convertible preferred stock tranche liability	19	—
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	158	118
Other non-current assets	(169)	(3,313)
Accounts payable	674	618
Accrued expenses and other current liabilities	(452)	(1,022)
Deferred rent and other lease liabilities	(182)	—
Operating lease liabilities	—	(384)
Other non-current liabilities	(8)	—
Net cash used in operating activities	(8,238)	(15,789)
Cash flows from investing activities:		
Purchases of property and equipment	(435)	(4,323)
Proceeds from maturities of marketable securities	2,753	—
Net cash provided by (used in) investing activities	2,318	(4,323)
Cash flows from financing activities:		
Proceeds from issuance of Series B convertible preferred stock, net of issuance costs	30,667	—
Proceeds from issuance of Series C convertible preferred stock, net of issuance costs	—	19,986
Proceeds from exercise of stock options	3	29
Net cash provided by financing activities	30,670	20,015
Net increase (decrease) in cash, cash equivalents and restricted cash	24,750	(97)
Cash, cash equivalents and restricted cash at beginning of period	24,271	129,083
Cash, cash equivalents and restricted cash at end of period	$ 49,021	$ 128,986
Components of cash, cash equivalents and restricted cash:		
Cash and cash equivalents	$ 48,622	$ 128,439
Restricted cash, non-current	399	547
Cash, cash equivalents and restricted cash	$ 49,021	$ 128,986
Supplemental disclosure of cash operating activities:		
Cash paid for leases that were included in operating cash outflows	$ —	$ 1,389
Supplemental disclosure of non-cash operating activities:		
Lease liability obtained in exchange for right-of-use asset	$ —	$ 213
Supplemental disclosure of non-cash investing and financing activities:		
Deferred offering costs related to initial public offering included in accounts payable	$ —	$ 74
Property and equipment included in accounts payable and accrued expenses and other current liabilities	$ 162	$ 452
Partial settlement of convertible preferred stock tranche liability in connection with the issuance of Series B convertible preferred stock	$ 27	$ —
Offering costs related to Series B convertible preferred stock included in accounts payable and accrued expenses and other current liabilities	$ 23	$ —
Offering costs related to Series C convertible preferred stock included in accounts payable	$ —	$ 5

The accompanying notes are an integral part of these unaudited condensed financial statements.

1. Organization and Description of the Business

Description of the Business

Tenaya Therapeutics, Inc. (the Company) was incorporated in the state of Delaware in August 2016 and is headquartered in South San Francisco, California. The Company is a preclinical stage biotechnology company focused on discovering, developing and delivering curative therapies that address the underlying drivers of heart disease. The Company is advancing product candidates from three distinct but interrelated product platforms: gene therapy, cellular regeneration and precision medicine.

Liquidity

The Company has incurred net losses since inception and expects such losses to continue in the future as it conducts research and development activities. As of March 31, 2021, the Company had an accumulated deficit of $95.9 million. The Company incurred a net loss of $9.1 million and $13.1 million during the three months ended March 31, 2020 and 2021. The Company had $128.4 million of cash and cash equivalents as of March 31, 2021.

Management recognizes the need to raise capital to fully implement its business plan. The Company has historically financed its operations primarily with proceeds from the issuance of its convertible preferred stock and may seek to raise capital through equity financings, debt financings, license agreements, collaborative agreements or other sources of financing. Management believes that its existing cash and cash equivalents as of March 31, 2021 are sufficient to fund the Company's operations for at least the next twelve months following the filing date of these condensed financial statements.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying condensed financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (GAAP) and follow the requirements of the Securities and Exchange Commission (SEC) for interim reporting. As permitted under those rules, certain footnotes or other financial information that are normally required by GAAP can be condensed or omitted.

Use of Estimates

The preparation of condensed financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, and the disclosure of contingent assets and liabilities at the date of the condensed financial statements and the reported amounts of expenses during the reporting period. Significant estimates and assumptions made in the accompanying condensed financial statements include, but are not limited to, the fair value of common stock, the valuation of equity-based awards, the useful lives of property and equipment, the fair value of the convertible preferred stock tranche liability, accrued expenses related to research and development activities and the valuation allowance for deferred tax assets. Management bases its estimates on historical experience, the current economic environment, and on various other assumptions that are believed to be reasonable under the circumstances. Actual results may differ from those estimates or assumptions.

Unaudited Interim Condensed Financial Statements

The interim condensed balance sheet as of March 31, 2021, and the interim condensed statements of operations and comprehensive loss, convertible preferred stock and stockholders' deficit and cash flows for the three months ended March 31, 2020 and 2021 are unaudited. These unaudited interim condensed financial statements have been prepared on the same basis as the Company's annual financial statements and, in the opinion of management, reflect all adjustments (consisting only of normal recurring adjustments) that are

necessary for the fair statement of the Company's financial position, results of operations and cash flows for the interim periods presented. The condensed results of operations for the three months ended March 31, 2021 are not necessarily indicative of the results to be expected for the full year or for any other future annual or interim period. The condensed balance sheet as of December 31, 2020 included herein was derived from the audited financial statements as of that date. These interim condensed financial statements should be read in conjunction with the Company's audited financial statements included elsewhere in this prospectus.

Cash and Cash Equivalents

The Company considers all highly liquid investments purchased with an original maturity of three months or less on the date of purchase to be cash equivalents. Cash equivalents primarily consist of money market funds that are stated at fair value.

Leases

The Company adopted Accounting Standards Codification (ASC) Topic 842, *Leases* (ASC 842) on January 1, 2021, as discussed below in the section titled "Recently Adopted Accounting Standards". Under ASC 842, the Company determines if an arrangement is a lease at inception.

Operating lease right-of-use (ROU) assets represent the Company's right to use an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. Operating lease ROU assets and liabilities are recognized based on the present value of lease payments over the lease term at the commencement date of the lease. ROU assets also include any initial direct costs incurred and any lease payments made at or before the lease commencement date, less any lease incentive received. The Company uses the rate implicit in the lease in determining the present value of lease payments and, if that rate is not readily determinable, the Company uses its incremental borrowing rate based on the information available at the date of lease commencement. The incremental borrowing rate reflects the rate of interest that a lessee would have to pay to borrow, on a collateralized basis over a similar term, an amount equal to the lease payments in a similar economic environment. The Company's lease terms may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. Lease expense for lease payments is recognized on a straight-line basis over the lease term.

The Company's non-lease components are primarily related to property taxes, insurance, and common area maintenance, which vary based on future outcomes, and are recognized as rent expense when incurred.

Deferred Offering Costs

Deferred offering costs, consisting of legal, accounting, audit and filing fees relating to the Company's initial public offering, are capitalized. Deferred offering costs will be offset against offering proceeds upon the completion of the offering. In the event the offering is terminated or delayed, deferred offering costs will be expensed. As of December 31, 2020, the Company did not incur any deferred offering costs. As of March 31, 2021, $0.1 million of deferred offering costs were capitalized, which are included in other non-current assets in the accompanying condensed balance sheet.

Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss by the weighted-average number of shares of the Company's common stock outstanding for the period, without consideration for potential dilutive shares of common stock. As the Company is in a loss position for the periods presented, diluted net loss per share is the same as basic net loss per share, since the effects of potentially dilutive securities are antidilutive. Shares related to early exercised stock options and restricted stock that are subject to repurchase are excluded from the basic and diluted net loss per share calculation until the Company's repurchase right lapses.

Recently Adopted Accounting Standards

On January 1, 2020, the Company adopted Financial Accounting Standards Board (FASB) Accounting Standard Update (ASU) No. 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement*. This standard eliminates, modifies and adds disclosure requirements for fair value measurements. The Company adopted the removed and modified disclosures on a retrospective basis and the new disclosures on a prospective basis. The adoption of this standard did not have a material impact on the Company's financial statements.

On January 1, 2021, the Company adopted ASC 842 using the modified retrospective transition method and elected the practical expedients to not reassess whether any expired or existing contracts are or contain leases, carry forward its historical lease classification and not reassess initial direct costs for existing leases. The Company elected to not separate non-lease components from the associated lease components and to not recognize ROU assets and lease liabilities for leases with a term of twelve months or less. Upon adoption of ASC 842, the Company recorded an operating right-of-use asset of $4.6 million, operating lease liabilities of $9.1 million and derecognized deferred rent and other lease liabilities of $4.5 million. Results for the three months ended March 31, 2021 are presented under ASC 842. Prior period amounts before January 1, 2021 have not been adjusted and continue to be reported in accordance with the Company's historical accounting under previous lease guidance, ASC 840: *Leases (Topic 840)*.

Recently Issued Accounting Pronouncements Not Yet Adopted

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* (ASU 2016-13), which replaces the existing incurred loss impairment model with an expected credit loss model. This standard will require companies to recognize an allowance for credit losses on available-for-sale debt securities rather than the current approach of recording a reduction to the carrying value of the asset. As an emerging growth company, ASU 2016-13 is effective for the Company beginning January 1, 2023. The Company is evaluating the impact of this standard on its financial statements.

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* (ASU 2019-12), which is intended to simplify the accounting for income taxes. This standard eliminates certain exceptions to the approach for intra period tax allocation, the methodology for calculating income taxes in an interim period and the recognition of deferred tax liabilities for outside basis differences. As an emerging growth company, ASU 2019-12 is effective for the Company beginning January 1, 2022. The Company is evaluating the impact of this standard on its financial statements.

In August 2020, the FASB issued ASU No. 2020-06, Debt—*Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40)* (ASU 2020-06), which is intended to simplify the accounting for convertible debt instruments and convertible preferred stock. This standard removes the existing guidance in ASC 470-20 that requires companies to account for cash conversion features and beneficial conversion features in equity, separately from the host convertible debt or preferred stock. As an emerging growth company, ASU 2020-06 is effective for the Company beginning January 1, 2024. The Company currently does not expect the adoption of this standard to have a material impact on its financial statements.

3. Fair Value Measurements

Financial assets and liabilities are recognized at fair value on a recurring basis. The following tables summarize the Company's financial assets measured at fair value on a recurring basis by level within the fair value hierarchy:

	Valuation Hierarchy	December 31, 2020			
		Amortized Cost	Unrealized Gain	Unrealized Loss	Fair Value
		(in thousands)			
Assets:					
Cash equivalents:					
Money market funds	Level 1	$ 127,535	$ —	$ —	$ 127,535
Total financial assets		$ 127,535	$ —	$ —	$ 127,535

	Valuation Hierarchy	March 31, 2021			
		Amortized Cost	Unrealized Gain	Unrealized Loss	Fair Value
		(in thousands)			
Assets:					
Cash equivalents:					
Money market funds	Level 1	$ 127,433	$ —	$ —	$ 127,433
Total financial assets		$ 127,433	$ —	$ —	$ 127,433

Money market funds are classified as Level 1 because they are valued using quoted market prices in active markets for identical assets.

There were no unrealized losses as of December 31, 2020 and March 31, 2021.

Convertible Preferred Stock Tranche Liability

The Company's convertible preferred stock tranche liability (see Note 7) was determined based on significant inputs not observable in the market, which represents a Level 3 measurement within the fair value hierarchy. Fair value was calculated using an option pricing model that required significant unobservable inputs supported by little or no market activity. The convertible preferred stock tranche liability is considered a non-contingent forward and the standard forward pricing model was used with the following key assumptions: (a) calculation of an expected term and (b) a risk-free interest rate. On the second and third closings of the Company's Series B convertible preferred stock financings in March and August 2020, the convertible preferred stock tranche liability was settled and reclassified to Series B convertible preferred stock. Accordingly, there is no convertible preferred stock tranche liability as of December 31, 2020 and March 31, 2021.

The following table summarizes the significant unobservable assumptions used to value the convertible preferred stock tranche liability as of March 31, 2020:

	March 31, 2020
Term to valuation date (in years)	0.5
Discount rate	5.0%

The following table summarizes the changes in the estimated fair value of the Company's convertible preferred stock tranche liability measured on a recurring basis using significant Level 3 inputs:

	March 31, 2020
	(in thousands)
Beginning balance	$ 786
Partial settlement upon second closing of Series B convertible preferred stock	(27)
Change in fair value upon remeasurement	19
Ending balance	$ 778

4. Balance Sheet Components

Property and Equipment, Net

Property and equipment, net consists of the following:

	December 31, 2020	March 31, 2021
	(in thousands)	
Laboratory equipment	$ 8,182	$ 8,676
Construction in progress	7,678	11,937
Leasehold improvements	7,237	7,237
Furniture and fixtures	534	534
Computer equipment and software	257	272
Total property and equipment	23,888	28,656
Less: accumulated depreciation and amortization	(6,703)	(7,389)
Total property and equipment, net	$ 17,185	$ 21,267

Depreciation and amortization expense for the three months ended March 31, 2020 and 2021 was $0.6 million and $0.7 million. Construction in progress consists primarily of capitalized machinery and equipment that is expected to be placed in service in the Company's manufacturing and office space located in Union City, California after the lease commencement date in May 2021.

Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consist of the following:

	December 31, 2020	March 31, 2021
	(in thousands)	
Accrued compensation and related expenses	$ 2,090	$ 1,122
Accrued research and development expenses	391	134
Accrued professional services	328	631
Accrued property and equipment	231	100
Other current liabilities	121	141
Total accrued expenses and other current liabilities	$ 3,161	$ 2,128

5. Collaboration and License Agreements

Gladstone License Agreement

In October 2016, the Company entered into a license agreement with Gladstone Institutes (Gladstone), pursuant to which Gladstone granted the Company a worldwide, royalty-bearing exclusive patent license and a non-exclusive technology license to develop and commercialize certain products for certain diseases (Gladstone License Agreement). Pursuant to the Gladstone License Agreement, the Company is obligated, among other things, to pay Gladstone (i) annual license maintenance fees ranging from $25,000 to $0.1 million per year, which will be creditable against royalties paid in the following twelve month period, (ii) milestone payments up to $4.1 million for royalty-bearing products directed to a particular target, which are contingent upon achieving specific clinical and commercialization milestone events, and (iii) tiered low-single digit royalties on future net sales of each royalty-bearing product. Under the agreement, the Company is subject to diligence requirements to develop and commercialize at least one royalty-bearing product. The Company may pay $50,000 to $100,000 to extend the deadline for its diligence milestone obligations for up to four additional one-year terms. As of March 31, 2021, the Company has not recognized any milestone and royalty payments under the Gladstone License Agreement.

During the three months ended March 31, 2020 and 2021, there were no amounts recorded related to annual license fees payable pursuant to the Gladstone License Agreement.

University of Texas Southwestern License Agreement

In January 2020, the Company entered into a license agreement with the University of Texas Southwestern (UTSW License), pursuant to which UTSW granted the Company a royalty-bearing exclusive and sublicensable patent license and a non-exclusive, non-sublicensable license for mutually agreed upon development activities. Under the UTSW License, the Company is obligated to pay UTSW (i) a non-refundable upfront license fee of $0.1 million, (ii) milestone payments up to a total of $14.8 million in aggregate, which are contingent upon achieving specific development and commercialization milestone events, and (iii) royalties on future net sales of each royalty-bearing product ranging in the low-single digits. As of March 31, 2021, the Company has not recognized any milestone and royalty payments under the UTSW License.

During the three months ended March 31, 2020, the Company recorded research and development expenses of $0.1 million related to the upfront license fee payable pursuant to the UTSW License.

Other License Agreements

In addition to the agreements described above, the Company has also entered into other license agreements with various institutions and business entities, none of which are material individually or in the aggregate.

6. Commitments and Contingencies

Facility Leases

In December 2016, the Company entered into a lease agreement for office and laboratory space in South San Francisco, California. The lease expires in May 2025 and the Company may renew the lease term for two additional five-year periods. Pursuant to the lease agreement, the Company received a tenant improvement allowance of $5.8 million in aggregate for leasehold improvements to the facility.

In December 2020, the Company entered into a short-term sublease agreement for additional office and laboratory space in South San Francisco, California with a lease term that expires on November 30, 2021.

On January 1, 2021, the Company adopted ASC 842 (see Note 2) and the following disclosures as of and for the three months ended March 31, 2021 are presented under ASC 842. As of March 31, 2021, the remaining lease term was 4.4 years and the incremental borrowing rate used to determine the operating lease liability was 9.0%.

For the three months ended March 31, 2021, the Company incurred $1.2 million in rent expense, of which $0.6 million is related to the Company's short-term lease. Variable lease payments were $0.4 million for the three months ended March 31, 2021. For the three months ended March 31, 2020, the Company incurred $0.6 million in rent expense.

As of March 31, 2021 the undiscounted future minimum lease payments due under the Company's non-cancelable operating lease are as follows:

	Amount (in thousands)
2021 (remaining 9 months)	$ 1,788
2022	2,446
2023	2,523
2024	2,603
2025	1,099
Total undiscounted future minimum lease payments	10,459
Present value adjustment for minimum lease commitments	(1,733)
Total operating lease liabilities	$ 8,726

As of December 31, 2020, undiscounted future minimum lease payments due under the Company's non-cancelable operating lease are as follows:

	Amount (in thousands)
2021	$ 3,752
2022	2,206
2023	2,283
2024	2,363
2025	999
Total future minimum lease payments	$ 11,603

In February 2021, the Company entered into a lease agreement for manufacturing and office space located in Union City, California. The lease commenced in May 2021 and has a ten-year term with one five-year renewal option. Upon the execution of the lease agreement, the Company provided the landlord with a refundable security deposit of $3.3 million, which is included in other non-current assets on the condensed balance sheets. The total undiscounted future minimum lease payments associated with this operating lease are $13.9 million and are not included in the table above.

The Company has previously entered into agreements to sublease portions of the Company's facilities in South San Francisco to two different subtenants, both of which expired as of December 31, 2020. Pursuant to the sublease agreements, the Company received sublease income of $0.2 million during the three months ended March 31, 2020, which is included in other income (expense), net on the condensed statements of operations and comprehensive loss.

Purchase Commitments

The Company enters into contractual agreements with various suppliers in the normal course of its business, including vendors that provide machinery and equipment. All contracts are terminable, with varying provisions regarding termination. If a contract with a specific vendor were to be terminated, the Company would only be obligated for the products or services that the Company had received through the time of termination.

Indemnification

In the normal course of business, the Company enters into agreements that may include indemnification provisions. Pursuant to such agreements, the Company may indemnify, hold harmless and defend an indemnified party for losses suffered or incurred by the indemnified party. In some cases, the indemnification will continue after the termination of the agreement. The maximum potential amounts of future payments the Company could be required to make under these provisions is not determinable. In addition, the Company has entered into indemnification agreements with its directors and certain officers that may require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. As of December 31, 2020 and March 31, 2021, the Company does not have any material indemnification claims that were probable or reasonably possible and, consequently, has not recorded any related liabilities.

7. Convertible Preferred Stock

Series B Convertible Preferred Stock Financing

In August 2019, the Company entered into a Series B preferred stock purchase agreement (Series B SPA) for the issuance of up to 9,259,254 shares of the Company's Series B convertible preferred stock at a purchase price of $9.936 per share in multiple closings. The Company completed the initial closing in August 2019, whereby 3,086,415 shares of Series B convertible preferred stock were issued for gross proceeds of $30.7 million. Pursuant to the Series B SPA, the Company was permitted to sell additional shares in subsequent closings contingent upon the approval of the Company's board of directors.

On issuance, the Company determined that its obligation to issue additional shares of Series B convertible preferred stock in future closings was a freestanding instrument that should be classified as a liability on the Company's balance sheets. The freestanding financial instrument, or convertible preferred stock tranche liability, was recorded at fair value on issuance of $0.8 million with the remaining proceeds being allocated to the Series B convertible preferred stock. Any changes in fair value of the convertible preferred stock tranche liability in subsequent reporting periods are recognized as a component of other income (expense), net in the statements of operations and comprehensive loss (see Note 3).

In March 2020, the Company completed its second closing of Series B convertible preferred stock financing and issued 3,086,415 shares of Series B convertible preferred stock at the fixed purchase price of $9.936 per share for gross proceeds of $30.7 million, thereby settling a portion of the convertible preferred stock tranche liability. Immediately prior to the second closing, the Company measured the convertible preferred stock tranche liability to its then fair value. Upon the closing of the second tranche, the convertible preferred stock tranche liability was partially settled and the related balance of the liability of $27,000 was reclassified to Series B convertible preferred stock.

In August 2020, the Company completed its third closing of Series B convertible preferred stock financing and issued 3,086,415 shares of Series B convertible preferred stock at the purchase price of $9.936 per share for gross proceeds of $30.7 million, thereby settling the remainder of the convertible preferred stock tranche liability. Immediately prior to the third closing, the Company measured the convertible preferred stock tranche liability to its then fair value. Upon the closing of the third tranche, the remaining convertible preferred stock tranche liability was settled and the balance of the liability of $0.7 million was reclassified to Series B convertible preferred stock.

Series C Convertible Preferred Stock Financing

In December 2020, the Company entered into a Series C preferred stock purchase agreement (Series C SPA) for the issuance of up to 8,526,381 shares of the Company's Series C convertible preferred stock at a purchase price of $12.432 per share in two closings. The Company completed the initial closing in December 2020,

whereby 6,917,621 shares of Series C convertible preferred stock were issued for gross proceeds of $86.0 million.

In January 2021, the Company sold an additional 1,608,750 shares of Series C convertible preferred stock at a purchase price of $12.432 per share for gross proceeds of $20.0 million.

The Company's convertible preferred stock consists of the following:

	December 31, 2020			
	Shares Authorized	Shares Issued and Outstanding	Net Carrying Value	Liquidation Preference
	(in thousands, except shares)			
Convertible Preferred Stock				
Series A	8,316,666	8,316,662	$ 43,393	$ 49,900
Series B	9,259,254	9,259,245	91,644	92,000
Series C	8,526,381	6,917,621	85,717	86,000
Total	26,102,301	24,493,528	$ 220,754	$ 227,900

	March 31, 2021			
	Shares Authorized	Shares Issued and Outstanding	Net Carrying Value	Liquidation Preference
	(in thousands, except shares)			
Convertible Preferred Stock				
Series A	8,316,666	8,316,662	$ 43,393	$ 49,900
Series B	9,259,254	9,259,245	91,644	92,000
Series C	8,526,381	8,526,371	105,698	106,000
Total	26,102,301	26,102,278	$ 240,735	$ 247,900

The Company classifies its convertible preferred stock outside of total stockholders' deficit because, in the event of certain change of control events that are not solely within the control of the Company (including liquidation, sale or transfer of the Company), the shares would become redeemable at the option of the holders. As a result, the Company has classified its convertible preferred stock as mezzanine equity on the balance sheets as the preferred stock is contingently redeemable. The Company did not adjust the carrying values of the convertible preferred stock to the deemed liquidation values of such shares since a liquidation event was not probable as of each reporting date. Subsequent adjustments to increase or decrease the carrying values to the ultimate liquidation values will be made only if and when it becomes probable that such liquidation event will occur.

8. Common Stock

The holders of the common stock are entitled to one vote per share on all matters to be voted on by the stockholders of the Company and are entitled to dividends, if and when declared by the board of directors, subject to the prior rights of the preferred stockholders. Common stock issued and outstanding on the condensed balance sheets and condensed statements of convertible preferred stock and stockholders' deficit includes shares related to early exercised options and restricted stock that are subject to repurchase. Common stock issued and outstanding is reduced for any repurchases of early exercised stock options and restricted stock. As of December 31, 2020 and March 31, 2021, outstanding common stock included 138,127 and 101,592 shares, respectively, related to early exercised stock options and restricted stock that are unvested and subject to repurchase.

The Company has reserved the following shares of common stock for issuance, on an as-if converted basis as follows:

	December 31, 2020	March 31, 2021
Conversion of outstanding shares of convertible preferred stock	24,493,528	26,102,278
Options outstanding under the 2016 Plan	1,160,808	1,727,968
Options available for future grant	412,170	379,271
Total	26,066,506	28,209,517

9. Stock-Based Compensation

2016 Equity Incentive Plan

In October 2016, the Company adopted the 2016 Equity Incentive Plan (the 2016 Plan), which provides for the granting of incentive and non-statutory stock options, stock appreciation rights, restricted stock and restricted stock units and other forms of stock awards to its employees, directors and non-employee service providers.

Total shares reserved and available for grant under the 2016 Plan as of March 31, 2021 are 379,271.

Stock Option Activity

The following table summarizes stock option activity under the 2016 Plan:

	Number of Options Outstanding	Weighted-Average Exercise Price Per Share	Weighted-Average Remaining Contractual Life (years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2020	1,160,808	$ 1.74	8.40	$ 6,060
Options granted	596,855	5.64		
Options exercised	(12,508)	2.49		
Options cancelled	(17,187)	3.14		
Outstanding as of March 31, 2021	1,727,968	$ 3.06	8.74	$ 10,178
Exercisable as of March 31, 2021	520,105	$ 1.39	7.93	$ 3,935

The total intrinsic value of options exercised during the three months ended March 31, 2020 and 2021 was $6,000 and $70,000. The aggregate intrinsic value is the difference between the fair value of the Company's common stock, as approved by the Company's board of directors, and exercise price of the option.

The weighted average grant-date fair value of options granted during the three months ended March 31, 2020 and 2021 was $4.74 and $7.74 per share.

Stock-Based Compensation

The following table summarizes stock-based compensation recognized in the Company's condensed statements of operations and comprehensive loss:

	Three Months Ended March 31,	
	2020	2021
	(in thousands)	
Research and development	$ 82	$ 154
General and administrative	72	278
Total stock-based compensation	$ 154	$ 432

As of March 31, 2021, there was $6.4 million of unrecognized stock-based compensation, which the Company expects to recognize over a weighted-average period of 3.5 years.

Stock Option Valuation

The fair value of the Company's stock option awards is estimated on the date of grant using the Black-Scholes option pricing model using the following assumptions:

	Three Months Ended March 31,	
	2020	2021
Expected term (in years)	6.0	6.0 – 6.1
Expected volatility	178%	183%
Risk-free interest rate	0.7% – 1.5%	0.6% – 1.0%
Expected dividend yield	—%	—%

Restricted Stock

Shares related to early exercised stock options and restricted stock are subject to the Company's lapsing repurchase right upon termination at the original purchase price. In order to vest, the holders are required to provide continued service to the Company.

A summary of restricted stock activity is as follows:

	Number of Shares	Weighted Average Fair Value at Date of Grant per Share
Unvested as of December 31, 2020	138,127	$ 0.90
Granted	442	1.08
Vested	(36,612)	0.54
Repurchased	(365)	1.50
Unvested as of March 31, 2021	101,592	$ 0.96

Employee Recourse Notes

In 2017 and 2018, the Company entered into full recourse notes with certain employees, including one of its officers, upon the exercise of stock options that are treated as substantive exercises for accounting purposes. The Company has the right to repurchase unvested shares up to 90 days after employment is terminated. As of March 31, 2021, the principal and accrued interest amount of the notes was $87,000. The notes are presented in the condensed statements of convertible preferred stock and stockholders' deficit.

10. Income Taxes

For the three months ended March 31, 2020 and 2021, the Company did not record any income tax expense. The Company has recorded a full valuation allowance against its U.S. federal and state deferred tax assets as the Company believes it is not more likely than not that the benefit will be realized.

11. Net Loss Per Share

The following potentially dilutive securities were not included in the calculation of diluted net loss per share for the periods presented because the effect would have been anti-dilutive:

	Three Months Ended March 31,	
	2020	2021
Convertible preferred stock	14,489,492	26,102,278
Series B convertible preferred stock issuable in a future closing	3,086,415	—
Outstanding stock options	1,043,247	1,727,968
Restricted stock subject to future vesting	278,790	101,592
Total	18,897,944	27,931,838

12. Related Party Transactions

Scientific Founders

During the three months ended March 31, 2020 and 2021, the Company recognized a total of $62,000 in each period in consulting expense paid to five of its scientific founders.

13. Subsequent Events

The Company evaluated subsequent events through June 15, 2021, the date the condensed financial statements were available to be filed, except for the 1-for-6 reverse stock split discussed below, which was evaluated through July 26, 2021.

Stock Options Grants

In June 2021, the Company granted 388,475 stock options at an exercise price of $9.36 per share. In July 2021, the Company granted 446,998 stock options at an exercise price of $10.56 per share. The awards generally vest over a four-year vesting schedule.

Reverse Stock Split

In July 2021, the Company's board of directors and the stockholders approved an amendment to the Company's amended and restated certificate of incorporation to effect a reverse split of shares of the Company's common stock, convertible preferred stock and authorized shares on a 1-for-6 basis (the Reverse Stock Split) effective on July 23, 2021. The par value of the common stock and preferred stock was not adjusted as a result of the Reverse Stock Split. Accordingly, all share data and per share data amounts for all periods presented in the accompanying financial statements and notes thereto have been retrospectively adjusted to reflect the effect of the Reverse Stock Split.

12,000,000 Shares

Common Stock

PROSPECTUS

Morgan Stanley *Cowen* *Piper Sandler*

Chardan

July 29, 2021