UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2022

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

FOR THE TRANSITION PERIOD FROM_____TO_____

Commission File Number 001-40656

TENAYA THERAPEUTICS, INC.

(Exact name of Registrant as specified in its Charter)

Delaware	**81-3789973**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
171 Oyster Point Boulevard, Suite 500	
South San Francisco, CA	**94080**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (650) 825-6990

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock $0.0001 par value per share	TNYA	Nasdaq Global Select Market

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
Emerging growth company	☒		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the Registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on the Nasdaq Global Select Stock Market on June 30, 2022 was $156,445,652.

The number of shares of Registrant's Common Stock outstanding as of March 2, 2023 was 66,865,250.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive proxy statement for the Registrant's 2022 Annual Meeting of Stockholders are incorporated by reference in Part III of this Form 10-K. Such definitive proxy statement will be filed with the Securities and Exchange Commission within 120 days after the end of the Registrant's 2022 fiscal year ended December 31, 2022.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or Annual Report, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. All statements other than statements of historical facts contained in this Annual Report, 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,” “vision,” or “continue” or the negative of these terms or other similar expressions. These forward-looking statements include, but are not limited to, statements about:

- our vision to change the treatment paradigm for heart disease;
- the ability of our ongoing preclinical studies and ongoing or planned clinical trials to demonstrate safety and efficacy of our product candidates, and other positive results;
- the timing, dosing, patient enrollment and populations, progress, and results of preclinical studies and ongoing or planned clinical trials for our current product candidates and other product candidates we may develop;
- the timing, scope and likelihood of regulatory filings and approvals, including timing of investigational new drugs (INDs), clinical trial applications (CTAs), U.S. Food and Drug Administration (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 trials;
- the size and the number of patients of the market opportunities we address with our product candidates;
- our manufacturing, commercialization, and marketing capabilities and strategy;
- our competitive position and the success of competing therapies that are or may become available;
- our plans relating to the further development of our product candidates, including 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 intellectual property position, including the scope and length 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 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, operating losses, future revenue, cash outlays, capital requirements and needs for additional financing, including expenses arising as a result of being a public company;
- our financial performance;
- our facilities;
- the period over which we estimate our existing cash, cash equivalents and investments in marketable securities will be sufficient to fund our future operating expenses and capital expenditure requirements;
- the impact of critical accounting policies on investor's ability to understand our financial performance; and
- our expectations regarding the period during which we will remain an emerging growth company under the JOBS Act.

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 Annual Report and are subject to a number of risks, uncertainties and assumptions described in the section titled "Risk Factors" and elsewhere in this Annual Report. 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, 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 Annual Report, 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.

PART I

Item 1. Business.

Overview

We are a clinical-stage biotechnology company committed to a bold mission: to discover, develop and deliver potentially curative therapies that address the underlying drivers of heart disease. Heart disease is the leading cause of death in the world, representing an estimated 32% of all global fatalities. In the United States (U.S.), one in every five deaths is attributable to heart disease, and an estimated 40,000 infants are born each year with congenital heart disease. While there is a clear need for improved treatments, the rate of cardiovascular drug product approvals has declined in recent years and few of the approved treatments address the underlying cause of such diseases.

Leveraging an improved understanding of the genetic causes of heart disease as well as an increased recognition that precision medicine initiatives may accelerate the advancement of scientific breakthroughs, our vision is to change the treatment paradigm for heart disease and in doing so, improve and extend the lives of patients. Roughly one-third to one-half of all heart diseases are linked to genetic risks, regardless of major racial and ethnic backgrounds, and there are over 250 known genetically defined disorders where the primary source of morbidity and mortality involves the heart. Our collective understanding of the links between heart disease and genetic factors is increasing exponentially, creating new opportunities for the advancement of novel disease-modifying therapeutics that target the underlying cause of disease.

We are advancing a deep and diverse pipeline of therapeutic programs intended for both rare and highly prevalent forms of heart disease. Each of our lead product candidates, TN-201, a gene therapy for myosin binding protein C3 (*MYBPC3*)-associated hypertrophic cardiomyopathy (HCM), TN-301, a small molecule for heart failure with preserved ejection fraction (HFpEF), and TN-401, a gene therapy for plakophilin 2 (*PKP2)*-associated arrhythmogenic right ventricular cardiomyopathy (ARVC), emerged from our proprietary integrated drug discovery platforms and has progressed to the clinic or late-stage preclinical development with the support of our core internal capabilities.

In addition to our lead product candidates, we have multiple early-stage programs progressing through pre-clinical development. These programs include an adeno-associated virus (AAV)-based gene therapy designed to express the Dwarf Open Reading Frame (*DWORF*) gene in the heart with potentially broad utility in dilated cardiomyopathy (DCM), as well as our reprogramming program for cardiac regeneration which aims to replace heart cells lost in patients experiencing heart failure due to prior myocardial infarction (MI). While these named programs have reached candidate selection stage, we also have numerous earlier-stage programs emerging from our proprietary product platforms to address other forms of heart failure.

Our distinct, but interrelated Gene Therapy, Cellular Regeneration and Precision Medicine platforms and suite of integrated capabilities support our efforts to discover disease-modifying treatments focused on heart disease in a modality-agnostic manner. We also continue to invest in complementary new technologies and the optimization of our existing proprietary capabilities, including the use of human-induced Pluripotent Stem Cell (iPSC) disease models, machine learning and phenotypic screening, capsid engineering and novel promoter constructs to enable the discovery, design, delivery and development of therapeutics that are best suited to a given cardiovascular condition. In 2022 we also launched operations of our Genetic Medicines Manufacturing Center (GMMC) based in Union City, CA. The facility utilizes a modular, scalable design to produce AAV-based gene therapies under current Good Manufacturing Practice (cGMP) standards.

Our Product Pipeline

Our pipeline includes programs that have emerged from our internal efforts, as well as programs that are based on intellectual property licensed from academic institutions.

* US Prevalence refers to the number of patients in the U.S. with the indication based on publicly available market data

TN-201: TN-201 is our potential first-in-class gene therapy for adults and children with HCM due to *MYBPC3* gene mutations, the most common cause of familial HCM. *MYBPC3*-associated HCM is estimated to affect more than 115,000 patients in the U.S. These mutations can cause the heart walls of affected individuals to become significantly thickened, leading to fibrosis, abnormal heart rhythms, cardiac dysfunction and heart failure. HCM is a chronic, progressive condition and those diagnosed with disease often experience significant impairment in overall heart function and quality of life. Those with sarcomeric genetic mutations, such as *MYBPC3*, are at increased risk of early disease onset, accelerated disease progression and disease-related mortality. TN-201 uses a differentiated approach to deliver a functional *MYBPC3* gene to the heart utilizing a recombinant AAV serotype 9 (AAV9) capsid to restore expression of the cardiac myosin binding protein (MyBP-C) to halt disease progression and potentially reverse the course of genetic HCM following a single intravenous injection. TN-201 has received orphan drug designation from the FDA and orphan medicinal product designation from the European Commission (EC). In January 2023, we received notification from the FDA that clinical testing of TN-201 may proceed, and in the third quarter of 2023, we expect to begin dosing patients in a Phase 1b multi-center, open-label clinical trial, designed to assess the safety, tolerability and efficacy of a one-time intravenous infusion of TN-201. Data from the trial is anticipated in 2024.

TN-301: TN-301 is our highly specific small molecule inhibitor of histone deacetylase 6 (HDAC6). TN-301 is initially being developed for the potential treatment of HFpEF. HFpEF is characterized by a stiffening of the heart muscle resulting in an inability for the left ventricle (LV) to relax properly during normal heart rhythm, referred to as diastolic dysfunction. There are several cellular processes thought to underly the pathophysiology of HFpEF including increases in fibrosis and inflammation and defects in metabolism. Although HFpEF accounts for approximately 50% of all heart failures, there are few proven treatment options. We are currently conducting a Phase 1 clinical trial in healthy adult participants to evaluate the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of escalating oral doses of TN-301. The Phase 1 clinical trial is being conducted in two stages: a single-ascending dose (SAD) stage and a multiple-ascending dose (MAD) stage. Data from both the SAD and MAD stages of the trial are anticipated in the second half of 2023.

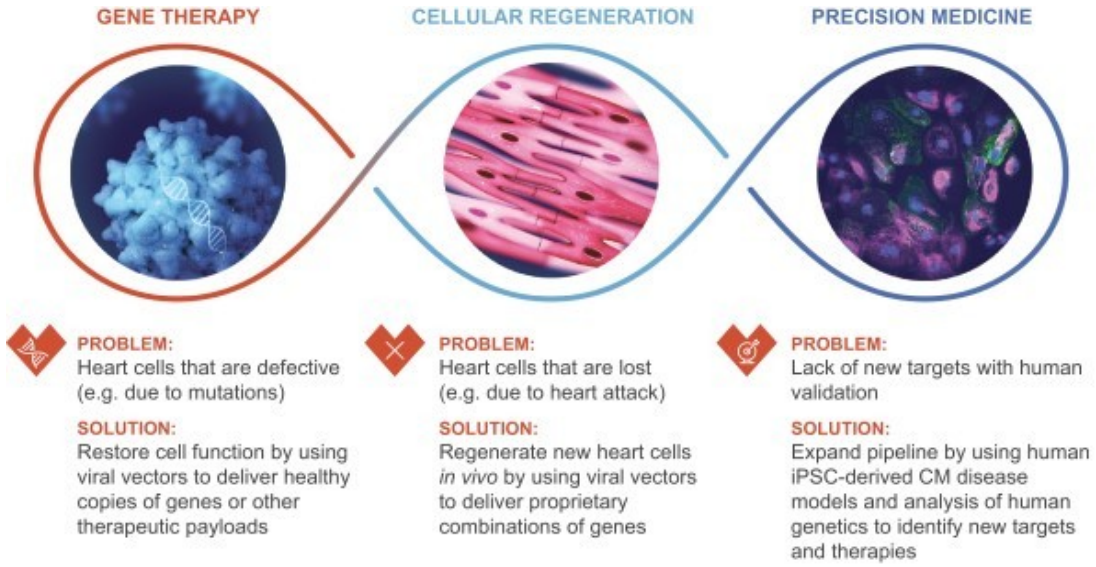
TN-401: We are developing a potential first-in-class AAV-based gene therapy, TN-401, designed to deliver a functional *PKP2* gene in adults with ARVC due to a *PKP2* genetic mutation. *PKP2*-associated ARVC is estimated to affect more than 70,000 patients in the U.S. *PKP2* mutations can cause enlargement 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. Our product candidate, TN-401, has demonstrated prevention of disease progression and survival benefit after a single dose in a mouse model of ARVC, as well as tolerability in a pilot non-Good Laboratory Practices (GLP) toxicology and biodistribution study. TN-401 has received orphan drug designation from the FDA. We have initiated investigational new drug application (IND)-enabling studies for TN-401 and expect to submit an IND to the FDA in the second half of 2023 to enable clinical development of TN-401.

Early-Stage Research Efforts: In addition to our lead product candidates, we have multiple early-stage programs progressing through preclinical development, including an AAV-based gene therapy designed to express the DWORF gene in the heart with potentially broad utility in DCM and a cellular reprogramming program for cardiac regeneration which aims to replace heart cells lost due to prior MI. Our researchers are conducting preclinical testing of these and several other genetically targeted leads emerging from our proprietary product platforms to address other forms of heart failure. In addition to our novel drug discovery efforts, we continue to invest in the further development of our gene therapy-enabling technologies and capabilities. Among the most advanced of these initiatives is an effort to identify novel AAV capsids designed to deliver cardiac gene therapy with enhanced specificity and expression compared to current AAV vectors, with the goal of optimizing gene therapy safety, dosing and efficacy.

Our Product Platforms

We have established three distinct but interrelated product platforms -- Gene Therapy, Cellular Regeneration and Precision Medicine -- 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. We believe these three product platforms, together with our suite of proprietary capabilities, provide us greater insight into disease processes, create more opportunities for successful drug development, mitigate scientific risks, and differentiate our efforts relative to competitors.



1. Our ***Gene Therapy*** platform uses AAVs to deliver healthy genes to specific cells in the heart to correct or compensate for functional defects. While our lead gene therapy programs utilize AAV9 to deliver healthy genes to the heart, we have the ability to use both known AAV capsids as well as novel capsids identified through our internal capsid engineering capabilities. In the future, we may also explore other delivery options, including non-viral delivery. Depending on the nature of the disease, we may target cardiomyocytes, cardiac fibroblasts, 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 rare and prevalent 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 cardiomyocytes through two distinct *in vivo* approaches: One approach uses AAV vectors to deliver proprietary combinations of genes that induce the resident cardiac fibroblasts to convert to cardiomyocytes. Another approach uses non-integrating lentiviruses to deliver proprietary combinations of genes that induce the resident cardiomyocytes 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 cardiomyocytes. We believe this platform has potentially broad utility across a range of heart conditions that result in the loss of cardiomyocytes, including MI, chemotherapy-related toxicity, and viral infection.

3. Our ***Precision Medicine*** platform for target identification uses human genetic information combined with phenotypic high throughput screening in our proprietary human iPSC-CM models of human disease and machine learning algorithms for the identification and validation of novel targets for heart diseases. Targets may be further characterized using three-dimensional human engineered heart tissues. By leveraging human cells and tissues to identify and/or validate heart disease targets, this platform is intended to overcome the shortcomings of traditional drug development efforts that rely more heavily on insights from animal models. 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 Core Capabilities

Foundational to our research and drug discovery efforts are our proprietary integrated core capabilities that collectively support discovery of novel targets, *in vitro* optimization and validation of leads, rapid product development, precise product delivery, and efficient production, which ultimately improves the probability of technical and regulatory success of our product candidates.

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, as existing models of human heart disease may not be adequate to assess the efficacy or safety of novel therapies. Our disease modelling capabilities serve to facilitate the discovery of new leads and to characterize the activity of existing leads as we move through preclinical development. For our *in vitro* human iPSC-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 17 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 against multiple attributes to assess their potential to translate across species and into humans. Our next-generation 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 future 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 that support our gene therapy and cellular regeneration programs by controlling 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 internalized and integrated both cGMP and non-GMP AAV manufacturing capabilities to support our emerging portfolio of gene therapy and cellular regeneration product candidates. This includes an in-house team of approximately 45 personnel that can support process development, analytical development, quality control (QC) and GMP manufacturing. In addition, we have established a Quality Management System to oversee our GxP operations, including cGMP, GLP and Good Clinical Practices (GCP). To date, we have produced non-clinical material involving multiple parental AAV capsids at the 50L and 200L scales to support early research and IND-enabling studies in small and large animal models, as well as clinical material at the 1000L scale to support our first-in-human clinical studies. Our GMMC, a cGMP facility, is strategically located near our research labs in the San Francisco Bay Area to enable smooth scale-up of production to support our clinical studies. We have both in-licensed and internally developed manufacturing technologies to support programs emerging from our Gene Therapy and Cellular Regeneration Platforms.

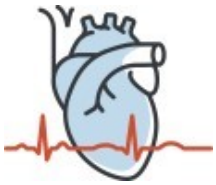
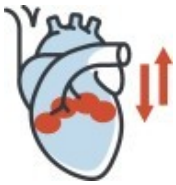
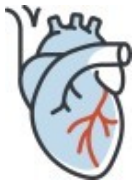
Overview of Heart Disease

Heart disease is the leading cause of death in the world, representing an estimated 32% of all global fatalities. In the U.S., 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 34 seconds, a gruesome statistic that translates to approximately one in five deaths in the U.S. The picture is equally bleak at the other end of the age spectrum, as approximately 40,000 infants are born in the U.S. every year with congenital heart disease, 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 genetic causes of such heart diseases. Recent analysis has shown that after decades of reduction in the mortality rate due to heart failure, 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, heart failure, 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	Heart failure 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. Heart failure 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 heart failure include a heart attack, uncontrolled high blood pressure, congenital heart defects, 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 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 heart failure and arrhythmia, particularly when these diseases can be traced to some underlying genetic defect.

Historic Challenges in the Development of Novel Therapies for Heart Disease

- ***Most development efforts have focused on treating symptoms rather than targeting the underlying causes of diseases.*** First-line therapies for heart failure such as generic small molecules, including angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers, beta blockers, aldosterone antagonists, and diuretics, act by reducing blood pressure or fluids to mitigate disease symptoms rather than altering the course of disease.
- ***Identifying relevant 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 an approximately 5% 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. This lack of genetic testing 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

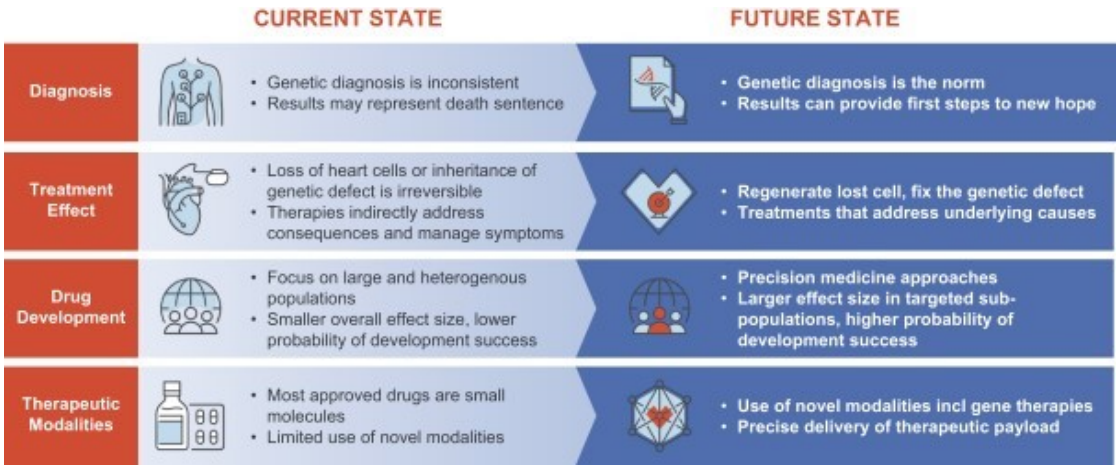
new cells surviving rejection by the immune system, (2) only modest efficacy from the surviving cells, and (3) arrhythmia caused by abnormal electric activity and connections between new cells and the existing cells.

- ***Gene therapy science for the heart is still maturing*.** Early gene therapy efforts, including an AAV-based effort using AAV1 to deliver sarcoplasmic/endoplasmic reticulum Ca2+ ATPase 2a (SERCA2a) for the treatment of heart failure saw promising preclinical and early clinical results, but were stymied following unsuccessful later-stage studies. These first-generation gene therapy efforts for the heart did not have the benefit of more recent advances in capsids, promoters, delivery, and manufacturing. More recent efforts directed at rare, genetic cardiomyopathies have provided encouraging early clinical evidence of disease-modification.
- ***Regulatory requirements focus on survival and hospitalization outcomes*.** Historically, cardiovascular drug development has involved large clinical studies to demonstrate a survival benefit or reductions in hospitalizations over and above standard-of-care. This has translated into a need for very large, long, and expensive randomized and placebo-controlled clinical studies. Only more recently has the FDA indicated a willingness to consider endpoints demonstrating measurable improvements in symptoms and heart function as being potentially approvable for certain types of heart diseases, including HCM.
- ***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 a leading cause of death, heart disease is one of the largest and most expensive categories for payers. The U.S. spends approximately $219 billion per year on cardiovascular disease. The total direct and indirect costs of heart failure 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 a 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 and American Heart Association recommendations for patients with 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. In addition, the FDA continues to issue important guidance to help streamline the development of gene therapies and mitigate safety and tolerability concerns that can delay the drug development timeline.

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.



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 of genetics and disease models to discover, develop, manufacture and ultimately commercialize a deep and diverse pipeline of novel heart disease therapies. The key components of our strategy to achieve these goals are:

- ***Focus exclusively on heart disease.*** Heart disease remains a leading cause of death globally, 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 integrated product platforms.*** To address the wide range of issues in heart diseases, we are advancing science from three distinct product platforms that tackle different problems that have historically plagued drug development in the field of cardiology: (i) our Gene Therapy platform enables the development and delivery of a wide variety of therapeutic payloads more precisely to heart tissue, (ii) our Cellular Regeneration platform enables the replacement of heart cells lost to disease and (iii) our Precision Medicine platform enables the discovery of targeted therapies in a modality-agnostic fashion. Underpinning these platforms is a suite of bespoke internal core capabilities designed to increase the speed with which we can conduct discovery, improve the precise delivery of drug products to the tissues where they can have the desired effect while maximizing safety and productivity. 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 heart failure populations, such as HFpEF and heart failure with reduced ejection fraction (HFrEF), through the use of genetics or biomarkers to improve selection of patients with attributes that are more suited to the specific mechanism of action of a given therapeutic candidate. We believe this strategy can accelerate clinical development, reduce overall development costs, and improve the probability of clinical and regulatory success.
- ***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, contract research organizations (CROs), or contract development and manufacturing organizations (CDMOs)—providing us better control of our timelines and costs.
- ***Advance a deep and diverse pipeline of therapies.*** The diversity of our programs illustrates the ambition of our vision and the versatility and depth of our scientific approach. We are currently advancing therapeutics for both rare and prevalent heart diseases across multiple treatment modalities. Our most advanced rare disease programs include two AAV-based gene therapy candidates: TN-201, our product candidate for *MYBPC3*-associated HCM and TN-401, our product candidate for PKP2-associated ARVC. We are also advancing TN-301, a small molecule inhibitor of HDAC6 intended to address HFpEF. Following closely at the candidate selection stage is a DWORF gene therapy for the potential treatment of DCM and a cellular reprogramming program for cardiac regeneration which aims to replace heart cells lost in patients experiencing heart failure due to prior MI. We are also working on several other early-stage programs, that we believe will add to our future pipeline opportunities.
- ***Seek partnerships that can expand our reach and accelerate our efforts.*** We believe our singular focus on heart disease and extensive platform and core capabilities make us a potential 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.
- ***Become a fully integrated biopharmaceutical company with commercial capabilities.*** We aim to discover, develop, manufacture, and eventually commercialize therapies, with an initial focus on those therapies for rare disease populations that could be marketed by a relatively small salesforce.

Our Programs

TN-201: Gene Therapy for MYBPC3-associated HCM

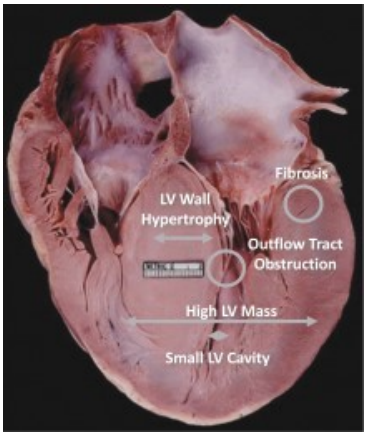
We are developing TN-201, an investigational and potential first-in-class gene therapy for *MYBPC3*-associated HCM. *MYBPC3* genetic mutations are the most common cause of familial HCM, estimated to affect more than 115,000 patients in the U.S. These mutations can cause the heart walls of affected individuals to become significantly thickened, leading to fibrosis, abnormal heart rhythms, cardiac dysfunction, heart failure, and increased risk of sudden cardiac death. TN-201 is an AAV-based gene therapy designed to deliver a fully functional *MYBPC3* gene to restore normal levels of the cardiac MyBP-C protein and in order to halt disease progression and reverse the course of genetic HCM after a single treatment. Based on publicly available information we believe TN-201 has the potential to be the first treatment to address the underlying genetic cause of this disease.

Overview of HCM

HCM is a condition in which the heart walls become thickened (hypertrophy), resulting in a reduced ability of the LV to relax and fill (diastole) and pump (systole) blood effectively with each contraction. HCM is a chronic, progressive disease associated with significant impairment to patients' overall quality of life, as well as an elevated risk of sudden cardiac death. Symptoms include chest pain, shortness of breath (dyspnea), fainting (syncope), fatigue and palpitations. As the disease progresses, patients may suffer premature death due to end-stage heart failure or malignant ventricular arrhythmia (VA) sometimes leading to sudden cardiac death or stroke. Disease onset can occur at any age, with HCM most frequently emerging in adults in their mid-40s. When HCM emerges in children and young adults, disease course is typically more aggressive and prognosis is worse than that observed in older patients. While a relatively rare occurrence, HCM is the leading cause of sudden cardiac death in young adults.

HCM is estimated to affect one in every 500 people, approximating more than 600,000 people in the U.S. 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 electrocardiogram (ECG) pattern. A clinical diagnosis of HCM in adults is defined as a left ventricular wall thickening of greater than 15mm. Patients with HCM can present with either the obstructive form (oHCM) or the nonobstructive form (nHCM) of the disease. Both forms of the disease involve significant LV hypertrophy; 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 to the rest of the body. Nonobstructive HCM is more frequently characterized by diastolic dysfunction resulting in increased LV filling pressures that leads to chest pain and dyspnea.

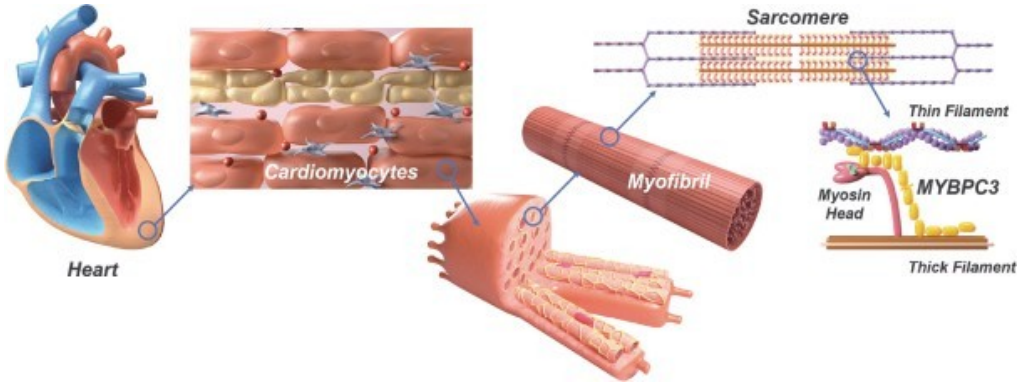
An example of a heart from a patient who had oHCM is shown below, characterized by LV hypertrophy, high LV mass, LVOT narrowing, an overall small LV, and fibrosis.



The genetic causes of HCM may be diverse, but approximately 60% of patients with HCM have clearly identifiable familial disease with an autosomal dominant pattern of inheritance. To date, more than 2,000 mutations in eleven or more genes have been linked to HCM. Those with sarcomeric genetic mutations, including the *MYBPC3* gene, are at increased risk of early disease onset, accelerated disease progression and disease-related mortality. Mutations in the *MYBPC3* gene are 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 U.S.

The *MYBPC3* gene encodes the MyBP-C protein, which forms a key component of the cardiac sarcomere, the fundamental contractile unit of the cardiomyocyte. MyBP-C protein is central to regulation of both contraction and relaxation of the cardiac muscle. *MYBPC3* gene mutations result in both oHCM and nHCM, with one study involving a series of more than 1000 patients finding that 69% of patients with truncating *MYBPC3* mutations had nHCM, while 31% presented with LVOT characteristic of oHCM. The schematic below illustrates the cellular localization of MyBP-C within the heart. Cardiomyocytes 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.



The reduced MyBP-C 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 an LV assist device (LVAD) or transplantation, in the most severely affected patients. Fibrosis and muscle cell disarray may also lead to arrhythmias in some patients, including life-threatening VA 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. With no ability to produce MyBP-C protein and no available treatment to address the underlying genetic mutation, the only option for this young patient population is a heart transplant.

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 MyBP-C protein. In the most severe cases in which both copies of the gene are affected, there is a complete lack of functional MyBP-C 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 MyBP-C 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, calcium channel blockers and antiarrhythmics. 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 oHCM patients with severe and disabling disease, invasive interventions, such as myectomy and septal ablation in which portions of the enlarged septum are removed, may be appropriate. For patients with severe nHCM implantation of an LVAD or a heart transplant may be the only options.

In recent years, a class of agents known as myosin inhibitors have emerged as potential treatments for oHCM and nHCM. One of these agents, mavacamten, was approved by the FDA in April 2022 for the treatment of oHCM. Other agents continue to be evaluated in clinical studies. Currently, there are no therapies approved or in clinical development specifically for HCM patients with *MYBPC3* gene mutations.

Our Solution

We are developing TN-201, a potential first-in-class AAV-based gene therapy designed to deliver a fully functional *MYBPC3* gene and to restore normal levels of MyBP-C protein, driven by our proprietary cardiac specific promoter. We believe TN-201 has the potential to address the underlying biological basis of disease in adult and pediatric HCM patients with homozygous or heterozygous *MYBPC3* gene mutations.

Based on our preclinical data, we believe that gene therapy can achieve highly selective and robust expression of the *MYBPC3* gene and has the potential to slow or even reverse the course of *MYBPC3*-associated HCM, including LV hypertrophy, outflow tract obstruction, heart failure, 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. 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.

TN-201 Clinical Development Plan

In January 2023, we received clearance of our IND from the FDA to conduct a Phase 1b clinical trial of TN-201 in symptomatic adults with the nonobstructive form of *MYBPC3*-associated HCM. We expect to commence patient dosing in the Phase 1b in the third quarter of 2023 and have completed all necessary manufacturing of TN-201 to supply the clinical trial.

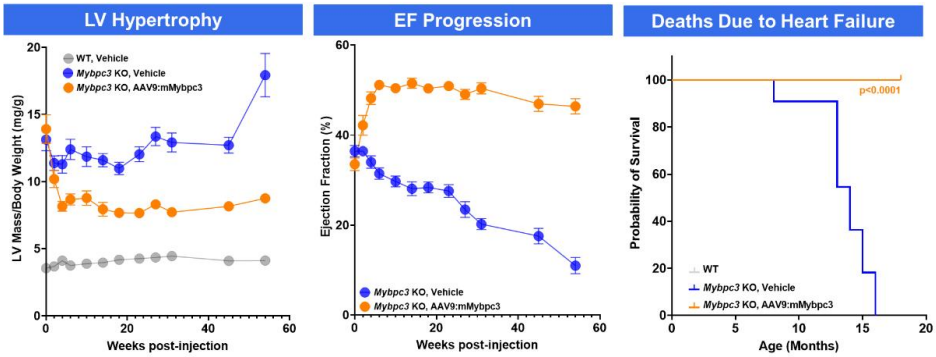
The TN-201 Phase 1b is a multi-center, open-label clinical trial designed to assess the safety, tolerability and efficacy of a one-time intravenous infusion of TN-201. The trial will seek to enroll at least six symptomatic (New York Heart Association class II or III) adults (ages 18-65) with low tiers of AAV9 neutralizing antibodies who have been diagnosed with *MYBPC3*-associated nHCM and have an implantable cardioverter defibrillator (ICD). The primary endpoints for the trial include safety and tolerability, PK (as measured by transgene and mRNA expression via cardiac biopsies at 8 weeks and 52 weeks) and PD (as measured by imaging and plasma biomarkers). Additional endpoints include exercise capacity (as measured by a six-minute walk test and peak maximal oxygen consumption (VO2)) and patient-reported outcomes (as measured by a Kansas City Cardiomyopathy Questionnaire). The trial will include a preventative immunosuppressive regimen and close safety monitoring, as well as a 5-year follow-up on safety and efficacy. We expect to assess two dose levels of TN-201 in the trial, starting with 3×10^{13} vg/kg, a dose associated with near-maximal efficacy in preclinical studies. Three patients are expected to be enrolled in the first dose cohort and will be dosed sequentially, with a pause between patient doses to monitor for safety. An independent safety review following the initial cohort will inform plans for dose escalation to 6×10^{13} vg/kg, as needed, and/or enrollment of additional patients in the initial cohort. TN-201 has received orphan drug designation from the FDA and orphan medicinal product designation from the EC. Data from the trial is anticipated in 2024.

The Phase 1b clinical trial will be conducted at multiple centers in the U.S. In order to support our development efforts for TN-201, we have initiated two noninterventional studies: a study evaluating seroprevalence to AAV9 antibodies among adults with *MYBPC3*-associated HCM, and MyClimb, a prospective and retrospective global natural history study focused on pediatric patients with *MYBPC3* mutation-associated cardiomyopathy. The objective of the natural history study is to characterize the outcomes, burden of illness, risk factors, quality of life, and biomarkers associated with disease progression in pediatric patients with cardiomyopathy due to *MYBPC3* gene mutations, as well as treatments, procedures, and patient outcomes. This study complements existing disease registries focused primarily on adult patient HCM populations and may support and expedite the development of TN-201 in the pediatric patient population. We have activated more than 15 sites in the U.S. and Europe and enrolled more than 100 subjects in the MyClimb study.

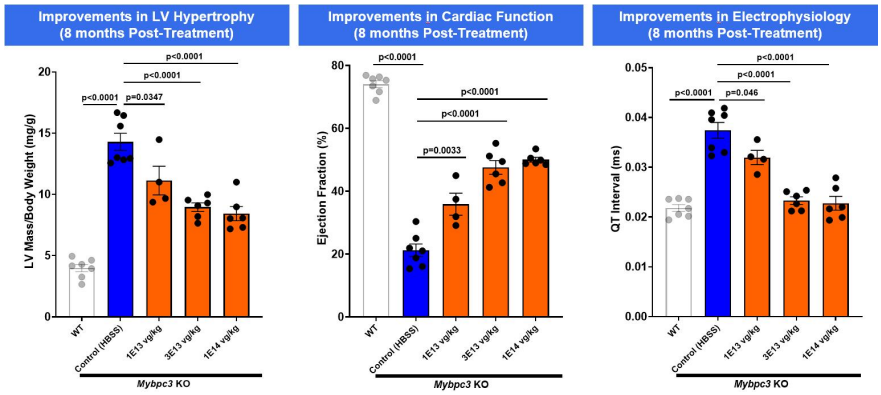
Preclinical Evidence Supporting TN-201 Clinical Development Plan

In preclinical studies, we systemically administered a mouse surrogate of TN-201 (AAV:mMybpc3 or mTN-201) in two-week-old *Mybpc3* KO mice. The *Mybpc3* KO model develops marked LV hypertrophy, poor cardiac function, and dilation at two-weeks of age, comparable to HCM patients with truncating or null mutations. Due to the severe phenotype of the *Mybpc3* KO mice and the lack of any MyBP-C protein, this is considered a demanding model to demonstrate efficacy particularly for modeling heterozygous patients, who lack only 35% to 40% of normal sarcomeric MyBP-C protein levels. As shown in the figures below, treatment with mTN-201 improved LV hypertrophy and cardiac function compared to their pre-treatment baseline levels, indicating partial reversal of the disease and dramatically extended lifespan. Treated mice exhibited an absolute improvement of EF of more than

20% versus untreated controls that eventually increases to more than 30% at 13 months, the last echocardiography measurement. EF and LV hypertrophy (LV mass normalized to body weight (BW)) improvements did not diminish over time, suggesting that a single systemic dose may be sufficient for a durable reversal of *MYBPC3-associated* HCM. Additionally, we observed improvements in LV diameter and ECG measurements. There is also a clear survival benefit with 100% survival in the mTN-201 arm and 100% mortality in the untreated control arm out to 18 months following dosing.

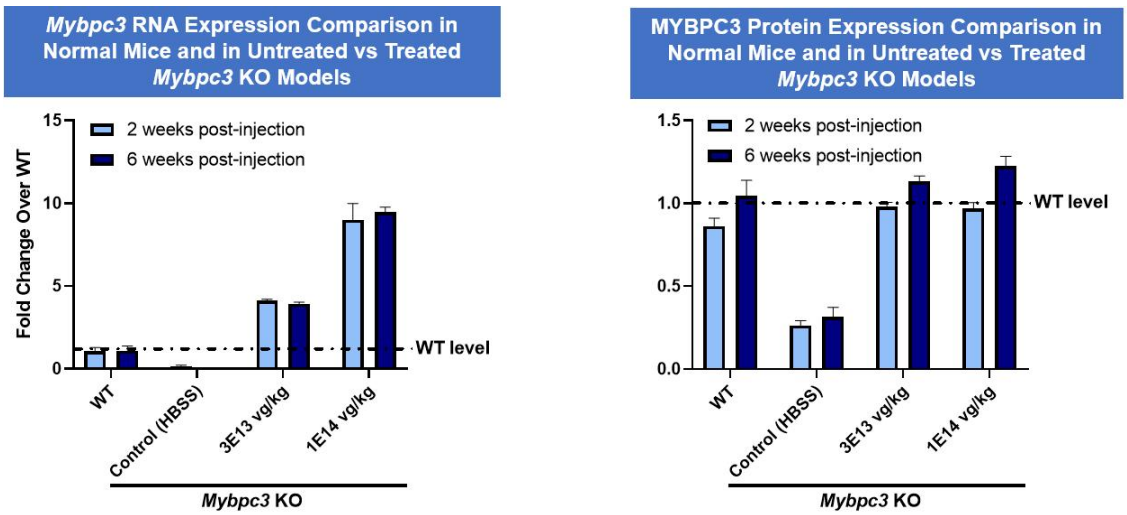


In addition, a dose-response relationship has been demonstrated with mTN-201. As shown below, 1×10^{13} vg/kg, 3×10^{13} vg/kg and 1×10^{14} vg/kg weight-based doses all produced significant improvements in EF, LV hypertrophy, and measures of electrophysiological function (QT interval) at eight months 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.



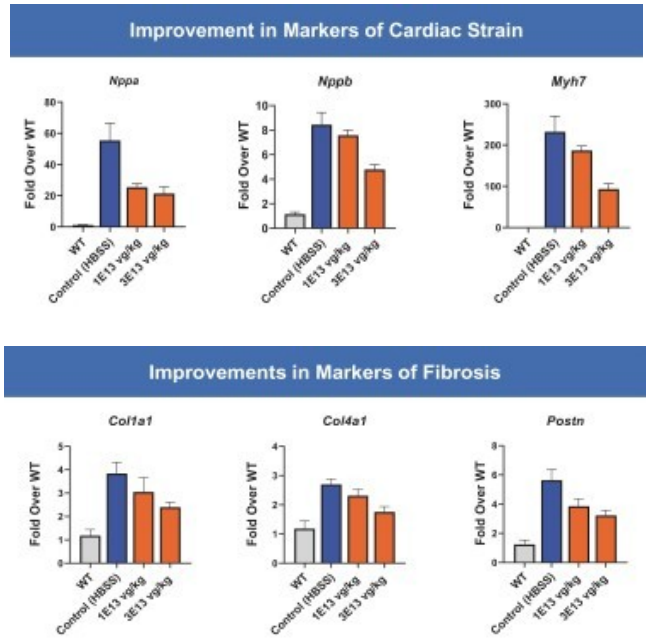
In our preclinical studies with the *Mybpc3* KO model, we have not observed MyBP-C protein levels substantially above normal levels, suggesting that protein accumulation does not occur and lowers the potential concern of overexpression-related toxicities. In addition, histological assessments of mTN-201 treated *Mybpc3* KO model murine hearts support the uniform and robust distribution of expression following mTN-201 infusion, suggesting gene therapy may be able to replace the missing *MYBPC3* gene uniformly across the heart. 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 MyBP-C protein levels to wildtype levels within two weeks following a single dose of mTN-201 at the 3×10^{13} vg/kg and 1×10^{14} vg/kg dose levels.



Consistent with observed therapeutic benefit, treatment of the *Mybpc3* KO mice with mTN-201 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 cardiac wall stress.

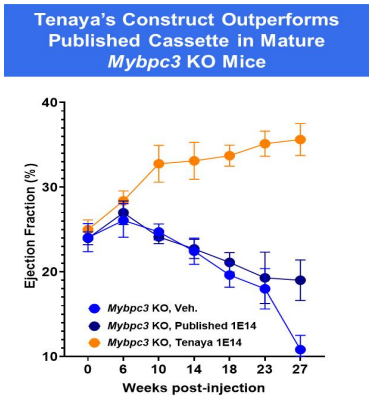
The figures below show dose-dependent inhibition of expression of genes associated with cardiac strain (Nppa, Nppb, and Myh7) and fibrosis (*Col1a1*, *Col4a1*, *and Postn*) following a single dose of mTN-201 at the 1×10^{13} vg/kg and 3×10^{13} vg/kg dose levels.



Treatment with either TN-201 or mTN-201 in the *Mybpc3* KO model was not associated with significant BW differences, clinical observations, or differences in histopathological assessments across dose levels. In addition, no impact on BW was observed at dose levels between 3×10^{13} vg/kg and 6×10^{14} vg/kg in pilot safety studies in wildtype neonatal mice twelve weeks after dosing.

Differentiating Characteristics for TN-201

During optimization of our *MYBPC3* gene therapies, we discovered a cardiomyocyte-specific promoter, TNP-CM1, with improved performance attributes as compared to the standard cardiac troponin T (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 Core Capabilities—3. Promoters and Regulatory Elements*." TNP-CM1 has been tested in a human iPSC-CM disease model, in multiple murine models, and in non-human primates (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.



TN-301: HDAC6 Inhibitor Program for HFpEF

We are developing an HDAC6 small molecule inhibitor for the potential treatment of HFpEF. HFpEF is one of the greatest areas of unmet need in heart disease with more than three million patients in the U.S. and currently no approved disease-modifying therapies. A complex syndrome, the causes of HFpEF are diverse, but result in a shared pathophysiology with systemic inflammation and metabolic dysfunction leading to hypertrophy, fibrosis, and diastolic dysfunction among other characteristic consequences. The result is high morbidity and mortality in affected individuals. Our product candidate, TN-301, is a differentiated compound with unique chemical structures and high specificity for HDAC6 and based on publicly available information to date, we believe, is the first HDAC6i being developed for HFpEF.

Overview of HFpEF

HFpEF is generally defined as heart failure 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 a progressive disease 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.

Patients with HFpEF represent approximately half of heart failure patients, with prevalence of the disease 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 U.S. and globally. At least half of all hospital admissions for heart failure 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 heart failure and mortality rates over a five-year period are as high as 40% and 75%, respectively.

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. Recently, a class of glucose lowering drugs known as sodium-glucose cotransporter-2 (SGLT2) inhibitors have demonstrated encouraging evidence of reducing hospitalizations and mortality versus placebo in HFpEF patients, with one such agent approved by the FDA for the treatment of HFpEF. In spite of this recent progress, HFpEF remains one of the greatest unmet needs in cardiovascular medicine.

Our Solution

We are developing TN-301, a highly specific small molecule inhibitor of HDAC6 for the potential treatment of HFpEF. HDAC6 is localized to the cell cytoplasm where it interacts with multiple proteins to coordinate cellular processes. In animal models intended to mimic human HFpEF, our highly selective HDAC6 inhibitors reversed preexisting cardiac hypertrophy and diastolic dysfunction, and improved lung congestion and exercise capacity, all of which are hallmarks of HFpEF.

TN-301 and our related HDAC6 inhibitors were discovered using our distinct Precision Medicine targeted drug discovery platform technologies, involving phenotypic screening and deep learning to human iPSCs. *In vitro*, our HDAC6 inhibitors demonstrated up to 2500-fold preferential selectivity for HDAC6, reduced sarcomeric damage and enhanced cardiac energetics. In *in vivo* studies in multiple mouse models of HFpEF, TN-301 and TYA-018, a structurally and functionally equivalent compound used for preclinical testing, demonstrated reductions in inflammation and metabolic dysfunction, as well as decreased fibrosis, hypertrophy and diastolic dysfunction. In a comparison study with the SGLT2 inhibitor empagliflozin, which is approved by the FDA in 2022 for the treatment of HFpEF, both TN-301 and TYA-018 improved glucose tolerance, reduced LV mass and end diastolic pressure and increased diastolic function with comparable efficacy, providing validation for our proprietary HFpEF mouse model and suggesting that preclinical results may translate to the clinic.

TN-301 Clinical Development Plan

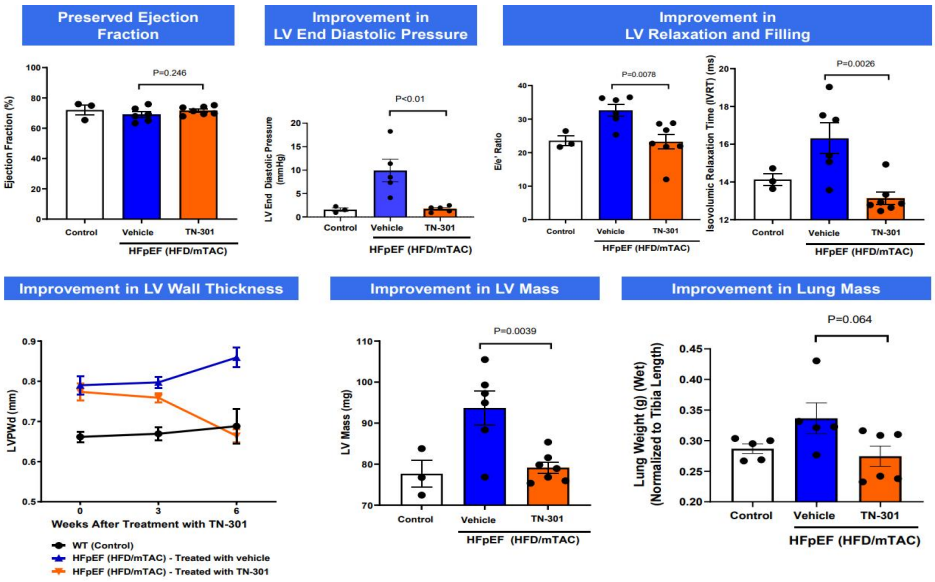
We are conducting a randomized (3:1), double-blind, placebo-controlled Phase 1 clinical trial designed to assess the safety and tolerability of escalating oral doses of TN-301 in healthy adult participants. Secondary objectives of the clinical trial will be to assess PK and PD measures. The trial is being conducted in two stages. In the first stage, participants receive single ascending doses of either TN-301 or placebo and based on data from the SAD stage of the trial, including PD evidence of target engagement, participants in the second stage receive multiple ascending doses of TN-301 at dose levels of interest to help guide dosing in future trials. Dosing in the SAD stage of the trial began in September 2022. To date, TN-301 has been generally well tolerated. Initial target engagement (as measured by the PD biomarker of tubulin acetylation) was achieved at dose levels thought to be in therapeutic ranges, enabling the initiation of the MAD stage of the clinical trial, which commenced in February 2023. Data from both the SAD and MAD stages of the trial are anticipated in the second half of 2023.

Preclinical Evidence Supporting TN-301 Clinical Development

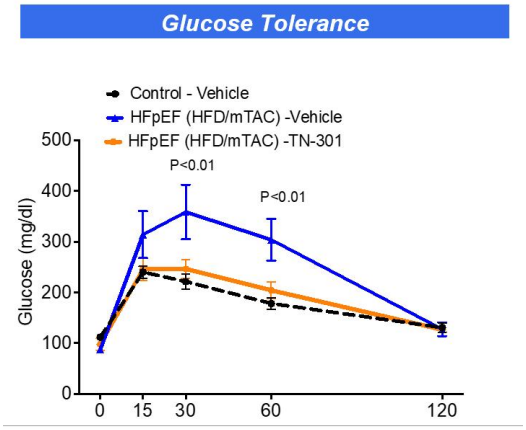
Treatment with TN-301 has reversed measures of HFpEF, including heart filling defects known as diastolic dysfunction, in multiple animal models. In one HFpEF model developed in-house, we surgically applied moderate aortic banding (mTAC) in wild type mice fed a high fat diet for eight weeks. These interventions induced a cardio-metabolic heart failure 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, while maintaining EF at or above 50%.

After the HFpEF phenotypes were established, animals were dosed orally with TN-301 or vehicle for six weeks. As illustrated below, TN-301 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,

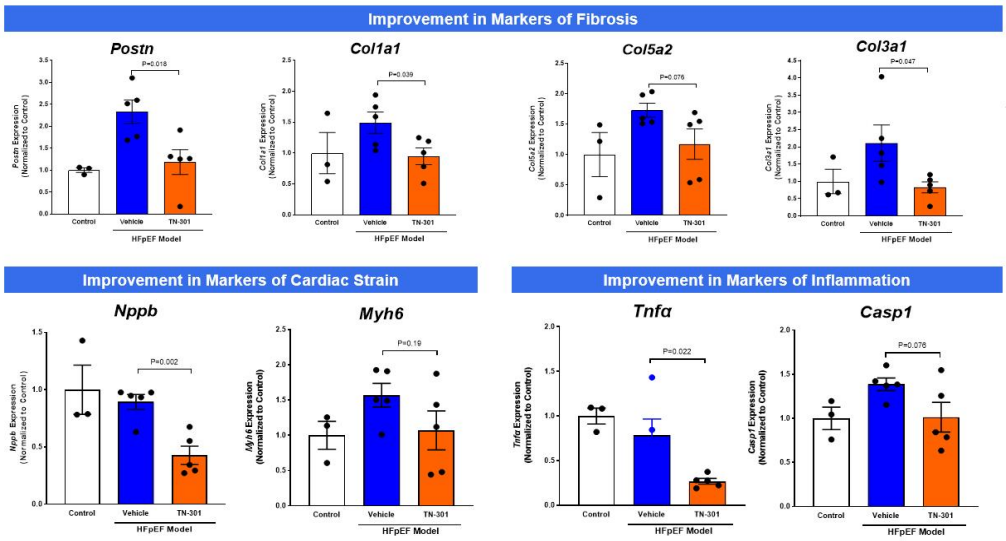
compared to control. In addition, as shown below, the treated mice exhibited a clear trend of decreased lung weight, indicative of improvement in pulmonary congestion consistent with the reduction of filling pressure.



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.



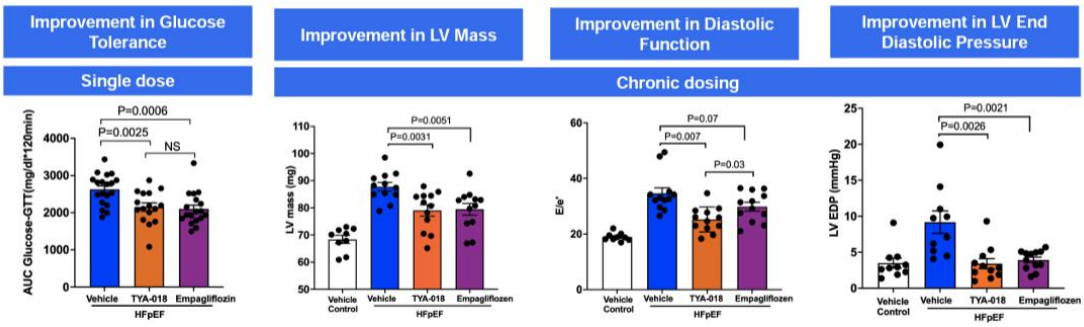
Consistent with the observed improvement in HFpEF phenotype, TN-301 treatment in this HFpEF model was also associated with reductions of key biomarkers of fibrosis, hypertrophy and cardiac damage, and inflammation in heart samples compared to levels observed in control animals, as shown in the figure below:



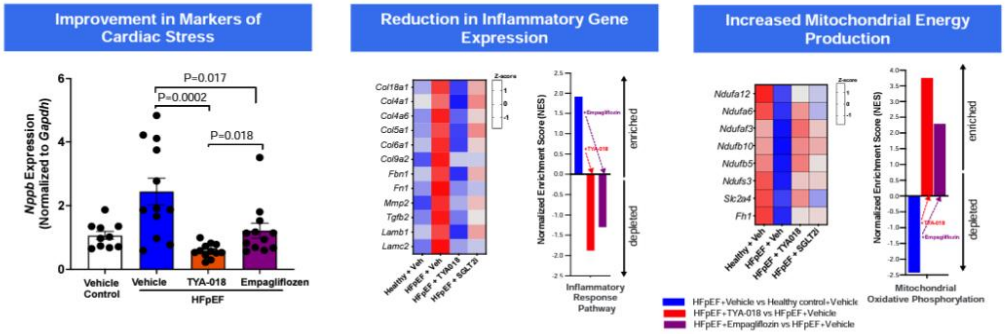
Comparison with SGLT2 Inhibitors

In order to validate our proprietary murine model of HFpEF we evaluated the efficacy of TYA-018 in comparison with empagliflozin, an SGLT2 inhibitor approved by the FDA for the treatment of HFpEF. HFpEF was induced with a combination of transaortic constriction and DIO to simulate a HFpEF phenotype. Maximally efficacious doses of TYA-018, empagliflozin or vehicle were administered for nine-weeks and compared.

In this model, empagliflozin behaved as anticipated based on the data generated from large clinical trials: fasting glucose and glucose tolerance were improved, and LV hypertrophy and diastolic dysfunction were reduced. TYA-018 demonstrated comparable benefits across multiple measures, including improvements in glucose tolerance, LV mass, LV end diastolic function and diastolic pressure.



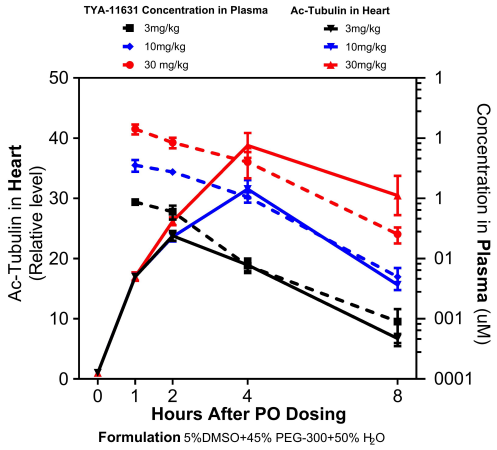
TYA-018 also demonstrated superiority in improving markers of cardiac stress, reducing inflammatory markers and improving mitochondrial energy.



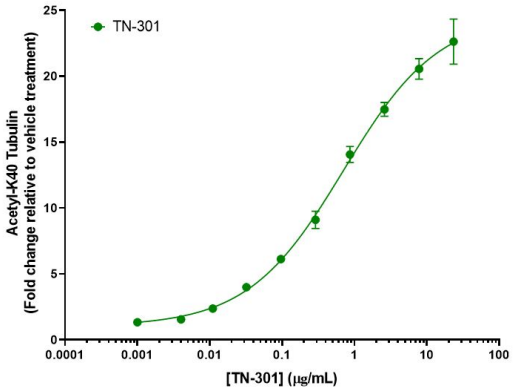
Taken together, data from our preclinical comparison studies elucidate the differentiated mechanism of action for HDAC6 inhibition and support the potential of our HDAC6 inhibition preclinical data to translate to the clinic.

PD Biomarker: Measurement of Target Engagement

HDAC6 is a cytoplasmic enzyme and one of its main substrates is tubulin. Increase in acetylated tubulin is a robust and reproducible PD marker with a high dynamic range that can be measured in both the heart and in circulating cells. We have developed an assay suitable for testing PD effect in human peripheral blood mononuclear cells that we intend to use to demonstrate proof-of-activity and target engagement in our clinical trials. The figure below illustrates dose-dependent increases in tubulin acetylation levels in the heart of a mouse model following administration of TN-301 (previously referred to as TYA-11631) (left axis), and how tubulin acetylation levels appear to correspond to levels of TN-301 as measured in plasma over time.



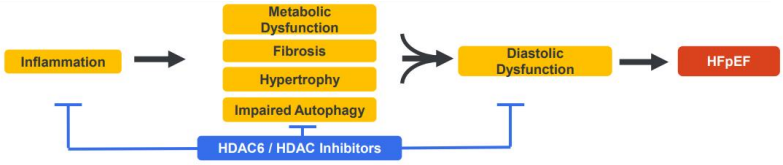
As part of our efforts to validate tubulin acetylation as a biomarker for target engagement, we undertook a series of experiments testing the effects of standard-of-care heart failure medication on tubulin acetylation and found that there was no impact, meaning it is a unique PD marker for TN-301.The figure below illustrates dose-dependent increases in tubulin acetylation levels in human peripheral blood mononuclear cells, illustrating how this PD biomarker can also be measured in human blood, including in healthy volunteers. This PD assay format is the same as what is being used for testing clinical samples from the TN-301 Phase 1 clinical trial.



Multi-Modal 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 HFpEF 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 HDAC6 inhibitors, including TN-301, in HFpEF.



		Inflammation	Metabolic Dysfunction	Fibrosis	Hypertrophy	Impaired Autophagy	Diastolic Dysfunction
	Role of HDAC6 or HDAC inhibition In cardiovascular indications supported by literature	✓	✓	✓	✓	✓	✓
Tenaya Results	*Cardiac fibroblasts (in vitro)*						
	hiPSC-cardiomyocytes (in vitro)						
	BAG3 DCM mouse model (in vivo)						
	Diet induced obesity mouse model (in vivo)						
	HFpEF mouse model (ex vivo analysis of heart and adipose tissue)						
	HFpEF mouse model (in vivo)						

= TNYA results support proposed mechanism of action of HDAC6 inhibition

1. *Inflammation / Oxidative stress:* In our preclinical studies, TN-301 has shown improvement in inflammatory markers in adipose tissue from a diet-induced obesity (DIO) model, while TYA-018 has shown improvement in inflammatory markers in a BAG3 model of DCM. Published studies have linked inhibition of HDAC6 with inflammasome biology and enhancement of regulatory T cell activity.

2. *Defective metabolism / glucose metabolism:* In our preclinical studies, TN-301 has 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-018 has also shown improvement in dysregulated metabolic pathways in a BAG3 model of DCM. 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.

3. *Fibrosis:* In our preclinical studies, TN-301 significantly improved markers of cardiac fibrosis in a HFpEF model. Published studies support our findings, having shown HDAC6 inhibition by siRNA or partially selective inhibitors attenuated myofibroblast markers and HDAC6 knockdown has been demonstrated to inhibit cardiac fibroblast proliferation.

4. *Hypertrophy:* In our preclinical studies, TN-301 has also shown improved in LV hypertrophy in multiple HFpEF models. In published studies, HDAC inhibitors prevented cardiac hypertrophy in animal models in response to various hypertrophic stimuli, and HDAC inhibition suppressed cardiac hypertrophy and fibrosis in a model of hypertension through regulation of HDAC6/HDAC8 enzyme activity.

5. *Impaired autophagy:* In our preclinical studies, TYA-018, has shown improvement in autophagy in a BAG3 model of DCM that was correlated with improvement in heart function. Published studies illustrate the role of reduced autophagy in HFpEF and in aging hearts.

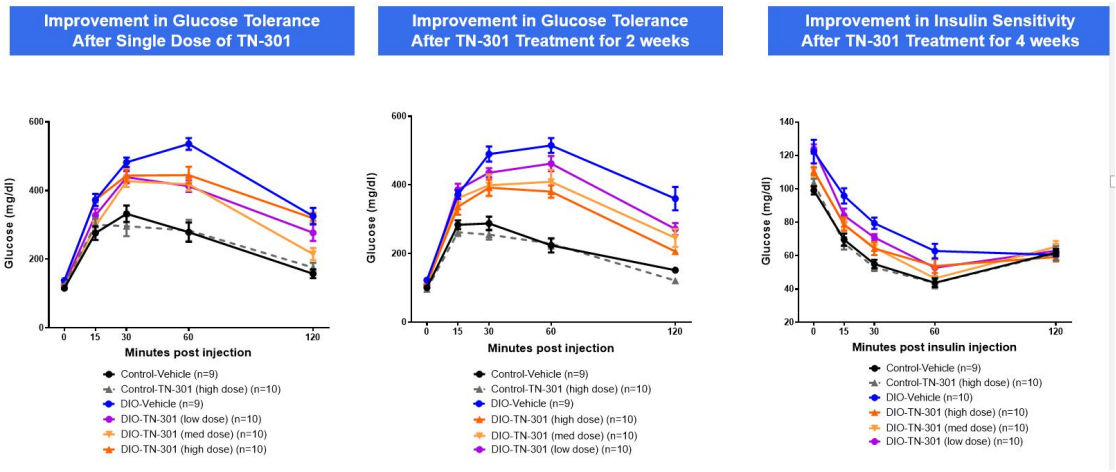
6. *Diastolic dysfunction:* TN-301 has also shown improved diastolic dysfunction in multiple preclinical HFpEF models. Published studies have shown pan-HDAC inhibitors improved diastolic dysfunction in two distinct murine models of HFpEF and HDAC inhibition improved cardiopulmonary function in a feline model of diastolic dysfunction.

Potential Indications Beyond HFpEF

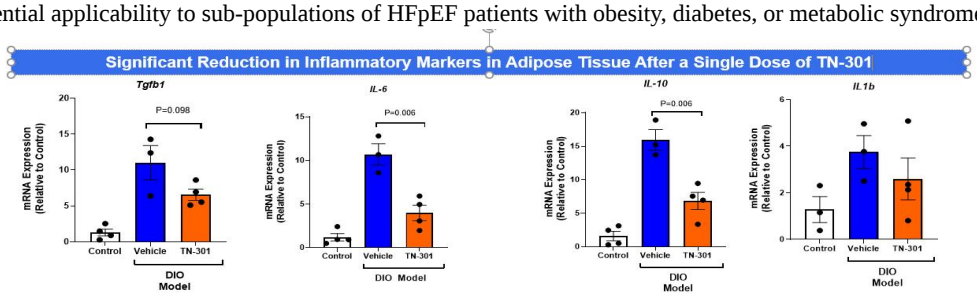
Data from preclinical studies evaluating TN-301 as a treatment for HFpEF suggest that there may also be a role for TN-301 in the treatment of sub-populations of HFpEF patients with obesity, diabetes or metabolic syndrome as well as potentially in sub-populations of DCM where there is strong alignment between the multi-modal mechanism of action of TN-301 with the pathophysiology of the disease.

TN-301: Preclinical Studies in Models of Metabolic Disease

In addition to improvements in glucose metabolism associated with TN-301 treatment in HFpEF mouse models, treatment with TN-301 has also led to improvements in glucose tolerance and insulin sensitivity in a DIO mouse model. As shown below, treatment with a single dose of TN-301 improves glucose tolerance in a dose-dependent manner in the DIO model. Furthermore, TN-301 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.



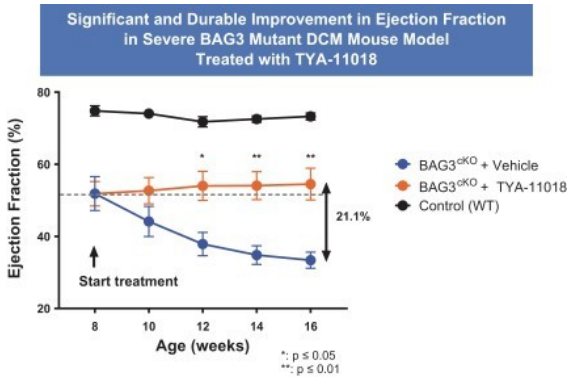
A single dose treatment of TN-301 in the DIO model is also associated with a significant reduction in inflammatory markers in adipose tissue relative to controls as shown below. Inflammatory biomarkers in adipose tissue are thought to be linked to glucose tolerance and insulin sensitivity. For example, 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 human 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-018 resulted in a greater than 20% improvement in EF after eight weeks of treatment compared to a control group treated with vehicle.



TN-401: Gene Therapy for PKP2-associated ARVC

PKP2 gene mutations are estimated to affect more than 70,000 patients in the U.S. 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 are developing TN-401, a potential first-in-class AAV-based gene therapy designed to address ARVC caused by *PKP2* gene mutations. We have demonstrated prevention of disease progression, reversal of RV remodeling and survival

benefit in a murine model after a single dose. We expect to submit an IND to the FDA in the second half of 2023, and those efforts are being aided by our learnings from the TN-201 IND filing experience.

Overview of ARVC

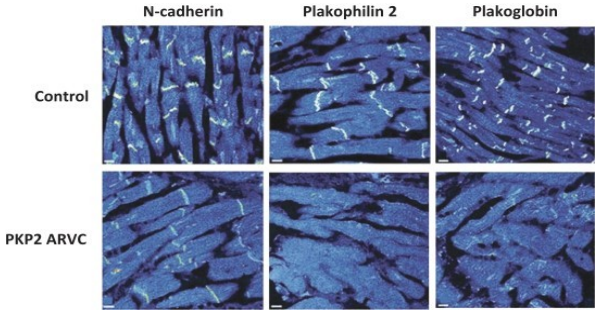
ARVC is largely an inherited disease characterized by the progressive loss of muscle cells in the heart's RV and replacement with a composite of fibrotic tissue and fatty deposits. As a result of this structural change, the heart becomes dilated and is prone to VA and particularly ventricular tachycardia (abnormally high heart rate).

Patients with ARVC most commonly present with symptoms related to VA (such as palpitations, lightheadedness, and fainting) or cardiac arrest, with the mean age of diagnosis in patients occurring before the age of 40. 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. In an effort to reduce the risk of sudden cardiac death, patients with ARVC are typically discouraged from competitive or endurance sports activities and physical exercise may be limited.

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 U.S. 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.

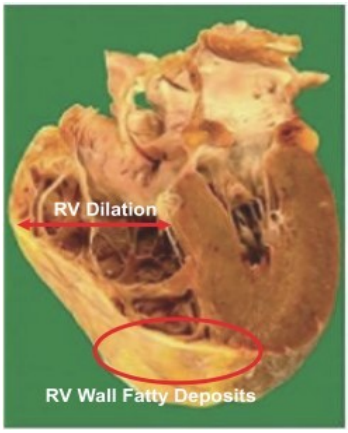
As illustrated below, the PKP2 protein is an integral component of cell adhesion protein complexes known as desmosomes which connect adjacent cardiomyocytes in the heart. Desmosomes are responsible for stabilizing the heart and for maintaining channels called gap junctions that allow for cellular communication among heart cells, which in turn is important to proper synchronization of cardiomyocyte contractions across the myocardium contributing to each heartbeat.

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 cardiomyocytes 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. As a result of this impairment, cardiomyocytes 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, illustrating the crucial role the PKP2 protein plays in maintaining the structural integrity of the desmosome, and that mutations in the *PKP2* gene are enough to disrupt this complex in human hearts.



(2) Source: Asimaki et. al. **NEJM** 2009.

An example of a 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.



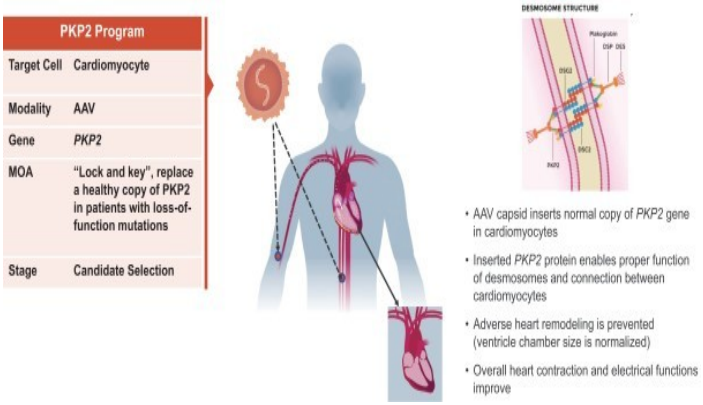
Following a diagnosis, ARVC patients are typically implanted with an ICD to control arrhythmias and prevent sudden cardiac death. ICD implantation is currently the only proven effective treatment for preventing sudden cardiac death in ARVC patients, but ICDs are also associated with complications, including inappropriate shocks, potential for heart perforation and need for 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. Pharmacologic options for ARVC treatment typically include beta blockers and other anti-arrhythmic or heart failure medications, intended to reduce VAs, but studies comparing the efficacy of such treatment have not been conducted. Despite the availability of these treatments, clinical heart failure 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 heart failure symptoms. There are currently no approved therapies that address the underlying genetic causes of ARVC.

Our Solution

We are developing a potential first-in-class AAV-based gene therapy to deliver a fully functional copy of the human *PKP2* gene to the hearts of ARVC patients carrying *PKP2* mutations. We believe that delivery of a working *PKP2* gene to cardiomyocytes represents a promising 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 cardiomyocytes is expected to restore proper structure and function of the desmosome. This in turn can help prevent adverse heart remodeling and improve heart contraction and electrical function. The *PKP2*

gene will be delivered using AAV9 capsid with well-established tropism for the heart and expression of the PKP2 protein will be targeted to the heart through use of a cardiomyocyte-specific promoter.

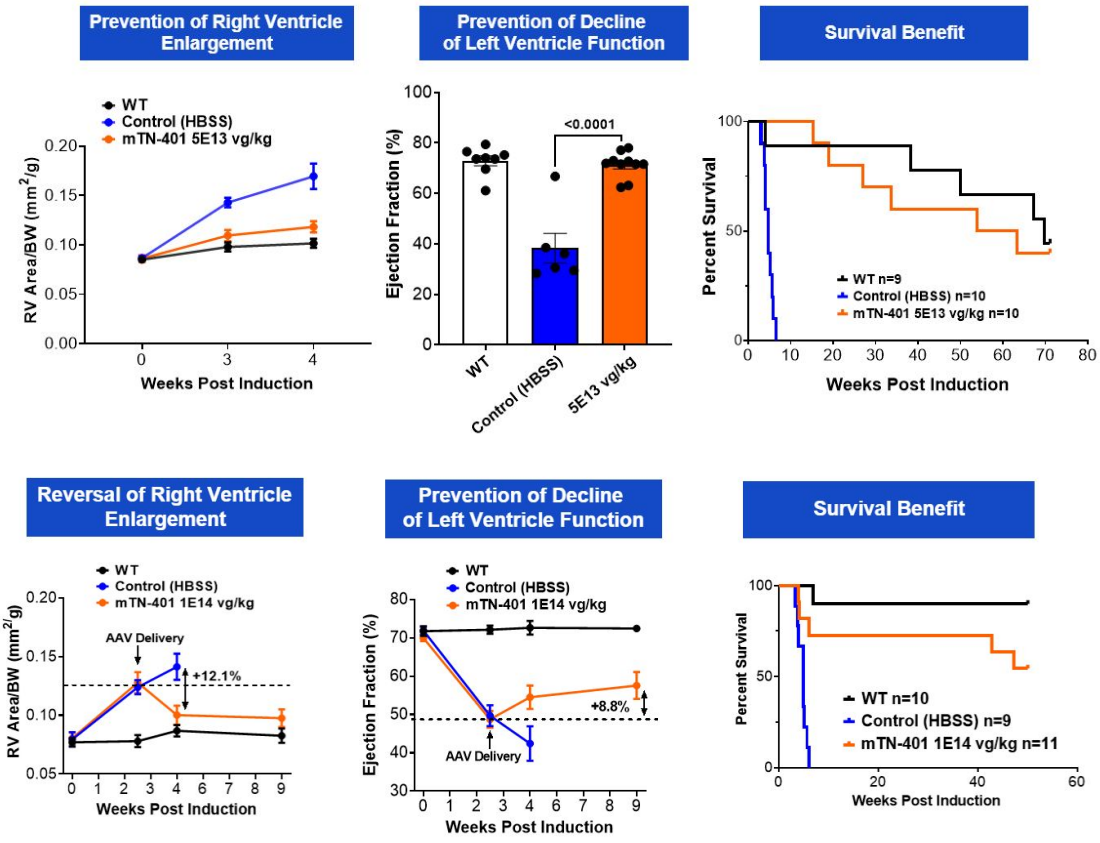
(3) Source: Pinamonti et. al **World J Cardiol** 2014.



TN-401 Preclinical Studies

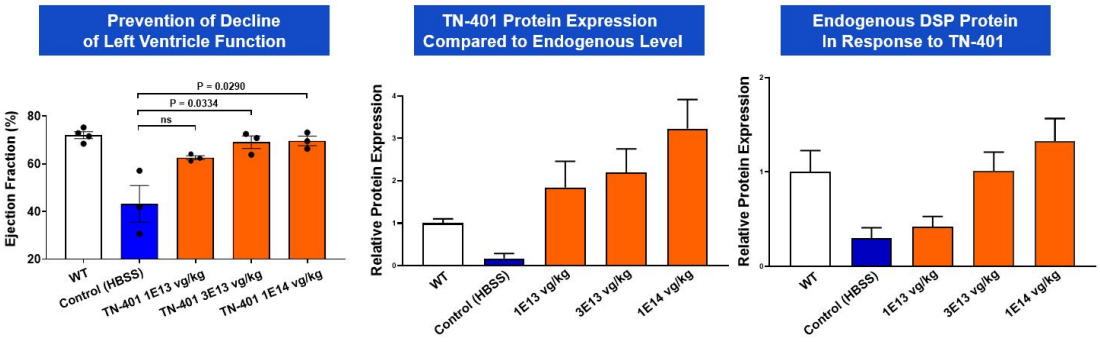
We developed a *Pkp2* conditional knockout (*Pkp2*-cKO) mouse model that simulates key aspects of ARVC including dilation of the RV, decline in LV heart function, severe arrhythmia, abnormal ECG trace, and early mortality. The onset of symptoms in this model is very rapid and occurs within three weeks after induction of the gene deletion. 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 mouse model 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 systemically administered a mouse surrogate of TN-401 (AAV:mPkp2 or mTN-401) in *Pkp2*-cKO mice at the 5×10^{13} vg/kg and 1×10^{14} vg/kg dose levels. Data from these studies showed that whether mTN-401 gene therapy was administered at the time of disease onset or following disease progression, several ARVC phenotypes improved compared to saline-treated controls (HBSS), including preventing RV enlargement, preventing decline of LV function, and improving survival after a single IV dose. Further, mTN-401's beneficial effects have been shown to be durable following a single dose lasting the remainder of the *Pkp2*-cKO mice model's natural life span.



We are also encouraged by the preclinical safety profile and dose-responses observed in our studies of *Pkp2*-cKO mice following treatment with various doses of TN-401. In these studies, we observed dose-dependent efficacy against disease attributes, including prevention of LV functional decline, with relatively low doses achieving near maximal efficacy. Single doses of TN-401 administered in *Pkp2*-cKO mice at the 1×10^{13} vg/kg, 3×10^{13} vg/kg and 1×10^{14} vg/kg dose levels were shown to achieve robust protein expression of PKP2 transgene and desmoplakin (DSP). DSP is one of the five protein components of desmosome in addition to PKP2 and its expression in response to TN-401 is an indicator of improved desmosome integrity following PKP2 protein replacement. The specificity of TN-401 for the heart and its therapeutic index have also proven to be promising in our preclinical studies with low tropism for other organs even at doses greater than ten-fold higher than those with near maximal efficacy. Taken

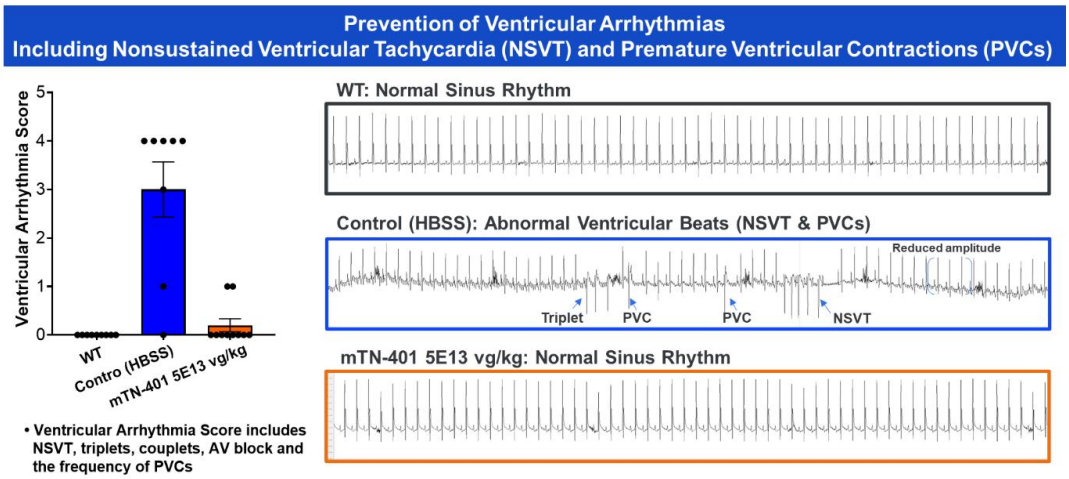
together, we believe these observations position TN-401 well for successful clinical development, with an encouraging safety and efficacy profile.



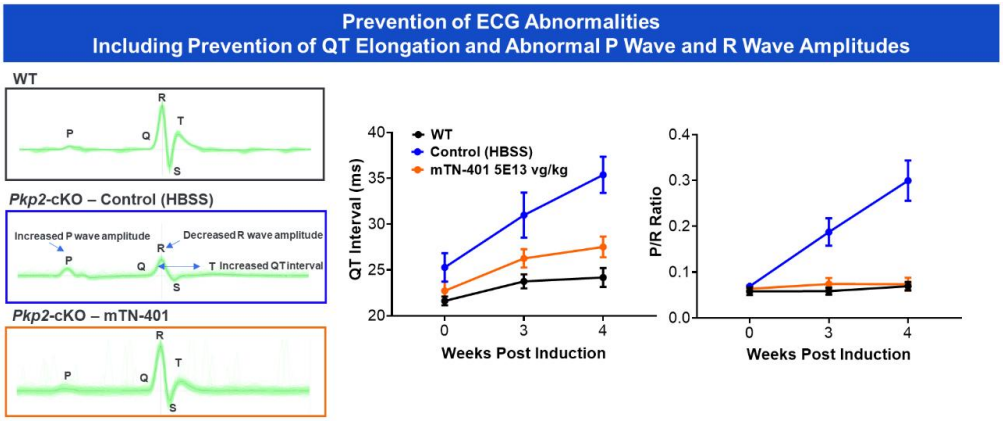
PD Biomarker: Preventing Ventricular Arrhythmias

PKP2 gene therapy has been shown preclinically to correct the hallmark electrophysiological defects associated with ARVC. The graphs below show nearly complete prevention of arrhythmia in *Pkp2*-cKO animals treated with mTN-401 versus controls, including prevention of nonsustained ventricular tachycardia (NSVT) and premature ventricular contractions (PVCs). NSVTs and PVCs were reduced to near healthy levels as evidenced by

the ECG trace and the quantification with a Ventricular Arrythmia Score measuring the incidence of spontaneous arrhythmias during 30 minutes of recording.



The graphs below show normalization of the QRS complex in *Pkp2*-cKO animals treated with mTN-401 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 the preclinical evidence that *PKP2* gene therapy is able to correct the arrhythmias associated with ARVC, we believe this measurement may provide a meaningful early PD biomarker for monitoring TN-401's activity in the clinic.

TN-401 Planned Clinical Development

We have initiated IND-enabling activities and plan to submit an IND to the FDA for TN-401 in the second half of 2023. We intend to use our experience from the TN-201 IND filing and to seek feedback from multiple regulatory agencies, including the FDA, as necessary. If our IND is approved, we plan to initiate global FIH clinical trials in patients with mutations of the *PKP2* gene. Additionally, in support of our development efforts for TN-401, we have initiated a global non-interventional study to collect treatment history and seroprevalence to AAV9 antibodies data among ARVC patients who carry pathogenic or likely pathogenic *PKP2* gene mutations.

DWORF Program for DCM

We are developing an AAV-based gene therapy designed to deliver the *DWORF* gene for patients with DCM.

Dilated cardiomyopathies are estimated to affect about one million patients in the U.S. DCM is a progressive and life-threatening disease that causes enlargement and wall thinning of the LV, insufficient contraction, reduced blood flow, VA, and can result in premature morbidity and need for heart transplant in affected individuals. DWORF is a muscle-specific micro-peptide that acts on the SERCA2a pathway, widely considered to be a promising target in heart failure. We and our academic collaborators have accumulated significant preclinical proof-of-concept evidence for the therapeutic benefit and tolerability of over-expression of the *DWORF* gene in multiple murine models, including models of DCM. 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 heart failure where the EF is below 40% and the walls of the LV 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, CAD, high blood pressure, heart attack, and viral infection.

DCM is a life-threatening and progressive disease. Once symptoms appear, a patient's condition typically declines progressively. Typical symptoms of heart failure 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.

It is estimated that DCM affects about one million people in the U.S., with genetic abnormalities linked to DCM estimated to be present in about 30% to 40% of DCM patients.

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 heart failure over time. Some patients with PLN mutations have a high severity of disease, including patients with R9C and R14del mutations. PLN mutations are rare with an estimated 0.5% of DCM patients carrying PLN mutations. Notwithstanding, founder effects in certain communities have led to higher concentrations of affected individuals in specific regions in the world, enabling patient identification.

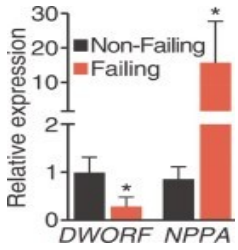
DCM treatment generally utilizes medications developed and approved for HFrEF. While current pharmacologic therapies have improved prognosis and the quality of life of DCM patients, the premature morbidity and mortality rate remains unacceptably high. End-stage DCM is the leading indication for use of 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 targeted, disease-modifying options.

Our Solution

We have licensed intellectual property from University of Texas Southwestern Medical Center (UTSW) to develop and commercialize products relating to therapeutics overexpressing *DWORF* and are developing an AAV-based gene therapy to deliver the *DWORF* gene to cardiomyocytes for the treatment of DCM. 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 cardiomyocytes 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.

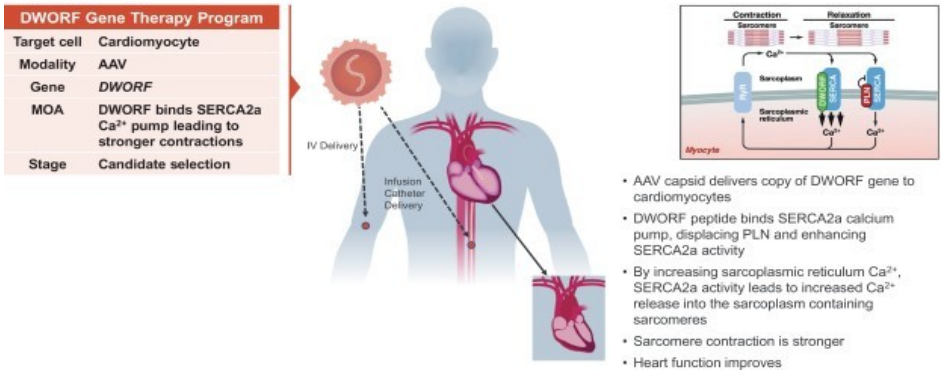
We believe DWORF is an ideal target for the treatment of particular forms of heart failure. DWORF is a small peptide that is readily expressed when delivered by AAV. The small size of the *DWORF* gene leaves additional room in the AAV capsid to include optimized combinations of promoters and regulatory 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 heart failure tissue. DWORF mRNA is reduced in failing hearts whereas atrial natriuretic peptide (NPPA) mRNA, a marker of congestive heart failure, 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 cardiomyocytes and increase contractile strength in DCM patients, as well as the broader HFrEF patient population. In addition, in patients with DCM caused by specific PLN mutations, the mutant PLN peptides are excessively inhibitory to SERCA2a, thereby reducing cardiac contractility. *DWORF* gene therapy produces DWORF peptides that directly compete with mutant PLN peptides by preferentially binding with SERCA2a, which can increase muscle contraction, potentially halting or even reversing disease progression.

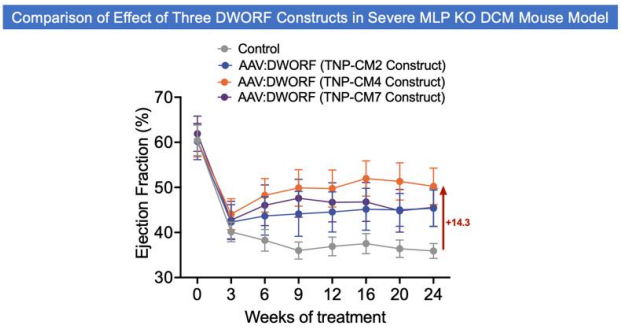
Our DWORF program, illustrated below, is currently at the candidate selection stage with multiple constructs under consideration. *DWORF* gene expression is limited to the cardiomyocyte through use of a novel cardiomyocyte-specific promoter. Our intended product candidate will use an AAV capsid with 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.



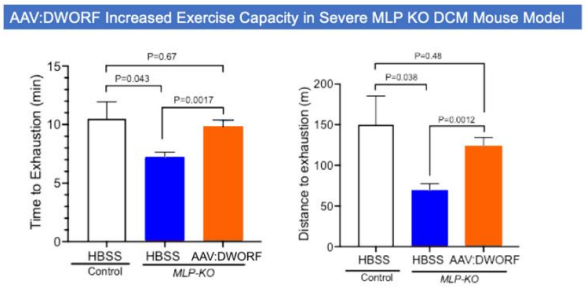
Preclinical Studies

Results in DCM (with Muscle Lim Protein (*MLP) KO model)*: AAV:DWORF constructs have shown improvements in heart remodeling following treatment in mouse models of DCM. As shown below, 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 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. The increase in heart function was durable throughout the duration of this 24-week study:



AAV9:DWORF also improved exercise capacity, including running distance and time to exhaustion, in the MLP KO DCM mouse model 26 weeks post-treatment.



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 and Potential Indications Beyond DCM

After selection of our product candidate, we plan to initiate IND-enabling studies. Should an IND for this program be cleared by the FDA, 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. Approximately 50% of heart failure cases are HFrEF, representing a prevalence of nearly four million patients in the U.S. 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.

Reprogramming Program for Heart Failure due to Prior MI

We are developing an AAV-based approach to cellular regeneration that involves converting (or reprogramming) existing cardiac fibroblasts within the heart to turn into new cardiomyocytes and to replace cells permanently lost due to MI. There are estimated to be more than four million patients in the U.S. living with heart failure due to prior MI. The loss of cardiomyocytes in affected individuals permanently impairs heart contraction, leading to heart failure 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 cardiomyocytes 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 cardiac fibroblasts to cardiomyocytes when delivered together in a single AAV capsid. Based on publicly available information to date, we believe our results in a pig model of heart failure 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 failure due to prior MI

CAD is the single most common cause of heart failure and 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 cardiomyocytes and cardiac fibroblasts, to die. The heart cannot replace the lost cardiomyocytes while the cardiac fibroblasts 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 heart failure, these patients also have a persistent risk of arrhythmias and increased likelihood of a second heart attack or sudden death.

In the U.S., 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 cardiomyocytes associated with MI and the resulting morbidity and mortality.

Our Solution: Direct In Vivo Reprogramming of Resident Cardiac Fibroblasts to Create Cardiomyocytes

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 cardiac fibroblasts into cardiomyocytes in both *in vitro* and *in vivo* models, creating the potential for a new approach to cardiac regeneration.

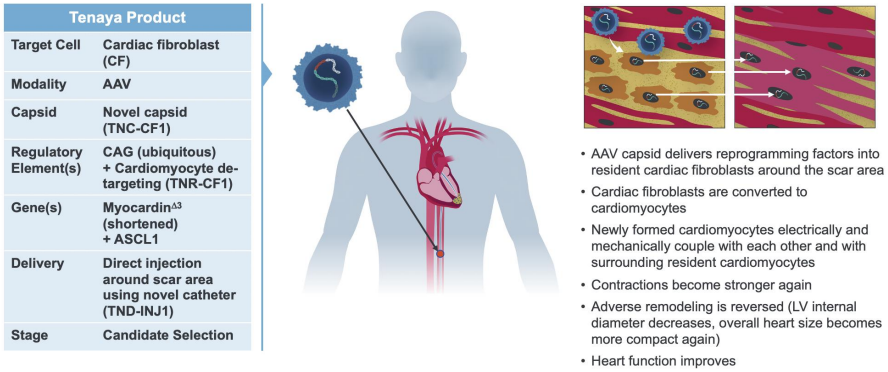
Building on this pioneering work, we have developed a novel AAV-based therapy for direct *in vivo* reprogramming of resident cardiac fibroblasts into cardiomyocytes to replace the cardiomyocytes lost due to an MI. Our goal is to convert the cardiac fibroblasts into new cardiomyocytes to help repair the heart after an MI, and ultimately slow down, stabilize or even potentially reverse the progression to heart failure. 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 cardiac fibroblasts, we identified a unique combination of genes encoding Myocardin and ASCL1, that together, can drive robust direct *in vivo* reprogramming of cardiac fibroblasts to cardiomyocytes, 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 cardiac fibroblasts, result in the direct reprogramming of the cardiac fibroblasts into cardiomyocytes.
- *Capsid engineering*. While AAV9 can be used to target cardiomyocytes, it does not sufficiently transduce cardiac fibroblasts. We have discovered a novel capsid, TNC-CF1, which has a higher transduction efficiency for human cardiac fibroblasts 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 cardiomyocytes by including a miR-208 binding site that decreases reprogramming factor expression in mature cardiomyocytes 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.

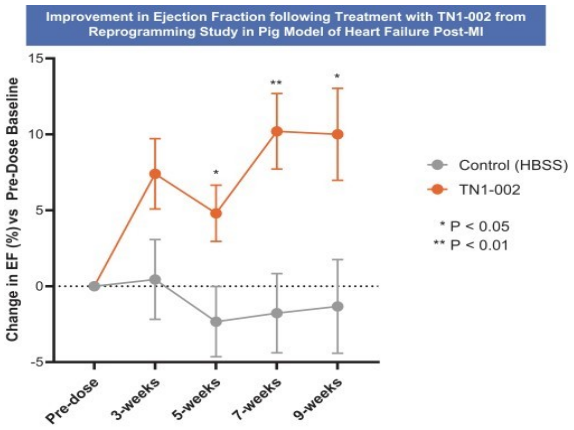


Preclinical Studies

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 cardiac fibroblasts. Our reprogramming approach has been optimized *in vitro* in adult human cardiac fibroblasts. We have conducted extensive iterative experiments to compare the relative efficiency of various constructs to convert cardiac fibroblasts to cardiomyocytes, whereby cardiomyocyte-specific markers like cTnT and a-Actinin are measured to determine the proportion of cells that have been converted from cardiac fibroblasts to cardiomyocytes. Results from one such an experiment demonstrate that our TN1-006 construct can convert approximately 40% of human cardiac fibroblasts to cardiomyocytes.

Results from pig disease model. We have demonstrated durable improvement in EF in a pig model of heart failure 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%.

Our preclinical findings to date provide direction to our ongoing candidate selection efforts. Further analyses of effects in individual animals revealed a clear correlation between levels of TN1-002 vector, reprogramming factor expression, and degree of functional improvement. This provides additional support that the improvements in EF seen in this experiment were a direct result of the delivery and expression of the reprogramming factors by our AAV capsid. We continue to seek ways to ensure more consistent delivery and expression of our reprogramming factors to cardiac fibroblasts, 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.

Our development plan is anticipated to include patients with advanced heart failure 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 heart failure caused by a loss of cardiomyocytes, 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.

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.

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.

Third-party clinical studies have demonstrated that 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, data suggest that AAV9 is a highly effective parental vector for the purpose of cardiac gene therapy where the target cells are cardiomyocytes (one of the most abundant cell types in the heart responsible for contraction). In addition, we are aware of over 2,300 patients worldwide that have been treated using Novartis Pharmaceutical's Zolgensma (developed by AveXis), a therapy utilizing IV AAV9. Based on the totality of preclinical and clinical evidence, we have also chosen to use AAV9 to support our TN-201 and TN-401 programs.

However, AAV9 has limitations. AAV9 has a well-established ability to transduce the liver and the central nervous system, in addition to the heart, which may create safety considerations. Also, some individuals have neutralizing antibodies to AAV9, making them ineligible for AAV9-based treatments. Cardiac-specific promoters like cTnT, can help limit the expression of AAV-delivered genes to cardiomyocytes, but do not enable targeted gene expression in other heart cells (e.g. cardiac fibroblasts). Additionally, the level of gene expression from these promoters may not be sufficient for therapeutic effect for some targets.

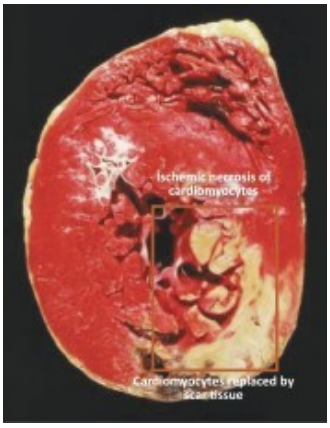
Therefore, there is significant room for improvement, and we aim to improve gene therapy for the heart in ways that expand its utility. We believe our five core internal capabilities will allow us to identify, engineer, validate, deliver and manufacture novel AAV vectors to optimize the delivery and 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. Additionally, we have established know-how to enable more optimal manufacturing, including of novel AAV capsids.

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. We believe our proprietary capabilities open the opportunity to deliver novel gene therapies to patients with heart disease and 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.

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 cardiomyocytes 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. 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 re-hospitalized within one year of their first MI. The loss of healthy functional cells is a contributing factor to other forms of heart disease as well. One reason that disease is so prevalent and a leading cause of death in the world is due to the lack of regenerative potential of the heart. 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: cardiomyocytes, which are the cells that are responsible for contraction during each heartbeat, and cardiac fibroblasts, that produce and secrete growth factors, cytokines and other signaling molecules contributing to structural, biochemical, mechanical and electrical properties of the myocardium. While cardiac fibroblasts are able to divide and proliferate, cardiomyocytes are post-mitotic, meaning they are incapable of regenerating. cardiomyocytes that are lost due to aging or disease are replaced by fibrotic scar tissue that is permanent and irreparable.



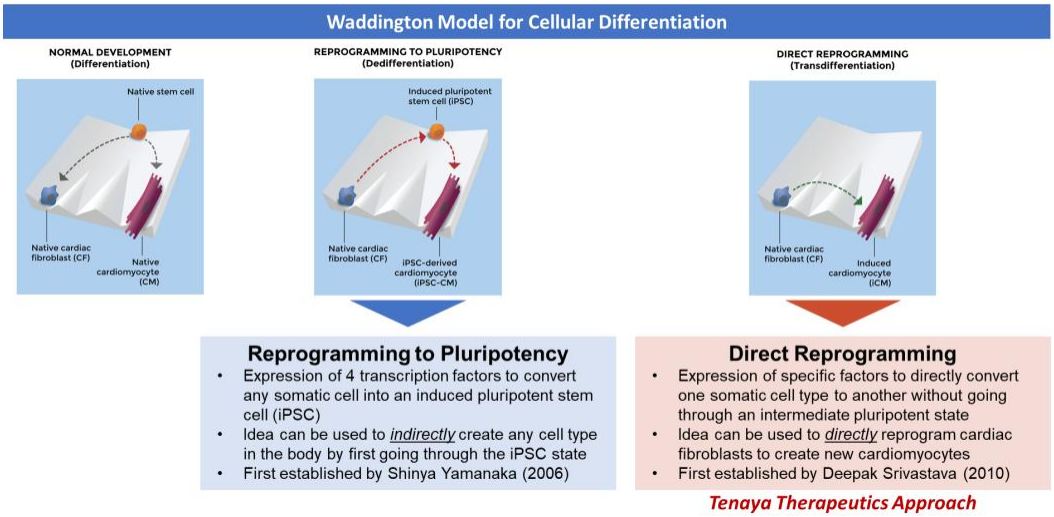
The field of cardiac regeneration has historically been dominated by *ex vivo* cell therapy approaches using autologous (from self) or allogeneic (from donors) cell sources to replace lost cardiomyocytes. However, there have been no successful therapies after scores of clinical studies involving thousands 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, 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 cardiomyocytes. 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 cardiac fibroblasts into new cardiomyocytes.

This approach was inspired by the Nobel-prize winning discoveries of Shinya Yamanaka. He first discovered that human cells can be "reprogrammed" with certain specific factors—which became known as the "Yamanaka factors"—to become 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 cardiac fibroblasts to cardiomyocytes 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 cardiac fibroblasts to cardiomyocytes 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 cardiac fibroblasts to cardiomyocytes, 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 using viral gene therapy to deliver cardiac reprogramming factors 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 heart failure following MI (i.e. following some period of time after the heart attack has occurred) 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 cardiac fibroblasts when compared to existing parental capsids. We have demonstrated higher transdifferentiation rates *in vitro* using human cardiac fibroblasts 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 heart failure post-MI. Most importantly, based on publicly available information to date, we believe our results in a pig model of heart failure 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 cardiomyocytes are generated from the patients' own cells, they are not rejected by the body and no immunosuppression is needed. Since these newly formed cardiomyocytes 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.

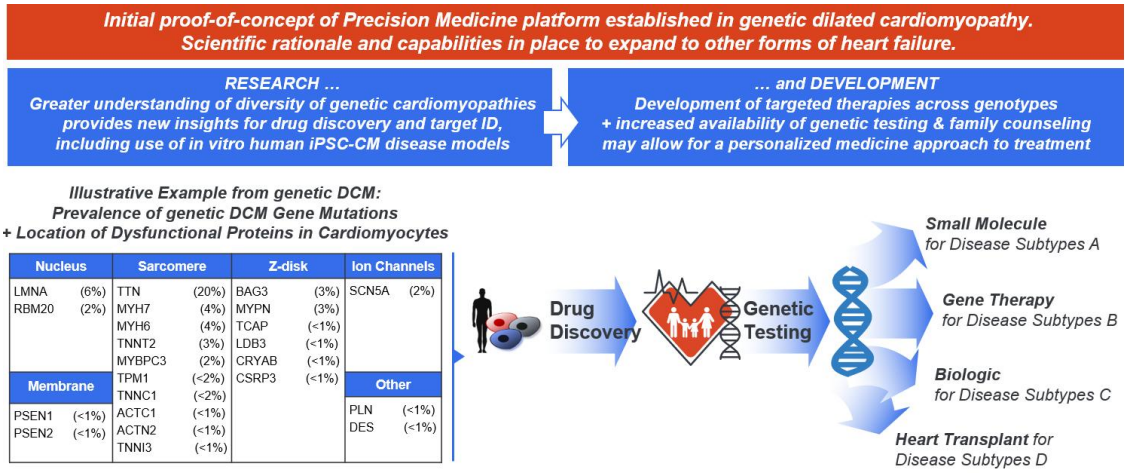
The initial focus of our Cellular Regeneration platform is on the development of disease-modifying treatments for heart failure due to prior MI. We believe the versatility of this product platform and related differentiated capabilities position us to expand our portfolio of therapies rapidly and pursue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

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 DCM, with more than 50% of patients presenting with multiple mutations. These mutations affect different parts of the cellular apparatus of patients' cardiomyocytes, 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 heart failure. 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.

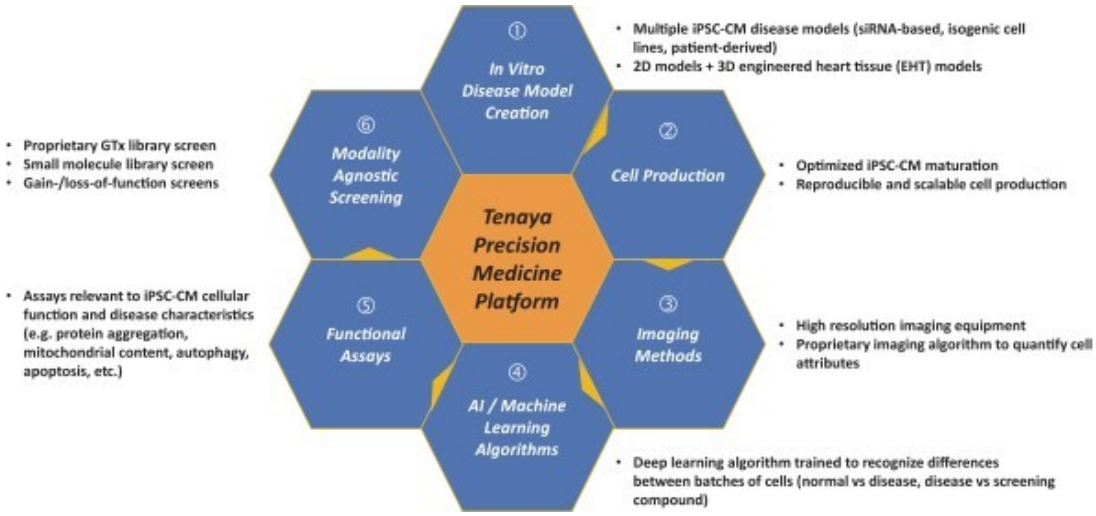
The figure below helps illustrate our vision for "precision medicine" research and development for heart disease through the lens of DCM:



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 DCM 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 human iPSC-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 human iPSC-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 human iPSC-CMs:



We have demonstrated proof of concept of this approach using a human iPSC-CM disease model representing a specific genetic DCM 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, TN-301, with *in vivo* activity and tolerability demonstrated in multiple heart disease models of HFpEF and DCM and evidence of target engagement during clinical evaluation.

We are currently conducting target identification screens for both gene therapy and small molecule targets in multiple human iPSC-CM disease models of DCM. 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 TN-301.

Our Core 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

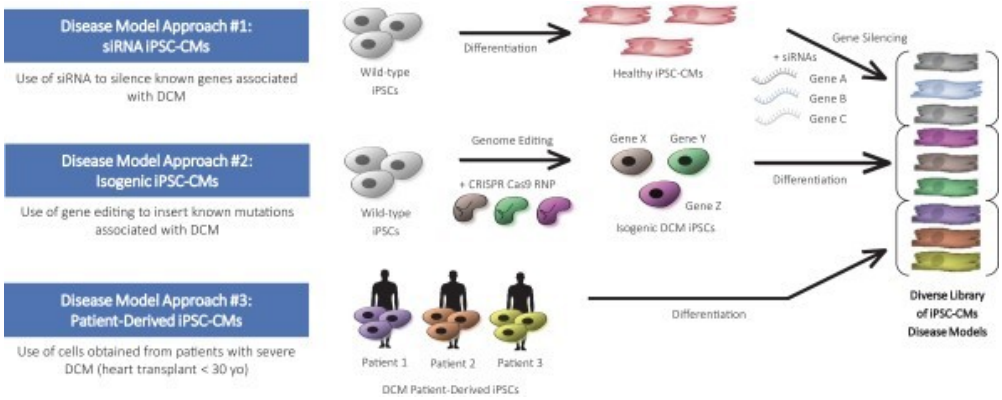
development of product candidates that, if approved, could address the high unmet need of patients with heart diseases.

1. Disease Models

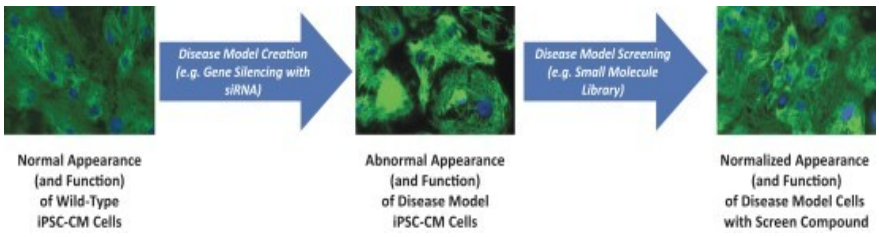
We have internalized the ability to create and integrate *in vitro* and *in vivo* models within our research organization, which allows us to simulate human heart disease phenotypes. We believe our success will be supported by the know-how we are developing and the proprietary integration of these disease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

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



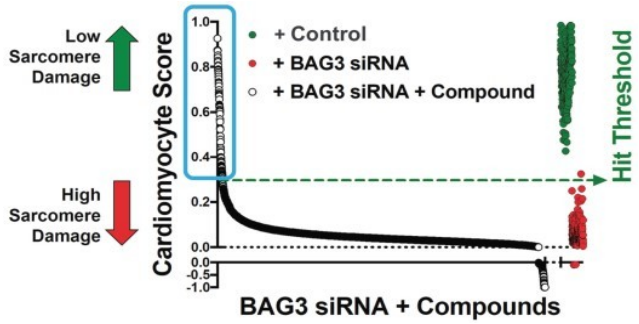
These disease models can collectively help simulate the impact of human disease-causing mutations on the appearance and function of cardiomyocytes and model the impact of potentially disease-modifying treatments on such cells. In the figure below, we illustrate how, through use of gene editing and gene 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 human iPSC-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.
- *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 17 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.

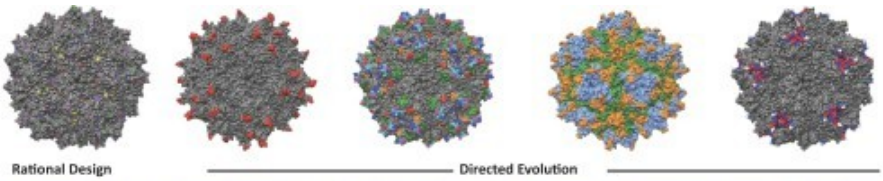
2. Capsid Engineering

Our goal is to discover, design, and develop novel heart-tropic AAV capsids with superior attributes in order to enable more precise cardiomyocytes targeting and to improve the safety profile of our product candidates by reducing tropism for other organs, particularly the liver. A capsid is the protective protein shell which contains the

AAV vector and AAV tropism is determined by interaction of capsid proteins and host cell surface receptors. To achieve our goals related to capsid engineering, 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.

- *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 to target the two most abundant cell types in the heart: cardiomyocytes and cardiac fibroblasts. 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 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.



Capsid Modification	Surface-Exposed Residues Prone to Phosphorylation	Peptide Insertion Library	Randomly Altered Variable Region Library	Chimeric Library Generation	Systematic Alteration of Variable Regions
Tenaya Efforts	• Mutagenesis screen of surface-exposed residues prone to phosphorylation	• Generated peptide insertion libraries with multiple AAV parental capsids	• Generated multiple modified variable region libraries with modified VRs to screen for CM tropism	• Generated chimeric libraries to identify CM capsids with improved properties for cardiac gene transfer	• Modified parental VRs

- *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. Several capsids identified have equivalent 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. Additionally, we have shown that several capsids we identified have overall better ability to evade human neutralizing antibodies compared to AAV9. We have also generated additional data that demonstrate that certain of these capsids have a greater ability to improve heart function compared to AAV9 in specific disease models.

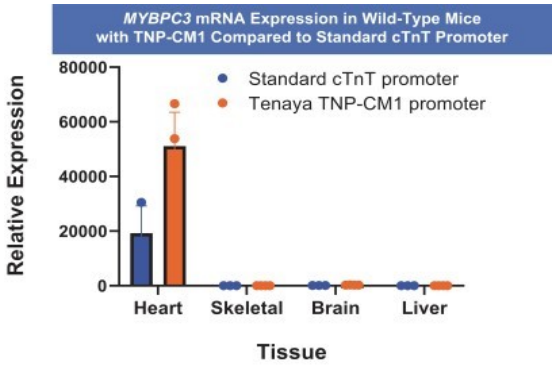
Overall, these data provide important proof of concept of the potential utility of capsid engineering. Therefore, we have taken steps to protect the intellectual property that support the novel capsids identified from our initial capsid engineering screens, and intend to continue this practice as we generate additional data from our ongoing capsid engineering efforts.

3. Promoters and Regulatory Elements

Promoters and regulatory elements are DNA sequences whose function is to determine the level of gene expression at the RNA level and in which cells transcription will occur. These elements can therefore be essential to the success of gene therapy. Enabled by our in-house molecular biology capabilities, we have created novel heart-specific promoters, as well as regulatory elements which control gene expression within the cells to support our AAV-based programs. 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 these elements may further support the successful clinical development of our product candidates.

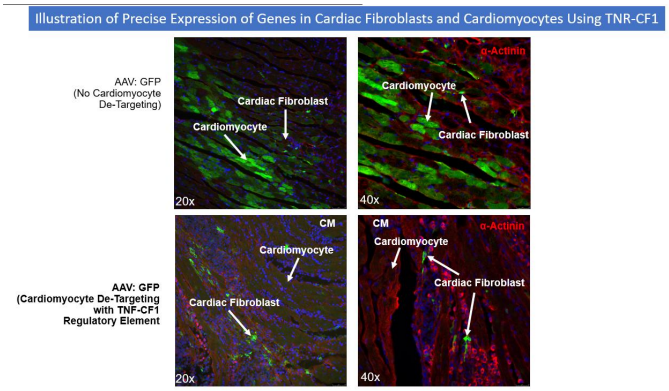
Illustrative examples of our innovations in this area include:

- *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 TN-201, we developed a cardiomyocyte-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, in a mouse model we observed 1000-fold selectivity of expression in cardiac tissue relative to other tissues, including skeletal muscle, brain and liver.



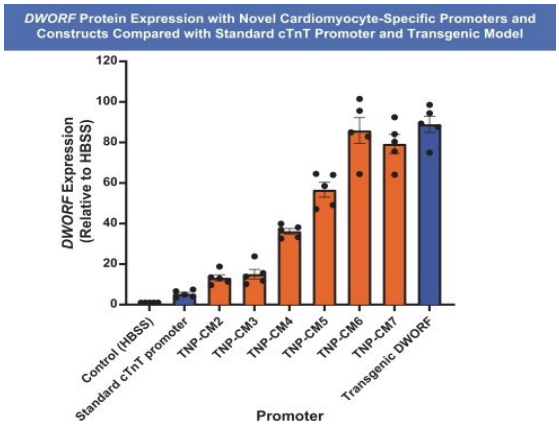
- *Cell specificity:* We have also developed a proprietary combination of regulatory elements that enable more optimal and selective expression in one cell type in the heart compared to others. For our Reprogramming program for cellular regeneration, we discovered ways to optimize the robust co-expression of two protein-coding genes and one micro-RNA gene delivered within a single AAV in cardiac fibroblasts, 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 cardiomyocytes as well as newly created cardiomyocytes, 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 in the cardiomyocytes of a mouse model and only allowed expression in the cardiac fibroblasts. We have used this regulatory element in our Reprogramming program to focus the expression of our proprietary factors in resident cardiac fibroblasts for the creation of new cardiomyocytes, but to prevent the expression of those factors both in resident cardiomyocytes and in newly created cardiomyocytes, 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 cardiomyocytes, by combining various combinations of enhancer elements from different cardiomyocyte selective genes. Through data (not shown in the figure below) generated in our DWORF program, more than ten promoters were designed and tested *in vitro* in human iPSC-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:



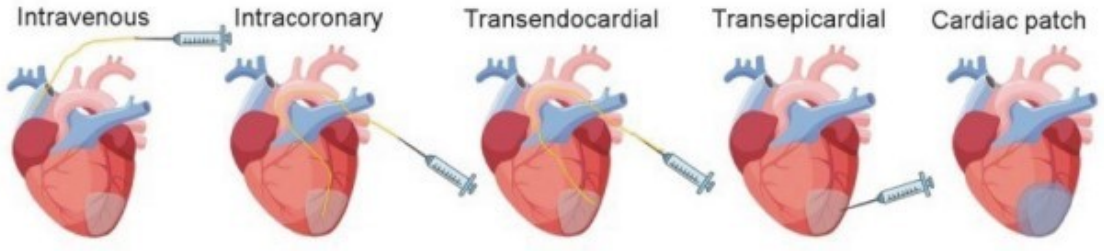
4. Drug Delivery

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)]



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

For the initial product candidates emerging from our Gene Therapy platform, including TN-201, 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.
- *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 example, for TN-201, we conducted experiments in NHPs to compare the degree of drug uptake and biodistribution for peripheral IV infusion and infusions delivered directly in the heart. Based on the results, we chose systemic IV infusions as the ROA for TN-201. In addition, for our Reprogramming program, we conducted experiments in pig models to demonstrate that a less invasive catheter-based 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.

5. Manufacturing

We have fully integrated and internalized AAV manufacturing capabilities to support our Gene Therapy and Cellular Regeneration platforms. Our overall strategy is to have complete ownership of our PD, analytical development, MFG and QC so that we have deep insight into the attributes of our drug substance and drug product. Internalized manufacturing enables continuous process improvement, consistency (quality and productivity) and innovation that can support manufacturing requirements for clinical development and commercialization not only for rare populations, but also for more prevalent indications, and allows 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 support our future capacity expansion needs or swiftly transfer technology know-how to CDMOs to achieve dual sourcing for product candidates for risk mitigation purposes.

- *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 process development, analytical development and QC personnel to internalize those capabilities. We have also established the necessary process development 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.
- *Manufacturing Technology Development Center (MTDC):* We have established in-house operations at the 200L scale to support all non-clinical studies including those involving large animal models, such as pigs and NHPs, under GLP regulations. We also rely on the MTDC for assay development and technology transfer to our dedicated cGMP facility. Our initial production at this scale has been at yields and with full/empty capsid ratios that compare favorably to industry standards.
- *Genetic Medicines Manufacturing Center:* Our GMMC is a dedicated cGMP facility for AAV drug product manufacturing and is located in the San Francisco Bay Area. The facility operates at the 1000L scale to support all clinical development activities from FIH clinical trials through to late stage development, as well as initial commercialization, if regulatory approval is obtained. It uses a modular design that will support scale-out and/or scale-up of manufacturing capacity in response to evolving needs.
- *Intellectual property:* We have in-licensed and internally developed certain manufacturing-related intellectual property to support our programs. We have filed multiple patent applications covering improvements that will support scale-up of AAV manufacturing for supply of our gene therapy product candidates intended for more prevalent heart disease populations.

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:

TN-201: We believe the principal competition for TN-201 will be programs that address the underlying genetic cause of *MYBPC3*-associated HCM. Based on publicly available data, we don't believe any such treatments have received approval from a regulatory agency or reached clinical development. Based on publicly available data, BioMarin and DiNAQOR's BMV-293 is only program in preclinical development for treating the underlying cause of *MYBPC3*-associated HCM. We may also face competition from treatments for both nHCM and oHCM, including Bristol Myers Squibb's myosin inhibitor Camzyos approved for oHCM. There are also several other programs in clinical development for HCM.

TN-301: We believe that the principal competition for TN-301 in HFpEF includes agents approved in the U.S. and/or Europe for the treatment of HFpEF, including Novartis' Entresto and Eli Lilly and Boehringer Ingleheim's SGLT2 inhibitor, Jardiance. While there are no approved HDAC6 inhibitors for cardiovascular indications, HFpEF clinical development is an area of robust investment and multiple additional agents for the treatment of HFpEF are in clinical development.

TN-401: We believe the principal competition for TN-401 will be programs that address the underlying genetic cause of *PKP2*-associated ARVC. Based on publicly available data, we don't believe any such treatments

have received approval from a regulatory agency or reached clinical development. However, there are several programs in preclinical development for treating the underlying cause of *PKP2*-associated ARVC, including Rocket Pharmaceutical's RP-A601, Lexeo Therapeutics' LX2020 and Stridebio's STRX-330. We may also face competition from therapies and medical devices directed to treat the symptoms of ARVC.

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, manufacturing processes and know-how, to operate without infringing, misappropriating or otherwise violating the intellectual property or other 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 agreements, including 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 U.S. and in certain jurisdictions outside of the U.S. related to our proprietary technology, inventions, improvements and product candidates that are important to our business. Our patent portfolio is intended to cover our product candidates and components thereof, their methods of use and processes for their manufacture, medical devices and systems for their administration, our proprietary reagents and assays and any other inventions that are commercially important to our business.

Product Pipeline

Lead products in our gene therapy, small molecule and cellular reprogramming programs are already covered by at least one or more issued U.S. patents, which are described below. Beyond these issued patents, our owned and exclusively licensed patent portfolio covers various aspects of our programs and technology, including our small-molecule compounds, gene delivery vectors, recombinant capsid proteins, gene editing technology, heart disease therapy including using gene therapy programs, medical devices, and manufacturing processes. Further details on certain segments of our patent portfolio are included below.

TN-201: With regard to TN-201, we own two issued U.S. patents covering a recombinant adeno-associated virus (rAAV) virion whose vector genome encodes *MYBPC3*, two pending non-provisional U.S. patent applications, and twenty six pending foreign patent applications. Any U.S. or foreign patents issued from the pending patent applications 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. The pending U.S. non-provisional patent applications disclose various aspects of TN-201, including *MYBPC3* gene expression vectors, rAAV virions, rAAV viral genomes, expression cassettes, and cover methods of using such compositions for therapeutic indications.

TN-301: With regard to TN-301, we own one issued U.S. patent, one pending non-provisional U.S. patent application and twenty-eight pending foreign patent applications. Any U.S. or foreign patents issued from these pending patent applications are expected to expire in 2040, assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees, and without taking potential patent term extensions or adjustments into account. The pending patent applications cover TN-301 and various analogs. We also own two patent families that

cover methods of treatment of various diseases and disorders with TN-301 and its analogs, with two pending PCT patent applications and one foreign patent application. Any U.S. or foreign patents issued from national stage filings of these PCT patent applications or the pending foreign patent application are expected to expire in 2042, 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. We also own one patent family that covers additional HDAC6i compounds, with one pending non-provisional U.S. patent application and three pending foreign patent applications. Any U.S. or foreign patents issued from these pending patent applications are expected to expire in 2040, assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees, and without taking potential patent term extensions or adjustments into account.

TN-401: With regard to TN-401, we own four pending U.S. non-provisional patent applications, one pending PCT patent application and three foreign counterparts of these patent applications from national stage filings. Patents claiming priority to these patent applications, if issued, are expected to expire by 2041, assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees and without taking potential patent term extensions or adjustments into account. These patent applications are related to proprietary *PKP2* gene expression vectors and methods of use. We own one pending U.S. provisional patent application related to *PKP2* therapeutic treatment methods. Patents claiming priority to this U.S. provisional patent application, if issued, are expected to expire in 2043, assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees, and without taking potential patent term extensions or adjustments into account. We own one pending U.S. provisional patent application related to capsids for *PKP2* therapy and methods of use. Patents claiming priority to this U.S. provisional patent application, if issued, are expected to expire in 2043, assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees, and without taking potential patent term extensions or adjustments into account.

DWORF: With regard to our DWORF program, we exclusively licensed two issued U.S. patents and one pending U.S. patent application from UTSW (the UT Patents). The U.S. patents and the pending U.S. patent application, if issued, are 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 cover a polynucleotide encoding a DWORF peptide, a vector comprising the same, and methods of enhancing activity of the SERCA pump in a subject using the same. In addition, we exclusively licensed from UTSW one pending non-provisional U.S. patent application, and fourteen pending foreign patent applications, covering a rAAV virion whose vector genome encodes DWORF and methods of use. Any U.S. or foreign patents issued from the pending patent applications 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. Furthermore, we own one pending PCT, one pending non-provisional U.S., and two pending foreign patent applications covering proprietary vectors, including proprietary DWORF vectors, and methods of use. Any U.S. or foreign patents if issued from the pending patent applications or from national stage filings of the PCT, are expected to expire in 2042, 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 application, and without taking potential patent term extensions or adjustments into account.

Reprogramming: We own four patent families directed to product candidates in our Reprogramming program, including one issued U.S. patent, three pending non-provisional U.S. patent application, twenty-one foreign counterparts of these patent applications, and a pending PCT patent application. Any U.S. or foreign patents issued from these pending patent applications, or national stage filings of the PCT patent application, are expected to expire between 2039 and 2042, 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 application, and without taking potential patent term extensions or adjustments into account. The four patent families cover various aspects of our Reprogramming program, including recombinant enhancers, gene delivery vectors, methods of treating a heart condition, engineered myocardin proteins, vectors encoding engineered myocardins, methods of making and methods of use. Additionally, we own a fifth patent family that is directed to AAV-based gene vectors and recombinant capsid proteins for cardiac cell transduction, with one pending non-provisional U.S. patent application and nine pending foreign counterparts of this patent application. Any U.S. or foreign patents issued from these pending patent applications are expected to expire in 2040, assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees, and without taking potential patent term extensions or adjustments into account.

Core Capabilities: Capsid Engineering, Manufacturing and Drug Delivery

Capsid Engineering: In support of our efforts to develop novel heart-tropic AAV capsids, we own two patent families directed to AAV-based recombinant capsid proteins, with one pending non-provisional U.S. patent application, twenty five pending foreign patent applications, and two pending provisional U.S. patent applications. Any U.S. or foreign patents based on the pending patent applications, or claiming priority to the provisional U.S. patent applications, if issued, are expected to expire between 2041 and 2043, assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees, and without taking potential patent term extensions or adjustments into account.

Manufacturing: In support of our manufacturing activities, we own two patent families with one pending non-provisional U.S. patent application and one pending provisional U.S. patent application. The pending non-provisional U.S. patent application is directed to improved methods of baculovirus expression, and any U.S. patent issued from this patent application is expected to expire in 2041, assuming payment of all appropriate maintenance or other governmental fees, and without taking potential patent term extensions or adjustments into account. The pending provisional U.S. patent application is directed to improved methods of viral particle production, and any U.S. or foreign patents claiming priority to this provisional U.S. patent application, if issued, are expected to expire in 2043, assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees, and without taking potential patent term extensions or adjustments into account.

Drug Delivery: In support of our efforts to identify 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 own one pending provisional U.S. patent application directed to cardiac catheter devices and systems for administration of our product candidates such as gene delivery vectors. Any U.S. or foreign patents claiming priority to this provisional U.S. patent application, if issued, are expected to expire in 2044, assuming payment of all appropriate maintenance, renewal, annuity or other governmental fees, and without taking potential patent term extensions or adjustments into account.

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. 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.

For information regarding the risks related to our intellectual property, see "*Risk Factors—Risks Related to Our Intellectual Property.*"

Manufacturing

We rely on a combination of our internal manufacturing capabilities as well as on external CDMOs for the manufacture of the drug substance and/or drug product of our portfolio programs, and intend to continue to utilize this strategy as our programs progress through various stages of clinical development and eventually to commercialization, if approved.

AAV Manufacturing

We have fully integrated and internalized AAV manufacturing capabilities to support product candidates from our Gene Therapy and Cellular Regeneration platforms. Our MTDC is co-located with our research labs in the San Francisco Bay Area. The MTDC includes a Vector Core, upstream and downstream process development labs, as well as assay development and QC capabilities. The MTDC does non-GMP work and operates at the shake flask, 50L, and 200L scales to support all non-clinical studies including, IND-enabling efficacy, pharmacology, toxicology, and biodistribution studies involving both small and large animal models. We also rely on the MTDC for

technology transfer of our proprietary processes to our GMMC, a dedicated cGMP facility for AAV drug substance and drug product manufacturing also located in the San Francisco Bay Area. The GMMC facility operates at the 200L and 1000L scales to support all clinical development activities from FIH clinical trials through to late-stage development, as well as initial commercialization, if regulatory approval is obtained. We utilized the GMMC to produce drug product for our FIH clinical study for our TN-201 program in 2022 and expect to produce clinical supply for our TN-401 program at the facility as well. We customized approximately half of the 94,000 square foot GMMC facility using a modular design that will support our ability to scale-out and/or scale-up of manufacturing capacity in response to evolving needs, including future potential clinical and commercial production needs.

In addition to our internal cGMP manufacturing capabilities, we have also negotiated and entered into master service agreements with multiple CDMOs for additional AAV manufacturing and filling capacity and related risk mitigation. Additionally, we will rely on third parties for certain manufacturing of ancillary materials and release assays, for which we have already secured or intend to secure dual-sourced capacity for risk mitigation.

Small Molecule Manufacturing

To optimize our use of resources and to utilize extensive experience in small molecule manufacturing, we work with CDMOs for our small molecule programs. We initiated and completed cGMP manufacturing to support our FIH study for our HDAC6 inhibitor small molecule program, TN-301, in 2021.

Government Regulation

Government authorities in the U.S. at the federal, state and local level and in other countries regulate, among other things, the research, development, testing, manufacture, QC, 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 U.S., 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 QCs, or the small molecule product's identity, chemistry, and QCs;
- 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 risk evaluation and mitigation strategies (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 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 continue to monitor changes in FDA policies and work with our clinical sites and investigators to mitigate potential risks to our ongoing clinical trials. The FDA, along with other global health authorities, has issued various guidance on COVID-19 related matters, including, among others, conducting clinical trials during the pandemic; manufacturing, supply chain, and drug and biological product inspections during the COVID-19 public health emergency; and GMP considerations for responding to COVID-19 infection in employees in biopharmaceutical manufacturing. 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. Recently, President Biden announced that the administration intends to end the COVID-19 national and public health emergencies on May 11, 2023. The full impact of the termination of the public health emergencies on FDA and other regulatory policies and operations is unclear.

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 2023 fee schedule, effective through September 30, 2023, the user fee for an application requiring clinical data, such as a BLA or NDA, is approximately $3.2 million. PDUFA also imposes an annual program fee for each marketed human prescription drug product ($393,933 in 2023) 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.

In *Catalyst Pharms., Inc. v. Becerra*, 14 F.4th 1299 (11th Cir. 2021), the court disagreed with the FDA's longstanding position that the orphan drug exclusivity only applies to the approved use or indication within an eligible disease. In particular, the circuit court held that the orphan-drug exclusivity for Catalyst's drug blocked FDA's approval of another drug for all uses or indications within the same orphan-designated disease, or Lambert-Eaton myasthenic syndrome (LEMS), even though Catalyst's drug was approved at that time only for use in the treatment of LEMS in adults. Accordingly, the court ordered the FDA to set aside the approval of a drug indicated for LEMS in children. This decision created uncertainty in the application of the orphan drug exclusivity. On January 24, 2023, the FDA published a notice in the Federal Register to clarify that while the agency complies with the court's order in *Catalyst*, the FDA intends to continue to apply its longstanding interpretation of the regulations to matters outside of the scope of the *Catalyst* order – that is, the agency will continue tying the scope of orphan-drug exclusivity to the uses or indications for which a drug is approved, which permits other sponsors to obtain approval of a drug for new uses or indications within the same orphan designated disease or condition that have not yet been approved. It is unclear how future litigation, legislation, agency decisions, and administrative actions will impact the scope of the orphan drug exclusivity.

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. Further, in December 2022, the Consolidated Appropriations Act, 2023, including the Food and Drug Omnibus Reform Act (FDORA), was signed into law. FDORA made several changes to the FDA's authorities and its regulatory framework, including, among other changes, reforms to the accelerated approval pathway, such as requiring the FDA to specify conditions for post-approval study requirements and setting forth procedures for the FDA to withdraw a product on an expedited basis for non-compliance with post-approval requirements.

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, QC 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, 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 Premarket Approval Application (PMA). 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, which imposes extensive testing, control, documentation, and other Quality Assurance (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, including fines, penalties, injunctions, requests for recall, and exclusion from participating in government programs. 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. Changes in regulations, statutes or the interpretation of existing regulations could impact our business and increase our exposure to additional liabilities. For more information, see "*Risk Factors— Risks Related to Regulatory Approval and Other Legal Compliance Matters*."

U.S. Data Privacy and Security Laws

In the United States, a broad variety of laws, rules, regulations and standards relating to privacy, data protection and information security 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, as amended by the California Privacy Rights Act effective January 1, 2023 (CCPA)), state health information privacy laws, and federal and state consumer protection laws. The CCPA requires covered businesses that process personal information of California residents to disclose their data collection, use, sharing and retention practices, provides California residents with data privacy rights (including the ability to opt out of certain disclosures of personal information including for certain advertising purposes), imposes 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. 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. Other state legislatures have enacted or are currently considering, and may pass, their own comprehensive data privacy and security laws, with potentially greater penalties and more rigorous compliance requirements, and 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

Recently enacted Clinical Trials Regulation EU No 536/2014 (the Regulation), which went into application on January 31, 2022, replaces the Clinical Trials Directive No. 2001/20/EC and aims to harmonize the processes for assessment and supervision of clinical trials throughout the European Union. Under the Regulation, clinical trial

sponsors can use the Clinical Trials Information System (CTIS) from January 31, 2022, but are not required to use it immediately, in line with a three-year transition period. CTIS publishes certain clinical trial information on a searchable public website and supports the flow of information and interactions between clinical trial sponsors and regulatory authorities in European Union Member States, European Economic Area countries, and the European Commission.

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 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. We are also subject to the UK GDPR, which implements the GDPR in the UK post-Brexit. The GDPR has increased 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 European Economic Area (EEA), United Kingdom (UK) and Switzerland relating to privacy and data protection. 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. Further, 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. Moreover, there has been heightened governmental scrutiny over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries as well as proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, impose limitations on drug price increases and reform government program reimbursement methodologies for drug products, could also have a material and adverse effect on our business, financial condition and results of operations.

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 August 2022, Congress passed the Inflation Reduction Act of 2022 (IRA), which includes prescription drug provisions that have significant implications for the pharmaceutical industry and Medicare beneficiaries, including allowing the federal government to negotiate a maximum fair price for certain high-priced single source Medicare drugs, imposing penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, requiring inflation rebates for all Medicare Part B and Part D drugs, with limited exceptions, if their drug prices increase faster than inflation, and redesigning Medicare Part D to reduce out-of-pocket prescription drug costs for beneficiaries, among other changes. The impact of such legislative, executive, and administrative actions and any future healthcare measures and agency rules implemented by the Biden administration on us and the pharmaceutical industry as a whole is unclear. The implementation of cost containment measures, including the prescription drug provisions under the IRA, as well as other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates if approved.

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. For more information, see "*Risk Factors—Risks Related to Regulatory Approval and Other Legal Compliance Matters.*"

Human Capital Resources

As of December 31, 2022, we had 141 full-time employees, representing an over 33% increase in our employee workforce as compared to December 31, 2021. Of these employees, 101 are engaged in research, development and technical operations. 28 of our employees hold Ph.D. or M.D. (or foreign equivalent) degrees and 10 hold other professional degrees such as a J.D. or M.B.A. None of our employees are represented by a labor union or covered under a collective bargaining agreement. We focus on employee engagement and consider our relationship with our employees to be good, in part as measured by relatively high scores from employee surveys.

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. In addition, we provide a variety of programs and services to help employees meet and balance their needs at work, at home and in life, including a healthcare, insurance and other benefit plans. We regularly assess our benefit programs, employee engagement and turnover, recruitment initiatives, workforce diversity and other matters relevant to human capital management, and review those results with our board of directors on a periodic basis.

We are an equal opportunity employer and maintain policies that prohibit unlawful discrimination based on race, color, religion, gender, sexual orientation, gender identity/expression, national origin/ancestry, age, disability, marital and veteran status. We employ a diverse workforce that, as December 31, 2022, was approximately 65% non-white and 57% women based on our employees' voluntary self-identification. We strive to create a collaborative culture that fosters internal engagement around our company and our mission to discover, develop and deliver curative therapies that address the underlying drivers of heart disease.

We are committed to advancing diversity and inclusion (D&I) in our workforce and established a D&I Committee in 2020. We acknowledge that diversity in thought, experience, background, and culture makes our science and our community stronger. Our mission is to foster and create a unique culture where belonging and empowerment are at the forefront of our community. We advocate for diverse perspectives and encourage employees to be authentic, inclusive, and respectful to each other. We discourage behaviors that do not have a positive impact on our community or support our mission to discover, develop, and deliver curative therapies that target the underlying causes of heart disease.

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, California 94080. Our telephone number is (650) 825-6990. We maintain a site on the worldwide web at www.tenayatherapeutics.com; however, information found on our website is not incorporated by reference into this report.

Investors and others should note that we may announce material information to the public through filings with the SEC, our website (www.tenayatherapeutics.com), press releases, public conference calls, and public webcasts. We use these channels, as well as social media, to communicate with the public about us, our product candidates and other matters. As such, investors, the media and others are encouraged to review the information disclosed through our social media and other channels listed above as such information could be deemed to be material information. Please note that this list may be updated from time to time.

We make available free of charge on or through our website our Securities and Exchange Commission (SEC) filings, including our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The SEC maintains a site on the worldwide web that contains reports, proxy and information statements and other information regarding our filings at www.sec.gov.

Item 1A. 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 annual report and in our other public filings in evaluating our business. 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.

Risk Factors Summary

Our ability to execute on our business strategy is subject to a number of risks and uncertainties, including those outside of our control, that could cause our actual results to be harmed, including risks regarding the following:

- We are early in our development efforts, with a limited operating history, have not 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.
- We require substantial additional capital to finance our operations. Raising additional capital will cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates. 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 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.
- Drug development involves a lengthy and expensive process with an uncertain outcome. The preclinical studies, clinical trials and post-marketing studies 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 delay or prevent regulatory approval, or market acceptance, or even if approval is received, require them to be taken off the market, include new safety warnings, contraindications or precautions, or otherwise 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.
- Due to our limited manufacturing experience, there can be no assurance that we will be able to successfully manufacture product candidates to support our clinical development and commercialization plans.
- 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 operations and financial results could be adversely impacted by the effects of the COVID-19 pandemic in the United States (U.S.) and the rest of the world.
- 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.
- We rely on third parties to conduct our preclinical studies and our clinical trials, and plan to rely on third parties to conduct such future drug development activities. These third parties may not perform satisfactorily, including failing to meet completion deadlines, or to comply with applicable regulatory requirements, which may harm our business.

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 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 a limited operating history upon which you can evaluate our business and prospects. We commenced operations in 2016, have not 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. In September 2022, we initiated a Phase 1 clinical trial evaluating TN-301 and began dosing TN-301 in humans and in January 2023 the FDA cleared our IND for TN-201 for evaluation in humans. All of our other product candidates are still in preclinical development and have never been tested in humans. Since our inception, 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 and clinical trials, 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 limited experience conducting clinical trials and have not yet demonstrated our ability to successfully complete any clinical trials, obtain marketing approvals, manufacture a late stage 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 principally through issuances of our stock. Our net loss was $123.7 million for the year ended December 31, 2022. As of December 31, 2022, we had an accumulated deficit of $279.2 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. 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, including, but not limited to, 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, including as a result of factors related to the novel coronavirus disease (COVID-19) pandemic; sufficiency of our financial and other resources to complete the necessary preclinical studies and clinical trials and commercialization activities; and the operational, technical and clinical development challenges associated with novel drug development;
- submission of INDs or other regulatory applications for our planned clinical trials, obtaining regulatory approval to commence clinical trials of our product candidates, and achieving favorable results from clinical trials;
- establishing and maintaining relationships with contract research organizations (CROs) and clinical sites for the clinical development of our 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 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;
- operating a manufacturing facility and developing an efficient and scalable manufacturing process for our product candidates, and the timely manufacture of sufficient quantities of a product candidate for use in clinical trials and, if approved, commercialization;
- 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;
- the actual market-size, ability to identify patients and the demographics of patients eligible for our product candidates, which may be different than expected; and commercial acceptance of our product candidates by patients, the medical community and third-party payors;
- our ability to distribute our products to certain segments of the patient population only accessible through restricted or closed distribution channels;
- satisfying any required post-marketing approval commitments to applicable regulatory authorities, and maintaining consistent quality, purity, and potency across clinical supplies and commercial supplies for any approved products;
- identifying, assessing and developing new product candidates, and our ability to expand into multiple indications;
- obtaining, maintaining, and expanding patent and other intellectual property protection, trade secret protection and regulatory exclusivity, both in the U.S. 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; and
- attracting, hiring and retaining qualified and key 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 our value 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 require substantial additional capital to finance our operations. Raising additional capital will cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates. 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 December 31, 2022, we had $204.2 million in cash, cash equivalents and investments in marketable securities. We expect our current cash, cash equivalents and investments in marketable securities will be sufficient to fund our current operating plan for operations through at least the next twelve months from the date of this Annual Report on Form 10-K. Our estimate 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.

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.

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 the near- and long-term in connection with our ongoing activities, particularly as we initiate and conduct clinical trials of, and seek marketing approval for, our product candidates. 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, 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 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 also expect to incur 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;
- 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 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.

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. 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 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 pre-clinical development programs, platforms, manufacturing activities, ongoing or planned clinical trials or future commercialization efforts.

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, maintaining certain leverage ratios, 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, 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 on their use under U.S. tax law. 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 subsequent shifts in our stock ownership, some of which are outside our control. Consequently, our ability to use our NOLs and certain other tax attributes may be limited.

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. Before we are able to generate any revenue from product sales, each of our programs and product candidates will require additional preclinical and/or clinical development, expansion of manufacturing capabilities and expertise, regulatory approval, building a commercial organization or successfully outsourcing commercialization, substantial investment and significant marketing efforts. Consequently, because of the substantial operational and financial investment required to further develop and commercialize our product candidates, there is a high risk of failure and we may never succeed in developing marketable products.

If we are unable to optimize our manufacturing processes to produce product candidates that meet applicable regulatory standards, do not successfully initiate and complete our clinical trials in a timely manner or fail to achieve favorable results from our trials, we may experience significant delays or be unable to advance 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. Furthermore, any changes to our development programs may cause our product candidates to perform differently and affect the results of planned clinical trials, which 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.

There is a high failure rate for biopharmaceutical products proceeding through clinical trials. 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 or earlier clinical studies. In addition, 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 and we may experience the same. We may also encounter regulatory delays or rejections as a result of many factors, including varying interpretations of data or 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 those described in the Risk Factor entitled "*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 do not have control over many of these factors, including certain aspects of the manufacturing process, preclinical and clinical development, the regulatory review process and potential threats to our intellectual property rights. If we are not successful with respect to one or more of these factors, 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 product candidates 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. Even if we obtain approval and begin commercializing one or more of our product candidates, we may never generate revenue that is significant enough to achieve profitability, as 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.

Within the broader genetic medicine field, very few therapeutic products, including those that utilize AAV-mediated gene transfer, have received marketing authorization from the FDA, EMA or comparable foreign regulatory authorities. 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 U.S., the European Union (EU) 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. Even with respect to more established products that fit into the categories of gene therapies or cell therapies, the regulatory landscape is still developing. 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 U.S., 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 EU. 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 EU, 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 in the EU may be applied to any gene therapy product candidate we may develop, but that remains uncertain at this point. Furthermore, 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 gene therapy 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, EMA, and other regulatory bodies to revise the requirements for the conduct of the clinical trials and approval of our product candidates or limit the use of products utilizing gene regulation technologies, either of which could harm our business. For example, the FDA has imposed clinical holds on various clinical trials of gene therapy product candidates being developed by other companies. In addition, the clinical trial requirements of the FDA, 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, 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 our product candidates, or lead to significant post-approval limitations or restrictions. As we advance our research programs and develop our 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 our product candidates. 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 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 see for our compounds in preclinical models may not be replicated in subsequent preclinical studies or translate into similar results in humans in clinical trials, and results of early clinical trials in humans may not be predictive of the results of larger clinical trials or post-marketing studies 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.

Drug development involves a lengthy and expensive process with an uncertain outcome. The preclinical studies, clinical trials and post-marketing studies 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, European Commission, following a positive opinion from the EMA, or other comparable foreign regulatory authorities for the sale of our product candidates, we must complete lengthy, complex and extensive preclinical studies and clinical trials to demonstrate with substantial evidence the safety and efficacy of such product candidates.

Preclinical and 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 preclinical studies or clinical trials will be initiated, conducted or completed on schedule or as planned, or at all. Failure can occur at any stage of testing. Such 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, which could delay or prevent the submission of an IND, initiation of a clinical trial, receipt of marketing approval or our ability to commercialize our product candidates, or require us to suspended or terminate further development of our product candidates. Moreover, 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 preclinical studies, clinical trials or post-marketing studies that we conduct will demonstrate consistent or adequate efficacy and safety to support marketing approval.

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.

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 clinical trials;

- receipt of feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- preclinical study or clinical trial observations or results that require us to modify the design of our clinical trials;
- negative or inconclusive preclinical study or clinical trial results that may require us to conduct additional preclinical studies or clinical trials or abandon certain research and/or 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 suspension or termination of our clinical trials, as a result of a clinical hold by regulatory authorities, for various reasons, including non-compliance with regulatory requirements, a finding that our product candidates have undesirable side effects or other unfavorable or unexpected characteristics or risks;
- changes to clinical trial protocol;
- clinical sites deviating from trial protocol or dropping out of a trial;
- the costs of preclinical studies or clinical trials 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;
- an unsuccessful post-marketing study or failure to complete such a study;
- 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.

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 trials, 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.

If we are required to conduct additional preclinical studies or clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete preclinical studies or clinical trials of our product candidates or other testing in a timely manner and if the results of these studies, trials or tests are not positive or are only modestly positive or if there are safety concerns, we may incur unplanned costs and be delayed in submitting an IND, initiating clinical trials or seeking and obtaining marketing approval. We may also decide to change the design or protocol of one or more of our planned clinical trials, which could result in increased costs and expenses and/or delays. Any delays in initiating or completing our preclinical studies or clinical trials will increase our costs, slow down our development and approval process and jeopardize our ability to commence product sales and generate revenues, including by shortening any period during which we may have the exclusive right to commercialize our product candidates and permitting our competitors to bring products to market before we do. If we receive approval, it is possible that we may receive 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, which 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 delay or prevent regulatory approval or market acceptance, or even if approval is received, require them to be taken off the market, include new safety warnings, contraindications or precautions, or otherwise 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 clinical trials may suffer serious adverse events or other side effects not observed in our preclinical studies or previous clinical trials. Patients treated with our product candidates may also be undergoing other therapies which can cause side effects or adverse events that are unrelated to our product candidates 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, either during the course of or after participating in such trials, due to other therapies or medications that such patients may be using or due to the gravity of such patients' illnesses.

If serious adverse events or other side effects are observed in any of our 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 authority 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, result in marketing approval with restrictive label warnings or for limited patient populations, or result in potential product liability claims. 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. No regulatory agency has made any determination that any of our product candidates or discovery programs is safe or effective for use by the general public for any indication. We cannot predict whether our product candidates will cause toxicities in humans that would preclude regulatory approval, of if approved, 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. Patient enrollment is a significant factor in the timing of clinical trials and our ability to enroll eligible patients may be limited or slower 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, including the effects of new variants. 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 COVID-19 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 clinical trials may be affected by other factors, including:

- size and nature of the patient population;
- the 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;
- ongoing clinical trials evaluating other product candidates in the same 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;
- challenges associated with recruiting eligible patients;
- 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 U.S. 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 and anticipate substantial direct competition from a variety of competitors. 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. Due to the nature of gene therapy products, use of a competitor gene therapy product by a prospective patient may preclude use of our gene therapy product candidate at a later point in time. 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 and suppliers may encounter difficulties in production. If we or any of our third-party manufacturers or suppliers 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 or suppliers 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, problems in our manufacturing processes or facilities established for our gene therapy product candidates

also could restrict our ability to meet market demand for our products, if approved, which would prevent us from generating product revenue and seriously harm our business.

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.

Due to our limited manufacturing experience, there can be no assurance that we will be able to successfully manufacture product candidates to support our clinical development and commercialization plans.

We have fully integrated and internalized AAV manufacturing capabilities to support product candidates from our Gene Therapy and Cellular Regeneration platforms. However, to optimize our resources and to utilize extensive third-party experience in small molecule manufacturing, we intend to work with CDMOs for our small molecule programs.

Although some of our employees have experience in the manufacturing of biopharmaceutical products from prior employment at other companies, we as a company have limited experience in manufacturing. Furthermore, maintaining manufacturing operations requires significant resources, management time and capital expenditures, particularly in areas relating to operations, quality, regulatory, facilities and information technology.

We cannot guarantee that our facility will be able to produce sufficient quantities of product candidates needed to support our preclinical studies and ongoing and planned clinical trials. We may face delays or increased costs in the production of clinical supply at our manufacturing facility, including as a result of COVID-19 or otherwise. We also may encounter problems hiring and retaining the experienced scientific, quality control and manufacturing personnel needed to operate our manufacturing facility and 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 the ongoing development of 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. 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 operations 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. 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 and our Phase 1 clinical trials for TN-301 and TN-201. 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.

In addition, 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.

If we are unable to successfully manufacture 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.

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;
- perceived 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 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;
- 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 our 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 for our gene therapy product candidates 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 U.S. 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 U.S., 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 U.S., 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 EU, 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 U.S. 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 U.S., the reimbursement for our products may be reduced compared with the U.S. 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 have limited 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 a 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 U.S. 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.

We cannot provide assurance that any of the product candidates we develop will progress through required clinical testing and obtain the regulatory approvals necessary for us to begin selling them. Applications for our product candidates could be delayed or 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 refuse to accept an application or decide not to accept data from our clinical trials conducted in locations outside of their jurisdiction;
- 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;
- the FDA, EMA or other comparable foreign regulatory authorities may require that we conduct additional 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.

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 U.S., 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 U.S., 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 our product candidates receive regulatory approval, such approval may be for a narrower indication than we seek, and our product candidates will be subject to significant post-marketing regulatory requirements and oversight.

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. 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. The 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. 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. 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, and may significantly limit the size of the market for the drug and affect reimbursement by third-party payors.

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 cGMP and GCP for any clinical trials that we conduct post-approval. Manufacturers of drug products and their facilities are also 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 U.S. and the EU, 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 U.S., or a patient population greater than 200,000 in the U.S. where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U.S. Similarly, in the EU, 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 the EU, 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 U.S., 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 U.S. 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.

Our lead product candidates from our gene therapy platform have been granted orphan drug designation by the FDA (TN-201 and TN-401) and the EC (TN-201), and we may seek orphan drug designation for other product candidates in the U.S., 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 U.S. 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.

In *Catalyst Pharms., Inc. v. Becerra*, 14 F.4th 1299 (11th Cir. 2021), the court disagreed with the FDA's longstanding position that the orphan drug exclusivity only applies to the approved use or indication within an eligible disease. This decision created uncertainty in the application of the orphan drug exclusivity. On January 24, 2023, the FDA published a notice in the Federal Register to clarify that while the agency complies with the court's order in *Catalyst*, the FDA intends to continue to apply its longstanding interpretation of the regulations to matters outside of the scope of the *Catalyst* order – that is, the agency will continue tying the scope of orphan-drug exclusivity to the uses or indications for which a drug is approved, which permits other sponsors to obtain approval of a drug for new uses or indications within the same orphan designated disease or condition that have not yet been approved. It is unclear how future litigation, legislation, agency decisions, and administrative actions will impact the scope of the orphan drug exclusivity.

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 U.S. 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 U.S. 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, some of which have been successful, that create considerable uncertainty for our business. Although the U.S. Supreme Court held in 2021 that Texas and other challengers had no legal standing to challenge the ACA, we cannot predict how future challenges 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 U.S. since the ACA was enacted, including aggregate reductions to Medicare payments to providers, effective April 1, 2013, which will remain in effect through 2031and increasing the statute of limitations period for the government to recover overpayments to providers from three to five years. These and future 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.

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. In July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at increasing competition for prescription drugs. In response to this executive order, the HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and potential legislative policies that Congress could pursue to advance these principles. In August 2022, Congress passed the Inflation Reduction Act of 2022 (the IRA), which includes prescription drug provisions that have significant implications for the pharmaceutical industry and Medicare beneficiaries, including allowing the federal government to negotiate a maximum fair price for certain high-priced single source Medicare drugs, imposing penalties and excise tax for manufacturers that fail to comply with the drug price negotiation requirements, requiring inflation rebates for all Medicare Part B and Part D drugs, with limited exceptions, if their drug prices increase faster than inflation, and redesigning Medicare Part D to reduce out-of-pocket prescription drug costs for beneficiaries, among other changes. The impact of these legislative, executive, and administrative actions and any future healthcare measures and agency rules implemented by the Biden administration on us and the pharmaceutical industry as a whole is unclear. The implementation of cost containment measures, including the prescription drug provisions under the IRA, as well as other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates if approved.

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. A number of states are considering or have recently enacted state drug price transparency and reporting laws that could substantially increase our compliance burdens and expose us to greater liability under such state laws once we begin commercialization after obtaining regulatory approval for any of our products. We are unable to predict the future course of federal or state healthcare legislation in the U.S. 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.

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 U.S., relevant legal requirements continue to evolve. For example, the collection and use of health data and other personal data including personal data collected in clinical trials is governed in the EU by the General Data Protection Regulation (GDPR), which imposes substantial obligations upon companies and new rights for individuals, by certain EU member state-level legislation. The GDPR also forms part of the law of England and Wales, Scotland and Northern Ireland by virtue of section 3 of the European Union (Withdrawal) Act 2018 and as amended by the Data Protection, Privacy and Electronic Communications (Amendments etc.) (EU Exit) Regulations 2019 (SI 2019/419), known as UK GDPR. 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 has increased 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 Economic Area (EEA), United Kingdom (UK) and Switzerland relating to privacy and data protection. This may be onerous and if our efforts to comply with GDPR or other applicable laws, rules, regulations and standards are not successful, or are perceived to be unsuccessful, it could adversely affect our business. Further, following the July 2020 Court of Justice of the EU (CJEU) decision invalidating the EU-U.S. Privacy Shield, there remains uncertainty regarding the appropriate mechanism for transferring personal data to the United States. The CJEU's decision and other regulatory guidance or developments may impose additional obligations with respect to the transfer of personal data from the EEA and Switzerland to the U.S., all of which could restrict our activities in those jurisdictions, limit our ability to provide our products and services in those jurisdictions, require us to modify our policies and practices, and to engage in additional contractual negotiations, or increase our costs and obligations and impose limitations upon our ability to efficiently transfer personal data from the EEA and Switzerland to the U.S.

In the U.S., a variety of data privacy, protection and security laws, rules, regulations and standards potentially 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, as amended by the California Privacy Rights Act effective January 1, 2023 (CCPA)), state health information privacy laws, and federal and state consumer protection laws. The CCPA requires covered businesses that process personal information of California residents to disclose their data collection, use, sharing and retention practices, provides California residents with data privacy rights (including the ability to opt out of certain disclosures of personal information including for certain advertising purposes), imposes 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). 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. Other state legislatures have enacted or are currently contemplating, and may pass, their own comprehensive data privacy and security laws, with potentially greater penalties and more rigorous compliance requirements, and 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. 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 significantly, thus complicating compliance efforts and potentially requiring us to undertake additional measures to comply with them.

With the GDPR, CCPA, 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.

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. 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, including delays or disruptions due to the COVID-10 pandemic, travel restrictions and staffing shortages, 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 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 or other disruption occurs, it could significantly impact the ability of the FDA to timely review, provide feedback on our clinical trial plans and process our regulatory submissions, which could have a material adverse effect on our business. Further, 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 which 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), which 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), certain non-physician healthcare professionals (such as nurse practitioners and physician assistants, among others), and teaching hospitals as well as information regarding ownership and investment interests held by physicians and their immediate family members; 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 are 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, offering or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector. 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 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. As we increase our international business activities, our risks under these laws may increase. 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.

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. While we have policies and procedures to address compliance with such laws, 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.

Allegations or 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, suspension or debarment from government contracts 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. 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.

Changes in tax law could increase the tax burden on our orphan drug programs and adversely affect our business and financial condition.

Changes in tax law, including to the orphan drug tax credit and other changes to U.S. and non-U.S. taxation, could increase our tax liability and adversely affect our operating results. For example, in 2022, changes to U.S. tax law took effect that required taxpayers to amortize domestic research and development costs in the year incurred rather than deduct such costs in the year incurred. When and if we become profitable, these changes may cause us to pay federal income taxes earlier under the revised tax law than under the prior law and may increase our total federal tax liability attributable to orphan drug programs and other research and development. In addition, the current administration has proposed a number of other tax law changes applicable to our business. These changes could increase our total federal tax liability when and if we become profitable.

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

Our operations and financial results could be adversely impacted by the effects of the COVID-19 pandemic, including the emergence of recent variants, in the U.S. and the rest of the world.

In March 2020, the World Health Organization declared the 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. Many of our employees have been working remotely since March 2020, which has required that we devise new ways of working and collaborating. 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, including the effects of recent variants, that could severely impact our business, including:

- interruptions, difficulties or delays arising in our existing operations and company culture as a result of many of our employees working remotely, including those hired during the COVID-19 pandemic;
- delays in the receipt of materials integral to the production of drug product to support our planned clinical trials;
- 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 or difficulties in obtaining supplies, supply chain specialists, vendors or other contractors related to clinical trial operations and logistics, which can delay the submission of an IND or our ability to commence a clinical trial in a timely manner;
- changes made to manufacturing plans due to delays or interruptions in obtaining manufacturing supplies or other disruptions to the supply chain, which can negatively impact our clinical plans, delay our clinical development timelines, and increase our costs; if supply chain or manufacturing issues result in material changes to our manufacturing process, such material changes could impact the quality and performance of our product candidates, which could delay our clinical trials, require the conduct of

bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, and delay approval of our product candidates;

- delays, difficulties or increased costs to comply with COVID-19 protocols at our 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 ongoing and 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 U.S.;
- 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 continue to assess the impact that the COVID-19 pandemic 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 and build-out our manufacturing facility. 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 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.

Recently, President Biden announced that the administration intends to end the COVID-19 national and public health emergencies on May 11, 2023. The full impact of the termination of the public health emergencies on FDA and other regulatory policies and operations is unclear. 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.

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, our scientific founders and other scientific and clinical advisors and consultants, and our scientific and medical staff. If we do not succeed in attracting and retaining such 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 long-term plans and strategies, we will need to grow the size of our organization, and we may experience difficulties in managing this growth.

In order to successfully implement our development and commercialization plans and strategies, we expect to need additional managerial, operational, sales, marketing, financial and other personnel in the future. Future growth would impose significant added responsibilities on members of management.

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.

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 and incidents from inadvertent or intentional actions by our employees, contractors, consultants, business partners, and other third parties, cyber-attacks and other hacking attempts 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, distributed 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 other data that we process or maintain or 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 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, including consequential damages, financial harm and reputational damage and the development and commercialization of our product candidates could be delayed. The loss of clinical trial data for our product candidates also could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data. 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 support the development and manufacture of 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. We maintain limited 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. 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 identify, remediate or otherwise address 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. Any data breach, disruption or security incident resulting 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, or if any of these is believed or reported to have occurred, 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 earthquake, flood, blizzard, wildfire, 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 development and marketing our product candidates internationally, subject to regulatory approval in applicable jurisdictions, could materially adversely affect our business.

We may seek regulatory approval of our product candidates outside of the U.S. and/or work with contractors or partners in foreign jurisdictions, and, accordingly, we expect that we will be subject to additional risks and foreign laws and regulatory requirements related to our operations in foreign countries, including:

- differing regulatory requirements and reimbursement regimes;
- 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 U.S.;
- 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 U.S.;
- 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, including effects of the recent Russia-Ukraine conflict.

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

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 relating to our product candidates and platforms and to operate without infringing, misappropriating or otherwise violating the intellectual property of others. We rely on patent, copyright, trade secret and trademark laws in the U.S. and certain other countries to protect our technology, and we generally seek to protect our position by filing patent applications in the U.S. and abroad and by acquiring or in-licensing relevant issued patents or pending applications from third parties. However, these efforts may provide only limited protection. 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.

Pending patent applications cannot be enforced until issued, and then only to the extent the issued claims cover the product candidate or relevant 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 designed around or invalidated by third parties.

Even issued patents may later be found invalid or unenforceable, or they may be modified, narrowed in scope, or revoked in proceedings instituted by third parties before various patent offices or in courts in the U.S. 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. 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 and platforms 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.

We may be unable 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. 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. Furthermore, 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. 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 and platforms or which effectively prevent others from commercializing competitive product candidates and technologies 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.

While we believe our intellectual property allows us to pursue our current development programs, we may not be aware of all third-party intellectual property rights potentially relating to our technology and product candidates. 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. Publications of discoveries in the scientific literature often lag the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all. 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.

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 U.S. and abroad. For example, we may be subject to a third-party pre-issuance submission of prior art, post-grant review (PGR) or inter partes review (IPR) at the USPTO, or other similar proceedings including, opposition, derivation, revocation or reexamination proceedings in the U.S. or abroad. A third party may also claim that our 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. Such proceedings also may result in substantial cost and require significant time from our scientists, manufacturing staff 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 our product candidates.

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.

Our commercial success depends in part on avoiding infringement, misappropriation or other violation of the patents or other intellectual property 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 of others. Other entities may have, develop or obtain patents that could impair our competitive position or limit our ability to make, use, sell, offer for sale or import our product candidates. There is a substantial amount of litigation, both within and outside the U.S., involving patent and other intellectual property rights in the biotechnology industry. Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields in which we are developing product candidates. Third-party patents or patent applications may include 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/or 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 U.S., 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 against such assertions, including that such patent rights are invalid and/or not infringed. 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.

Although no third party has asserted a claim of patent infringement against us as of the date of this periodic report, there can be no assurance that we will not be subject to claims of patent or other intellectual property infringement in the future. 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. We may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by our activities. 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. 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. 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 ambiguity in the meaning of patent claims.

Third parties may assert patent infringement claims 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 would involve substantial litigation expense and would be a substantial diversion of management and employee resources from our business. 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. 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.

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 our 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 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.

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.

Changes in either the patent laws or in the interpretations of patent laws in the U.S. 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, the U.S. 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.

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 U.S. 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. Similarly, foreign courts have made and will 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 U.S. and foreign legislative bodies. 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 product candidates. 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 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 U.S., 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. 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 U.S. 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.

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 U.S. can be less extensive than those in the U.S. 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 U.S., 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 U.S., even in jurisdictions where we or our licensors do pursue patent protection. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own competing 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 U.S.

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.

In Europe, expected by the end of 2023, European applications will soon have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the Unitary Patent Court (UPC). This will be a significant change in European patent practice. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation. As a single court system can invalidate a European patent, we, where applicable have opted out of the UPC and as such, each European patent would need to be challenged in each individual country.

Geo-political actions in the U.S. and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors. For example, the U.S. and foreign government actions related to Russia's invasion of Ukraine may limit or prevent filing, prosecution and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia. If such an event were to occur, it could have a material adverse effect on our business. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees that have citizenship or nationality in, are registered in, or have predominately primary place of business or profit-making activities in the U.S. and other countries that Russia has deemed unfriendly without consent or compensation. Consequently, we would not be able to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia. Accordingly, 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 U.S. at various points over the lifetime of our potential future patents and patent applications and those of our licensors. 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 U.S. 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 on 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, that these parties will not breach such agreements and disclose our proprietary information, including our trade secrets, or that we would be able to obtain adequate remedies for such breaches should they occur. We may not be able to prevent the unauthorized disclosure or use of our trade secrets. 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 U.S. are less willing or unwilling to protect trade secrets. 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.

Moreover, third parties may still derive similar information independently, and we would have no right to prevent them from using that information to compete with us. We expect know-how and information to be disseminated over time within the industry through independent development, publication of journal articles, and movement of personnel between companies and from academic to industry scientific positions. We 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.

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.

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 confidential or other information proprietary of their former employers or their former or current clients.

In addition, we have entered into and may in the future enter into non-disclosure and confidentiality agreements to protect the proprietary positions of third parties, such as collaborators, CROs, third-party manufacturers, consultants, potential partners 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 any such claims, regardless of their merit, could involve substantial litigation expense and be a substantial diversion of resources from our business. We cannot predict whether we would prevail in any such claims. 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, including the loss of valuable intellectual property rights or personnel, all of 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 us obtaining licenses from others and the terms and conditions of such licenses. If we fail to comply with our obligations in any agreement under which we license intellectual property rights from third parties, we could lose licensed rights that are important to our business.

We have entered into and may in the future enter into additional license agreements with third parties to advance our research or allow commercialization of product candidates. These licenses may not provide us with exclusive rights in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products.

In addition, 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 If our licensors fail to prosecute, maintain, enforce, and defend, or lose rights to such patents or patent applications, the rights we have licensed may be reduced or eliminated, and our right to develop and commercialize any product that is the subject of such licensed rights could be adversely affected. Even where we have the right to control patent prosecution of patents and patent applications we have licensed from third parties, we may still be adversely affected or prejudiced by actions or inactions taken by or on behalf of our licensors prior to the date upon which we assumed control over patent prosecution.

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, our rights to use the licensed intellectual property would not be exclusive and they may be able to license such patents to our competitors, permitting our competitors to market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

For example, the intellectual property we license from UTSW is subject to certain non-commercial rights reserved by UTSW. 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.

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. If any such event occurs, competitors or other third parties may gain the freedom to seek regulatory approval of, and to market, products identical to ours. Further, 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. This could have a material adverse effect on our competitive position, business, financial condition, results of operations, and prospects.

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. Disputes may arise between us and our current and future licensors. 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. 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.

Our licensors may also 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 our 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.

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, and we may acquire or in-license in the future, certain patents, patent applications or other intellectual property generated using 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 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 generated using 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 U.S. 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, and 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 U.S. or that under the circumstances domestic manufacture is not commercially feasible. 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 our clinical trials, and plan to rely on third parties to conduct such future drug development activities. These third parties may not perform satisfactorily, including failing to meet completion deadlines, or to comply with applicable regulatory requirements, which may harm our business.

The third parties upon which we rely to conduct our preclinical studies and clinical trials have a significant role in the conduct of such drug development activities 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 devotes to our preclinical studies or our clinical trials. Furthermore, the competition for third parties has increased as a result of the COVID-19 pandemic. 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. If we need to enter into alternative arrangements with, or replace or add any third parties, it would involve a transition period, and may require substantial cost and extensive management time and focus. Any of these events may delay our drug development activities, increase costs, and materially impact our ability to meet our desired clinical development timelines.

Our heavy reliance on these third parties for such drug development activities reduces our control over these activities. As a result, we have less direct control over the conduct, timing and completion of preclinical studies and clinical trials and the management of data developed through such drug development activities than if we were relying entirely upon our own staff. Nevertheless, we are responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with applicable protocol, legal and regulatory requirements and scientific standards, such as GCP and cGMP, and our reliance on third parties does not relieve us of these responsibilities. Regulatory authorities enforce these requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable requirements, such as GCP or cGMP, 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 applicable regulations. 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, or may be delayed in, obtaining marketing approvals for our product candidates or otherwise successfully commercializing our product candidates.

We rely on third parties to produce certain of our product candidates. This increases the risk that we will not have sufficient quality and quantities of product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our business.

We completed the build-out and operational launch of our cGMP manufacturing facility in June 2022 and have established end-to-end in-house AAV manufacturing capabilities to support our Gene Therapy and Cellular Regeneration platforms. However, in order to optimize our use of resources and availability of 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 the COVID-19 pandemic and we have experienced delays in supply chain activities as a result.

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 may have, 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 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. Furthermore, any decision by us to change a third-party manufacturer 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 may be unable to maintain or establish required agreements with third-party manufacturers on acceptable terms. Even if we are able to do so, 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 manufacture our product candidates according to our specifications or comply with applicable regulatory requirements, including cGMP;
- 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.

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 provide us with necessary quantities of API, drug substance and drug product based on our development needs. As we advance our product candidates through development, we will consider our lack of redundant supply 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.

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 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, especially in light of the supply chain issues caused by the effects of the COVID-19 pandemic, that we require or satisfy our anticipated specifications and quality requirements. 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 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.

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;
- unauthorized use or disclosure of our confidential information accessed in connection with partnership activities;
- 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;
- 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; and
- our inability to realize anticipated efficiencies and strategic benefits from such acquisitions or strategic partnerships.

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.

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

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. The collaboration negotiation process is time-consuming and

complex. 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. 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 stage of development, 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, alternative product candidates or technologies, and industry and market conditions generally.

If we are unable to reach a definitive agreement, 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.

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;
- the relationship 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;
- 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 an agreement with a collaborator 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.

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.

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 the Securities Market and Ownership of Our Common Stock

An active, liquid and orderly trading market may not continue to be developed or sustained for our common stock and as a result it may be difficult for you to sell your shares of our common stock.

The trading market for our common stock on the Nasdaq Global Select Market has been limited and an active trading market for our shares may not be sustained. The lack of an active market may also reduce the fair market

value of your shares of common stock. 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 is volatile, and you could lose all or part of your investment.

The trading price of our common stock is 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 periodic report, these factors include:

- the timing of achievement of our research, clinical, regulatory and other milestones for our product candidates;
- the 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 product candidates or those of our competitors;
- actual or anticipated changes in our growth rate relative to our competitors;
- regulatory or legal developments in the U.S. and other countries;
- litigation, including 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 coverage and/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;
- fluctuations in interest rates and inflation rates; 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, 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;
- the cost of operating a manufacturing facility and manufacturing our 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;
- our ability to enroll patients in clinical trials and the timing of enrollment;
- the need to conduct unanticipated clinical trials or trials that are larger or more complex than anticipated;
- competition from existing and potential future products 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;
- our ability to establish and maintain collaborations, licensing or other arrangements;
- 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 U.S., either independently or working with third parties;
- 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 the COVID-19 pandemic 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.

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 December 31, 2022, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately 45% of our common stock. 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.

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. For example, we filed: (i) on August 10, 2022, a shelf registration statement on Form S-3 with the SEC that became effective on August 17, 2022 and allows us to undertake various equity and debt offerings up to $300.0 million (the Shelf Registration); (ii) on August 17, 2022, a prospectus supplement to the shelf registration statement that covers the offering, issuance and sale of up to $75.0 million of our common stock from time to time through an “at-the-market” program under the Securities Act and (iii) on November 17, 2022, a prospectus supplement to the Shelf Registration that covered the offering, issuance and sale of 25,429,716 shares of our common stock, at a public offering price of $2.60 per share, and pre-funded warrants to purchase 6,236,693 shares of our common stock, at a public offering price of $2.599 per pre-funded warrant (the Follow-On Prospectus Supplement), pursuant to which we received aggregate net proceeds of $76.9 million, after deducting the underwriting commissions and offering expenses. To date, we have not sold any shares under our “at-the-market” program.

Moreover, certain holders of our common stock 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. Registration of these shares under the Securities Act of 1933, as amended (Securities Act), would result in the shares becoming freely tradeable in the public market, subject to the restrictions of Rule 144 in the case of our affiliates. If these shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

We will incur 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 are 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). As a result of our initiatives to comply with such regulatory requirements, we incur significant legal, accounting and other expenses which may increase after we are no longer an “emerging growth company.” Moreover, our management and other personnel need to devote a substantial amount of time to these compliance initiatives.

In particular, as a public company we are required 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 are 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, unless we continue to qualify as a "smaller reporting company" at such time. To achieve compliance with Section 404 within the prescribed periods, we engage 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 deadlines imposed by the Sarbanes-Oxley Act.

Our internal control over financial reporting will not prevent or detect all errors and all fraud or prevent material weaknesses from being identified in such reporting. 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.

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.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws 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 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.

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 provide that the Court of Chancery of the State of Delaware and the federal district courts of the United States of America are 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 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.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

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., Suite 500, 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. In addition, we currently sublease approximately 105,000 square feet of additional office and laboratory space located at 131 Oyster Point Blvd, South San Francisco, CA 94080 through November 30, 2023.

We also have a leased space at a facility in Union City containing manufacturing and office space located at 33498 Central Avenue, Union City, CA 94587. The lease expires in July 2031, 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.

Item 3. Legal Proceedings.

From time to time, we may become involved in litigation or other legal proceedings that arise in the ordinary course of our business. We are not currently a party to any litigation or legal proceedings that 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.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Our common stock is traded on the Nasdaq Global Select Market under the symbol "TNYA". Public trading of our common stock began on July 30, 2021. Prior to that, there was no public market for our common stock.

Holders of Common Stock

As of March 2, 2023, there were 48 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees.

Dividend Policy

We have never declared or paid any cash dividends on our common stock and do not anticipate paying cash dividends in the foreseeable future.

Recent Sales of Unregistered Securities

None.

Securities Authorized for Issuance under Equity Compensation Plans

Information about our equity compensation plans is incorporated herein by reference to Part III, Item 12 of this Annual Report.

Use of Proceeds from Public Offering of Common Stock

On August 3, 2021, we completed our initial public offering (IPO) and issued an aggregate of 13,800,000 shares of our common stock (inclusive of 1,800,000 shares pursuant to the underwriters' overallotment option) at a price of $15.00 per share. The gross proceeds from the offering for shares sold in our IPO was $207.0 million. We received net proceeds from the IPO of $188.5 million, after deducting underwriting discounts and commissions of approximately $14.5 million and offering expenses of approximately $4.0 million. None of the expenses associated with the IPO were paid to directors, officers, persons owning 10% or more of any class of equity securities, or to their associates. Morgan Stanley & Co. LLC, Piper Sandler & Co. and Cowen and Company, LLC acted as book-running managers for the IPO. Shares of our common stock began trading on the Nasdaq Global Select Market on July 30, 2021. The offer and sale of the shares were registered under the Securities Act on a registration statement on Form S-1 (Registration No. 333-257820), which was declared effective on July 29, 2021. There has been no material change in the planned use of proceeds from our IPO as described in the registration statement on Form S-1.

Issuer Purchases of Equity Securities

Not applicable.

Item 6. Reserved

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our financial statements and related notes included elsewhere in this Annual Report on Form 10-K. The following discussion contains forward-looking statements that are based upon current expectations that involve risks, uncertainties and assumptions. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of many factors, including those discussed under "Risk Factors" and elsewhere in this Annual Report on Form 10-K. Please also see the section titled "Special Note Regarding Forward-Looking Statements."

Overview

We are a clinical-stage biotechnology company focused on discovering, developing and delivering 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 deep and diverse pipeline of disease-modifying therapies that includes both gene therapies and small molecules discovered internally and developed using our product platforms and core capabilities to target defined sub-populations of patients with rare or highly prevalent forms of heart disease. All of our programs are currently being assessed in clinical trials or are in the preclinical stage; we do not have any products approved for sale and have not generated any revenue to date.

Our lead product candidates include, TN-201, a gene therapy for *MYBPC3*-associated HCM, TN-301, a small molecule for HFpEF, and TN-401, a gene therapy for *PKP2*-associated ARVC.

TN-201 is our first-in-class gene therapy for adults and children with HCM due to *MYBPC3* gene mutations. These mutations can cause the heart walls of affected individuals to become significantly thickened, leading to fibrosis, abnormal heart rhythms, cardiac dysfunction and heart failure. HCM is a chronic, progressive condition and those diagnosed with disease often experience significant impairment in overall quality of life. TN-201 uses a differentiated approach to deliver a functional *MYBPC3* gene to the heart utilizing a recombinant AAV9 capsid to restore expression of the cardiac myosin binding protein to halt disease progression and potentially reverse the course of genetic HCM following a single intravenous injection. In January 2023, we received notification from the FDA that clinical testing of TN-201 may proceed, and in the third quarter of 2023, we expect to begin dosing patients in a Phase 1b multi-center, open-label clinical trial, designed to assess the safety, tolerability and efficacy of a one-time intravenous infusion of TN-201. TN-201 has received orphan drug designation from FDA and orphan medicinal product designation from the EC.

In order to support our development efforts for TN-201, we have initiated two noninterventional studies: a study evaluating seroprevalence to AAV9 antibodies among adults with *MYBPC3*-associated HCM, and MyClimb, a prospective and retrospective global natural history study focused on pediatric patients with *MYBPC3* mutation-associated cardiomyopathy. The objective of the natural history study is to characterize the outcomes, burden of illness, risk factors, quality of life, and biomarkers associated with disease progression in pediatric patients with cardiomyopathy due to *MYBPC3* gene mutations, as well as treatments, procedures, and patient outcomes. MyClimb complements existing disease registries focused primarily on adult patient HCM populations and may support and expedite the development of TN-201 in the pediatric patient population.

TN-301 is our highly specific small molecule inhibitor of histone deacetylase 6. TN-301 is initially being developed for the potential treatment of HFpEF. HFpEF is characterized by a stiffening of the heart muscle resulting in an inability for the left ventricle to relax properly during normal heart rhythm, referred to as diastolic dysfunction. There are several cellular processes thought to underly the pathophysiology of HFpEF including increases in fibrosis and inflammation and defects in metabolism. Although HFpEF accounts for approximately 50% of all heart failures, there are few proven treatment options. We are currently conducting a Phase 1 clinical trial in healthy adult participants to evaluate the safety, tolerability, pharmacokinetics and PD of escalating oral doses of TN-301. The Phase 1 clinical trial is being conducted in two stages: a SAD stage and a MAD stage. In the SAD stage of the trial, initial target engagement (as measured by the PD biomarker of tubulin acetylation) was achieved at dose levels thought to be in therapeutic ranges, enabling the initiation of the MAD stage of the clinical trial, which commenced in February 2023. In preclinical studies, dose dependent tubulin acetylation measured in circulating blood cells was found to correlate to levels in the heart. Data from both the SAD and MAD stages of the trial are anticipated in the second half of 2023.

TN-401 is our other AAV-based gene therapy designed to deliver a functional *PKP2* gene in adults with ARVC due to a *PKP2* genetic mutation. *PKP2* 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. TN-401, has demonstrated prevention of disease progression and survival benefit after a single dose in a mouse model of ARVC, as well as tolerability in a pilot non-Good Laboratory Practices toxicology and biodistribution study. We have initiated IND-enabling studies for TN-401 and expect to submit an IND to the FDA in the second half of 2023 to enable clinical development of TN-401. TN-401 has received orphan drug designation from the FDA. Additionally, in support of our development efforts for TN-401, we have initiated a global non-interventional study to collect treatment history and seroprevalence to AAV9 antibodies data among ARVC patients who carry pathogenic or likely pathogenic *PKP2* gene mutations.

In addition to our lead product candidates, we have multiple early-stage programs progressing through pre-clinical development. These programs include an AAV-based gene therapy designed to express the DWORF gene in the heart with potentially broad utility in DCM, as well as our reprogramming program for cardiac regeneration which aims to replace heart cells lost in patients experiencing heart failure due to prior MI. While these named programs have reached candidate selection stage, we also have numerous earlier-stage programs emerging from our proprietary product platforms to address other forms of heart failure.

Our distinct, but interrelated Gene Therapy, Cellular Regeneration and Precision Medicine platforms and suite of integrated capabilities support our efforts to discover disease-modifying treatments focused on heart disease in a modality-agnostic manner. We also continue to invest in complementary new technologies and the optimization of our existing proprietary capabilities, including the use of human-iPSC disease models, machine learning and phenotypic screening, capsid engineering and novel promoter constructs to enable the discovery, design, delivery and development of therapeutics that are best suited to a given cardiovascular condition. In 2022, we also launched operations of our GMMC based in Union City, CA. The facility utilizes a modular, scalable design to produce AAV-based gene therapies under current GMP standards.

Results of Operations

Comparison of the Years Ended December 31, 2022 and 2021

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

	Year Ended December 31,		$	%
(in thousands, except percentages)	**2022**	**2021**	**Change**	**Change**
Operating expenses:				
Research and development	$ 94,537	$ 54,393	$ 40,144	74%
General and administrative	31,084	18,413	12,671	69%
Total operating expenses	125,621	72,806	52,815	73%
Loss from operations	(125,621)	(72,806)	(52,815)	73%
Other income (expense), net:				
Interest income	1,954	108	1,846	1,709%
Other income (expense), net	2	(23)	25	109%
Total other income (expense), net	1,956	85	1,871	2,201%
Net loss	$ (123,665)	$ (72,721)	$ (50,944)	70%

Research and Development Expenses

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, employee-related costs (including salaries, benefits and stock-based compensation for employees engaged in research and development functions), laboratory supplies, other non-capital equipment utilized for in-house research and allocated overhead costs. External research and development expenses include, among others, fees paid to CROs to execute preclinical studies and clinical trials on our behalf, consulting fees and fees related to 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.

We expense all research and development costs in the periods in which they are incurred. We enter into various agreements with CROs. Costs of certain research and development activities are recognized based on estimates generally based on an evaluation of the progress and input from external service providers.

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

	Year Ended December 31,		$	%
(in thousands, except percentages)	**2022**	**2021**	**Change**	**Change**
Facility and laboratory costs	$ 33,095	$ 22,833	$ 10,262	45%
Outside services	30,930	13,406	17,524	131%
Personnel-related costs	29,369	17,729	11,640	66%
Other research and development expenses	1,143	425	718	169%
Total research and development expenses	$ 94,537	$ 54,393	$ 40,144	74%

Research and development expenses were $94.5 million and $54.4 million for the years ended December 31, 2022 and 2021, respectively. The increase of $40.1 million, or 74%, was primarily due to:

- an increase of $10.3 million in facility and laboratory costs, including manufacturing and laboratory supplies and materials and other allocated costs;
- an increase of $17.5 million in outside services, including costs incurred for CROs on the IND-enabling and other research and development activities, preclinical studies and other external research expenses; and
- an increase of $11.6 million in employee-related costs reflecting higher stock-based compensation from growth in the number of our research and development employees, partially offset by benefits from estimated employee tax credits.

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 cannot reasonably estimate or know the nature, timing or estimated costs of the efforts that will be necessary to complete the development of, and obtain regulatory approval for, 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 and stock-based compensation for our employees in finance, human resources and other administrative functions), legal fees, professional fees incurred for accounting, audit and tax services, information technology and facility costs not otherwise included in research and development expenses. Legal fees primarily include those related to corporate and intellectual property related matters.

We expect that our general and administrative expenses will generally increase for the foreseeable future to support our continued research and development activities, future business development opportunities and professional fees. In addition, we will continue to incur legal, accounting, insurance and other expenses in operating our business as a public company, including costs associated with regulatory and compliance activities.

General and administrative expenses were $31.1 million and $18.4 million for the years ended December 31, 2022 and 2021, respectively. The increase of $12.7 million, or 69%, was primarily due to an $8.2 million increase in employee-related expenses reflecting higher stock-based compensation from growth in the number of employees, partially offset by benefits from estimated employee tax credits. The increase is also due to a $2.2 million increase in professional and outside service expenses and a $1.0 million increase in insurance costs.

Interest Income

Interest income primarily consists of interest earned on our cash, cash equivalents and investment balances. The year-over-year increase of $1.8 million was primarily due to rising interest rates during the year ended December 31, 2022.

Other Income (Expense), Net

Other income (expense), net primarily consists of gain and loss on disposal of assets and foreign exchange.

Net Loss

Net loss for the year ended December 31, 2022, was $123.7 million, compared to a net loss of $72.7 million for the year ended December 31, 2021.

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. From our inception through December 31, 2022, we have funded our operations primarily from the sale and issuance of our equity securities. As of December 31, 2022, we had cash, cash equivalents and investments in marketable securities of $204.2 million and an accumulated deficit of $279.2 million.

Follow-on Offering

On November 21, 2022, we completed an underwritten public offering of 22,613,307 shares of our common stock at a price of $2.60 per share and, to certain investors in lieu of common stock, pre-funded warrants to purchase 6,236,693 shares of our common stock at a price of $2.599 per pre-funded warrant under our registration statement on Form S-3 (File No. 333-266741) (the Shelf Registration Statement). The pre-funded warrants can be exercised at any time after issuance for an exercise price of $0.001 per share, subject to certain ownership limitations. In addition, we granted the underwriters a 30-day option to purchase up to an additional 4,327,500 shares of our common stock to cover overallotments, if any, at $2.60 per share. On November 29, 2022, the underwriters partially exercised the option and purchased an additional 2,816,409 shares of our common stock. We received total net proceeds of $76.9 million after deducting underwriting discounts and commissions of $4.9 million and offering expenses of $0.5 million. The offering expenses were paid in January 2023.

"At-the-Market" Equity Offering

On August 10, 2022, we entered into a sales agreement (Sales Agreement) with SVB Securities LLC (SVB Securities). Pursuant to the Sales Agreement we may sell, from time to time up to an aggregate of $75.0 million of our common stock through an "at-the-market" offering defined in Rule 415 under the Securities Act. We will pay SVB Securities a commission equal to 3.0% of the gross proceeds from the sale of shares of our common stock under the Sales Agreement. The $75.0 million of common stock that may be offered, issued and sold under the Sales Agreement is included in the $300.0 million of securities that may be offered, issued and sold by us under the Shelf Registration Statement. As of December 31, 2022, no shares have been sold pursuant to the Sales Agreement.

Funding Requirements

We expect our expenses and operating losses will continue to increase 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 lead product candidates, TN-201, TN-301 and TN-401, in and toward the clinic;
- continue preclinical development of our earlier-stage product candidates and initiate additional preclinical studies using our Gene Therapy, Cellular Regeneration and Precision Medicine platforms and core capabilities;

- operate our manufacturing facility and develop our manufacturing capabilities;
- seek regulatory approval of our product candidates that successfully complete clinical trials;
- expand our operational, financial, and information systems, including personnel to support our preclinical and clinical development, manufacturing, system infrastructure, regulatory compliance and future commercialization efforts;
- continue to develop, grow, perfect, enforce and defend our intellectual property portfolio; and
- continue to incur legal, accounting, insurance and other expenses in operating our business as a public company, including costs associated with regulatory and compliance activities.

Based on our current operating plan, we believe that our existing cash, cash equivalents and investments in marketable securities will be sufficient to meet our working capital and capital expenditure needs through at least the next twelve months following the date of this Annual Report on Form 10-K.

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 continued worsening global economic conditions and the recent disruptions to, and volatility in, the credit and financial markets in the United States and worldwide. 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,	
	2022	2021
	(In thousands)	
Net cash provided by (used in):		
Operating activities	$ (104,424)	$ (60,812)
Investing activities	83,652	(238,564)
Financing activities	77,767	208,970
Net change in cash, cash equivalents and restricted cash	$ 56,995	$ (90,406)

Operating Activities

Net cash used in operating activities for the year ended December 31, 2022 was $104.4 million, which consisted of a net loss of $123.7 million and a net change in operating assets and liabilities of $0.8 million, partially offset by $20.0 million in non-cash charges. The change in net operating assets and liabilities was due to a decrease

in operating lease liabilities of $3.1 million, a decrease in prepaid expenses and other current assets of $2.9 million and an increase in other noncurrent assets of $0.8 million, partially offset by an increase in accounts payable and accrued expenses and other current liabilities of $6.0 million. Cash flows from operations are generally impacted by the timing of payments to vendors and vendor payment terms. The non-cash charges primarily consisted of stock-based compensation of $11.5 million and depreciation and amortization of $6.5 million.

Net cash used in operating activities for the year ended December 31, 2021, was $60.8 million, which consisted primarily of a net loss of $72.7 million, offset by $7.2 million in non-cash charges and a net change in net operating assets and liabilities of $4.7 million. The non-cash charges primarily consisted of depreciation and amortization of $3.0 million, stock-based compensation of $3.0 million and non-cash operating lease expense of $1.1 million. The change in net operating assets and liabilities was primarily due to an increase in accounts payable and accrued expenses and other current liabilities of $11.9 million, partially offset by an increase in other non-current assets of $3.1 million related to a security deposit for a lease entered into in February 2021, an increase in prepaid expenses and other current assets of $2.7 million, and a decrease in operating lease liabilities of $1.5 million.

Investing Activities

Net cash provided by investing activities for the year ended December 31, 2022 was $83.7 million, which consisted primarily of proceeds from maturities of marketable securities of $244.8 million, partially offset by purchases of marketable securities of $140.5 million and purchases of property and equipment of $20.6 million primarily related to our manufacturing and office space in Union City, California.

Net cash used in investing activities for the year ended December 31, 2021, was $238.6 million, which consisted of purchases of marketable securities of $213.4 million and purchases of property and equipment of $25.1 million.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2022, was $77.8 million, which primarily consisted of proceeds from our follow-on public offering, net of issuance costs, of $77.4 million.

Net cash provided by financing activities for the year ended December 31, 2021, was $209.0 million, which primarily consisted of proceeds from our initial public offering, net of issuance costs, of $188.5 million, net proceeds received from the sale and issuance of our Series C convertible preferred stock of $20.0 million, and proceeds from the exercise of stock options of $0.4 million.

Contractual and Other Obligations

We lease office space for our corporate headquarters in South San Francisco under a lease that expires in May 2025. We expect to pay rent of approximately $2.5 million during 2023 for this lease. We also lease the Union City Facility under a lease that expires in July 2031. We expect to pay rent of approximately $1.3 million in 2023 for this lease. In addition, we sublease additional office and laboratory space in South San Francisco through November 30, 2023 and expect to pay rent of approximately $1.4 million in 2023 for this sublease. As of December 31, 2022, undiscounted future minimum lease payments of $6.2 million and $12.2 million remain on the South San Francisco and Union City leases, respectively.

In addition, we enter into agreements in the normal course of business with vendors for preclinical research studies, clinical trials and other services and products for operating purposes. These contracts do not contain any minimum purchase commitments and are generally cancelable upon written notice. Payments due upon cancellation consist only of payments for services provided and expenses incurred up to the date of cancellation.

We have also entered into license agreements under which we are obligated to make specified milestone and royalty payments. The payment obligations under these agreements are contingent upon future events, such as our achievement of specified development, regulatory, and sales milestones, or generating product sales. Generally, the timing or likelihood of achieving these milestones or generating future product sales are not determinable.

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 (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 Annual Report, 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 expenses 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 expenses and actual expenses 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 made upon regulatory approval are capitalized and amortized over the remaining useful life of the related product.

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, we recognize the expense 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 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*—Prior to our IPO, there was no public market for our common stock. As such, the estimated fair value of our common stock and underlying stock options was determined at each grant date by our board of directors, with input from management, based on the information known to us on the grant date and upon a review of any recent events and their potential impact on the estimated per share fair value of our common stock. As part of these fair value determinations, our board of directors obtained and considered valuation reports prepared by a third-party valuation firm in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting & Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. For grants

subsequent to our IPO, the grant date fair value of common stock was determined by using the closing price per share of common stock as reported on the Nasdaq Global Select Market.

- *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 we have limited trading history of 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. We expect to continue to apply this process until enough historical information regarding the volatility of our own stock price becomes available.
- *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 financial statements 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.

Recent Accounting Pronouncements

See *Note 2* to our financial statements 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 $1.235 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) December 31, 2026.

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 by 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 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 if either (i) the market value of our stock held by non-affiliates is less than $250 million or (ii) our annual revenue is 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 company’s smaller reporting companies have reduced disclosure obligations regarding executive compensation.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are a smaller reporting company, as defined by Rule 12b-2 under the Securities and Exchange Act of 1934 and in Item 10(f)(1) of Regulation S-K, and are not required to provide the information under this item.

Item 8. Financial Statements and Supplementary Data.

INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the stockholders and the 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, 2022 and 2021, the related statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit), and cash flows, for each of the two years in the period ended December 31, 2022, 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, 2022 and 2021, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2022, 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 & Touche LLP

San Francisco, California
March 8, 2023

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, 2022	December 31, 2021
ASSETS		
Current assets:		
Cash and cash equivalents	$ 95,272	$ 38,129
Short-term investments in marketable securities	91,255	213,171
Prepaid expenses and other current assets	7,227	4,058
Total current assets	193,754	255,358
Property and equipment, net	51,032	43,020
Operating lease right-of-use assets	11,663	11,685
Long-term investments in marketable securities	17,703	—
Other noncurrent assets	4,793	4,126
Total assets	$ 278,945	$ 314,189
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 9,578	$ 10,721
Accrued and other current liabilities	10,664	9,059
Operating lease liabilities, current	4,006	1,994
Total current liabilities	24,248	21,774
Operating lease liabilities, noncurrent	11,093	13,707
Other noncurrent liabilities	228	182
Total liabilities	35,569	35,663
Commitments and contingencies (Note 6)		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 200,000,000 shares authorized as of December 31, 2022 and 2021; no shares issued and outstanding as of December 31, 2022 and 2021	—	—
Common stock, $0.0001 par value; 1,000,000,000 shares authorized as of December 31, 2022 and 2021; 66,857,113 and 41,291,374 shares issued and outstanding as of December 31, 2022 and 2021	7	4
Additional paid-in capital	522,945	434,196
Accumulated other comprehensive loss	(378)	(141)
Accumulated deficit	(279,198)	(155,533)
Total stockholders' equity	243,376	278,526
Total liabilities and stockholders' equity	$ 278,945	$ 314,189

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,	
	2022	**2021**
Operating expenses:		
Research and development	$ 94,537	$ 54,393
General and administrative	31,084	18,413
Total operating expenses	125,621	72,806
Loss from operations	(125,621)	(72,806)
Other income (expense), net:		
Interest income	1,954	108
Other income (expense), net	2	(23)
Total other income (expense), net	1,956	85
Net loss before income tax expense	(123,665)	(72,721)
Income tax expense	—	—
Net loss	(123,665)	(72,721)
Other comprehensive loss:		
Net unrealized loss on marketable securities	(237)	(141)
Comprehensive loss	$ (123,902)	$ (72,862)
Net loss per share, basic and diluted	$ (2.76)	$ (4.10)
Weighted-average shares used in computing net loss per share, basic and diluted	44,823,597	17,734,166

The accompanying notes are an integral part of these financial statements.

	Convertible Preferred Stock		Common Stock		Additional Paid-In	Notes Receivable from Stockholders	Accumulated Other Comprehensive	Accumulated	Total Stockholders' Equity
	Shares	Amount	Shares	Amount	Capital		Loss	Deficit	(Deficit)
Balance as of January 1, 2021	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	—	—	—	—	—	—	—
Conversion of convertible preferred stock to common stock upon completion of initial public offering	(26,102,278)	(240,735)	26,102,278	3	240,732	—	—	—	240,735
Issuance of common stock upon initial public offering, net of issuance costs of $18,459	—	—	13,800,000	1	188,540	—	—	—	188,541
Issuance of common stock upon exercise of stock options	—	—	195,749	—	358	—	—	—	358
Repurchase of common stock related to early exercise of options	—	—	(16,959)	—	—	—	—	—	—
Vesting of early exercised stock options	—	—	—	—	32	—	—	—	32
Notes receivable from stockholders	—	—	—	—	—	87	—	—	87
Stock-based compensation	—	—	—	—	2,950	—	—	—	2,950
Other comprehensive loss	—	—	—	—	—	—	(141)	—	(141)
Net loss	—	—	—	—	—	—	—	(72,721)	(72,721)
Balance as of December 31, 2021	—	$ —	41,291,374	$ 4	$ 434,196	$ —	$ (141)	$ (155,533)	$ 278,526
Issuance of common stock and pre-funded warrants, net of issuance costs of $5,441	—	—	25,429,716	3	76,883	—	—	—	76,886
Issuance of common stock upon exercise of stock options and vesting of restricted stock units	—	—	32,609	—	51	—	—	—	51
Issuance of common stock pursuant to employee stock purchase plan	—	—	106,192	—	329	—	—	—	329
Repurchase of common stock related to early exercise of options	—	—	(2,778)	—	—	—	—	—	—
Vesting of early exercised stock options	—	—	—	—	19	—	—	—	19
Stock-based compensation	—	—	—	—	11,467	—	—	—	11,467
Other comprehensive loss	—	—	—	—	—	—	(237)	—	(237)
Net loss	—	—	—	—	—	—	—	(123,665)	(123,665)
Balance as of December 31, 2022	—	$ —	66,857,113	$ 7	$ 522,945	$ —	$ (378)	$ (279,198)	$ 243,376

The accompanying notes are an integral part of these financial statements.

TENAYA THERAPEUTICS, INC.
Statements of Cash Flows
(in thousands)

	Year Ended December 31,	
	2022	**2021**
Cash flows from operating activities:		
Net loss	$ (123,665)	$ (72,721)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	6,467	2,961
Amortization (accretion) of premium (discount) on marketable securities	(307)	131
Stock-based compensation	11,467	2,950
Non-cash operating lease expense	2,246	1,064
Other	217	61
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(2,934)	(2,730)
Other noncurrent assets	(815)	(3,114)
Accounts payable	1,660	8,600
Accrued and other current liabilities	4,348	3,295
Operating lease liabilities	(3,107)	(1,472)
Other noncurrent liabilities	(1)	163
Net cash used in operating activities	(104,424)	(60,812)
Cash flows from investing activities:		
Purchases of property and equipment	(20,630)	(25,121)
Purchases of marketable securities	(140,476)	(213,443)
Proceeds from maturities of marketable securities	244,750	—
Other	8	—
Net cash provided by (used in) investing activities	83,652	(238,564)
Cash flows from financing activities:		
Proceeds from issuance of common stock and pre-funded warrants in follow-on offering, net of issuance costs	77,387	—
Proceeds from issuance of Series C convertible preferred stock, net of issuance costs	—	19,981
Proceeds from initial public offering, net of issuance costs	—	188,541
Proceeds from exercise of stock options and employee stock purchase plan	380	374
Repurchase of common stock	—	(13)
Proceeds from repayments on notes receivable from stockholders	—	87
Net cash provided by financing activities	77,767	208,970
Net change in cash, cash equivalents and restricted cash	56,995	(90,406)
Cash and cash equivalents and restricted cash at beginning of period	38,676	129,082
Cash and cash equivalents and restricted cash at end of period	$ 95,671	$ 38,676
Components of cash, cash equivalents and restricted cash:		
Cash and cash equivalents	$ 95,272	$ 38,129
Restricted cash included in other noncurrent assets	399	547
Cash, cash equivalents and restricted cash	$ 95,671	$ 38,676
Supplemental disclosure of non-cash investing and financing activities:		
Conversion of convertible preferred stock to common stock upon completion of initial public offering	$ —	$ 240,735
Offering costs related to November 2022 public offering included in accounts payable and accrued and other current liabilities	$ 501	$ —
Property and equipment included in accounts payable and accrued and other current liabilities	$ 549	$ 4,100

The accompanying notes are an integral part of these financial statements.

Note 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 clinical-stage biotechnology company focused on discovering, developing and delivering curative therapies that address the underlying drivers of heart disease. The Company's lead product candidates include, TN-201, a gene therapy for myosin binding protein C3-associated hypertrophic cardiomyopathy, TN-301, a small molecule for heart failure with preserved ejection fraction, and TN-401, a gene therapy for plakophilin 2-associated arrhythmogenic right ventricular cardiomyopathy (ARVC).

Reverse Stock Split

In July 2021, the Company's board of directors approved an 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 convertible preferred stock was not adjusted as a result of the Reverse Stock Split. All share data, per share data and related information for all periods presented in the accompanying financial statements have been retrospectively adjusted to reflect the effect of the Reverse Stock Split.

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, 2022, the Company had an accumulated deficit of $279.2 million. The Company incurred a net loss of $123.7 million and $72.7 million during the years ended December 31, 2022 and 2021, respectively. The Company had $204.2 million of cash, cash equivalents and investments in marketable securities as of December 31, 2022.

Management recognizes the need to raise additional capital to fully implement its business plan. The Company 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, cash equivalents and investments in marketable securities as of December 31, 2022 will be sufficient to fund the Company's operations for at least the next twelve months following the date these financial statements are filed with the Securities and Exchange Commission (SEC).

Note 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).

Reclassification

Certain prior year balances have been reclassified in order to conform to current year presentation for the condensed balance sheets. These reclassifications have no effect on the previously reported financial position.

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. The Company 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 price that would be received to sell an asset or paid to transfer a liability (an exit price) in an orderly transaction between market participants at the reporting date. The accounting guidance establishes a three-tiered hierarchy, which prioritizes the inputs used in the valuation methodologies in measuring fair value as follows:

Level 1 - Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date.

Level 2 - Inputs other than quoted market prices included in Level 1 are either directly or indirectly observable for the asset or liability through correlation with market data at the measurement date and for the duration of the instrument's anticipated life.

Level 3 - Inputs reflect management's best estimate of what market participants would use in pricing the asset or liability at the measurement date. Consideration is given to the risk inherent in the valuation technique and the risk inherent in the inputs to the model.

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 that potentially subject the Company to concentration of risk consist principally of cash, cash equivalents and marketable securities. The Company maintains deposits in cash and cash equivalents in federally insured financial institutions that it believes have high credit quality. Such deposits may exceed federally insured limits. The Company is exposed to credit risk in the event of default by the financial institutions holding its cash and cash equivalents and the issuers of its investments in marketable securities to the extent recorded in the balance sheets. 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.

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 that are stated at fair value.

Restricted Cash

The restricted cash represents security deposits for the Company's operating leases in South San Francisco, and Union City, 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, commercial paper and corporate bonds. 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. Impairment of long-lived assets were not material for any of the periods presented.

Leases

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.

Asset Retirement Obligation

The Company records asset retirement obligations (AROs) for the estimated cost of removing constructed leasehold improvement assets and restoring the leased premises back to their original condition, at the time when the contractual obligations are incurred. AROs represent the present value of the expected costs for the related restoration activities. The ARO assets and liabilities are recorded in property, plant and equipment and other long-term liabilities, respectively, in the Company's balance sheets. The Company records accretion expense, which represents the increase in the asset retirement obligations, over the remaining or operational life of the associated leasehold improvements. Accretion expense is recorded as operating expense in the statements of operations using an accretion rate based on the credit adjusted risk-free interest rate. Changes resulting from revisions to the timing or amount of the original estimate of cash flows are recognized as an increase or a decrease in the asset retirement cost, or income when the asset retirement cost is depleted.

Research and Development Expenses

Research and development (R&D) costs are expensed as incurred. Research and development expenses 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, fees related to licensing agreements, fees 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.

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.

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.

For purposes of determining the estimated fair value of options granted to employees and nonemployees, the Company uses the Black-Scholes option pricing model. See *Note 8* to the Company's financial statements for the specific assumptions used in applying the Black-Scholes valuation model.

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. As of December 31, 2022 and 2021, 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. Basic shares of common stock outstanding include the weighted-average effect of the Company's pre-funded warrants issued in November 2022 because the pre-funded warrants have a nominal exercise price. 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 that are subject to repurchase are excluded from the basic and diluted net loss per share calculation until the Company's repurchase right lapses.

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

In December 2019, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (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 became effective for the Company beginning January 1, 2022. The adoption of this standard did not have any impact on the Company's financial statements.

In November 2021, the FASB issued ASU No. 2021-10, *Government Assistance (Topic 832): Disclosures by Business Entities about Government Assistance (ASU 2021-10)*, which requires business entities to make annual disclosures about transactions with a government they account for by analogizing to a grant or contribution accounting model. The required annual disclosures include the nature of the transaction, the entity's related accounting policy, the financial statement line items affected and the amounts reflected in the current period financial statements, and any significant terms and conditions. ASU 2021-10 became effective for the Company beginning January 1, 2022. 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 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 will become effective for the Company beginning January 1, 2023. The Company does not expect the adoption of this standard will have a material impact on its financial statements.

Note 3. Fair Value Measurements

Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability (an exit price) in an orderly transaction between market participants at the reporting date. The accounting guidance establishes a three-tiered hierarchy, which prioritizes the inputs used in the valuation methodologies in measuring fair value as follows:

Level 1 - Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date.

Level 2 - Inputs other than quoted market prices included in Level 1 are either directly or indirectly observable for the asset or liability through correlation with market data at the measurement date and for the duration of the instrument's anticipated life.

Level 3 - Inputs reflect management's best estimate of what market participants would use in pricing the asset or liability at the measurement date. Consideration is given to the risk inherent in the valuation technique and the risk inherent in the inputs to the model.

The following tables summarize the Company's financial assets measured at fair value on a recurring basis by level within the fair value hierarchy:

		December 31, 2022			
	Valuation Hierarchy	Amortized Cost	Unrealized Gain	Unrealized Loss	Fair Value
		(In thousands)			
Assets:					
Cash equivalents:					
Cash equivalents	Level 1	$ 20,532	—	—	$ 20,532
Money market funds	Level 1	7,203	—	—	7,203
Commercial paper	Level 2	11,972	—	(4)	11,968
Government agencies bonds	Level 2	54,569	12	—	54,581
Marketable securities:					
U.S. treasuries	Level 1	25,273	1	(147)	25,127
Commercial paper	Level 2	43,605	4	(125)	43,484
Corporate bonds	Level 2	2,696	—	(18)	2,678
Government agencies bonds	Level 2	37,770	9	(110)	37,669
Total financial assets		$ 203,620	$ 26	$ (404)	$ 203,242

		December 31, 2021			
	Valuation Hierarchy	Amortized Cost	Unrealized Gain	Unrealized Loss	Fair Value
		(In thousands)			
Assets:					
Cash equivalents:					
Money market funds	Level 1	$ 37,129	$ —	$ —	$ 37,129
Marketable securities:					
U.S. treasuries	Level 1	78,097	—	(85)	78,012
Commercial paper	Level 2	121,634	—	(50)	121,584
Corporate bonds	Level 2	8,979	—	(3)	8,976
Government agencies bonds	Level 2	4,602	—	(3)	4,599
Total financial assets		$ 250,441	$ —	$ (141)	$ 250,300

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 observable inputs or can be derived from non-binding quotes from the Company's 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. To validate the fair value determination provided by its investment managers, the Company reviews the pricing movement in the context of overall market trends and trading information from its investment managers. In addition, the Company considers the inputs and methods used in determining the fair value in order to determine the classification of securities in the fair value hierarchy.

The Company believes it is more likely than not that its marketable securities in an unrealized loss position will be held until maturity or the recovery of the cost basis of the investment. To date, the Company has not recorded any impairment charges on marketable securities related to other-than-temporary declines in market value.

As of December 31, 2022, the fair value of available-for-sale marketable securities was $109.0 million. $91.3 million of available-for-sale marketable securities had remaining maturities of less than one year. The remaining $17.7 million of marketable securities had remaining maturities between one and two years.

The carrying amount of the Company's remaining financial assets and liabilities, which include cash, receivables and payables, approximate their fair values due to their short-term nature.

Note 4. Balance Sheet Components

Property and Equipment, Net

Property and equipment, net, consists of the following:

	December 31, 2022	December 31, 2021
	(In thousands)	
Leasehold improvements	$ 23,605	$ 7,241
Laboratory equipment	20,537	11,891
Manufacturing equipment	17,468	—
Construction in progress	3,128	32,561
Computer equipment and software	1,060	218
Furniture and fixtures	910	534
Total property and equipment	$ 66,708	$ 52,445
Less: accumulated depreciation and amortization	(15,676)	(9,425)
Total property and equipment, net	$ 51,032	$ 43,020

Depreciation and amortization expense for the years ended December 31, 2022 and 2021, was $6.5 million and $3.0 million, respectively. Leasehold improvements represent certain enhancements made to the Company's leased manufacturing and office space located in Union City, California (Union City Facility). During the quarter ended June 30, 2022, the Company completed the build out and operational launch of the Union City Facility. As a result, the Company reclassified the related capitalized machinery and equipment from construction in progress to manufacturing and laboratory equipment in that period.

Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consist of the following:

	December 31, 2022	December 31, 2021
	(In thousands)	
Accrued compensation and related expenses	$ 6,299	$ 3,667
Accrued research and development expenses	3,214	2,023
Accrued professional services	482	344
Accrued property and equipment	139	2,863
Other current liabilities	530	162
Total accrued and other current liabilities	$ 10,664	$ 9,059

Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets include a receivable of approximately $2 million relating to the employee retention credit (ERC) under the Coronavirus Aid, Relief, and Economic Security Act. The ERC is a refundable tax credit, which was provided to encourage businesses to keep employees on the payroll during the COVID-19 pandemic. During the year ended December 31, 2022, the Company recorded the receivable with the offsetting benefit included in operating expenses.

Note 5. License Agreements

Gladstone License Agreement

In October 2016, the Company entered into a license agreement with the J. David Gladstone Institute (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 up 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. Dr. Deepak Srivastava, M.D., a member of the Company's board of directors, serves as President of Gladstone. As of December 31, 2022, the Company has not recognized any milestone and royalty payments under the Gladstone License Agreement.

During the years ended December 31, 2022 and 2021, amounts recorded related to annual license fees payable pursuant to the Gladstone License Agreement were immaterial.

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, which was paid by the Company in 2020, (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, 2022, the Company has not recognized any milestone and royalty payments under 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.

Note 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.

In February 2021, the Company entered into a lease agreement for the Union City Facility. 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 was included in other noncurrent assets on the balance sheets.

In November 2021, 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 was initially set to expire on June 30, 2022. In May 2022, the Company entered into an amendment to extend the term for the existing sublease premise through December 31, 2022. Under the amendment, the Company also subleased additional office and laboratory space at the same sublease premise through November 30, 2023.

Information related to operating lease activity during the year ended December 31, 2022 was as follows (in thousands):

	Year Ended December 31,	
	2022	2021
Operating lease cost	$ 3,714	$ 2,364
Variable lease cost	1,209	$ 1,095
Short-term lease cost	952	2,241
Total lease cost	$ 5,875	$ 5,700
Operating lease-right-of-use assets obtained in exchange for lease obligations	$ 2,224	$ 8,558
Cash paid for leases included in operating cash outflows	$ 6,454	$ 6,110
Cash paid for amounts included in the measurement of lease liabilities	$ 4,293	$ 2,774

As of December 31, 2022, the Company's operating leases had a weighted average remaining lease term of 5.6 years and a weighted average discount rate of 9.3%. Future minimum lease payments under the Company's operating leases as of December 31, 2022 were as follows:

	Amount (In thousands)
2023	$ 5,223
2024	3,910
2025	2,445
2026	1,386
2027	1,428
Thereafter	5,477
Total undiscounted future minimum lease payments	$ 19,869
Imputed interest	(4,770)
Total operating lease liabilities	$ 15,099

Asset Retirement Obligation

Under the lease agreement for the Union City Facility, the Company is contractually obligated to remove constructed leasehold improvements related to capitalized machinery and equipment (see *Note 4*) and to restore the leased space to its original condition upon termination of the lease agreement. As of December 31, 2022, the balance of the asset retirement obligation liability was not material.

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

From time to time, the Company may become involved in litigation and other legal actions. The Company estimates the range of liability related to any pending litigation where the amount and range of loss can be estimated. The Company records its best estimate of a loss when the loss is considered probable. Where a liability is probable and there is a range of estimated loss with no best estimate in the range, the Company records a charge equal to at least the minimum estimated liability for a loss contingency when both of the following conditions are met: (i)

information available prior to issuance of the consolidated financial statements indicates that it is probable that a liability had been incurred at the date of the consolidated financial statements and (ii) the range of loss can be reasonably estimated. The Company was not involved in any material litigation as of December 31, 2022 and 2021.

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, 2022 and 2021, the Company did not have any material indemnification claims that were probable or reasonably possible and, consequently, has not recorded any related liabilities.

Note 7. Convertible Preferred Stock and Stockholders' Equity (Deficit)

Convertible Preferred Stock

On August 3, 2021, immediately prior to the completion of the Company's IPO, all outstanding shares of convertible preferred stock were converted into 26,102,278 shares of the Company's common stock.

The Company classified 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.

Common Stock

The holders of 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' equity (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, 2022 and 2021, outstanding common stock included 853 and 28,905 shares, respectively, related to early exercised stock options and restricted stock that are unvested and subject to repurchase.

Initial Public Offering

On August 3, 2021, the Company completed its IPO, at which time the Company issued an aggregate of 13,800,000 shares of its common stock (inclusive of 1,800,000 shares pursuant to the underwriters' overallotment option) at a price of $15.00 per share. The Company received net proceeds of $188.5 million, after deducting underwriting discounts and commissions of $14.5 million and other offering expenses of $4.0 million. Immediately prior to the completion of the IPO, all of the Company's outstanding shares of convertible preferred stock automatically converted into 26,102,278 shares of common stock.

"At-the-Market" Equity Offering

On August 10, 2022, the Company entered into a sales agreement with a sales agent to establish an at-the-market (ATM) offering defined in Rule 415 under the Securities Act. Pursuant to the sales agreement, the Company is permitted to offer and sell, from time to time, shares of its common stock having a maximum aggregate offering price of up to $75.0 million. As of December 31, 2022, no shares have been sold pursuant to the ATM program.

Follow-On Offering

On November 21, 2022, the Company completed an underwritten public offering of 22,613,307 shares of its common stock at a price of $2.60 per share and, to certain investors in lieu of common stock, pre-funded warrants to purchase 6,236,693 shares of its common stock at a price of $2.599 per pre-funded warrant. The pre-funded warrants can be exercised at any time after issuance for an exercise price of $0.001 per share, subject to certain ownership limitations. The Company determined the pre-funded warrants qualified for equity accounting. In addition, the

Company granted the underwriters a 30-day option to purchase up to an additional 4,327,500 shares of its common stock to cover overallotments, if any, at $2.60 per share. On November 29, 2022, the underwriters partially exercised the option and purchased an additional 2,816,409 shares of Company's common stock. The Company received net proceeds of $76.9 million, inclusive of the additional shares purchased by the underwriters, after deducting underwriting discounts and commissions of $4.9 million and other offering expenses of $0.5 million. The offering expenses were paid in January 2023.

As of December 31, 2022, total shares of common stock reserved for issuance, on an as-if converted basis, are as follows:

	December 31, 2022
Outstanding stock options and awards	5,669,374
Outstanding pre-funded warrants	6,236,693
Stock options and awards available for future grant	2,318,761
Shares available for further issuance under the employee stock purchase plan	1,106,721
Total	15,331,549

Note 8. Stock-Based Compensation

2021 Equity Incentive Plan

In July 2021, the Company adopted the 2021 Equity Incentive Plan (2021 Plan), which became effective in connection with the initial public offering (IPO). Under the 2021 Plan, 4,000,000 shares of the Company's common stock were initially reserved for issuance of equity awards to employees, directors, and consultants, under terms and provisions established by the Board of Directors. The number of shares of common stock available for issuance under the 2021 Plan automatically increases on the first day of January for a period of ten years, commencing on January 1, 2022, in an amount equal to the lesser of: 4,000,000 shares; 4% of the outstanding shares of the Company's common stock as of the last day of the immediately preceding year; or such other amount as the Company's Board of Directors may determine. In addition, the Company's 2016 Equity Incentive Plan (2016 Plan) was terminated in connection with the IPO. Shares subject to awards granted under the 2016 Plan that are repurchased by or forfeited to the Company will be reserved for issuance under the 2021 Plan.

Total shares reserved and available for grant under the 2021 Plan as of December 31, 2022 are 2,318,761.

Stock Option Activity

The following table summarizes stock option activity:

	Shares	Weighted-Average Exercise	Weighted-Average Remaining Contractual Life	Aggregate Intrinsic Value
		(in dollars)	(Years)	(In thousands)
Outstanding as of December 31, 2021	2,772,154	$ 7.90		
Options granted	2,632,302	$ 12.58		
Options exercised	(23,677)	$ 2.14		
Options cancelled	(170,597)	$ 16.54		
Outstanding as of December 31, 2022	5,210,182	$ 10.01	8.45	$ 751
Exercisable as of December 31, 2022	1,719,533	$ 7.15	7.56	$ 691

The aggregate intrinsic value is the value of the Company's closing stock price on the last trading day of the year in excess of the weighted-average exercise price multiplied by the number of options outstanding or exercisable. The total intrinsic value of options exercised during the years ended December 31, 2022 and 2021, was $0.2 million and $1.7 million.

The weighted-average grant-date fair value of options granted during the years ended December 31, 2022 and 2021 was $9.80 and $9.50 per share.

As of December 31, 2022, there was $30.3 million of unrecognized stock-based compensation cost related to stock options, which is expected to be recognized over an estimated weighted-average period of 2.6 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:

The assumptions used to determine the fair value of options granted were as follows. Each of these inputs is subjective, involve inherent uncertainties, and generally requires significant judgment. The assumptions used to determine the fair value of the awards represent management's best estimates.

	Year Ended December 31,	
	2022	**2021**
Expected term (in years)	5.5 – 6.1	5.0 – 6.1
Expected volatility	95% – 97%	95% – 103%
Risk-free interest rate	1.6% – 4.2%	0.6% – 1.4%
Expected dividend yield	—%	—%

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 limited 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 Units

The Company began granting restricted stock units (RSUs) during the quarter ended March 31, 2022. RSUs are awards that entitle the holder to receive freely tradable shares of the Company's common stock upon the completion of a specific period of continued service. RSUs are generally subject to forfeiture if employment terminates prior to the release of vesting restrictions. RSUs are valued at the market price of the underlying common stock on the date of grant. The Company recognizes noncash compensation expense for the fair value of RSUs on a straight-line basis over the requisite service period of the awards. The following table summarizes activity of RSUs granted to employees with service-based vesting under the 2021 Plan.

	Shares	**Weighted Average Grant Date Fair Value per Share**	**Weighted-Average Remaining Contractual Life**	**Aggregate Intrinsic Value**
		(in dollars)	**(Years)**	**(In thousands)**
Unvested as of December 31, 2021	—	$ —		
Granted	489,153	$ 4.44		
Vested	(8,932)	$ 15.19		
Forfeited	(21,029)	$ 7.93		
Unvested as of December 31, 2022	459,192	$ 4.07	1.41	$ 923

As of December 31, 2022, there was $1.7 million of unrecognized stock-based compensation cost related to RSUs, which is expected to be recognized over an estimated weighted-average period of 2.3 years.

2021 Employee Stock Purchase Plan

In July 2021, the Company adopted the 2021 Employee Stock Purchase Plan (ESPP), which became effective in connection with the IPO. The Company initially reserved 800,000 shares for future issuance under the ESPP. The number of shares of common stock available for issuance under the ESPP automatically increases on the first day of each fiscal year beginning with 2022 in an amount equal to the lesser of: 800,000 shares; 1% of the outstanding shares of the Company's common stock as of the last day of the immediately preceding year; or such other amount as the board of directors may determine. As of December 31, 2022, 1,106,721 shares were reserved for future issuance under the ESPP. Under the Company's ESPP, employees are generally eligible to participate and can purchase shares on each purchase date established semi-annually through payroll deductions at the lower of 85% of the fair market value of the Company's stock at the commencement of the offering period or each purchase date of the offering period. Each offering period spans 6 months. The ESPP permits eligible employees to purchase common stock through payroll deductions for up to 15% of qualified compensation, up to an annual limit of $25,000 per the Internal Revenue Service. The first offering period commenced in January 2022. For the year ended December 31, 2022, the stock-based compensation expense for ESPP was not material.

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,	
	2022	2021
	(In thousands)	
Research and development	$ 4,914	$ 1,179
General and administrative	6,553	1,771
Total stock-based compensation	$ 11,467	$ 2,950

Note 9. Income Taxes

No provision for or benefit from income taxes was recorded during the years ended December 31, 2022 and 2021. 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 temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes, as well as 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,	
	2022	2021
U.S. federal taxes at statutory rate	21.0 %	21.0 %
State taxes (net of federal benefit)	1.2	0.6
Credits	2.8	3.1
Stock-based compensation	(0.3)	(0.3)
Section 382 limitation on tax attribute carryforwards	0.0	0.0
Change in valuation allowance	(24.1)	(23.3)
Other	(0.6)	(1.1)
Total	—%	—%

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows:

	December 31,	
	2022	2021
	(In thousands)	
Balance at beginning of year	$ 1,470	$ 571
Additions based on tax positions related to current year	1,588	901
Additions based on tax positions related to prior years	83	—
Reductions for tax positions related to prior years	—	(2)
Balance at end of year	$ 3,141	$ 1,470

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 jurisdictions with varying statutes of limitations. Due to net operating loss and credit carryforwards, all of the tax years since inception through the 2022 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,	
	2022	2021
	(In thousands)	
Deferred tax assets:		
Net operating losses	$ 41,256	$ 34,746
Capitalized research and development expenditure	17,045	—
Tax credits	9,347	4,443
Lease liability	3,176	3,362
Stock-based compensation	1,631	309
Accrued expenses and other	1,368	727
Property and equipment	—	152
Total deferred tax assets	73,823	43,739
Valuation allowance	(71,129)	(41,281)
Deferred tax assets, net of valuation allowance	2,694	2,458
Deferred tax liabilities:		
Right-of-use asset	(2,453)	(2,458)
Property and equipment	(241)	—
Net deferred tax assets	$ —	$ —

Beginning January 1, 2022, the Tax Cuts and Jobs Act eliminated the option to deduct research and development expenditures in the current year and requires taxpayers to capitalize such expenses pursuant to Internal Revenue Code (IRC) Section 174. The capitalized expenses are amortized over a 5-year period for domestic expenses and a 15-year period for foreign expenses.

The tax benefit of net operating losses, capitalized research expenses, 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 $29.8 million and $17.0 million during the years ended December 31, 2022 and 2021. The increase in valuation allowance during the year ended December 31, 2022, was primarily due to the increase in deferred tax assets from 2022 federal net operating losses and the IRC Section 174 capitalized expenses.

Net Operating Loss and Tax Credit Carryforwards

As of December 31, 2022, 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)	$ 171,533	Do Not Expire
Net operating losses, federal (pre-January 1, 2018)	$ 3,093	Begins to Expire 2036
Net operating losses, state	$ 62,973	Begins to Expire 2036
Tax credits, federal	$ 8,544	Begins to Expire 2036
Tax credits, state	$ 5,067	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, 2022, a study was updated and the Company concluded that there were no ownership changes during 2022. 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, 2022 and 2021, no interest and penalties were accrued by the Company.

Note 10. Net Loss Per Share

Basic and diluted loss per share are computed by dividing net loss by the weighted-average number of common shares outstanding during the reporting period. Basic weighted-average shares of common stock outstanding includes the weighted-average effect of the Company's pre-funded warrants issued in November 2022 (see *Note 7*), the exercise of which requires nominal consideration for the delivery of Company's common shares.

The following potentially dilutive securities were excluded from the calculation of diluted net loss per share for the periods presented because the effect would have been anti-dilutive:

	December 31,	
	2022	2021
Outstanding stock options and awards	5,669,374	2,772,154
Restricted stock subject to future vesting	853	28,905
Total	5,670,227	2,801,059

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation and supervision of our Chief Executive Officer and our Chief Financial Officer, have evaluated our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act) as of the end of the period covered by this Annual Report on Form 10-K. Based on that evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of the end of the period covered by this Annual Report on Form 10-K, our disclosure controls and procedures are effective to provide reasonable assurance that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in SEC rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure. We believe that a control system, no matter how well designed and operated, cannot provide absolute assurance that the objectives of the control system are met, and no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within a company have been detected.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act). Under the supervision of and with the participation of our principal executive officer and principal financial officer, our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2022 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in "Internal Control—Integrated Framework" (2013). Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2022.

As an emerging growth company, we are not required to provide, and this Annual Report on Form 10-K does not include an attestation report on our internal control over financial reporting issued by our independent registered public accounting firm. Our auditors will not be required to opine on the effectiveness of our internal control over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act of 2002 until we are no longer an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012, and are no longer a non-accelerated filer.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) during the quarter ended December 31, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations on Effectiveness of Controls

A control system, no matter how well designed and operated, can provide only reasonable and not absolute assurance of achieving the desired control objectives. In reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the benefits of possible controls and procedures relative to their costs. In addition, the design of any system of controls is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, controls may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

Item 9B. Other Information.

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not Applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Information required by this item will be contained in our definitive Proxy Statement to be filed with the SEC on Schedule 14A within 120 days of December 31, 2022, and is incorporated herein by reference.

Code of Ethics

We have adopted a Code of Business Conduct and Ethics that applies to all of our directors, officers and employees, including our principal executive officer, principal financial officer and principal accounting officer. The Code of Business Conduct and Ethics is posted on our website at www.tenayatherapeutics.com under the caption "Investors—Corporate Governance—Governance Documents."

We intend to satisfy the disclosure requirement under Item 5.05 of Form 8-K regarding an amendment to, or waiver from, a provision of this Code of Business Conduct and Ethics by posting such information on our website, at the address and location specified above and, to the extent required by the listing standards of the Nasdaq Stock Market, by filing a Current Report on Form 8-K with the SEC, disclosing such information.

Item 11. Executive Compensation.

Information required by this item will be contained in our definitive Proxy Statement to be filed with the SEC on Schedule 14A within 120 days of December 31, 2022, and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

Information required by this item will be contained in our definitive Proxy Statement to be filed with the SEC on Schedule 14A within 120 days of December 31, 2022, and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

Information required by this item will be contained in our definitive Proxy Statement to be filed with the SEC on Schedule 14A within 120 days of December 31, 2022, and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

Information required by this item will be contained in our definitive Proxy Statement to be filed with the SEC on Schedule 14A within 120 days of December 31, 2022, and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) The following documents are filed as a part of the report:

(1) Financial Statements: The financial statements filed as part of this Annual Report are included in Part II, Item 8 of this Annual Report.

(2) Financial Statement Schedules: Financial statement schedules have been omitted in this Annual Report because they are not applicable, not required under the instructions or the information requested is set forth in the financial statements or related notes thereto.

(3) Exhibits: The exhibits listed in the accompanying index to exhibits are filed or incorporated by reference as part of this Annual Report.

Item 16. Form 10-K Summary

None.

Exhibit Index

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date
3.1	Amended and Restated Certificate of Incorporation of the Registrant.	8-K	001-40656	3.1	8-3-2021
3.2	Amended and Restated Bylaws of the Registrant.	8-K	001-40656	3.2	8-3-2021
4.1	Specimen common stock certificate of the Registrant.	S-1/A	333-257820	4.2	7-26-2021
4.2	Amended and Restated Investors' Rights Agreement by and among the Registrant and certain of its stockholders, dated December 17, 2020.	S-1/A	333-257820	4.1	7-26-2021
4.3	Description of Securities of the Registrant.	10-K	001-40656	4.3	3-23-2022
10.1	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers.	S-1/A	333-257820	10.1	7-26-2021
10.2+	2021 Equity Incentive Plan and forms of agreements thereunder.	10-K	001-40656	10.2	3-23-2022
10.3+	2021 Employee Stock Purchase Plan and forms of agreements thereunder.	S-1/A	333-257820	10.4	7-26-2021
10.4+	Employment Letter between the Registrant and Faraz Ali, M.B.A.	S-1/A	333-257820	10.5	7-26-2021
10.5+	Employment Letter between the Registrant and Timothy Hoey, Ph.D.	S-1/A	333-257820	10.6	7-26-2021
10.6+	Employment Letter between the Registrant and Leone D. Patterson, M.B.A.	S-1/A	333-257820	10.7	7-26-2021
10.7+	Employment Letter between the Registrant and Whittemore (Whit) Tingley, M.D., Ph.D.	S-1/A	333-257820	10.8	7-26-2021
10.8+	Executive Change in Control and Severance Plan.	S-1/A	333-257820	10.12	7-26-2021
10.9+	Executive Incentive Compensation Plan.	S-1/A	333-257820	10.13	7-26-2021
10.10+*	Outside Director Compensation Policy.				
10.11+	Amended and Restated 2016 Equity Incentive Plan and forms of agreement thereunder.	S-1/A	333-257820	10.2	7-26-2021
10.13	Lease between HCP Oyster Point III LLC and the Registrant dated as of September 6, 2016.	S-1/A	333-257820	10.10	7-26-2021
10.14	Lease between Terreno Park Union City LLC and the Registrant dated as of February 12, 2021.	S-1/A	333-257820	10.11	7-26-2021
23.1*	Consent of Deloitte & Touche LLP, Independent Registered Public Accounting Firm.				
24.1*	Power of Attorney (included on the signature page to this Annual Report on Form 10-K).				
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				
32.1†	Certification of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				

101.INS*	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104*	Cover Page Interactive Data File (embedded within the Inline XBRL document)

***** Filed herewith**.**

+ Management contract, compensatory plan or agreement.

† The certifications attached as Exhibit 32.1 that accompany this Annual Report on Form 10-K are not deemed filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of the Registrant under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Annual Report on Form 10-K, irrespective of any general incorporation language contained in such filing.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

TENAYA THERAPEUTICS, INC.

Date: March 8, 2023

By: /s/ Faraz Ali, M.B.A.
Faraz Ali, M.B.A.
Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Faraz Ali and Leone Patterson as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and substitution, for him or her and in his or her name, place, and stead, in any and all capacities (including his or her capacity as a director and/or officer of Tenaya Therapeutics, Inc.) to sign any or all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and all other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as they, he or she might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agents or any of them, or their, his, or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Faraz Ali, M.B.A. **Faraz Ali, M.B.A.**	Chief Executive Officer and Director *(Principal Executive Officer)*	March 8, 2023
/s/ Leone D. Patterson, M.B.A. **Leone D. Patterson, M.B.A.**	Chief Financial and Business Officer *(Principal Financial and Accounting Officer)*	March 8, 2023
/s/ Amy L. Burroughs **Amy L. Burroughs, M.B.A.**	Director	March 8, 2023

/s/ Jin-Long Chen, Ph.D. **Jin-Long Chen, Ph.D.**	Director	March 8, 2023
/s/ David V. Goeddel, Ph.D. **David V. Goeddel, Ph.D.**	Director	March 8, 2023
/s/ June Lee, M.D. **June Lee, M.D.**	Director	March 8, 2023
/s/ Karah Parschauer **Karah Parschauer**	Director	March 8, 2023
/s/ Deepak Srivastava, M.D. **Deepak Srivastava, M.D.**	Director	March 8, 2023
/s/ Catherine Stehman-Breen, M.D. **Catherine Stehman-Breen, M.D.**	Director	March 8, 2023
/s/ Jeffrey T. Walsh, M.B.A. **Jeffrey T. Walsh, M.B.A.**	Director	March 8, 2023
/s/ R. Sanders (Sandy) Williams, M.D. **R. Sanders (Sandy) Williams, M.D.**	Director	March 8, 2023

Exhibit 10.10

TENAYA THERAPEUTICS, INC.

OUTSIDE DIRECTOR COMPENSATION POLICY

(as most recently amended and restated December 5, 2022 (the "Restatement Date"))

Tenaya Therapeutics, Inc. (the "Company") believes that the granting of equity and cash compensation to members of the Company's Board of Directors (the "Board," and members of the Board, "Directors") represents an effective tool to attract, retain and reward Directors who are not employees of the Company ("Outside Directors"). This Outside Director Compensation Policy (the "Policy") is intended to formalize the Company's policy regarding cash compensation and grants of equity awards to its Outside Directors. Unless otherwise defined herein, capitalized terms used in this Policy will have the meaning given such term in the Company's 2021 Equity Incentive Plan, as amended from time to time, or if such plan no longer is in use at the time of the grant of an equity award, the meaning given such term or similar term in the equity plan then in place under which the equity award is granted (the "Plan"). Each Outside Director will be solely responsible for any tax obligations incurred by such Outside Director as a result of the equity awards and cash and other compensation such Outside Director receives under this Policy.

1. Effective Date; Restatement Date. This Policy originally became effective as of the effective date of the first registration statement that is filed by the Company and declared effective pursuant to Section 12(b) of the U.S. Securities Exchange Act of 1934, as amended, with respect to any class of the Company's securities (such date, the "Effective Date"). This amended and restated Policy is effective as of the Restatement Date.

2. Cash Compensation

2.1 Board Member Annual Cash Retainer. Each Outside Director will be paid an annual cash retainer of $35,000. There are no per-meeting attendance fees for attending Board meetings or meetings of any committee of the Board.

2.2 Additional Annual Cash Retainers. As of the Effective Date, each Outside Director who serves as the Chair of the Board, or the chair or a member of a committee of the Board, will be eligible to earn additional annual fees as follows:

Non-Executive Chair of the Board:	$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

For clarity, each Outside Director who serves as the chair of a committee will receive only the additional annual fee as the chair of the committee and not the additional annual fee as a member of such committee while serving as such chair, provided, that the Outside Director who serves as the Chair of the Board will receive the annual fee for services provided in such role as well as the annual fee as an Outside Director.

2.3 Payment Timing and Proration. Each annual cash retainer (a "Annual Cash Retainer") under this Policy will be paid quarterly in arrears on a prorated basis to each Outside Director who has served in the relevant capacity at any time during the immediately preceding fiscal quarter of the Company ("Fiscal Quarter"), and such payment will be made no later than thirty (30) days following the end of such immediately preceding Fiscal Quarter. For clarity, an Outside Director who has served as an Outside Director, as a member of an applicable committee (or chair thereof) during only a portion of the relevant Fiscal Quarter will receive a prorated payment of the quarterly installment of the applicable Annual Cash Retainer(s), calculated based on the number of days during such Fiscal Quarter such Outside Director has served in the relevant capacities. For clarity, an Outside Director who has served as an Outside Director or as a member of an applicable committee (or chair thereof) from the Effective Date through the end of the Fiscal Quarter containing the Effective Date (the "Initial Period"), as applicable, will receive a prorated payment of the quarterly installment of the applicable Annual Cash Retainer(s), calculated based on the number of days during the Initial Period that such Outside Director has served in the relevant capacities.

3. Equity Compensation. Outside Directors will be eligible to receive all types of Awards (except Incentive Stock Options) under the Plan, including discretionary Awards not covered under this Policy, subject to Section 5 hereof. All grants of Awards to Outside Directors pursuant to Sections 3.2 and 3.3 of this Policy will be automatic and nondiscretionary, except as otherwise provided herein, and will be made in accordance with the following provisions:

3.1 No Discretion. No person will have any discretion to select which Outside Directors will be granted Annual Awards (as defined below) under this Policy or to determine the number of Shares to be covered by such Awards (except as provided in Sections 3.4.4 and 10 below).

3.2 Initial Awards. Each individual who first becomes an Outside Director on or following the Restatement Date automatically will be granted an Option (an "Initial Award") to purchase Shares with a grant date fair value as determined in accordance with U.S. generally accepted accounting principles (the "Grant Value") equal to $320,000 (with any resulting fractional Share rounded down to the nearest whole Share), provided that, notwithstanding the foregoing, no more than 40,000 Shares may be subject to an Initial Award. The grant date of the Initial Award will be the first Trading Day on or after the date on which such individual first becomes an Outside Director (such first date as an Outside Director, the "Initial Start Date"), whether through election by the stockholders of the Company or appointment by the Board to fill a vacancy. If an individual was an Employee-Director, becoming an Outside Director due to termination of the individual's status as an Employee will not entitle the Outside Director to an Initial Award. Each Initial Award will be scheduled to vest

as to one thirty-sixth (1/36th) of the Shares subject to the Initial Award on a monthly basis following the Initial Award's grant date on the same day of the month as such grant date (or on the last day of the month, if there is no corresponding day in such month), subject to the Outside Director remaining a Service Provider through the applicable vesting date.

3.3 Annual Award. On the first Trading Day immediately following each Annual Meeting of the Company's stockholders (an "Annual Meeting" and such first Trading Day immediately following the Annual Meeting, the "Annual Award Date") that occurs on or after the Restatement Date, (i) each Outside Director who, as of the date of such Annual Meeting (the "Current Meeting") has been in continuous service as an Outside Director since the date of the most recently preceding Annual Meeting (the "Prior Meeting"), automatically will be granted an Option (the "Annual Award") to purchase Shares with a Grant Value equal to $160,000 (with any resulting fractional Share rounded down to the nearest whole Share), and (ii) each Outside Director who, as of the date of the Current Meeting, has not been in continuous service as an Outside Director since the Prior Meeting, automatically will be granted a prorated Annual Award having a Grant Value equal to the product of (A) $160,000 multiplied by (B) a fraction, (x) the numerator of which is the number of full months (not to exceed 12) during which the individual served as an Outside Director between such individual's Initial Start Date and the date of the Current Meeting, and (y) the denominator of which is 12 (with any resulting fractional Share rounded down to the nearest whole Share). Notwithstanding the foregoing, no more than 20,000 Shares may be subject to an Annual Award. The 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 that occurs after the Annual Award's grant date, subject to the Outside Director remaining a Service Provider through the applicable vesting date. For the avoidance of doubt, for purposes of this Policy, a "full month" will have elapsed on each one-month anniversary of the Initial Start Date (e.g., if the Initial Start Date is September 15 of a given year, a full month will elapse on October 15 of such year and the next full month will elapse on November 15 of such year) or, if there is no monthly anniversary of the applicable date, on the last date of the applicable month (e.g., if the Initial Start Date is October 31 of a given year, a full month will elapse on November 30 of such year and the next full month will elapse on December 31 of such year).

3.4 Additional Terms of Initial Awards and Annual Awards. The terms and conditions of each Initial Award and Annual Award will be as follows.

3.4.1 The term of each Initial Award and Annual Award will be ten (10) years, subject to earlier termination as provided in the Plan.

3.4.2 The per Share exercise price of each Initial Award and Annual Award will be equal to one hundred percent (100%) of the Fair Market Value per Share on such Award's grant date.

3.4.3 Each Initial Award and Annual Award will be granted under and subject to the terms and conditions of the Plan and the applicable form of Award Agreement previously approved by the Board or its Committee, as applicable, for use thereunder.

3.4.4 The Board or its Committee, as applicable and in its discretion, may change and otherwise revise the terms of Initial Awards and Annual Awards granted pursuant to this Policy, including without limitation the number of Shares subject thereto and type of Award.

4. Change in Control. In the event of a Change in Control, each Outside Director will fully vest in his or her outstanding Company equity awards as of immediately prior to the Change in Control, including any Initial Award and Annual Award, provided that the Outside Director continues to be an Outside Director through the date of such Change in Control.

5. Annual Compensation Limit. No Outside Director may be granted, in any Fiscal Year, Awards with values (based on their grant date fair value determined in accordance with U.S. generally accepted accounting principles), and be provided any other compensation (including without limitation any cash retainers or fees) in amounts that, in any Fiscal Year, in the aggregate, exceed $500,000. Any Awards or other compensation provided to an individual (a) for his or her services as an Employee, or for his or her services as a Consultant other than as an Outside Director, or (b) prior to the Registration Date, will be excluded for purposes of this Section 5.

6. Travel Expenses. Each Outside Director's reasonable, customary and properly documented travel expenses to meetings of the Board and any of its committees, as applicable, will be reimbursed by the Company.

7. Adjustments. In the event that any 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, reclassification, repurchase, or exchange of Shares or other securities of the Company, or other change in the corporate structure of the Company affecting the Shares occurs (other than any ordinary dividends or other ordinary distributions), the Administrator, in order to prevent diminution or enlargement of the benefits or potential benefits intended to be made available under this Policy, will adjust the number and class of the shares of stock issuable pursuant to Awards that may be granted pursuant to Section 3 of this Policy.

8. Section 409A. In no event will cash compensation or expense reimbursement payments under this Policy be paid after the later of (a) the fifteenth (15th) day of the third (3rd) month following the end of the Company's taxable year in which the compensation is earned or expenses are incurred, as applicable, or (b) the fifteenth (15th) day of the third (3rd) month following the end of the calendar year in which the compensation is earned or expenses are incurred, as applicable, in compliance with the "short-term deferral" exception under Section 409A. It is the intent of this Policy that this Policy and all payments hereunder be exempt from or otherwise comply with the requirements of Section 409A so that none of the compensation to be provided hereunder will be subject to the additional tax imposed under Section 409A, and any ambiguities or ambiguous terms herein will be interpreted to be so exempt or comply. In no event will the Company or any of its Parents or Subsidiaries have any responsibility, liability, or obligation to reimburse, indemnify, or hold harmless an Outside Director (or any other person) for any taxes imposed, or other costs incurred, as a result of Section 409A.

9. Stockholder Approval. The initial adoption of this Policy was approved by the Company's stockholders prior to the Effective Date. Unless otherwise required by applicable law, following such approval, this Policy will not be subject to approval by the Company's stockholders, including, for

clarity, as a result of or in connection with any action taken with respect to this Policy as contemplated in Section 10.

10. Revisions. The Board or any committee of the Board that has been designated appropriate authority with respect to Outside Director compensation (or with respect to any applicable element or elements thereof, authority with respect to such element or elements) (the "Committee") may amend, alter, suspend or terminate this Policy at any time and for any reason. Further, the Board may provide for cash, equity, or other compensation to Outside Directors in addition to the compensation provided under this Policy. No amendment, alteration, suspension or termination of this Policy will materially impair the rights of an Outside Director with respect to compensation that already has been paid or awarded, unless otherwise mutually agreed between the Outside Director and the Company. Termination of this Policy will not affect the Board's or the Committee's ability to exercise the powers granted to it with respect to Awards granted under the Plan pursuant to this Policy before the date of such termination, including without limitation such applicable powers set forth in the Plan.

* * *

EXHIBIT 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement No. 333-266741 on Form S-3 and No. 333-258337 and No. 333-263802 on Form S-8 of our report dated March 8, 2023, relating to the financial statements of Tenaya Therapeutics, Inc. appearing in this Annual Report on Form 10-K for the year ended December 31, 2022.

/s/ Deloitte & Touche LLP

San Francisco, California
March 8, 2023

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Faraz Ali, M.B.A., certify that:

1. I have reviewed this Annual Report on Form 10-K of Tenaya Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 8, 2023

TENAYA THERAPEUTICS, INC.

By:	/s/ Faraz Ali, M.B.A.
Name:	Faraz Ali, M.B.A.
Title:	Chief Executive Officer and Director *(Principal Executive Officer)*

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER
PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Leone D. Patterson, M.B.A., certify that:

1. I have reviewed this Annual Report on Form 10-K of Tenaya Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 8, 2023

TENAYA THERAPEUTICS, INC.

By:	/s/ Leone D. Patterson, M.B.A.
Name:	Leone D. Patterson, M.B.A.
Title:	Chief Financial and Business Officer *(Principal Financial and Accounting Officer)*

Exhibit 32.1

CERTIFICATIONS OF PRINCIPAL EXECUTIVE OFFICER AND PRINCIPAL FINANCIAL OFFICER
PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

I, Faraz Ali, M.B.A., certify, pursuant to 18 U.S.C. Section 1350 as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, (1) the Annual Report on Form 10-K of Tenaya Therapeutics, Inc. (the "Company") for the year ended December 31, 2022, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934 and (2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ Faraz Ali, M.B.A.

Faraz Ali, M.B.A.

Chief Executive Officer and Director
(Principal Executive Officer)

Date: March 8, 2023

I, Leone D. Patterson, M.B.A., certify, pursuant to 18 U.S.C. Section 1350 as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, (1) the Annual Report on Form 10-K of Tenaya Therapeutics, Inc. (the "Company") for the year ended December 31, 2022, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934 and (2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ Leone D. Patterson, M.B.A.

Leone D. Patterson, M.B.A.

Chief Financial and Business Officer
(Principal Financial and Accounting Officer)

Date: March 8, 2023