PROSPECTUS SUPPLEMENT (To prospectus dated August 17, 2022)

8,888,890 SHARES OF COMMON STOCK PRE-FUNDED WARRANTS TO PURCHASE 2,222,271 SHARES OF COMMON STOCK



We are offering an aggregate of 8,888,890 shares of our common stock and, in lieu of common stock to certain investors that so choose, pre-funded warrants to purchase 2,222,271 shares of our common stock in a registered direct offering. The purchase price of each pre-funded warrant equals the price per share at which shares of our common stock are being sold in this offering, minus \$0.001 multiplied by the number of shares subject to the warrant, and the exercise price of each pre-funded warrant equals \$0.001 per share. This prospectus supplement also relates to the offering of the shares of our common stock issuable upon the exercise of such pre-funded warrants.

Certain existing stockholders, including stockholders affiliated with certain of our directors, are participating in this offering and are expected to purchase an aggregate of 2,222,222 shares of common stock, on the same terms as other investors in this offering.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "TNYA." On February 7, 2024, the last reported sale price of our common stock was \$4.42 per share. There is no established public trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to list the pre-funded warrants on the Nasdaq Global Select Market, any other national securities exchange or any other recognized trading system.

We are an "emerging growth company" and a "smaller reporting company" as defined under U.S. federal securities laws and as such, we have elected to comply with certain reduced public company reporting requirements for this prospectus supplement and may elect to do so for future filings. See "Prospectus Supplement Summary—Implications of Being an Emerging Growth Company and a Smaller Reporting Company."

	Per Share	Per Pre-Funded Warrant	Total
Offering price	\$4.500	\$4.499	\$49,998,002
Underwriting discounts and commissions (1)	\$0.270	\$0.270	\$3,000,013
Proceeds to Tenaya Therapeutics, Inc., before expenses	\$4.230	\$4.229	\$46,997,989

⁽¹⁾ See "Underwriting" for a description of the compensation payable to the underwriters.

INVESTING IN OUR SECURITIES INVOLVES SIGNIFICANT RISKS. YOU SHOULD REVIEW CAREFULLY THE "RISK FACTORS" ON PAGE S-12 OF THIS PROSPECTUS SUPPLEMENT, AND IN THE DOCUMENTS INCORPORATED BY REFERENCE IN THIS PROSPECTUS SUPPLEMENT AND ACCOMPANYING PROSPECTUS BEFORE INVESTING IN OUR SECURITIES.

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

The underwriters expect to deliver the shares of common stock and pre-funded warrants to purchasers on or about February 12, 2024.

Joint Bookrunning Managers

Leerink Partners

TD Cowen

Lead Manager

LifeSci Capital

The date of this prospectus supplement is February 7, 2024

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus are part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission (the SEC), using a "shelf" registration process.

We are providing information to you about this offering of our common stock and pre-funded warrants in two parts. The first part is this prospectus supplement, which provides you with specific information regarding the terms of this offering of our common stock and pre-funded warrants, and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus. The second part is the accompanying prospectus, which provides more general information, some of which does not apply to this offering of our common stock and pre-funded warrants. Generally, when we refer to this prospectus, we are referring to both parts of this document combined.

Before buying any of the common stock or pre-funded warrants that we are offering, we urge you to carefully read this prospectus supplement, the accompanying prospectus and all of the information incorporated by reference herein and therein, as well as the additional information described under the headings "Where You Can Find More Information" and "Incorporation of Certain Information by Reference." These documents contain important information that you should consider when making your investment decision.

To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in any document incorporated by reference in this prospectus supplement that was filed with the SEC before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in this prospectus supplement—the statement in the document having the later date modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in this prospectus supplement or the accompanying prospectus, and the documents herein or therein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreement, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Neither we nor the underwriters have authorized anyone to provide you with any information or to make any representation, other than those contained or incorporated by reference in this prospectus supplement and in the accompanying prospectus or in any related free writing prospectus that we authorize for use in connection with this offering and to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, and the documents incorporated by reference herein and therein or any free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

We are offering to sell, and seeking offers to buy, our common stock and pre-funded warrants only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the common stock and pre-funded warrants in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and pre-funded warrants and the distribution of this prospectus supplement and the accompanying prospectus outside the United States.

This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

Unless the context otherwise indicates, references in this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein to "Tenaya Therapeutics," "Tenaya," "we," "our" and "us" refer, collectively, to Tenaya Therapeutics, Inc. We have proprietary rights to trademarks that are used in this prospectus supplement and the documents incorporated by reference herein, which are important to our business and many of which are registered under applicable intellectual property laws. Solely for convenience, the trademarks, service marks, logos and trade names referred to in this prospectus supplement and the documents incorporated by reference herein may be without the ® and ™ symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights to these trademarks, service marks and trade names. This prospectus supplement and the documents incorporated by reference herein contain additional trademarks, service marks and trade names of others, which are the property of their respective owners. All trademarks, service marks and trade names appearing in this prospectus supplement and the documents incorporated by reference herein are, to our knowledge, the property of their respective owners. We do not intend our use or display of other companies' trademarks, service marks, copyrights or trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus, and the documents incorporated by reference herein and therein, contain forward-looking statements within the meaning of Section 27A of the Securities Act, and Section 21E of the Exchange Act. All statements other than statements of historical facts contained in this prospectus supplement, the accompanying prospectus, and the documents incorporated by reference herein and therein, including statements regarding our future results of operations and financial position, business strategy, development plans, planned preclinical studies and clinical trials, future results of preclinical studies and 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. The words "may," "will," "should," "would," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms and similar expressions and variations thereof are intended to identify forward-looking statements but are not the exclusive means of identifying such statements. These forward-looking statements include, but are not limited to, statements about:

- 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, 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), 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;
- our manufacturing, commercialization, and marketing capabilities and strategy;
- our plans relating to commercializing our product candidates, if approved;
- the need to hire additional personnel and our ability to attract and retain such personnel;
- 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 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, as well as our ability to realize the potential benefits of any such agreements;
- 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, capital requirements and needs for additional financing;
- our financial performance;
- 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;
- our expectations regarding the period during which we will remain an emerging growth company; and
- our expectations related to the use of proceeds from this offering.

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

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus supplement 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 you are cautioned not to unduly rely upon these statements.

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

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in this prospectus supplement, the accompanying prospectus and in the documents we incorporate by reference. This summary is not complete and does not contain all of the information you should consider before making an investment decision. You should carefully read this entire prospectus supplement and the accompanying prospectus, including the information incorporated by reference herein and therein, especially the risks of investing in our common stock discussed under "Risk Factors" beginning on page S-12 of this prospectus supplement, the "Risk Factors" section of our most recent Quarterly Report on Form 10-Q and other filings we make with the SEC, along with our consolidated financial statements and notes to those consolidated financial statements and the other information incorporated by reference in this prospectus supplement and the accompanying prospectus and in our filings with the SEC.

Company Overview

We are a clinical-stage biotechnology company focused on discovering, developing and delivering potentially 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 extensive 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 are: TN-201, a gene therapy for myosin binding protein C3 (MYBPC3)-associated hypertrophic cardiomyopathy (HCM), TN-401, a gene therapy for plakophilin 2 (PKP2)-associated arrhythmogenic right ventricular cardiomyopathy (ARVC), and TN-301, a small molecule for heart failure with preserved ejection fraction (HFpEF).

TN-201 is our investigational AAV9-based 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 the disease often experience significant impairment in overall quality of life. TN-201 is designed to deliver a functional MYBPC3 gene to the heart utilizing a recombinant adeno-associated virus serotype 9 (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 October 2023, we began dosing patients in the MyPeak™ -1 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. Initial data from the trial is anticipated in the second half of 2024.

In order to support our development efforts for TN-201, we have initiated two non-interventional 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-201 has received orphan drug designation and Fast Track Designation from the FDA and orphan medicinal product designation from the European Commission (EC) for the treatment of MYBPC3-associated HCM.

TN-401 is our AAV9-based investigational gene therapy product candidate for the treatment of ARVC caused by mutations in the PKP2 gene. ARVC, also known as arrhythmogenic cardiomyopathy or ACM, is a chronic, progressive, familial disease characterized by ventricular arrhythmias, adverse remodeling of the heart and an increased risk of sudden cardiac death. PKP2 mutations are the most common genetic cause of ARVC and result in a loss of key proteins needed to maintain the structural integrity and cell-to-cell signaling of heart muscle cells.

In October 2023, the FDA provided clearance of our IND application to initiate clinical testing of TN-401. We plan to initiate patient dosing in RIDGE™ -1, our Phase 1b multi-center, open-label clinical trial, designed to assess the safety, tolerability and efficacy of a one-time intravenous infusion of TN-401, during the second half of 2024. 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. TN-401 has received orphan drug designation and Fast Track Designation from the FDA and orphan medicinal product designation from the EC.

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 to relax properly during normal heart rhythm, referred to as diastolic dysfunction. There are several cellular processes thought to underlie 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.

In October 2023, Tenaya shared positive data from its Phase 1 clinical trial of TN-301 in healthy participants at the 2023 Heart Failure Society of America (HFSA) Annual Scientific Meeting. The Phase 1 trial enrolled participants in two stages. In Stage 1, participants received single ascending doses (SAD) and in Stage 2, participants received multiple ascending doses (MAD). TN-301 was generally well tolerated across the broad range of doses studied. Pharmacokinetic results showed overall dose proportionality in the SAD and MAD stages of the study with a half-life supportive of once-daily dosing. Robust HDAC6 inhibition was observed and increasing doses and exposures with TN-301 correlated with increased pharmacodynamic effects. There were no changes in histone acetylation with TN-301, underscoring the selectivity of TN-301 for HDAC6 and potentially reducing the risk of off target effects observed with less selective HDAC6 inhibitors or pan-HDAC inhibition. In preclinical studies, selective HDAC6 inhibition has been shown to have comparable efficacy to empagliflozin, a sodium-glucose cotransporter-2 (SGLT2) inhibitor which is approved for the treatment of HFpEF. More recently, using a validated mouse model of disease, we demonstrated that HDAC6 inhibition co-administered with an SGLT2 inhibitor demonstrated additive benefit, improving several measures of heart function. Taken together, these data support continued development of TN-301 as a potential treatment for patients with HFpEF. We believe late-stage clinical development of TN-301 is best suited for development by or with a well-resourced partner.

In addition to our lead product candidates, we have multiple early-stage programs to address other forms of heart failure progressing through preclinical development.

Our distinct, but interrelated 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, gene editing, 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.

We have internalized and integrated both current Good Manufacturing Practices (GMP) and non-GMP AAV manufacturing capabilities to support our emerging portfolio of gene therapy and cellular regeneration product candidates. Our Genetic Medicines Manufacturing Center, 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 and utilizes a modular, scalable design to produce AAV-based gene therapies under current GMP standards.

Risk Factors Summary

The below summary of risk factors provides an overview of many of the risks we are exposed to in the normal course of our business activities and risks related to this offering. As a result, the below summary risks do not contain all of the information that may be important to you, and you should read the summary risks together with the more detailed discussion of risks set forth following this section under the heading "Risk Factors," as well as elsewhere in this prospectus supplement. Additional risks, beyond those summarized below or discussed elsewhere in this prospectus supplement and the documents incorporated herein by reference, may apply to our activities or operations as currently conducted or as we may conduct them in the future or in the markets in which we operate or may in the future operate. Consistent with the foregoing, we are exposed to a variety of risks, including risks associated with the following:

- We are early in our development efforts, with a limited operating history 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, which if available, may 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, European Medicines Agency (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.
- 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.
- 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.
- 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.
- There is no public market for the pre-funded warrants being offered in this offering.
- Holders of the pre-funded warrants will have no rights as common stockholders until such holders exercise their pre-funded warrants and acquire our common stock.
- Significant holders or beneficial owners of our common stock may not be permitted to exercise the pre-funded warrants that they hold.

Corporate Information

We were incorporated in Delaware in August 2016. Our principal executive offices are located at 171 Oyster Point Boulevard, Suite 500, South San Francisco, CA 94080. Our telephone number is (650) 825-6990. Our website address is www.tenayatherapeutics.com. Information contained on, or accessible through, our website is not incorporated by reference into this prospectus supplement and should not be considered to be part of this prospectus supplement. The inclusion of our website address in this prospectus supplement is an inactive textual reference only.

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 website that contains reports, proxy and information statements and other information regarding our filings at www.sec.gov.

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

We are an "emerging growth company" as defined in The Jumpstart Our Business Startups Act of 2012, as amended (the JOBS Act). We will remain an emerging growth company until the earliest to occur of: (1) the last day of the fiscal year in which we have more than \$1.235 billion in annual revenue; (2) the date we qualify as a "large accelerated filer," with at least \$700 million of equity securities held by non-affiliates; (3) the date on which we have issued more than \$1.0 billion in non-convertible debt securities during the prior three-year period; and (4) the last day of the fiscal year ending after the fifth anniversary of our initial public offering, which will be December 31, 2026. As a result of this status, we have taken advantage of reduced reporting requirements in this prospectus and may elect to take advantage of other reduced reporting requirements in our future filings with the SEC. In particular, in this prospectus supplement, we have incorporated only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards, delaying the adoption of these accounting standards until they would apply to private companies. We have elected to use the extended transition period to enable us to comply with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date we (1) are no longer an emerging growth company and (2) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

We are also a "smaller reporting company," meaning that the market value of our stock held by non-affiliates plus the proposed aggregate amount of gross proceeds to us as a result of this offering is less than \$700 million and our annual revenue was less than \$100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company after this offering if either (1) the market value of our stock held by non-affiliates is less than \$250 million or (2) our annual revenue was less than \$100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than \$700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

THE OFFERING

Common Stock and Pre-Funded Warrants Offered by Us

8,888,890 shares of our common stock. We are also offering, in lieu of common stock to certain investors that so choose, pre-funded warrants to purchase 2,222,271 shares of our common stock. The purchase price of each pre-funded warrant equals the price per share at which shares of common stock are being sold in this offering minus \$0.001, multiplied by the number of shares subject to the warrant, and the exercise price of each pre-funded warrant equals \$0.001 per share. Each pre-funded warrant will be exercisable from the date of issuance until the date the warrant is exercised in full, subject to an ownership limitation. See "Description of Pre-Funded Warrants." This prospectus supplement also relates to the offering of the shares of common stock issuable upon the exercise of such pre-funded warrants.

Common Stock to be Outstanding After this Offering

76,999,909 shares of our common stock.

Use of Proceeds

We intend to use the net proceeds from this offering, together with our existing cash, cash equivalents and marketable securities, to fund the ongoing and planned development of our lead gene therapy product candidates, the continued development of our earlier-stage research programs, the progression of our core capabilities, and for working capital and other general corporate purposes. See "Use of Proceeds" on page S-16 of this prospectus supplement.

Risk Factors

Investing in our securities involves significant risks. You should read the "Risk Factors" section on page S-12 of this prospectus supplement and in the documents incorporated by reference in this prospectus supplement and accompanying prospectus for a discussion of factors to consider carefully before deciding to purchase shares of our common stock or pre-funded warrants.

Nasdaq Global Select Market Symbol

Our common stock is listed on the Nasdaq Global Select Market under the symbol "TNYA." There is no established public trading market for the pre-funded warrants, and we do not expect a market to develop. We do not intend to list the pre-funded warrants on the Nasdaq Global Select Market or any other national securities exchange or nationally recognized trading system. Without an active trading market, the liquidity of the pre-funded warrants will be limited. See "Description of Pre-Funded Warrants."

The number of shares of our common stock outstanding after this offering is based on 68,111,019 shares of our common stock outstanding as of September 30, 2023, and excludes:

- 8,224,346 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2023, at a weighted average exercise price of \$7.57 per share;
- 1,094,781 shares of common stock issuable upon vesting of restricted stock units outstanding as of September 30, 2023;
- 253,600 shares of our common stock issuable upon the exercise of options granted subsequent to September 30, 2023, at a weighted average exercise price of \$2.38 per share;
- 5,934,176 shares of common stock issuable upon exercise of pre-funded warrants as of September 30, 2023, at an exercise price of \$0.001 per share;
- 1,078,248 shares of common stock reserved for issuance under our 2021 Equity Incentive Plan (the 2021 Plan) as of September 30, 2023, as well as shares that become available pursuant to provisions in our 2021 Plan that automatically increase the share reserve thereunder each year;
- 1,624,717 shares of common stock reserved for issuance under our 2021 Employee Stock Purchase Plan (the 2021 ESPP) as of September 30, 2023, as well as shares that become available pursuant to provisions in our 2021 ESPP that automatically increase the share reserve thereunder each year; and
- 2,222,271 shares of common stock issuable upon exercise of pre-funded warrants sold in this offering.

Up to \$75.0 million of shares of our common stock may be sold from time to time under our "at-the-market" program that we entered into on August 10, 2022, with Leerink Partners LLC. As of the date of this prospectus supplement, we have sold an aggregate of 535,767 shares of our common stock under this program for aggregate net proceeds of \$3.9 million.

Unless otherwise indicated, all information in this prospectus supplement assumes no exercise of outstanding options or warrants or vesting of outstanding restricted stock units after September 30, 2023, and no purchase and exercise of pre-funded warrants by any purchaser in this offering.

Certain existing stockholders, including stockholders affiliated with certain of our directors, are participating in this offering and are expected to purchase an aggregate of 2,222,222 shares of common stock, on the same terms as the other investors in this offering.

RISK FACTORS

Investing in our securities involves a high degree of risk. Before making a decision to invest in our securities, in addition to carefully considering the other information contained in this prospectus supplement, in the accompanying prospectus and in the documents incorporated by reference herein or therein, you should carefully consider the risks described below, as well as the risks discussed under the caption "Risk Factors" contained in our most recent annual report on Form 10-K and in our most recent quarterly reports on Form 10-Q, as well as any amendments thereto, which are incorporated by reference into this prospectus supplement in their entirety. The risks described in these documents are not the only ones we face. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could harm our future results. Past financial performance may not be a reliable indicator of future performance, and historical trends should not be used to anticipate results or trends in future periods. If any of these risks actually occurs, our business, financial condition, results of operations or prospects could be harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment. See "Where You Can Find More Information" and "Incorporation of Certain Information by Reference."

Risks Related to this Offering

The vesting of outstanding restricted stock units and the exercise of our outstanding options and warrants will dilute stockholders and could decrease our stock price.

The vesting of outstanding restricted stock units and the exercise of our outstanding options and warrants may adversely affect our stock price due to sales of a large number of shares or the perception that such sales could occur. These factors also could make it more difficult to raise funds through future offerings of our securities, and could adversely impact the terms under which we could obtain additional equity capital. Exercise of outstanding options and warrants or any future issuance of additional shares of common stock or other securities, including, but not limited to preferred stock, options, warrants, restricted stock units or other derivative securities convertible into our common stock, may result in significant dilution to our stockholders and may decrease our stock price.

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

As of September 30, 2023, we had 68,111,019 shares of our common stock outstanding. If our stockholders sell, or the market perceives that our stockholders intend to sell, a substantial amount of our common stock in the public market, the market price of our common stock could decline significantly. Sales of a substantial number of shares of our common stock in the public market could occur at any time, including by us pursuant to our existing "at-the-market" program, under which, as of February 7, 2024, we may issue and sell up to approximately \$71.0 million in additional shares of our common stock.

Shares issued upon the exercise of stock options or the vesting of restricted stock units outstanding under our equity incentive plans or pursuant to future awards granted under those plans will become available for sale in the public market to the extent permitted by the provisions of applicable vesting schedules and Rule 144 under the Securities Act.

Moreover, certain holders of our common stock have rights, subject to 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 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 any of these additional shares are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

Our management team will have broad discretion to use the net proceeds from this offering and its investment of these proceeds may not yield a favorable return.

Our management team will have broad discretion in the application of the net proceeds from this offering and could spend or invest the proceeds in ways that may not yield a favorable return or enhance the value of our common stock. Accordingly, investors will need to rely on our management team's judgment with respect to the use of these proceeds. We intend to use the proceeds from this offering in the manner described in the section titled "Use of Proceeds." The failure by management to apply these funds effectively could negatively affect our ability to operate and grow our business. We cannot specify with certainty all of the particular uses for the net proceeds to be received upon the completion of this offering. In addition, the amount, allocation and timing of our actual expenditures will depend upon numerous factors, including any milestone payments received from any future strategic partnerships. Accordingly, we will have broad discretion in using these proceeds. Until the net proceeds are used, they may be placed in investments that do not produce significant income or that may lose value.

We do not anticipate paying cash dividends and, accordingly, stockholders must rely on share appreciation for any return on their investment.

We have never paid any dividends on our capital stock. We currently intend to retain our future earnings, if any, to fund the development and growth of our businesses and do not anticipate that we will declare or pay any cash dividends on our capital stock in the foreseeable future. See the section titled "Dividend Policy." As a result, capital appreciation, if any, of our common stock will be your sole source of gain on your investment for the foreseeable future. Investors seeking cash dividends should not invest in our common stock.

You will experience immediate dilution in the book value per share of the securities you purchase in this offering.

Because the price per share of our common stock being offered is substantially higher than the net tangible book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. Our net tangible book value as of September 30, 2023, was approximately \$164.9 million, or \$2.42 per share of our common stock. Therefore, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of \$1.83 per share with respect to the net tangible book value of our common stock, based on the sale of 11,111,161 shares in total at an assumed offering price of \$4.50 per share (assuming the exercise of all pre-funded warrants sold in this offering). See the section titled "Dilution" in this prospectus supplement for a detailed discussion of the dilution you will incur if you purchase common stock in this offering.

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

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 of these new securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing, if available, may involve fixed payment obligations or agreements that include covenants limiting or restricting our ability to take specific actions such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through partnerships, collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, product candidates or future revenue streams, or grant licenses on terms that are not favorable to us. We cannot assure you that we will be able to obtain additional funding if and when necessary. If we are unable to obtain adequate financing on a timely basis, we could be required to delay, scale back or eliminate one or more of our clinical, preclinical or discovery programs or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. In addition, 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.

Our operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.

We expect our operating results to be subject to fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expense related to the ongoing development of our product candidates or future development programs;
- results of preclinical studies and clinical trials, or the addition or termination of preclinical studies and clinical trials or funding support by
 us or potential future collaborators;
- our execution of any collaboration, licensing or similar arrangements, and the timing of payments we may make or receive under potential future arrangements or the termination or modification of any of our existing or potential future collaboration, licensing or similar arrangements;
- any intellectual property infringement, misappropriation or violation lawsuit or opposition, interference or cancellation proceeding in which we may become involved;
- additions and departures of key personnel;
- strategic decisions by us or our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;
- if any of our product candidates receives regulatory approval, the terms of such approval and market acceptance and demand for such product candidates;
- competition from existing and potential future products and changes in the competitive landscape of our industry;
- regulatory developments affecting our product candidates or those of our competitors; and
- changes in general market and economic conditions.

If our operating results or announcements related to our product candidates fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any fluctuations in our operating results or announcements related to our product candidates may, in turn, cause the price of our stock to fluctuate substantially. We believe that comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

There is no public market for the pre-funded warrants being offered in this offering.

There is no public trading market for the pre-funded warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to list the pre-funded warrants on the Nasdaq Global Select Market or any other national securities exchange or nationally recognized trading system. Without an active trading market, the liquidity of the pre-funded warrants will be limited.

Holders of the pre-funded warrants will have no rights as common stockholders until such holders exercise their pre-funded warrants and acquire our common stock.

Until holders of the pre-funded warrants exercise their pre-funded warrants and acquire shares of our common stock, such holders will have no rights with respect to the shares of our common stock underlying such pre-funded warrants.

Significant holders or beneficial owners of our common stock may not be permitted to exercise the pre-funded warrants that they hold.

A holder of the pre-funded warrants will not be entitled to exercise any portion of any pre-funded warrant that, upon giving effect to such exercise, would cause (i) the aggregate number of shares of our common stock

beneficially owned by such holder (together with its affiliates) to exceed 9.99% of the number of shares of our common stock outstanding immediately after giving effect to the exercise; or (ii) the combined voting power of our securities beneficially owned by such holder (together with its affiliates) to exceed 9.99% of the combined voting power of all of our securities outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants and subject to such holder's rights under the pre-funded warrants to increase or decrease such percentage to any other percentage not in excess of 19.99% upon at least 61 days' prior notice from the holder to us. As a result, you may not be able to exercise your pre-funded warrants for shares of our common stock at a time when it would be financially beneficial for you to do so. In such a circumstance, you could seek to sell your pre-funded warrants to realize value, but you may be unable to do so in the absence of an established trading market.

USE OF PROCEEDS

We estimate that the net proceeds to us from the issuance and sale of shares of common stock and pre-funded warrants in this offering will be approximately \$46.5 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering, together with our existing cash, cash equivalents and marketable securities, to fund the ongoing and planned development of our lead gene therapy product candidates, the continued development of our earlier-stage research programs, the progression of our core capabilities, and for working capital and other general corporate purposes.

Pending the specific use of net proceeds as described in this prospectus supplement, we intend to invest the net proceeds to us from this offering in short and intermediate-term investment grade instruments, certificates of deposit or guaranteed obligations of the U.S. government in accordance with our investment policy.

Our expected use of proceeds from this offering represents our current intentions based on our present plans and business condition. As of the date of this prospectus supplement, we cannot predict with certainty all of the particular uses for the proceeds to be received upon the completion of this offering or the actual amounts that we will spend on the uses set forth above. We may also use a portion of the proceeds to in-license, acquire or invest in additional businesses, technologies, products or assets. Although we have no specific agreements, commitments or understandings with respect to any in-licensing activity or acquisition, we evaluate these opportunities and engage in related discussions with other companies from time to time.

The net proceeds from this offering, together with our existing cash, cash equivalents and marketable securities, will not be sufficient for us to fund our clinical programs, and we will need to raise additional capital to achieve our business objectives.

The amount and timing of our actual expenditures will depend on numerous factors, including the results of our research and development efforts, the timing and outcome of any ongoing or future preclinical studies and clinical trials the timing and outcome of regulatory submissions and any unforeseen cash needs. As a result, our management will have broad discretion over the use of the proceeds from this offering.

DILUTION

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

Our historical net tangible book value as of September 30, 2023, was approximately \$164.9 million, or approximately \$2.42 per share of common stock based upon 68,111,019 shares outstanding as of September 30, 2023. Historical net tangible book value per share represents the amount of our total tangible assets less total liabilities, divided by the number of shares of our common stock outstanding as of September 30, 2023.

After giving effect to the sale by us of 11,111,161 shares of our common stock in this offering (which assumes the exercise of all pre-funded warrants sold in this offering) based on the offering price of \$4.50 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2023 would have been \$211.4 million, or \$2.67 per share of common stock. This represents an immediate increase in net tangible book value of \$0.25 per share to our existing stockholders and an immediate dilution of \$1.83 in net tangible book value per share to new investors purchasing common stock in this offering. Dilution per share to new investors is determined by subtracting as adjusted net tangible book value per share after this offering from the offering price per share paid by new investors.

The following table illustrates this calculation on a per share basis.

Offering price per share		\$4.50
Net tangible book value per share as of September 30, 2023	\$2.42	
Increase in net tangible book value per share attributable to this offering	0.25	
As adjusted net tangible book value per share after to this offering		2.67
Dilution per share to new investors purchasing in this offering		\$1.83

The above discussion and table are based on 68,111,019 shares of our common stock outstanding as of September 30, 2023 and excludes:

- 8,224,346 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2023, at a weighted average exercise price of \$7.57 per share;
- 1,094,781 shares of common stock issuable upon vesting of restricted stock units outstanding as of September 30, 2023;
- 253,600 shares of our common stock issuable upon the exercise of options granted subsequent to September 30, 2023, at a weighted average exercise price of \$2.38 per share;
- 5,934,176 shares of common stock issuable upon exercise of pre-funded warrants as of September 30, 2023 at an exercise price of \$0.001 per share:
- 1,078,248 shares of common stock reserved for issuance under our 2021 Equity Incentive Plan (the 2021 Plan) as of September 30, 2023, as well as shares that become available pursuant to provisions in our 2021 Plan that automatically increase the share reserve thereunder each year; and
- 1,624,717 shares of common stock reserved for issuance under our 2021 Employee Stock Purchase Plan (the 2021 ESPP) as of September 30, 2023, as well as shares that become available pursuant to provisions in our 2021 ESPP that automatically increase the share reserve thereunder each year.

To the extent that outstanding options or restricted stock awards or warrants outstanding as of September 30, 2023 have been or may be exercised or other shares issued, including pursuant to our 2021 ESPP, investors purchasing our common stock in this offering may experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities or other equity-linked securities, the issuance of these securities could result in further dilution to our stockholders.

DIVIDEND POLICY

We have never declared or paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends to holders of our common stock in the foreseeable future. Payment of future cash dividends, if any, will be at the discretion of our board of directors after taking into account various factors, including our financial condition, operating results, current and anticipated cash needs, the requirements and contractual restrictions of then-existing debt instruments, and other factors that our board of directors deems relevant.

DESCRIPTION OF PRE-FUNDED WARRANTS

The following is a brief summary of certain terms and conditions of the pre-funded warrants being offered by this prospectus supplement. The following description is subject in all respects to the provisions contained in the pre-funded warrants.

Form

The pre-funded warrants will be issued as individual warrant agreements to the investors. You should review the form of pre-funded warrant, which is filed as an exhibit to a Current Report on Form 8-K that we filed with the SEC.

Term

The pre-funded warrants will expire on the date the warrant is exercised in full.

Exercisability

The pre-funded warrants are exercisable at any time on or after their original issuance. The pre-funded warrants will be exercisable, at the option of each holder, in whole or in part by delivering to us a duly executed exercise notice and by payment in full in immediately available funds for the number of shares of common stock purchased upon such exercise. As an alternative to payment in immediately available funds, the holder may, in its sole discretion, elect to exercise the pre-funded warrant through a cashless exercise, in which case the holder would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the pre-funded warrant. No fractional shares of common stock will be issued in connection with the exercise of a pre-funded warrant. In lieu of fractional shares, we will pay the holder an amount in cash equal to the fractional amount multiplied by the fair market value of the common stock on the exercise date.

Exercise Limitations

We may not effect the exercise of any pre-funded warrant, and a holder will not be entitled to exercise any portion of any pre-funded warrant that, upon giving effect to such exercise, would cause: (i) the aggregate number of shares of our common stock beneficially owned by such holder (together with its affiliates) to exceed 9.99% of the number of shares of our common stock outstanding immediately after giving effect to the exercise; or (ii) the combined voting power of our securities beneficially owned by such holder (together with its affiliates) to exceed 9.99% of the combined voting power of all of our securities outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants. However, any holder of a pre-funded warrant may increase or decrease such percentage to any other percentage not in excess of 19.99% upon at least 61 days' prior notice from the holder to us.

Exercise Price

The exercise price per whole share of our common stock purchasable upon the exercise of the pre-funded warrants is \$0.001 per share of common stock. The exercise price of the pre-funded warrants is subject to appropriate adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our common stock and also upon any distributions of assets, including cash, stock or other property to our stockholders.

Transferability

Subject to applicable laws, the pre-funded warrants may be offered for sale, sold, transferred or assigned without our consent.

Exchange Listing

There is no established trading market for the pre-funded warrants, and we do not expect a market to develop. We do not plan on applying to list the pre-funded warrants on the Nasdaq Global Select Market, any other national securities exchange or any other nationally recognized trading system.

Fundamental Transactions

In the event of a fundamental transaction, as described in the pre-funded warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding common stock, or any person or group becoming the beneficial owner of 50% of the voting power represented by our outstanding common stock, the holders of the pre-funded warrants will be entitled to receive upon exercise of the pre-funded warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the pre-funded warrants immediately prior to such fundamental transaction. In the event a holder does not exercise its pre-funded warrants in connection with a fundamental transaction, such holder's pre-funded warrants will be deemed exercised in full pursuant to the "cashless exercise" mechanism described above upon the consummation of such transaction.

Rights as a Stockholder

Except by virtue of such holder's ownership of shares of our common stock, the holder of a pre-funded warrant does not have the rights or privileges of a holder of our common stock, including any voting rights, until the holder exercises the pre-funded warrant.

MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES FOR HOLDERS OF COMMON STOCK AND PRE-FUNDED WARRANTS

The following is a summary of the material U.S. federal income tax consequences of the ownership and disposition of our common stock and pre-funded warrants acquired in this offering, but does not purport to be a complete analysis of all the potential tax considerations relating thereto. This summary is based upon the provisions of the United States Internal Revenue Code of 1986, as amended, or the Code, Treasury regulations promulgated thereunder, administrative rulings and judicial decisions, all as of the date hereof. These authorities may be changed, possibly retroactively, so as to result in U.S. federal income tax consequences different from those set forth below. We have not sought, and do not intend to seek, any ruling from the Internal Revenue Service, or IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS or a court will agree with such statements and conclusions.

This summary also does not address the tax considerations arising under the laws of any non-U.S., state or local jurisdiction, under U.S. federal gift and estate tax rules nor does it address any aspects of the alternative minimum tax, the special tax accounting rules under Section 451(b) of the Code, or the Medicare tax on net investment income. In addition, this discussion does not address tax considerations applicable to an investor's particular circumstances or to investors that may be subject to special tax rules, including, without limitation:

- banks, insurance companies, regulated investment companies, real estate investment trusts or other financial institutions;
- tax-exempt organizations or governmental organizations;
- pension plans and tax-qualified retirement plans;
- controlled foreign corporations, passive foreign investment companies and corporations that accumulate earnings to avoid U.S. federal income tax:
- brokers or dealers in securities or currencies;
- traders in securities that elect to use a mark-to-market method of accounting for their securities holdings;
- persons that own, or are deemed to own, more than five percent of our capital stock and/or pre-funded warrants (except to the extent specifically set forth below);
- certain former citizens or long-term residents of the United States;
- persons who acquired our common stock pursuant to the exercise of any employee stock option or otherwise as compensation;
- persons who hold our common stock or pre-funded warrants as a position in a hedging transaction, "straddle," "conversion transaction" or other risk reduction transaction;
- persons who do not hold our common stock or pre-funded warrants as a capital asset within the meaning of Section 1221 of the Code (generally, property held for investment); or
- persons deemed to sell our common stock or pre-funded warrants under the constructive sale provisions of the Code.

In addition, if a partnership, entity or arrangement classified as a partnership or flow-through entity for U.S. federal income tax purposes holds our common stock or pre-funded warrants, the tax treatment of a partner in such partnership or other entity generally will depend on the status of the partner and upon the activities of the partnership or other entity. A partner in a partnership or other such entity that will hold our common stock or pre-funded warrants should consult his, her or its own tax advisor regarding the tax consequences of the ownership and disposition of our common stock or pre-funded warrants through a partnership or other such entity, as applicable.

You are urged to consult your tax advisor with respect to the application of the U.S. federal income tax laws to your particular situation, as well as any tax consequences of the purchase, ownership and disposition of our common stock, or pre-funded warrants, arising under the U.S. federal gift or estate tax rules or under the laws of any state, local, non-U.S. or other taxing jurisdiction or under any applicable tax treaty.

U.S. Holder and Non-U.S. Holder Defined

For purposes of this discussion, you are a "U.S. holder" if you are a beneficial owner (other than a partnership or other entity or arrangement classified as a partnership for U.S. federal income tax purposes) of our common stock or pre-funded warrants that, for U.S. federal income tax purposes, is:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity taxable as a corporation, created or organized in the United States or under the laws of the United States or any political subdivision thereof, or otherwise treated as such for U.S. federal income tax purposes;
- an estate whose income is subject to U.S. federal income tax regardless of its source; or
- a trust (1) whose administration is subject to the primary supervision of a U.S. court and that has one or more U.S. persons (within the meaning of the Code) who have the authority to control all substantial decisions of the trust or (2) that has made a valid election under applicable Treasury regulations to be treated as a U.S. person.

For purposes of this discussion, you are a "non-U.S. holder" if you are a beneficial owner of our common stock or pre-funded warrants that is not a U.S. holder or a partnership (or other entity or arrangement classified as a partnership for U.S. federal income tax purposes).

General Treatment of Pre-Funded Warrants

Although the law in this area is not completely settled, the pre-funded warrants are generally expected to be treated as outstanding stock for U.S. federal income tax purposes. Accordingly, upon exercise, no income, gain or loss should be recognized upon the exercise of a prefunded warrant except to the extent of cash received in exchange for a fractional share, which will be treated as a sale subject to the rules described below under "Tax Consequences Applicable to U.S. Holders—Gain on Disposition of Common Stock or Pre-Funded Warrants," and "Tax Consequences Applicable to Non-U.S. Holders—Gain on Disposition of Common Stock or Pre-Funded Warrants," and the holding period of a pre-funded warrant should carry over to the share of common stock received. The tax basis of the pre-funded warrant should carry over to the share of common stock received upon exercise of the pre-funded warrant increased by the exercise price. If you are contemplating the acquisition of pre-funded warrants, you should discuss with your personal tax advisor the consequences of the purchase, ownership and disposition of the pre-funded warrants, as well as the exercise of, certain adjustments to, and any payments in respect of the pre-funded warrants (including potential alternative characterizations).

Tax Consequences Applicable to U.S. Holders

Distributions

We have never declared or paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends to holders of our common stock in the foreseeable future. However, if we do make distributions on our common stock, those payments will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those distributions exceed both our current and our accumulated earnings and profits, the excess will

constitute a return of capital and will first reduce your basis in our common stock, but not below zero, and then will be treated as gain from the sale of stock as described below under "Tax Consequences Applicable to U.S. Holders—Gain on Disposition of Common Stock or Pre-Funded Warrants." If you are a non-corporate U.S. holder, and certain requirements are met, a preferential U.S. federal income tax rate will apply to any dividends paid to you if you meet certain holding period requirements.

If you are a corporate shareholder, distributions constituting dividends for U.S. federal income tax purposes will generally be eligible for the dividends received deduction, or DRD. No assurance can be given that we will have sufficient earnings and profits (as determined under U.S. federal income tax principles) to cause any distributions to be eligible for a DRD. In addition, a DRD is available only if certain holding periods and other taxable income requirements are satisfied.

The taxation of a distribution received with respect to a pre-funded warrant is unclear. It is possible such a distribution would be treated as a distribution as described in this section, although other treatments may also be possible. You should consult your tax advisors regarding the proper treatment of any payments in respect of the pre-funded warrants.

Gain on Disposition of Common Stock or Pre-Funded Warrants

Upon a sale or other taxable disposition of common stock or pre-funded warrants, you generally will recognize capital gain or loss in an amount equal to the difference between the amount realized and your adjusted tax basis in the common stock or pre-funded warrant. Capital gain or loss will constitute long-term capital gain or loss if your holding period for the common stock or pre-funded warrant exceeds one year. The deductibility of capital losses is subject to certain limitations. U.S. holders who recognize losses with respect to a disposition of our common stock or pre-funded warrants should consult their own tax advisors regarding the tax treatment of such losses.

Certain Adjustments to Pre-Funded Warrants

Under Section 305 of the Code, an adjustment to the number of shares of common stock that will be issued on the exercise of the pre-funded warrants, or an adjustment to the exercise price of the pre-funded warrants, may be treated as a constructive distribution to you of the pre-funded warrants if, and to the extent that, such adjustment has the effect of increasing your proportionate interest in our "earnings and profits" or assets, depending on the circumstances of such adjustment (for example, if such adjustment is to compensate for a distribution of cash or other property to our shareholders). Any such adjustment that is treated as a constructive distribution would be treated as a dividend, subject to withholding, to the extent described above under "Tax Consequences Applicable to U.S. Holders—Distributions." You should consult your tax advisor regarding the proper tax treatment of any such adjustment.

Backup Withholding and Information Reporting

Information reporting requirements generally will apply to payments of dividends (including constructive dividends) on the common stock or pre-funded warrants and to the proceeds of a sale or other disposition of common stock or pre-funded warrants paid to you unless you are an exempt recipient, such as certain corporations. Backup withholding at a current rate of 24% will apply to those payments if you fail to provide your taxpayer identification number (generally in the form of a properly completed and executed IRS Form W-9), or certification of exempt status, or if you otherwise fail to comply with applicable requirements to establish an exemption.

Backup withholding is not an additional tax; rather, the U.S. federal income tax liability of persons subject to backup withholding will be reduced by the amount of tax withheld. If withholding results in an overpayment of taxes, a refund or credit may generally be obtained from the IRS, provided that the required information is furnished to the IRS in a timely manner.

Tax Consequences Applicable to Non-U.S. Holders

Distributions

We have never declared or paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends to holders of our common stock in the foreseeable future. However, if we do make distributions on our common stock, those payments generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those distributions exceed both our current and our accumulated earnings and profits, the excess will constitute a return of capital and will first reduce your basis in our common stock, but not below zero, and then will be treated as gain from the sale of stock, treated as described below in "Tax Consequences Applicable to Non-U.S. Holders—Gain on Disposition of Common Stock or Pre-Funded Warrants."

Subject to the discussions below on effectively connected income and Foreign Account Tax Compliance Act, or FATCA, any dividend paid to you generally will be subject to U.S. federal withholding tax either at a rate of 30% of the gross amount of the dividend or such lower rate as may be specified by an applicable income tax treaty between the United States and your country of residence. In order to receive a reduced treaty rate, you must provide the applicable withholding agent with an IRS Form W-8BEN or W-8BEN-E or other appropriate version of IRS Form W-8 certifying qualification for the reduced rate. A non-U.S. holder of shares of our common stock or pre-funded warrants eligible for a reduced rate of U.S. federal withholding tax pursuant to an income tax treaty may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. If the non-U.S. holder holds our common stock or pre-funded warrants through a financial institution or other agent acting on the non-U.S. holder's behalf, the non-U.S. holder will be required to provide appropriate documentation to the agent, which then will be required to provide certification to the applicable withholding agent, either directly or through other intermediaries.

Dividends received by you that are treated as effectively connected with your conduct of a U.S. trade or business (and, if required by an applicable income tax treaty, such dividends are attributable to a permanent establishment or fixed base maintained by you in the United States) are generally exempt from the 30% U.S. federal withholding tax, subject to the discussion below on backup withholding and FATCA. In order to obtain this exemption, you must provide the applicable withholding agent with a properly executed IRS Form W-8ECI or other applicable IRS Form W-8 properly certifying such exemption. Such effectively connected dividends, although not subject to U.S. federal withholding tax, are taxed at the same rates applicable to U.S. persons, net of certain deductions and credits, subject to an applicable income tax treaty providing otherwise. In addition, if you are a corporate non-U.S. holder, dividends you receive that are effectively connected with your conduct of a U.S. trade or business may also be subject to a branch profits tax at a rate of 30% or such lower rate as may be specified by an applicable income tax treaty between the United States and your country of residence. You should consult your tax advisor regarding the tax consequences of the ownership and disposition of our common stock or pre-funded warrants, including any applicable tax treaties that may provide for different rules.

The taxation of a distribution received with respect to a pre-funded warrant is unclear. It is possible such a distribution would be treated as a distribution as described in this section, although other treatments may also be possible. You should consult your own tax advisors regarding the proper treatment of any payments in respect of the pre-funded warrants.

Gain on Disposition of Common Stock or Pre-Funded Warrants

Subject to the discussion below regarding backup withholding and FATCA, you generally will not be required to pay U.S. federal income tax on any gain realized upon the sale or other disposition of our common stock or pre-funded warrants unless:

• the gain is effectively connected with your conduct of a U.S. trade or business (and, if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by you in the United States);

- you are an individual who is present in the United States for a period or periods aggregating 183 days or more during the calendar year in which the sale or disposition occurs and certain other conditions are met; or
- our common stock constitutes a United States real property interest by reason of our status as a "United States real property holding corporation," or USRPHC, for U.S. federal income tax purposes at any time within the shorter of the five-year period preceding your disposition of, or your holding period for, our common stock.

We believe that we are not currently and will not become a USRPHC for U.S. federal income tax purposes, and the remainder of this discussion so assumes. However, because the determination of whether we are a USRPHC depends on the fair market value of our U.S. real property interests relative to the fair market value of our U.S. and worldwide real property interests plus our other business assets, there can be no assurance that we will not become a USRPHC in the future. Even if we become a USRPHC, however, as long as our common stock is regularly traded on an established securities market, your common stock will be treated as a U.S. real property interest only if you actually (directly or indirectly) or constructively hold more than five percent of such regularly traded common stock at any time during the shorter of the five-year period preceding your disposition of, or your holding period for, our common stock. Special rules may apply to non-U.S. holders of pre-funded warrants, who should consult their tax advisors.

If you are a non-U.S. holder described in the first bullet above, you generally will be required to pay tax on the gain derived from the sale (net of certain deductions and credits) under regular U.S. federal income tax rates applicable to U.S. persons, and a corporate non-U.S. holder described in the first bullet above also may be subject to the branch profits tax at a 30% rate, or such lower rate as may be specified by an applicable income tax treaty. If you are an individual non-U.S. holder described in the second bullet above, you will be subject to tax at 30% (or such lower rate specified by an applicable income tax treaty) on the gain derived from the sale, which gain may be offset by U.S. source capital losses for the year, provided you have timely filed U.S. federal income tax returns with respect to such losses. You should consult your tax advisor regarding any applicable income tax treaties or other agreements that may provide for different rules.

Certain Adjustments to Pre-Funded Warrants

Under Section 305 of the Code, an adjustment to the number of shares of common stock that will be issued on the exercise of the pre-funded warrants, or an adjustment to the exercise price of the pre-funded warrants, may be treated as a constructive distribution to you of the pre-funded warrants if, and to the extent that, such adjustment has the effect of increasing your proportionate interest in our "earnings and profits" or assets, depending on the circumstances of such adjustment (for example, if such adjustment is to compensate for a distribution of cash or other property to our shareholders). Any such adjustment that is treated as a constructive distribution would be treated as a dividend, subject to withholding, to the extent described above under "Tax Consequences Applicable to U.S. Holders—Distributions." You should consult your tax advisor regarding the proper tax treatment of any such adjustment.

Backup Withholding and Information Reporting

Generally, we or the applicable paying agent must report annually to the IRS the amount of dividends paid to you, your name and address, and the amount of tax withheld, if any. A similar report will be sent to you. Pursuant to applicable income tax treaties or other agreements, the IRS may make these reports available to tax authorities in your country of residence.

Payments of dividends on or of proceeds from the disposition of our common stock or pre-funded warrants made to you will generally be subject to information reporting and backup withholding at a current rate of 24% unless you establish an exemption, for example, by properly certifying your non-U.S. status on a properly

completed IRS Form W-8BEN or W-8BEN-E, or W-8ECI or another appropriate version of IRS Form W-8 or you otherwise meet the documentary evidence requirements for establishing that you are not a U.S. person or otherwise establish an exemption. Notwithstanding the foregoing, backup withholding and information reporting may apply if the applicable withholding agent has actual knowledge, or reason to know, that you are a U.S. person.

Backup withholding is not an additional tax; rather, the U.S. federal income tax liability of persons subject to backup withholding will be reduced by the amount of tax withheld. If withholding results in an overpayment of taxes, a refund or credit may generally be obtained from the IRS, provided that the required information is furnished to the IRS in a timely manner.

Foreign Account Tax Compliance Act

Provisions of the Code commonly referred to as FATCA, Treasury regulations issued thereunder and official IRS guidance generally impose a U.S. federal withholding tax of 30% on dividends on, and, subject to the discussion of certain proposed Treasury regulations below, the gross proceeds from a sale or other disposition of our common stock or pre-funded warrants, paid to a "foreign financial institution" (as specially defined under these rules), unless such institution enters into an agreement with the U.S. government to, among other things, withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding the U.S. account holders of such institution (which includes certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with U.S. owners) or otherwise establishes an exemption from FATCA withholding. FATCA also generally imposes a U.S. federal withholding tax of 30% on dividends on, and, subject to the discussion of certain proposed Treasury regulations below, the gross proceeds from, a sale or other disposition of our common stock or pre-funded warrants paid to a "non-financial foreign entity" (as specially defined under these rules), unless such entity provides the withholding agent with a certification identifying the substantial direct and indirect U.S. owners of the entity, certifies that it does not have any substantial U.S. owners, or otherwise establishes an exemption.

The withholding obligations under FATCA generally apply to dividends on our common stock or pre-funded warrants and subject to the proposed Treasury regulations described in the next sentence, will apply to the payment of gross proceeds of a sale or other disposition of our common stock or pre-funded warrants. The Treasury Department has released proposed Treasury regulations (the preamble to which specifies that taxpayers are permitted to rely on them pending finalization) that, if finalized in their present form, would eliminate the federal withholding tax of 30% applicable to the gross proceeds of a disposition of our common stock or pre-funded warrants. The withholding tax on dividends will apply regardless of whether the payment otherwise would be exempt from U.S. non-resident and backup withholding tax, including under the exemptions described above. Under certain circumstances, a non-U.S. holder might be eligible for refunds or credits of such taxes. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this section. Prospective investors are encouraged to consult with their own tax advisors regarding the application of FATCA withholding to their investment in, and ownership and disposition of, our common stock or pre-funded warrants.

The preceding discussion of U.S. federal tax considerations is for general information only. It is not tax advice to investors in their particular circumstances. Each prospective investor should consult its own tax advisor regarding the particular U.S. federal, state and local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock or pre-funded warrants, including the consequences of any proposed change in applicable laws.

UNDERWRITING

Leerink Partners LLC and Cowen and Company, LLC are acting as representatives of each of the underwriters named below and as joint bookrunning managers for this offering. Subject to the terms and conditions set forth in the underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of shares of common stock and pre-funded warrants set forth opposite its name below.

Underwriter	Number of Shares	Pre-Funded Warrants
Leerink Partners LLC	4,000,001	1,000,022
Cowen and Company, LLC	4,000,001	1,000,022
LifeSci Capital LLC	888,888	222,227
Total	8,888,890	2,222,271

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the shares and pre-funded warrants sold under the underwriting agreement if any of the shares or pre-funded warrants are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares and pre-funded warrants, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares and pre-funded warrants, and subject to other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officers' certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers and to reject orders in whole or in part.

Discounts and Commissions

The representatives have advised us that the underwriters propose initially to offer the shares and pre-funded warrants at the initial offering price set forth on the cover page of this prospectus supplement and to dealers at that price less a concession not in excess of \$0.162 per share or pre-funded warrant. After the initial offering of the shares and pre-funded warrants, the offering price, concession or any other term of this offering may be changed by the representatives.

The following table shows the initial offering price, underwriting discounts and commissions and proceeds, before expenses, to us.

		Per Pre-Funded			
	Per Share	Warrant		Total	
Offering price	\$ 4.500	\$	4.499	\$49,998,002	
Underwriting discounts and commissions	\$ 0.270	\$	0.270	\$ 3,000,013	
Proceeds before expenses, to us	\$ 4.230	\$	4.229	\$46,997,989	

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$485,000. We have agreed to reimburse the underwriters for certain expenses in an amount up to \$15,000.

No Sales of Similar Securities

We, our executive officers and directors and certain of our other existing security holders have agreed not to sell or transfer any common stock or securities convertible into or exchangeable or exercisable for common stock, for 60 days after the date of this prospectus supplement without first obtaining the written consent of the representatives on behalf of the underwriters. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly:

- offer, pledge, sell or contract to sell any common stock;
- sell any option or contract to purchase any common stock;
- purchase any option or contract to sell any common stock;
- grant any option, right or warrant for the sale of any common stock;
- otherwise dispose of or transfer any common stock;
- request or demand that we file a registration statement related to the common stock; or
- enter into any swap or other agreement or any transaction that transfers, in whole or in part, the economic consequence of ownership of
 any common stock, whether any such swap, agreement or transaction is to be settled by delivery of shares or other securities, in cash or
 otherwise

The lock-up provisions apply to common stock and to securities convertible into or exchangeable or exercisable for common stock. They also apply to common stock owned now or acquired later by the person executing the lock-up agreement or for which the person executing the lock-up agreement later acquires the power of disposition.

The lock-up provisions do not limit our ability to issue and sell shares of our common stock pursuant to placements under our "at-the-market" offering program.

Nasdaq Global Select Market Listing

Our common stock is listed on the Nasdaq Global Select Market under the symbol "TNYA."

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of the shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our common stock. However, the representatives may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with this offering, the underwriters may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in this offering. Stabilizing transactions permit bids to purchase shares of common stock so long as the stabilizing bids do not exceed a specified maximum, and are engaged in for the purpose of preventing or retarding a decline in the market price of the common stock while the offering is in progress. Syndicate covering transactions involve purchases of common stock in the open market after the distribution has been completed in order to cover syndicate short positions. If the underwriters sell more shares in excess of the number of shares the underwriters are obligated to purchase and, therefore, have a naked short position, the position can be closed out only by buying shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that after pricing there could be downward pressure on the price of the shares in the open market that could adversely affect investors who purchase in the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on the Nasdaq Global Select Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor any of the underwriters make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Electronic Distribution

In connection with this offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Some of the underwriters and certain of their affiliates may in the future engage in investment banking and other commercial dealings in the ordinary course of business with us and our affiliates, for which they may in the future receive customary fees, commissions and expenses.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Leerink Partners LLC is the sales agent for us under our "at-the-market" program. Under our "at-the-market" program, we may offer and sell, from time to time, shares of our common stock through Leerink Partners LLC through an "at-the-market offering," as defined in Rule 415(a)(4) promulgated under the Securities Act.

Selling Restrictions

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area (each, a "Relevant State"), no securities have been offered or will be offered pursuant to the offering to the public in that Relevant State prior to the publication of a prospectus in relation to the securities which has been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation, except that securities may be offered in that Relevant State at any time:

A. to any legal entity which is a qualified investor as defined under Article 2 of the Prospectus Regulation;

- B. to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the Prospectus Regulation), subject to obtaining the prior consent of the representatives for any such offer; or
- C. in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of securities shall require us or any of the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

For the purposes of this provision, the expression an "offer to the public" in relation to any securities in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any securities to be offered so as to enable an investor to decide to purchase or subscribe for any securities, and the expression "Prospectus Regulation" means Regulation (EU) 2017/1129, as amended

Notice to Prospective Investors in the United Kingdom

No securities have been offered or will be offered pursuant to the offering to the public in the United Kingdom prior to the publication of a prospectus in relation to the securities which has been approved by the Financial Conduct Authority, except that the securities may be offered to the public in the United Kingdom at any time:

- A. to any legal entity which is a qualified investor as defined under Article 2 of the UK Prospectus Regulation;
- B. to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the UK Prospectus Regulation), subject to obtaining the prior consent of the representatives for any such offer; or
- C. in any other circumstances falling within Section 86 of the Financial Services and Markets Act 2000 (the "FMSA"),

provided that no such offer of the securities shall require us or any representative to publish a prospectus pursuant to Section 85 of the FSMA or supplement a prospectus pursuant to Article 23 of the UK Prospectus Regulation. For the purposes of this provision, the expression an "offer to the public" in relation to the securities in the United Kingdom means the communication in any form and by any means of sufficient information on the terms of the offer and any securities to be offered so as to enable an investor to decide to purchase or subscribe for any securities and the expression "UK Prospectus Regulation" means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018.

Notice to Prospective Investors in Canada

The securities may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the securities must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Notice to Prospective Investors in Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange (SIX) or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company, or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority (FINMA), and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes (CISA). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

Notice to Prospective Investors in the Dubai International Financial Centre

This prospectus supplement relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority (DFSA). This prospectus supplement is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus supplement nor taken steps to verify the information set forth herein and has no responsibility for the prospectus supplement. The securities to which this prospectus supplement relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the securities offered should conduct their own due diligence on the securities. If you do not understand the contents of this prospectus supplement, you should consult an authorized financial advisor.

Notice to Prospective Investors in Australia

No placement document, prospectus supplement, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission (ASIC), in relation to the offering. This prospectus supplement does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001 (the Corporations Act), and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the securities may only be made to persons (the "Exempt Investors") who are "sophisticated investors" (within the meaning of section 708(8) of the Corporations Act), "professional investors" (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the securities without disclosure to investors under Chapter 6D of the Corporations Act.

The securities applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring securities must observe such Australian on-sale restrictions.

This prospectus supplement contains general information only and does not take account of the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus supplement is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

Notice to Prospective Investors in Hong Kong

The securities have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the securities has been or may be insued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Notice to Prospective Investors in Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) and, accordingly, will not be offered or sold, directly or indirectly, in Japan, or for the benefit of any Japanese Person or to others for re-offering or resale, directly or indirectly, in Japan or to any Japanese Person, except in compliance with all applicable laws, regulations and ministerial guidelines promulgated by relevant Japanese governmental or regulatory authorities in effect at the relevant time. For the purposes of this paragraph, "Japanese Person" shall mean any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

Notice to Prospective Investors in Singapore

This document has not been registered as a prospectus supplement with the Monetary Authority of Singapore. Accordingly, the securities have not been offered or sold or caused to be made the subject of an invitation for subscription or purchase and will not be offered or sold or caused to be made the subject of an invitation for subscription or purchase, and this prospectus supplement or any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the securities, has not been circulated or distributed, nor will it be circulated or distributed, whether directly or indirectly, to any person in Singapore other than (i) to an institutional investor (as defined in Section 4A of the Securities and Futures Act (Chapter 289) of Singapore, as modified or amended from time to time (the "SFA")) pursuant to Section 274 of the SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- a. a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- b. a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities or securities-based derivatives contracts (each term as defined in Section 2(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

- a. to an institutional investor or to a relevant person, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
- b. where no consideration is or will be given for the transfer;
- c. where the transfer is by operation of law;
- d. as specified in Section 276(7) of the SFA; or
- e. as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations of 2005 of Singapore (Regulation 32).

Singapore SFA *product classification*. In connection with Section 309B of the SFA and the CMP Regulations 2018, unless otherwise specified before an offer of shares, we have determined, and hereby notify all relevant persons (as defined in Section 309A(1) of the SFA), that the securities are "prescribed capital markets products" (as defined in the CMP Regulations 2018) and Excluded Investment Products (as defined in MAS Notice SFA 04-N12: Notice on the Sale of Investment Products and MAS Notice FAA-N16: Notice on Recommendations on Investment Products).

LEGAL MATTERS

The validity of the securities offered in this prospectus supplement will be passed upon for us by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California. Davis Polk & Wardwell LLP, Menlo Park, California, is acting as counsel for the underwriters.

EXPERTS

The financial statements of Tenaya Therapeutics, Inc., incorporated by reference in this prospectus supplement have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report. Such financial statements are incorporated by reference in reliance upon the report of such firm given their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at www.sec.gov.

This prospectus supplement and the accompanying prospectus are part of a registration statement on Form S-3 that we filed with the SEC and do not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. You may inspect a copy of the registration statement through the SEC's website, as provided above.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference much of the information that we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus supplement is considered to be part of this prospectus supplement. Because we are incorporating by reference future filings with the SEC, this prospectus supplement is continually updated and those future filings may modify or supersede some of the information included or incorporated by reference in this prospectus supplement. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus supplement or in any document previously incorporated by reference have been modified or superseded. This prospectus supplement incorporates by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (in each case, other than those documents or the portions of those documents furnished pursuant to Items 2.02 or 7.01 of any Current Report on Form 8-K and, except as may be noted in any such Form 8-K, exhibits filed on such form that are related to such information), until the offering of the securities under the registration statement of which this prospectus supplement forms a part is terminated or completed:

- our Annual Report on Form 10-K for the year ended December 31, 2022, filed with the SEC on March 8, 2023;
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2023, June 30, 2023, and September 30, 2023, filed with the SEC on May 10, 2023, August 9, 2023 and November 8, 2023, respectively;
- the portions of our Definitive Proxy Statement on Schedule 14A (other than information furnished rather than filed) that are incorporated by reference into our Annual Report on Form 10-K, filed with the SEC on April 27, 2023;
- our Current Reports on Form 8-K filed on March 21, 2023, June 12, 2023, and February 8, 2024; and
- the description of our common stock contained in the Registration Statement on Form 8-A relating thereto, filed on July 23, 2021, including any amendment or report filed for the purpose of updating such description.

We will furnish without charge to each person to whom this prospectus supplement is delivered, upon written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents. You can request a copy of these filings by writing or telephoning us at the following address or telephone number:

Tenaya Therapeutics, Inc.
171 Oyster Point Boulevard, Suite 500
South San Francisco, California 94080
Attention: Investor Relations
(650) 825-6990

The information accessible through any website referred to in this prospectus supplement or any document incorporated therein is not, and should not be deemed to be, a part of this prospectus supplement.

PROSPECTUS



Tenaya Therapeutics, Inc.

\$300,000,000

Common Stock
Preferred Stock
Debt Securities
Depositary Shares
Warrants
Subscription Rights
Purchase Contracts
Units

We may issue securities from time to time in one or more offerings, in amounts, at prices and on terms determined at the time of offering. This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide the specific terms of these securities in supplements to this prospectus, which will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this prospectus. You should read this prospectus and any applicable prospectus supplement before you invest. The aggregate offering price of the securities we sell pursuant to this prospectus will not exceed \$300,000,000.

The securities may be sold directly to you, through agents or through underwriters and dealers. If agents, underwriters or dealers are used to sell the securities, we will name them and describe their compensation in a prospectus supplement. The price to the public of those securities and the net proceeds we expect to receive from that sale will also be set forth in a prospectus supplement.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "TNYA." Each prospectus supplement will indicate whether the securities offered thereby will be listed on any securities exchange.

We are an "emerging growth company" and "smaller reporting company" as defined under the federal securities laws, and, as such, may elect to comply with certain reduced public company reporting requirements for this and future filings. We will provide information in any applicable prospectus supplement regarding any listing of securities other than shares of our common stock on any securities exchange.

Investing in these securities involves risks. Please carefully read the information under the headings "Risk Factors" beginning on page 5 of this prospectus, any similar section contained in the applicable prospectus supplement, and "Item 1A—Risk Factors" of our most recent report on Form 10-K or 10-Q that is incorporated by reference in this prospectus before you invest in our securities.

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

The date of this prospectus is August 17, 2022.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission (SEC), using a "shelf" registration process. Under this shelf registration process, we may from time to time sell any combination of the securities described in this prospectus in one or more offerings for an aggregate offering price of up to \$300,000,000.

This prospectus provides you with a general description of the securities that may be offered. Each time we sell securities, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement or free writing prospectus may also add, update or change information contained in this prospectus with respect to that offering. You should read both this prospectus and any applicable prospectus supplement and free writing prospectus together with the additional information described under the heading "Where You Can Find More Information" and "Incorporation by Reference." If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement or free writing prospectus, you should rely on the prospectus supplement or free writing prospectus, as applicable.

We have not authorized anyone to provide you with information that is different from that contained, or incorporated by reference, in this prospectus, any applicable prospectus supplement or in any related free writing prospectus. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus and any applicable prospectus supplement or any related free writing prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in the applicable prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

PROSPECTUS SUMMARY

This summary highlights selected information that is presented in greater detail elsewhere, or incorporated by reference, in this prospectus. It does not contain all of the information that may be important to you and your investment decision. Before investing in our securities, you should carefully read this entire prospectus, including the matters set forth under the section of this prospectus captioned "Risk Factors" and the financial statements and related notes and other information that we incorporate by reference herein, including our Annual Report on Form 10-K and our Quarterly Reports on Form 10-Q. Unless the context indicates otherwise, references in this prospectus to "Tenaya Therapeutics, Inc.," "we," "our" and "us" refer, collectively, to Tenaya Therapeutics, Inc., a Delaware corporation.

Company Overview

We are a biotechnology company focused on discovering, designing, 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 in the preclinical stage; we do not have any products approved for sale and have not generated any revenue to date.

The most advanced product candidate from our Gene Therapy Platform is TN-201. TN-201 is an adeno-associated virus (AAV)-based gene therapy that addresses genetic hypertrophic cardiomyopathy (HCM) caused by Myosin Binding Protein C3 (*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, heart failure, and sudden cardiac death in some adults and children. TN-201 is designed to deliver a fully functional *MYBPC3* gene driven by our proprietary heart-specific promoter to restore normal levels of MYBPC3 protein. We remain on track with our Investigational New Drug (IND) submission plans for TN-201 in the second half of 2022 and plan to focus on initial clinical development in adult *MYBPC3* gene mutation carriers with symptomatic non-obstructive HCM. TN-201 has been granted orphan drug designation by both the U.S. Food and Drug Administration (FDA) and the European Commission for the potential treatment of HCM due to mutations in the *MYBPC3* gene.

In 2021, we initiated a global natural history study to improve our understanding of disease progression and unmet need in individuals carrying mutations in the *MYBPC3* gene, with an initial focus on pediatric patients under the age of 18. We continue site activation and patient enrollment in the global natural history study to support the future clinical evaluation of TN-201 in pediatric patients after early safety has been established in adults. The natural history 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.

TN-301, the most advanced product candidate from our Precision Medicine Platform, is a highly specific small molecule inhibitor of histone deacetylase 6 (HDAC6i). It has potentially broad utility in both heart failure with preserved ejection fraction (HFpEF) as well as genetic dilated cardiomyopathy. HFpEF is one of the greatest areas of unmet need in heart disease, and is characterized by systemic inflammation, left ventricular hypertrophy, fibrosis, and diastolic dysfunction resulting in high morbidity and mortality in affected individuals. We remain on track with our IND submission plans for TN-301 in the second half of 2022.

TN-401, another product candidate from our Gene Therapy Platform, uses an AAV-based gene therapy to address genetic arrhythmogenic right ventricular cardiomyopathy (ARVC) caused by plakophilin 2 (*PKP2*) gene mutations. ARVC is characterized by enlargement of the right ventricle in affected individuals, replacement

of heart muscle with fibrotic tissue and fatty deposits, and severely abnormal heart rhythms (arrhythmia) that can make it difficult for the heart to function properly and result in sudden cardiac death in some adults and children. We have scaled up production of TN-401 to 200L and are initiating IND-enabling studies. We also intend to support establishment of a global natural history study in 2022 and expect to submit an IND for TN-401 in 2023.

Our earlier-stage discovery programs include an AAV-based gene therapy designed to express the Dwarf Open Reading Frame (*DWORF*) gene in the heart, which has potentially broad utility in dilated cardiomyopathy and heart failure with reduced ejection fraction (HFrEF) and is currently at the candidate selection stage. Another program is an AAV-approach based on science from our founders that involves converting (or reprogramming) cells to replace cardiomyocytes lost due to heart damage, such as myocardial infarction. This program is currently at the candidate selection stage. In addition, we have numerous emerging programs being explored to address other forms of heart failure.

We have invested in significant gene therapy enabling capabilities, most notably with the build out and operational launch of our Genetic Medicines Manufacturing Center to support the production of our AAV-based programs. In June 2022, this facility obtained a drug manufacturing license from the State of California, Department of Public Health, to enable current Good Manufacturing Practice (cGMP) production of drug product. Located in Union City near our research labs, our Genetic Medicines Manufacturing Center enables scale-up of production to support first-in-human studies. This facility will initially support the production of drug product at multiple scales for clinical studies for all AAV-based programs, including TN-201 and TN-401. We have also initiated cGMP to support the production of TN-301 at a contract development and manufacturing organization (CDMO).

Corporate Information

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

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 website that contains reports, proxy and information statements and other information regarding our filings at www.sec.gov.

The Securities That May Be Offered

We may offer or sell common stock, preferred stock, depositary shares, debt securities, warrants, subscription rights, purchase contracts and units in one or more offerings and in any combination. The aggregate offering price of the securities we sell pursuant to this prospectus will not exceed \$300,000,000. Each time securities are offered with this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and terms of the securities being offered and the net proceeds we expect to receive from that sale.

The securities may be sold to or through underwriters, dealers or agents or directly to purchasers or as otherwise set forth in the section of this prospectus captioned "Plan of Distribution." Each prospectus supplement will set forth the names of any underwriters, dealers, agents or other entities involved in the sale of securities described in that prospectus supplement and any applicable fee, commission or discount arrangements with them.

Common Stock

We may offer shares of our common stock, par value \$0.0001 per share, either alone or underlying other registered securities convertible into our common stock. Holders of our common stock are entitled to receive dividends declared by our board of directors out of funds legally available for the payment of dividends, subject to rights, if any, of preferred stockholders. We have not paid dividends in the past and have no current plans to pay dividends. Each holder of common stock is entitled to one vote per share. The holders of common stock have no preemptive rights.

Preferred Stock

Our board of directors has the authority, subject to limitations prescribed by Delaware law, to issue preferred stock in one or more series, to establish from time to time the number of shares to be included in each series, and to fix the designation, powers, preferences and rights of the shares of each series and any of its qualifications, limitations or restrictions, in each case without further vote or action by our stockholders. Each series of preferred stock offered by us will be more fully described in the particular prospectus supplement that will accompany this prospectus, including redemption provisions, rights in the event of our liquidation, dissolution or winding up, voting rights and rights to convert into common stock.

Depositary Shares

We may issue fractional shares of preferred stock that will be represented by depositary shares and depositary receipts.

Each series of depositary shares or depositary receipts offered by us will be more fully described in the particular prospectus supplement that will accompany this prospectus, including redemption provisions, rights in the event of our liquidation, dissolution or winding up, voting rights and rights to convert into common stock.

Debt Securities

We may offer secured or unsecured obligations in the form of one or more series of senior or subordinated debt. The senior debt securities and the subordinated debt securities are together referred to in this prospectus as the "debt securities." The subordinated debt securities generally will be entitled to payment only after payment of our senior debt. Senior debt generally includes all debt for money borrowed by us, except debt that is stated in the instrument governing the terms of that debt to be not senior to, or to have the same rank in right of payment as, or to be expressly junior to, the subordinated debt securities. We may issue debt securities that are convertible into shares of our common stock.

The debt securities will be issued under an indenture between us and a trustee to be identified in an accompanying prospectus supplement. We have summarized the general features of the debt securities to be governed by the indenture in this prospectus and the form of indenture has been filed as an exhibit to the registration statement of which this prospectus forms a part. We encourage you to read the indenture.

Warrants

We may offer warrants for the purchase of common stock, preferred stock, debt securities or depositary shares. We may offer warrants independently or together with other securities.

Subscription Rights

We may offer subscription rights to purchase our common stock, preferred stock, debt securities, depositary shares, warrants or units consisting of some or all of these securities. These subscription rights may be offered independently or together with any other security offered hereby and may or may not be transferable by the stockholder receiving the subscription rights in such offering.

Purchase Contracts

We may offer purchase contracts, including contracts obligating holders or us to purchase from the other a specific or variable number of securities at a future date or dates.

Units

We may offer units comprised of one or more of the other classes of securities described in this prospectus in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit.

RISK FACTORS

An investment in our securities involves a high degree of risk. The prospectus supplement applicable to each offering of our securities will contain a discussion of the risks applicable to an investment in our securities. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the section in the applicable prospectus supplement captioned "Risk Factors," together with all of the other information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus. You should also consider the risks, uncertainties and assumptions discussed under "Part I—Item 1A—Risk Factors" of our most recent Annual Report on Form 10-K and in "Part II—Item 1A—Risk Factors" in our most recent Quarterly Reports on Form 10-Q filed subsequent to such Form 10-K that are incorporated herein by reference, as may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations. See "Where You Can Find More Information" and "Incorporation by Reference."

FORWARD-LOOKING STATEMENTS

This prospectus, each prospectus supplement and the information incorporated by reference in this prospectus and each prospectus supplement contain certain statements that constitute "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended (Securities Act), and Section 21E of the Securities Exchange Act of 1934, as amended (Exchange Act). The words "may," "will," "should," "would," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential" or "continue" or the negative of these terms and similar expressions and variations thereof are intended to identify forward-looking statements, but are not the exclusive means of identifying such statements. Those statements appear in this prospectus, any accompanying prospectus supplement and the documents incorporated herein and therein by reference, particularly in the sections captioned "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and include statements regarding the intent, belief or current expectations of our management that are subject to known and unknown risks, uncertainties and assumptions. You are cautioned that any such forward-looking statements are not guarantees of future performance and involve risks and uncertainties, and that actual results may differ materially from those projected in the forward-looking statements as a result of various factors.

Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely upon forward-looking statements as predictions of future events. The events and circumstances reflected in the 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, including the securities laws of the United States and the rules and regulations of the SEC, we do not plan to publicly update or revise any forward-looking statements contained herein after we distribute this prospectus, whether as a result of any new information, future events or otherwise.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and although 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 a thorough 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.

This prospectus and the documents incorporated by reference in this prospectus may contain market data that we obtain from industry sources. These sources do not guarantee the accuracy or completeness of the information. Although we believe that our industry sources are reliable, we do not independently verify the information. The market data may include projections that are based on a number of other projections. While we believe these assumptions to be reasonable and sound as of the date of this prospectus, actual results may differ from the projections.

USE OF PROCEEDS

We will set forth in the prospectus supplement our intended use for the net proceeds received from the sale of any securities. We will retain broad discretion over the use of the net proceeds to us from the sale of our securities under this prospectus.

DESCRIPTION OF CAPITAL STOCK

The description of our capital stock is incorporated by reference to $\underline{\text{Exhibit 4.3}}$ to our Annual Report on Form 10-K for the year ended December 31, 2021, filed with the SEC on March 23, 2022.

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplement, summarizes certain general terms and provisions of the debt securities that we may offer under this prospectus. When we offer to sell a particular series of debt securities, we will describe the specific terms of the series in a supplement to this prospectus. We will also indicate in the supplement to what extent the general terms and provisions described in this prospectus apply to a particular series of debt securities.

We may issue debt securities either separately, or together with, or upon the conversion or exercise of or in exchange for, other securities described in this prospectus. Debt securities may be our senior, senior subordinated or subordinated obligations and, unless otherwise specified in a supplement to this prospectus, the debt securities will be our direct, unsecured obligations and may be issued in one or more series.

The debt securities will be issued under an indenture between us and a trustee to be identified in an accompanying prospectus supplement. We have summarized select portions of the indenture below. The summary is not complete. The form of the indenture has been filed as an exhibit to the registration statement of which this prospectus forms a part and you should read the indenture for provisions that may be important to you. In the summary below, we have included references to the section numbers of the indenture so that you can easily locate these provisions. Capitalized terms used in the summary and not defined herein have the meanings specified in the indenture.

General

The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors and set forth or determined in the manner provided in a resolution of our board of directors, in an officer's certificate or by a supplemental indenture. The particular terms of each series of debt securities will be described in a prospectus supplement relating to such series (including any pricing supplement or term sheet).

We can issue an unlimited amount of debt securities under the indenture that may be in one or more series with the same or various maturities, at par, at a premium, or at a discount. We will set forth in a prospectus supplement (including any pricing supplement or term sheet) relating to any series of debt securities being offered the aggregate principal amount and the following terms of the debt securities, if applicable:

- the title and ranking of the debt securities (including the terms of any subordination provisions);
- the price or prices (expressed as a percentage of the principal amount) at which we will sell the debt securities;
- any limit upon the aggregate principal amount of the debt securities;
- the date or dates on which the principal of the securities of the series is payable;
- the rate or rates (which may be fixed or variable) per annum or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable and any regular record date for the interest payable on any interest payment date;
- the place or places where principal of, and interest, if any, on the debt securities will be payable (and the method of such payment), where the securities of such series may be surrendered for registration of transfer or exchange, and where notices and demands to us in respect of the debt securities may be delivered;
- the period or periods within which, the price or prices at which and the terms and conditions upon which we may redeem the debt securities;

- any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund or analogous provisions or at the option of a
 holder of debt securities and the period or periods within which, the price or prices at which and the terms and conditions upon which
 securities of the series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;
- the dates on which and the price or prices at which we will repurchase debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;
- the denominations in which the debt securities will be issued, if other than denominations of \$1,000 and any integral multiple thereof;
- whether the debt securities will be issued in the form of certificated debt securities or global debt securities;
- the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;
- the currency of denomination of the debt securities, which may be United States dollars or any foreign currency, and if such currency of
 denomination is a composite currency, the agency or organization, if any, responsible for overseeing such composite currency;
- the designation of the currency, currencies or currency units in which payment of principal of, premium and interest on the debt securities will be made;
- if payments of principal of, premium or interest on the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined:
- the manner in which the amounts of payment of principal of, premium, if any, or interest on the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index;
- any provisions relating to any security provided for the debt securities;
- any addition to, deletion of or change in the Events of Default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;
- any addition to, deletion of or change in the covenants described in this prospectus or in the indenture with respect to the debt securities;
- any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents with respect to the debt securities;
- any other terms of the debt securities, which may supplement, modify or delete any provision of the indenture as it applies to that series, including any terms that may be required under applicable law or regulations or advisable in connection with the marketing of the securities; and
- whether any of our direct or indirect subsidiaries will guarantee the debt securities of that series, including the terms of subordination, if any, of such guarantees.

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

If we denominate the purchase price of any of the debt securities in a foreign currency or currencies or a foreign currency unit or units, or if the principal of and any premium and interest on any series of debt securities

is payable in a foreign currency or currencies or a foreign currency unit or units, we will provide you with information on the restrictions, elections, general tax considerations, specific terms and other information with respect to that issue of debt securities and such foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Transfer and Exchange

Each debt security will be represented by either one or more global securities registered in the name of a clearing agency registered under the Exchange Act, which we refer to as the depositary, or a nominee of the depositary (we will refer to any debt security represented by a global debt security as a "book-entry debt security"), or a certificate issued in definitive registered form (we will refer to any debt security represented by a certificated security as a "certificated debt security") as set forth in the applicable prospectus supplement. Except as set forth under the heading "Global Debt Securities and Book-Entry System" below, book-entry debt securities will not be issuable in certificated form.

Certificated Debt Securities

You may transfer or exchange certificated debt securities at any office we maintain for this purpose in accordance with the terms of the indenture. No service charge will be made for any transfer or exchange of certificated debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with a transfer or exchange.

You may effect the transfer of certificated debt securities and the right to receive the principal of, premium and interest on certificated debt securities only by surrendering the certificate representing those certificated debt securities and either reissuance by us or the trustee of the certificate to the new holder or the issuance by us or the trustee of a new certificate to the new holder.

Global Debt Securities and Book-Entry System

Each global debt security representing book-entry debt securities will be deposited with, or on behalf of, the depositary, and registered in the name of the depositary or a nominee of the depositary.

Covenants

We will set forth in the applicable prospectus supplement any restrictive covenants applicable to any issue of debt securities.

No Protection in the Event of a Change of Control

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions which may afford holders of the debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control) which could adversely affect holders of debt securities.

Consolidation, Merger and Sale of Assets

We may not consolidate with or merge with or into, or convey, transfer or lease all or substantially all of our properties and assets to any person, which we refer to as a successor person, unless:

we are the surviving corporation or the successor person (if other than us) is a corporation organized and validly existing under the laws of
any U.S. domestic jurisdiction and expressly assumes our obligations on the debt securities and under the indenture; and

immediately after giving effect to the transaction, no Default or Event of Default, shall have occurred and be continuing.

Notwithstanding the above, any of our subsidiaries may consolidate with, merge into or transfer all or part of its properties to us.

Events of Default

"Event of Default" means with respect to any series of debt securities, any of the following:

- default in the payment of any interest upon any debt security of that series when it becomes due and payable, and continuance of such default for a period of 30 days (unless the entire amount of the payment is deposited by us with the trustee or with a paying agent prior to the expiration of the 30-day period);
- default in the payment of principal of any security of that series at its maturity;
- default in the performance or breach of any other covenant or warranty by us in the indenture (other than a covenant or warranty that has been included in the indenture solely for the benefit of a series of debt securities other than that series), which default continues uncured for a period of 60 days after we receive written notice from the trustee, or we and the trustee receive written notice from the holders of not less than 25% in principal amount of the outstanding debt securities of that series as provided in the indenture;
- certain voluntary or involuntary events of bankruptcy, insolvency or reorganization of us; and
- any other Event of Default provided with respect to debt securities of that series that is described in the applicable prospectus supplement.

No Event of Default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an Event of Default with respect to any other series of debt securities. The occurrence of certain Events of Default or an acceleration under the indenture may constitute an event of default under certain indebtedness of ours or our subsidiaries outstanding from time to time.

We will provide the trustee written notice of any Default or Event of Default within 30 days of becoming aware of the occurrence of such Default or Event of Default, which notice will describe in reasonable detail the status of such Default or Event of Default and what action we are taking or propose to take in respect thereof.

If an Event of Default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than 25% in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the trustee if given by the holders), declare to be due and payable immediately the principal of (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) and accrued and unpaid interest, if any, on all debt securities of that series. In the case of an Event of Default resulting from certain events of bankruptcy, insolvency or reorganization, the principal (or such specified amount) of and accrued and unpaid interest, if any, on all outstanding debt securities will become and be immediately due and payable without any declaration or other act on the part of the trustee or any holder of outstanding debt securities. At any time after a declaration of acceleration with respect to debt securities of any series has been made, but before a judgment or decree for payment of the money due has been obtained by the trustee, the holders of a majority in principal amount of the outstanding debt securities of that series may rescind and annul the acceleration if all Events of Default, other than the non-payment of accelerated principal and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the indenture. We refer you to the prospectus supplement relating to any series of debt securities upon the occurrence of an Event of Default.

The indenture provides that the trustee may refuse to perform any duty or exercise any of its rights or powers under the indenture unless the trustee receives indemnity satisfactory to it against any cost, liability or expense which might be incurred by it in performing such duty or exercising such right or power. Subject to certain rights of the trustee, the holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to the debt securities of that series.

No holder of any debt security of any series will have any right to institute any proceeding, judicial or otherwise, with respect to the indenture or for the appointment of a receiver or trustee, or for any remedy under the indenture, unless:

- that holder has previously given to the trustee written notice of a continuing Event of Default with respect to debt securities of that series;
- the holders of not less than 25% in principal amount of the outstanding debt securities of that series have made written request, and offered indemnity or security satisfactory to the trustee, to the trustee to institute the proceeding as trustee, and the trustee has not received from the holders of not less than a majority in principal amount of the outstanding debt securities of that series a direction inconsistent with that request and has failed to institute the proceeding within 60 days.

Notwithstanding any other provision in the indenture, the holder of any debt security will have an absolute and unconditional right to receive payment of the principal of, premium and any interest on that debt security on or after the due dates expressed in that debt security and to institute suit for the enforcement of payment.

The indenture requires us, within 120 days after the end of our fiscal year, to furnish to the trustee a statement as to compliance with the indenture. If a Default or Event of Default occurs and is continuing with respect to the securities of any series and if it is known to a responsible officer of the trustee, the trustee shall send to each securityholder of the securities of that series notice of a Default or Event of Default within 90 days after it occurs or, if later, after a responsible officer of the trustee has knowledge of such Default or Event of Default. The indenture provides that the trustee may withhold notice to the holders of debt securities of any series of any Default or Event of Default (except in payment on any debt securities of that series) with respect to debt securities of that series if the trustee determines in good faith that withholding notice is in the interest of the holders of those debt securities.

Modification and Waiver

We and the trustee may modify, amend or supplement the indenture or the debt securities of any series without the consent of any holder of any debt security:

- to cure any ambiguity, defect or inconsistency;
- to comply with covenants in the indenture described above under the heading "Consolidation, Merger and Sale of Assets";
- to provide for uncertificated securities in addition to or in place of certificated securities;
- to add guarantees with respect to debt securities of any series or secure debt securities of any series;
- to surrender any of our rights or powers under the indenture;
- to add covenants or events of default for the benefit of the holders of debt securities of any series;
- to comply with the applicable procedures of the applicable depositary;
- to make any change that does not adversely affect the rights of any holder of debt securities;

- to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture;
- to effect the appointment of a successor trustee with respect to the debt securities of any series and to add to or change any of the provisions of the indenture to provide for or facilitate administration by more than one trustee; or
- to comply with requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act.

We may also modify and amend the indenture with the consent of the holders of at least a majority in principal amount of the outstanding debt securities of each series affected by the modifications or amendments. We may not make any modification or amendment without the consent of the holders of each affected debt security then outstanding if that amendment will:

- · reduce the amount of debt securities whose holders must consent to an amendment, supplement or waiver;
- reduce the rate of or extend the time for payment of interest (including default interest) on any debt security;
- reduce the principal of or premium on or change the fixed maturity of any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to any series of debt securities;
- reduce the principal amount of discount securities payable upon acceleration of maturity;
- waive a default in the payment of the principal of, premium or interest on any debt security (except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of that series and a waiver of the payment default that resulted from such acceleration);
- make the principal of or premium or interest on any debt security payable in currency other than that stated in the debt security;
- make any change to certain provisions of the indenture relating to, among other things, the right of holders of debt securities to receive payment of the principal of, premium and interest on those debt securities and to institute suit for the enforcement of any such payment and to waivers or amendments; or
- waive a redemption payment with respect to any debt security.

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration.

Defeasance of Debt Securities and Certain Covenants in Certain Circumstances

Legal Defeasance

The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, we may be discharged from any and all obligations in respect of the debt securities of any series

(subject to certain exceptions). We will be so discharged upon the irrevocable deposit with the trustee, in trust, of money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money or U.S. government obligations in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities.

This discharge may occur only if, among other things, we have delivered to the trustee an opinion of counsel stating that we have received from, or there has been published by, the United States Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable United States federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit, defeasance and discharge and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit, defeasance and discharge had not occurred.

Defeasance of Certain Covenants

The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, upon compliance with certain conditions:

- we may omit to comply with the covenant described under the heading "Consolidation, Merger and Sale of Assets" and certain other covenants set forth in the indenture, as well as any additional covenants which may be set forth in the applicable prospectus supplement; and
- any omission to comply with those covenants will not constitute a Default or an Event of Default with respect to the debt securities of that series

We refer to this as covenant defeasance. The conditions include:

- depositing with the trustee money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal of, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities;
- such deposit will not result in a breach or violation of, or constitute a default under the indenture or any other agreement to which we are a party;
- no Default or Event of Default with respect to the applicable series of debt securities shall have occurred or is continuing on the date of such deposit; and
- delivering to the trustee an opinion of counsel to the effect that we have received from, or there has been published by, the United States Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable United States federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred.

No Personal Liability of Directors, Officers, Employees or Stockholders

None of our past, present or future directors, officers, employees or stockholders, as such, will have any liability for any of our obligations under the debt securities or the indenture or for any claim based on, or in respect or by reason of, such obligations or their creation. By accepting a debt security, each holder waives and releases all such liability. This waiver and release is part of the consideration for the issue of the debt securities. However, this waiver and release may not be effective to waive liabilities under U.S. federal securities laws, and it is the view of the SEC that such a waiver is against public policy.

Governing Law

The indenture and the debt securities, including any claim or controversy arising out of or relating to the indenture or the securities, will be governed by the laws of the State of New York.

The indenture will provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably waive, to the fullest extent permitted by applicable law, any and all right to trial by jury in any legal proceeding arising out of or relating to the indenture, the debt securities or the transactions contemplated thereby.

The indenture will provide that any legal suit, action or proceeding arising out of or based upon the indenture or the transactions contemplated thereby may be instituted in the federal courts of the United States of America located in the City of New York or the courts of the State of New York in each case located in the City of New York, and we, the trustee and the holder of the debt securities (by their acceptance of the debt securities) irrevocably submit to the non-exclusive jurisdiction of such courts in any such suit, action or proceeding. The indenture will further provide that service of any process, summons, notice or document by mail (to the extent allowed under any applicable statute or rule of court) to such party's address set forth in the indenture will be effective service of process for any suit, action or other proceeding brought in any such court. The indenture will further provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably and unconditionally waive any objection to the laying of venue of any suit, action or other proceeding in the courts specified above and irrevocably and unconditionally waive and agree not to plead or claim any such suit, action or other proceeding has been brought in an inconvenient forum.

DESCRIPTION OF DEPOSITARY SHARES

General

We may, at our option, elect to offer fractional shares of preferred stock, or depositary shares, rather than full shares of preferred stock. If we do, we will issue to the public receipts, called depositary receipts, for depositary shares, each of which will represent a fraction, to be described in the applicable prospectus supplement, of a share of a particular series of preferred stock. Unless otherwise provided in the prospectus supplement, each owner of a depositary share will be entitled, in proportion to the applicable fractional interest in a share of preferred stock represented by the depositary share, to all the rights and preferences of the preferred stock represented by the depositary share. Those rights include dividend, voting, redemption, conversion and liquidation rights.

The shares of preferred stock underlying the depositary shares will be deposited with a bank or trust company selected by us to act as depositary under a deposit agreement between us, the depositary and the holders of the depositary receipts. The depositary will be the transfer agent, registrar and dividend disbursing agent for the depositary shares.

The depositary shares will be evidenced by depositary receipts issued pursuant to the depositary agreement. Holders of depositary receipts agree to be bound by the deposit agreement, which requires holders to take certain actions such as filing proof of residence and paying certain charges.

The summary of terms of the depositary shares contained in this prospectus is not complete. You should refer to the form of the deposit agreement, our certificate of incorporation and the certificate of designation for the applicable series of preferred stock that are, or will be, filed with the SEC.

Dividends and Other Distributions

The depositary will distribute all cash dividends or other cash distributions, if any, received in respect of the preferred stock underlying the depositary shares to the record holders of depositary shares in proportion to the numbers of depositary shares owned by those holders on the relevant record date. The relevant record date for depositary shares will be the same date as the record date for the underlying preferred stock.

If there is a distribution other than in cash, the depositary will distribute property (including securities) received by it to the record holders of depositary shares, unless the depositary determines that it is not feasible to make the distribution. If this occurs, the depositary may, with our approval, adopt another method for the distribution, including selling the property and distributing the net proceeds from the sale to the holders.

Liquidation Preference

If a series of preferred stock underlying the depositary shares has a liquidation preference, in the event of the voluntary or involuntary liquidation, dissolution or winding up of us, holders of depositary shares will be entitled to receive the fraction of the liquidation preference accorded each share of the applicable series of preferred stock, as set forth in the applicable prospectus supplement.

Withdrawal of Stock

Unless the related depositary shares have been previously called for redemption, upon surrender of the depositary receipts at the office of the depositary, the holder of the depositary shares will be entitled to delivery, at the office of the depositary to or upon his or her order, of the number of whole shares of the preferred stock and any money or other property represented by the depositary shares. If the depositary receipts delivered by the holder evidence a number of depositary shares in excess of the number of depositary shares representing the

number of whole shares of preferred stock to be withdrawn, the depositary will deliver to the holder at the same time a new depositary receipt evidencing the excess number of depositary shares. In no event will the depositary deliver fractional shares of preferred stock upon surrender of depositary receipts. Holders of preferred stock thus withdrawn may not thereafter deposit those shares under the deposit agreement or receive depositary receipts evidencing depositary shares therefor.

Redemption of Depositary Shares

Whenever we redeem shares of preferred stock held by the depositary, the depositary will redeem as of the same redemption date the number of depositary shares representing shares of the preferred stock so redeemed, so long as we have paid in full to the depositary the redemption price of the preferred stock to be redeemed plus an amount equal to any accumulated and unpaid dividends on the preferred stock to the date fixed for redemption. The redemption price per depositary share will be equal to the redemption price and any other amounts per share payable on the preferred stock multiplied by the fraction of a share of preferred stock represented by one depositary share. If less than all the depositary shares are to be redeemed, the depositary shares to be redeemed will be selected by lot or pro rata or by any other equitable method as may be determined by the depositary.

After the date fixed for redemption, depositary shares called for redemption will no longer be deemed to be outstanding and all rights of the holders of depositary shares will cease, except the right to receive the monies payable upon redemption and any money or other property to which the holders of the depositary shares were entitled upon redemption upon surrender to the depositary of the depositary receipts evidencing the depositary shares.

Voting the Preferred Stock

Upon receipt of notice of any meeting at which the holders of the preferred stock are entitled to vote, the depositary will mail the information contained in the notice of meeting to the record holders of the depositary receipts relating to that preferred stock. The record date for the depositary receipts relating to the preferred stock will be the same date as the record date for the preferred stock. Each record holder of the depositary shares on the record date will be entitled to instruct the depositary as to the exercise of the voting rights pertaining to the number of shares of preferred stock represented by that holder's depositary shares. The depositary will endeavor, insofar as practicable, to vote the number of shares of preferred stock represented by the depositary shares in accordance with those instructions, and we will agree to take all action that may be deemed necessary by the depositary in order to enable the depositary to do so. The depositary will not vote any shares of preferred stock except to the extent that it receives specific instructions from the holders of depositary shares representing that number of shares of preferred stock.

Charges of the Depositary

We will pay all transfer and other taxes and governmental charges arising solely from the existence of the depositary arrangements. We will pay charges of the depositary in connection with the initial deposit of the preferred stock and any redemption of the preferred stock. Holders of depositary receipts will pay transfer, income and other taxes and governmental charges and such other charges (including those in connection with the receipt and distribution of dividends, the sale or exercise of rights, the withdrawal of the preferred stock and the transferring, splitting or grouping of depositary receipts) as are expressly provided in the deposit agreement to be for their accounts. If these charges have not been paid by the holders of depositary receipts, the depositary may refuse to transfer depositary shares, withhold dividends and distributions and sell the depositary shares evidenced by the depositary receipt.

Amendment and Termination of the Deposit Agreement

The form of depositary receipt evidencing the depositary shares and any provision of the deposit agreement may be amended by agreement between us and the depositary. However, any amendment that materially and

adversely alters the rights of the holders of depositary shares, other than fee changes, will not be effective unless the amendment has been approved by the holders of a majority of the outstanding depositary shares. The deposit agreement may be terminated by the depositary or us only if:

- all outstanding depositary shares have been redeemed; or
- there has been a final distribution of the preferred stock in connection with our dissolution and such distribution has been made to all the holders of depositary shares.

Resignation and Removal of Depositary

The depositary may resign at any time by delivering to us notice of its election to do so, and we may remove the depositary at any time. Any resignation or removal of the depositary will take effect upon our appointment of a successor depositary and its acceptance of such appointment. The successor depositary must be appointed within 60 days after delivery of the notice of resignation or removal and must be a bank or trust company having its principal office in the United States and having the requisite combined capital and surplus as set forth in the applicable agreement.

Notices

The depositary will forward to holders of depositary receipts all notices, reports and other communications, including proxy solicitation materials received from us, that are delivered to the depositary and that we are required to furnish to the holders of the preferred stock. In addition, the depositary will make available for inspection by holders of depositary receipts at the principal office of the depositary, and at such other places as it may from time to time deem advisable, any reports and communications we deliver to the depositary as the holder of preferred stock.

Limitation of Liability

Neither we nor the depositary will be liable if either is prevented or delayed by law or any circumstance beyond its control in performing its obligations. Our obligations and those of the depositary will be limited to performance in good faith of our and its duties thereunder. We and the depositary will not be obligated to prosecute or defend any legal proceeding in respect of any depositary shares or preferred stock unless satisfactory indemnity is furnished. We and the depositary may rely upon written advice of counsel or accountants, on information provided by persons presenting preferred stock for deposit, holders of depositary receipts or other persons believed to be competent to give such information and on documents believed to be genuine and to have been signed or presented by the proper party or parties.

DESCRIPTION OF WARRANTS

We may issue warrants to purchase debt securities, preferred stock, depositary shares or common stock. We may offer warrants separately or together with one or more additional warrants, debt securities, preferred stock, depositary shares or common stock, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. If we issue warrants as part of a unit, the applicable prospectus supplement will specify whether those warrants may be separated from the other securities in the unit prior to the expiration date of the warrants. The applicable prospectus supplement will also describe the following terms of any warrants:

- the specific designation and aggregate number of, and the offering price at which we will issue, the warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;
- whether the warrants are to be sold separately or with other securities as parts of units;
- whether the warrants will be issued in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- any applicable material U.S. federal income tax consequences;
- the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;
- the designation and terms of any equity securities purchasable upon exercise of the warrants;
- the designation, aggregate principal amount, currency and terms of any debt securities that may be purchased upon exercise of the warrants:
- if applicable, the designation and terms of the debt securities, preferred stock, depositary shares or common stock with which the warrants are issued and the number of warrants issued with each security;
- if applicable, the date from and after which any warrants issued as part of a unit and the related debt securities, preferred stock, depositary shares or common stock will be separately transferable;
- the number of shares of preferred stock, the number of depositary shares or the number of shares of common stock purchasable upon exercise of a warrant and the price at which those shares may be purchased;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- information with respect to book-entry procedures, if any;
- the antidilution provisions, and other provisions for changes to or adjustment in the exercise price, of the warrants, if any;
- · any redemption or call provisions; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange or exercise of the warrants.

DESCRIPTION OF SUBSCRIPTION RIGHTS

We may issue subscription rights to purchase our common stock, preferred stock, debt securities, depositary shares, warrants or units consisting of some or all of these securities. These subscription rights may be offered independently or together with any other security offered hereby and may or may not be transferable by the stockholder receiving the subscription rights in such offering. In connection with any offering of subscription rights, we may enter into a standby arrangement with one or more underwriters or other purchasers pursuant to which the underwriters or other purchasers may be required to purchase any securities remaining unsubscribed for after such offering.

The prospectus supplement relating to any subscription rights we offer, if any, will, to the extent applicable, include specific terms relating to the offering, including some or all of the following:

- the price, if any, for the subscription rights;
- the exercise price payable for our common stock, preferred stock, debt securities, depositary shares, warrants or units consisting of some or all of these securities upon the exercise of the subscription rights;
- the number of subscription rights to be issued to each stockholder;
- the number and terms of our common stock, preferred stock, debt securities, depositary shares, warrants or units consisting of some or all of these securities which may be purchased per each subscription right;
- the extent to which the subscription rights are transferable;
- any other terms of the subscription rights, including the terms, procedures and limitations relating to the exchange and exercise of the subscription rights;
- the date on which the right to exercise the subscription rights shall commence, and the date on which the subscription rights shall expire;
- the extent to which the subscription rights may include an over-subscription privilege with respect to unsubscribed securities or an overallotment privilege to the extent the securities are fully subscribed; and
- if applicable, the material terms of any standby underwriting or purchase arrangement which may be entered into by us in connection with the offering of subscription rights.

The descriptions of the subscription rights in this prospectus and in any prospectus supplement are summaries of the material provisions of the applicable subscription right agreements. These descriptions do not restate those subscription right agreements in their entirety and may not contain all the information that you may find useful. We urge you to read the applicable subscription right agreements because they, and not the summaries, define your rights as holders of the subscription rights. For more information, please review the forms of the relevant subscription right agreements, which will be filed with the SEC promptly after the offering of subscription rights and will be available as described in the section of this prospectus captioned "Where You Can Find More Information."

DESCRIPTION OF PURCHASE CONTRACTS

The following description summarizes the general features of the purchase contracts that we may offer under this prospectus. Although the features we have summarized below will generally apply to any future purchase contracts we may offer under this prospectus, we will describe the particular terms of any purchase contracts that we may offer in more detail in the applicable prospectus supplement. The specific terms of any purchase contracts may differ from the description provided below as a result of negotiations with third parties in connection with the issuance of those purchase contracts, as well as for other reasons. Because the terms of any purchase contracts we offer under a prospectus supplement may differ from the terms we describe below, you should rely solely on information in the applicable prospectus supplement if that summary is different from the summary in this prospectus.

We will incorporate by reference into the registration statement of which this prospectus is a part the form of any purchase contract that we may offer under this prospectus before the sale of the related purchase contract. We urge you to read any applicable prospectus supplement related to specific purchase contracts being offered, as well as the complete instruments that contain the terms of the securities that are subject to those purchase contracts. Certain of those instruments, or forms of those instruments, have been filed as exhibits to the registration statement of which this prospectus is a part, and supplements to those instruments or forms may be incorporated by reference into the registration statement of which this prospectus is a part from reports we file with the SEC.

We may issue purchase contracts, including contracts obligating holders to purchase from us, and for us to sell to holders, a specific or variable number of our securities at a future date or dates. Alternatively, the purchase contracts may obligate us to purchase from holders, and obligate holders to sell to us, a specific or varying number of our securities.

If we offer any purchase contracts, certain terms of that series of purchase contracts will be described in the applicable prospectus supplement, including, without limitation, the following:

- the price of the securities or other property subject to the purchase contracts (which may be determined by reference to a specific formula described in the purchase contracts);
- whether the purchase contracts are issued separately, or as a part of units each consisting of a purchase contract and one or more of our other securities, including U.S. Treasury securities, securing the holder's obligations under the purchase contract;
- · any requirement for us to make periodic payments to holders or vice versa, and whether the payments are unsecured or pre-funded;
- any provisions relating to any security provided for the purchase contracts;
- whether the purchase contracts obligate the holder or us to purchase or sell, or both purchase and sell, the securities subject to purchase under the purchase contract, and the nature and amount of each of those securities, or the method of determining those amounts;
- whether the purchase contracts are to be prepaid or not;
- whether the purchase contracts are to be settled by delivery, or by reference or linkage to the value, performance or level of the securities subject to purchase under the purchase contract;
- any acceleration, cancellation, termination or other provisions relating to the settlement of the purchase contracts;
- a discussion of certain U.S. federal income tax considerations applicable to the purchase contracts;
- whether the purchase contracts will be issued in fully registered or global form; and
- any other terms of the purchase contracts and any securities subject to such purchase contracts.

DESCRIPTION OF UNITS

We may issue units comprising two or more securities described in this prospectus in any combination. For example, we might issue units consisting of a combination of debt securities and warrants to purchase common stock. The following description sets forth certain general terms and provisions of the units that we may offer pursuant to this prospectus. The particular terms of the units and the extent, if any, to which the general terms and provisions may apply to the units so offered will be described in the applicable prospectus supplement.

Each unit will be issued so that the holder of the unit also is the holder of each security included in the unit. Thus, the unit will have the rights and obligations of a holder of each included security. Units will be issued pursuant to the terms of a unit agreement, which may provide that the securities included in the unit may not be held or transferred separately at any time or at any time before a specified date. A copy of the forms of the unit agreement and the unit certificate relating to any particular issue of units will be filed with the SEC each time we issue units, and you should read those documents for provisions that may be important to you. For more information on how you can obtain copies of the forms of the unit agreement and the related unit certificate, see the section of this prospectus captioned "Where You Can Find More Information."

The prospectus supplement relating to any particular issuance of units will describe the terms of those units, including, to the extent applicable, the following:

- the designation and terms of the units and the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provision for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units; and
- whether the units will be issued in fully registered or global form.

PLAN OF DISTRIBUTION

We may sell securities:

- through underwriters;
- through dealers;
- · through agents;
- · directly to purchasers; or
- through a combination of any of these methods of sale.

In addition, we may issue the securities as a dividend or distribution or in a subscription rights offering to our existing securityholders.

We may directly solicit offers to purchase securities or agents may be designated to solicit such offers. We will, in the prospectus supplement relating to such offering, name any agent that could be viewed as an underwriter under the Securities Act and describe any commissions that we must pay. Any such agent will be acting on a best efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis. This prospectus may be used in connection with any offering of our securities through any of these methods or other methods described in the applicable prospectus supplement.

The distribution of the securities may be effected from time to time in one or more transactions:

- at a fixed price or prices that may be changed from time to time;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

- the name of the agent or any underwriters;
- the public offering or purchase price;
- if applicable, the names of any selling securityholders;
- any discounts and commissions to be allowed or paid to the agent or underwriters;
- all other items constituting underwriting compensation;
- any discounts and commissions to be allowed or paid to dealers; and
- any exchanges on which the securities will be listed.

If any underwriters or agents are utilized in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement or other agreement with them at the time of sale to them, and we will set forth in the prospectus supplement relating to such offering the names of the underwriters or agents and the terms of the related agreement with them.

If a dealer is utilized in the sale of the securities in respect of which the prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale.

If we offer securities in a subscription rights offering to our existing securityholders, we may enter into a standby underwriting agreement with dealers, acting as standby underwriters. We may pay the standby underwriters a commitment fee for the securities they commit to purchase on a standby basis. If we do not enter into a standby underwriting arrangement, we may retain a dealer-manager to manage a subscription rights offering for us.

Agents, underwriters, dealers and other persons may be entitled under agreements that they may enter into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of
 the jurisdiction to which that institution is subject; and
- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery.

The underwriters and other persons acting as agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Certain agents, underwriters and dealers, and their associates and affiliates may be customers of, have borrowing relationships with, engage in other transactions with, and/or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may over-allot in connection with the offering, creating a short position for their own accounts. In addition, to cover over-allotments or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in two business days, unless the parties to any such trade expressly agree otherwise. The applicable prospectus supplement may provide that the original issue date for your securities may be more than two scheduled business days after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the third business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are expected to settle in more than three scheduled business days after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement.

The securities may be new issues of securities and may have no established trading market. Any common stock will be listed on The Nasdaq Global Select Market, but any other securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

The specific terms of any lock-up provisions in respect of any given offering will be described in the applicable prospectus supplement.

LEGAL MATTERS

The validity of the issuance of our common stock offered in this prospectus supplement will be passed upon for us by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California. Additional legal matters may be passed on for us, or any underwriters, dealers or agents by counsel we will name in the applicable prospectus supplement.

EXPERTS

The financial statements of Tenaya Therapeutics, Inc. as of December 31, 2021 and 2020, and for each of the two years in the period ended December 31, 2021, incorporated by reference in this Prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2021 have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report. Such financial statements are incorporated by reference in reliance upon the report of such firm given their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at www.sec.gov. Copies of certain information filed by us with the SEC are also available on our website at www.tenayatherapeutics.com. Information accessible on or through our website is not a part of this prospectus.

This prospectus and any prospectus supplement is part of a registration statement that we filed with the SEC and do not contain all of the information in the registration statement. You should review the information and exhibits in the registration statement for further information on us and our consolidated subsidiaries and the securities that we are offering. Forms of any indenture or other documents establishing the terms of the offered securities are filed as exhibits to the registration statement of which this prospectus forms a part or under cover of a Current Report on Form 8-K and incorporated in this prospectus by reference. Statements in this prospectus or any prospectus supplement about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should read the actual documents for a more complete description of the relevant matters.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference much of the information that we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated by reference in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus incorporates by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (in each case, other than those documents or the portions of those documents furnished pursuant to Items 2.02 or 7.01 of any Current Report on Form 8-K and, except as may be noted in any such Form 8-K, exhibits filed on such form that are related to such information), until the offering of the securities under the registration statement of which this prospectus forms a part is terminated or completed:

- our Annual Report on <u>Form 10-K</u> for the year ended December 31, 2021;
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2022 and June 30, 2022;
- the portions of our <u>Definitive Proxy Statement</u> on Schedule 14A (other than information furnished rather than filed) that are incorporated by reference into our Annual Report on Form 10-K, filed with the SEC on April 28, 2022;
- our Current Reports on Form 8-K filed on June 10, 2022 and August 10, 2022; and
- the description of our common stock contained in the Registration Statement on Form 8-A relating thereto, filed on July 23, 2021, including any amendment or report filed for the purpose of updating such description.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number:

Tenaya Therapeutics, Inc.
171 Oyster Point Boulevard, 5th Floor
South San Francisco, California 94080
Attn: Investor Relations
(650) 825-6990



8,888,890 SHARES OF COMMON STOCK

PRE-FUNDED WARRANTS TO PURCHASE 2,222,271 SHARES OF COMMON STOCK

PROSPECTUS SUPPLEMENT

Joint Bookrunning Managers

Leerink Partners

TD Cowen

Lead Manager

LifeSci Capital

February 7, 2024