

PROSPECTUS

13,934,427 Shares



*Common Stock*

This prospectus relates to the resale of up to 13,934,427 shares of our common stock by the selling stockholders named in this prospectus or in supplements to this prospectus. See “Selling Stockholders.” We are registering the applicable shares of our common stock to provide the selling stockholders with freely tradable securities. The registration of the shares of our common stock covered by this prospectus does not necessarily mean that any shares of our common stock will be sold by any of the selling stockholders, and we cannot predict when or in what amounts any of the selling stockholders may sell any of our shares of common stock offered by this prospectus. The prices at which the selling stockholders may sell the shares of our common stock will be determined by prevailing market prices or at prices that may be obtained in negotiated transactions. We are filing the registration statement of which this prospectus is a part pursuant to contractual obligations that exist with the selling stockholders, as described in more detail in this prospectus under “Selling Stockholders” and “The Private Placement.”

We are not selling any shares of our common stock under this prospectus and will not receive any proceeds from any sale or disposition by the selling stockholders of the shares of our common stock covered by this prospectus. In addition, we have agreed to pay certain fees and expenses incident to our contractual obligations to register the shares of our common stock. The selling stockholders from time to time may offer and sell the shares of our common stock held by them directly or through one or more underwriters, broker-dealers or agents on terms to be determined at the time of sale, as described in more detail in this prospectus under “Plan of Distribution.” No shares of our common stock may be sold without delivery of this prospectus describing the method and terms of the offering of such shares.

Our common stock trades on the Nasdaq Global Select Market, or Nasdaq, under the symbol “TSVT.” On May 5, 2022, the last reported sale price of our common stock on Nasdaq was \$14.00 per share.

**INVESTING IN OUR SECURITIES INVOLVES A HIGH DEGREE OF RISK. YOU SHOULD CAREFULLY READ AND CONSIDER THE RISK FACTORS DESCRIBED IN THIS PROSPECTUS AND IN THE DOCUMENTS INCORPORATED BY REFERENCE INTO THIS PROSPECTUS. SEE “RISK FACTORS” ON PAGE 6 BEFORE MAKING A DECISION TO 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 MAY 6, 2022.**

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## ABOUT THIS PROSPECTUS

This document is called a prospectus and is part of a registration statement that we have filed with the SEC. The selling stockholders named in this prospectus may sell up to 13,934,427 shares of our common stock from time to time.

This prospectus provides you with a general description of the securities we may offer. Each time a selling stockholder sells shares of our common stock, we or the selling stockholder will provide a prospectus and any prospectus supplement containing specific information about the terms of the applicable offering, as required by applicable law. The prospectus supplement may also add, update or change information in this prospectus or in documents incorporated by reference in this prospectus. To the extent that any statement that we or the selling stockholders make in a prospectus supplement is inconsistent with statements made in this prospectus or in documents incorporated by reference in this prospectus, the statements made or incorporated by reference in this prospectus will be deemed modified or superseded by those made in the prospectus supplement. You should carefully read both this prospectus and any applicable prospectus supplement together with the additional information described under the heading “Where You Can Find More Information” and “Incorporation of Certain Documents by Reference” before buying any shares of our common stock offered in this offering.

No person has been authorized to give any information or make any representations in connection with this offering other than those contained or incorporated by reference in this prospectus in connection with the offering described in this prospectus, and, if given or made, such information or representations must not be relied upon as having been authorized by us. This prospectus shall not constitute an offer to sell or a solicitation of an offer to buy offered securities in any jurisdiction in which it is unlawful for such person to make such an offering or solicitation. Neither the delivery of this prospectus nor any sale made hereunder shall under any circumstances imply that the information contained or incorporated by reference in this prospectus is correct as of any date subsequent to the date of this prospectus or the date of the document incorporated by reference, as applicable. Our business, financial condition, results of operations and prospects may have changed since those dates.

The selling stockholders may from time to time offer and sell, transfer or otherwise dispose of any or all of the shares of our common stock covered by this prospectus directly or through one or more underwriters, broker-dealers or agents on terms to be determined at the time of sale. A prospectus supplement may describe the terms of the plan of distribution and set forth the names of any underwriters involved in the sale of our common stock. See “Plan of Distribution” for more information.

For purposes of this prospectus, references to the terms “TSVT,” “the Company,” “we,” “us” and “our” refer to 2seventy bio, Inc., together with its subsidiary, unless the context otherwise requires.

The registration statement containing this prospectus, including exhibits to the registration statement, provides additional information about us and the common stock offered under this prospectus. The registration statement can be read at the SEC’s website or at the SEC offices mentioned under the heading “Where You Can Find More Information.”

## PROSPECTUS SUMMARY

*This summary highlights information contained elsewhere in this prospectus. This summary does not contain all of the information that you should consider before deciding to invest in our common stock. You should read this entire prospectus carefully, including the “Risk Factors” section, as well as our historical financial statements and the notes thereto which are incorporated by reference in this prospectus.*

### Overview

We are a cell and gene therapy company focused on the research, development, and commercialization of transformative treatments for cancer. We are led by an accomplished team with significant expertise and experience in this field, from discovery through clinical development to regulatory approval of ABECMA (idecabtagene vicleucel, or ide-cel), the first chimeric antigen receptor, or CAR T, cell therapy approved by the U.S. Food and Drug Administration, or FDA, for multiple myeloma. Our approach combines our expertise in T cell engineering technology and lentiviral vector gene delivery approaches, experience in research, development, and manufacturing of cell therapies and a suite of technologies that can be selectively deployed to develop highly innovative, targeted cellular therapies for patients with cancer. We are advancing multiple clinical programs, including DARIC33, for the treatment of pediatric patients with relapsed and refractory acute myeloid leukemia and bbT369, for the treatment of patients with B-cell non-Hodgkins lymphoma as well as multiple preclinical programs, including bbT4015, an engineered CAR T cell therapy targeting MUC16. Additionally, together with our partner Bristol-Myers Squibb, or BMS, we are delivering ABECMA to multiple myeloma patients in the United States following approval by the FDA of ABECMA in March 2021 for the treatment of adults with multiple myeloma who have received at least four prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 (cyclic ADP ribose hydrolase) monoclonal antibody.

In recent years, growing understanding of cancer cell metabolism and genomics, as well as of the body’s immune response to tumor cells, has led to the development of new classes of therapies against cancer targets and pathways that have dramatically reshaped the treatment landscape. The advent of immunotherapy, particularly engineered cell therapies, has offered the potential to move past the treatment paradigm of maintenance of cancer as a “chronic” disease. Few curative therapies, however, exist and, in some settings, such as solid tumors, current approaches do not offer significant depth or durability of outcome for most cancer types and patients. Monotherapies have historically been of limited efficacy in cancer, and drugs are typically combined to deliver an outsized effect relative to the action of any of the individual components, with one potential advantage of combination therapies being the ability to address the heterogeneity of single target expression and/or mechanisms for relapse and resistance specific to a particular mechanism or target.

While medicines such as ABECMA have highlighted the power of first-generation CAR T cell therapy by achieving previously unobtainable levels of efficacy in the late line setting, we believe that to be broadly successful in the treatment of cancer, a combination therapy approach is necessary, and that our multiplex approach to next-generation autologous cellular therapy, which allows multiple encoded mechanisms of action to be delivered within a single drug product, may be a potential solution. Based on our experience in the research and development of ABECMA, we believe we can develop next-generation, engineered cell therapies to bring new options to patients suffering from a broad range of different tumor types.

In designing our next-generation product candidates, we aim to address the limitations of first-generation T cell therapies by augmenting them with additional technologies. These limitations include: (1) targeting a single tumor-associated antigen that may be lost or down regulated; (2) heterogeneous target expression resulting in the sparing of tumor cells devoid of antigen; (3) expression of immunosuppressive molecules such as transforming growth factor- $\beta$ , or TGF $\beta$ , or programmed death ligand 1, or PD-L1, in the tumor microenvironment and/or (4) poor T cell engraftment and persistence. Our approach is to create product candidates that are multiplex engineered cell therapies by combining: (1) CAR and T cell receptor technology, which programs T cells to recognize and kill cancer cells based on the cell surface expression or presentation of intracellular protein targets, respectively; (2) dual-targeting CAR architecture for multi-target tumor cell recognition; (3) our core lentiviral gene transfer technology, which delivers these genetic cargos (and more) to program a patient’s own T cells to the kill the cancer cells; (4) our megaTAL-based gene editing technology, which allows us to perform site specific gene addition or

deletion from the genome to improve the properties of the T cell; and (5) genetically encoded technologies for engineering T cells to enhance the cytotoxic activity and reprogram the tumor microenvironment for more effective anti-tumor responses.

### ***Our Strategy***

Our strategy is to apply our broad range of technologies to design multiplex product candidates that address the key treatment challenges in cancer. Unlike other oncology-focused companies in our space, we believe our breadth of technology enables us to develop tailored products focused on the specific areas of cancer biology we have identified. We selectively combine the relevant features and components from our range of tools and technologies to address the defined attributes of a cellular therapy that we believe are necessary for anti-tumor effect.

To execute on our strategy, we plan to:

- Commercialize ABECMA, including clinical expansion to earlier lines of therapy, through our collaboration with BMS, and leverage our clinical and operational experience under this collaboration and this product revenue stream to further invest in our next-generation proprietary programs.
- Leverage our leadership position in autologous CAR T therapies to advance through the clinic our next-generation programs in B-NHL, AML, and multiple myeloma.
- Apply our multiplex approach to the discovery and design of transformative cell and gene therapy products for the treatment of solid tumors.
- Seek to extend our approach to other cell types beyond T cells and to include off-the-shelf approaches, as we gain additional experience in our autologous T cell programs.
- Build upon our existing internal lentiviral vector manufacturing know-how and experience through both selective investments in manufacturing collaborations and through our internal capabilities, including the planned build-out of our drug product manufacturing capabilities at our Cambridge, Massachusetts headquarters, which will be designed to enable rapid translational research in our clinical trials, as well as allow us to manufacture drug product for preclinical and Phase 1 clinical development activities, over time, with the objectives of enabling rapid iteration on clinical learnings into research and development, increasing the efficiency of manufacturing processes, and improving the overall patient and healthcare professional experience.

### ***Our Technologies***

Our oncology programs use a lentiviral vector to deliver the genetic cargo with the potential to program a patient's own T cells to recognize specific proteins or protein fragments on the surface of cancer cells to kill the cancer cells. Our current programs are based on CAR technology designed to program T cells to recognize cancer cells based on expression of specific cell surface antigens, and T cell receptor technology designed to program T cells to recognize cancer cells based on protein fragments derived from either intracellular or extracellular proteins displayed on the tumor cell surface. The genetically engineered T cells are designed to supplement a patient's immune system, and we believe they have the potential to be further engineered to overcome immune evasion mechanisms employed by cancer cells. Our approach is to create multiplex engineered cell therapies by combining our foundational lentiviral vector and CAR/TCR, technology with next-generation tools to address the challenges in existing cancer treatments.

- **Dual-Targeting** Polyclonal responses are a hallmark of adaptive immunity, but most T cell therapies have been devised with antigen receptors specific to a single target antigen. There are many documented cases of cancer deploying its intrinsic genetic plasticity to escape mono-targeted T cell therapies (both with cellular and more classical modalities, such as small molecules and antibodies). In such cases, our solution is to utilize a dual-targeting antigen receptor, including a multi-chain, dual-targeting architecture, to respond when either target antigen is present on a cancer cell, as well as an architecture that leverages the unique properties of humanized single-domain camelid-derived antibodies.

- **DARIC.** We have developed a dimerizing agent-regulated immunoreceptor complex, which we refer to as DARIC, that comprises separate antigen targeting and signal transduction componentry. DARIC receptors become poised for anti-tumor function only when the two components are brought together as heterodimers, a process that is strictly dependent on the bridging function of the drug rapamycin. This technology can enable pharmacological, “on-demand” control of engineered T cell responses. Controlling the “on” and “off” states of engineered T cells also creates opportunities to pursue cancers and cancer targets with disease characteristics and expression profiles that are incompatible with constitutively responsive antigen receptors.
- **Reversal of immunosuppression.** Patients who present in the clinic with advanced metastatic disease host tumors that have evolved to evade endogenous immunity via a variety of mechanisms. Tumor infiltrating T cells lose potency over time due to repetitive antigen stimulation and exhaustion in a tumor microenvironment that suppresses T cell function. Checkpoint engagement, hypoxia, poor nutrient conditions, and exposure to immunosuppressive cell types and cytokines all significantly blunt T cell potency and thwart attempts to regress tumors in clinically meaningful ways. We have developed a suite of synthetic biology innovations that antagonize and rewire immunosuppressive signaling and response pathways. We have focused significant attention on transforming growth factor beta, or TGF $\beta$ , a profoundly immunosuppressive cytokine found at high levels in many solid tumors. Our chimeric TGF $\beta$  flip receptor, or CTBR, technology converts this suppressive signal into a supportive interleukin receptor signal that enhances T cell function. Suppressive to enhancing signal conversion operates in a localized, engineered T cell intrinsic manner, enhancing potency within the microenvironment of the tumor where the highest concentrations of activated TGF $\beta$  ligand are present. We have also developed several approaches to modulate T cell metabolism to allow for enhanced function and potency in the metabolically challenging tumor microenvironment.
- **Co-stimulation.** Parallel track costimulatory domains, also known as chimeric costimulatory receptors, offer a unique set of functional attributes that culminate in enhanced anti-tumor activity. This technology pairs enhanced targeting breadth with a qualitatively distinct and more potent functional response, simultaneously countering two potential mechanisms of resistance.
- **Gene-editing.** megaTALs are highly specific, compact nucleases that efficiently catalyze the formation and mutagenic resolution of double-stranded breaks at pre-specified genetic target sequences. Using our megaTAL gene-editing platform, we have demonstrated that disrupting genes that intersect with T cell signaling and response pathways can promote more potent immune responses. In addition, we have developed a full suite of on-target editing assays, functional bioassays, and off-target discovery and verification analytics to deeply characterize gene-editing events and their functional consequences in target cells, which may enable the potential application of this technology in the clinical setting.
- **mRNA capabilities.** We have also developed messenger RNA, or mRNA, capabilities that enable transient gene expression, both in cells cultured ex vivo and for organ-specific in vivo delivery. We manufacture mRNA starting from a proprietary plasmid template outfitted with an encoded poly-A tract, an approach that results in highly homogenous mRNA species following in vitro transcription. Our purification process includes double-stranded RNA, or dsRNA, depletion steps to minimize immunogenicity and optimize cell viability. A robust suite of analytical assays is in place to ensure that consistently pure and potent material is generated. We have developed clinical-scale electroporation processes for ex vivo mRNA delivery and are actively using these processes to improve T cell potency via our megaTAL gene-editing platform. This technology can potentially be further leveraged to transiently express other factors that may be advantageous to ex vivo manufactured T cells.

In addition, we continue to invest in our core foundational technologies and build upon our leadership position in autologous engineered cell therapy products based on CAR and TCR approaches:

- **Next-generation lentiviral vector design.** With a management team that collectively possesses decades of experience in this technology, we have extensively refined the componentry and methodology behind lentiviral vector design and manufacturing. Our transfer plasmid design elements include several

innovations that have created advanced gene expression tuning capabilities and the delivery of large and complex genetic payloads via transgene stacking. We have developed proprietary codon optimization algorithms, promoter variants, and regulatory elements that we believe together enable constitutive and/or responsive expression profiles across a range of transgene expression levels. These mature capabilities enable highly efficient transfer of sophisticated genetic modules, such as the multiplex product concepts represented by our next-generation programs.

- **Target selection and validation.** Cancer targets with profiles that make them appropriate for cell therapy development have diverse structural features, biochemical properties, and sub-cellular distribution characteristics. To support novel target identification, we have developed significant in-house expertise and external collaborations in the areas of data mining, functional genomics, and primary tissue analysis. We have also built a full suite of target validation assays to perform confirmatory studies assessing tumor and normal tissue expression properties. In addition, we have developed significant internal expertise specifically aimed at de-risking potential off-target liabilities of TCR engineered T cells. We have focused the bulk of our efforts on select hematological and solid tumor indications. We believe this approach allows us to deeply interrogate the target landscape in cancers where T cell therapies may have the highest potential for technical success.
- **Receptor engineering.** We have access to state-of-the-art binder capabilities through our collaboration arrangements that cover the full range of potential cancer targets. For intracellular targets of interest, our partners develop TCRs and fully humanized “peptide-in-groove”, or PiG, single-chain variable fragment, or scFv, reagents. For surface proteins, we have multiple providers of immunization-sourced, fully humanized scFv and single-domain reagents.
- **Manufacturing process innovations.** Our analytical development, clinical bioassays, correlative research, and data sciences teams have exceptional access to clinical trial data using CAR T therapies. We are regularly interrogating these data sets to isolate key manufacturing variables and correlates of clinical signals that enable hypothesis testing. These activities derive insights that inform process research directions for optimizing T cell manufacturing through reagents, processes, and culture timing, and for the discovery of underlying biological relationships between clinical and correlative data.

#### **Private Placement**

On March 17, 2022, we completed a private placement in which we issued and sold an aggregate of 13,934,427 shares of our common stock to the selling stockholders, which shares of common stock are being registered hereunder (the “Private Placement”). The shares were purchased pursuant to agreements (the “Purchase Agreements”) with each of the selling stockholders. At, and as a condition to, the closing of the Private Placement, the Company and the purchasers entered into a registration rights agreement (the “PIPE Registration Rights Agreement”). See “The Private Placement.”

#### **Corporate Information**

2seventy bio, Inc. was incorporated in the State of Delaware on April 26, 2021 for the purpose of holding bluebird bio, Inc.’s oncology portfolio and programs in connection with the separation of bluebird bio’s oncology portfolio and programs from its severe genetic disease portfolio and programs. The contribution of this business to us occurred over a period of time prior to the completion of the separation, and we had no operations prior to such contribution. The address of our principal executive offices is 60 Binney Street, Cambridge, Massachusetts 02142. We also maintain a website at [www.2seventybio.com](http://www.2seventybio.com). The information contained in or accessible from our website is not incorporated into this prospectus, and you should not consider it part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

## THE OFFERING

Common stock offered by the selling stockholders	13,934,427 shares
Common Stock to be Outstanding Immediately after this Offering	37,615,797 shares
Use of Proceeds	All proceeds from the sale of the shares of common stock under this prospectus will be for the account of the selling stockholders. We will not receive any proceeds from the sale of our shares of common stock offered pursuant to this prospectus.
Risk Factors	You should read the section entitled “Risk Factors” in Part I – Item 1A, “Risk Factors”, in our Annual Report on Form 10-K for the year ended December 31, 2021, as filed with the SEC on March 22, 2022, for a discussion of the risk factors to consider carefully before deciding to invest in shares of our common stock.
Nasdaq Global Select Market Symbol	TSVT

The number of shares of our common stock shown as issued and outstanding in the table above is based on 23,585,331 shares of our common stock outstanding as of December 31, 2021 and excludes:

- 1,489,784 shares of common stock issuable upon exercise of options outstanding under our 2021 Stock Option and Incentive Plan at a weighted-average exercise price of \$145.52 per share as of December 31, 2021;
- 1,079,932 shares of common stock issuable upon vesting and settlement of restricted stock units under our 2021 Stock Option and Incentive Plan as of December 31, 2021;
- 757,575 shares of common stock issuable upon the exercise of pre-funded warrants to purchase shares of common stock at an exercise price of \$0.0001 per share outstanding as of December 31, 2021;
- 2,125,485 shares of common stock reserved for future issuance under our 2021 Stock Option and Incentive Plan as of December 31, 2021; and
- 233,302 shares of common stock reserved for future issuance under our 2021 Employee Stock Purchase Plan as of December 31, 2021.



## **RISK FACTORS**

Before you invest in our securities, in addition to the other information, documents or reports incorporated by reference in this prospectus and any prospectus supplement or other offering materials, you should carefully consider the risk factors in the section entitled “Risk Factors” in any prospectus supplement, as well as our most recent Annual Report on Form 10-K and subsequent Quarterly Reports on Form 10-Q filed with the SEC. Each of the risks described in these sections and documents could materially and adversely affect our business, financial condition, results of operations and prospects, and could result in a partial or complete loss of your investment.

## CAUTIONARY NOTE REGARDING FORWARD-LOOKING INFORMATION

This prospectus, and the documents incorporated by reference in this prospectus, contain express or implied forward-looking statements that are based on our management's belief and assumptions and on information currently available to our management. These statements relate to future events or our future operational or financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements in this prospectus include, but are not limited to, statements about:

- our business and operations following the separation and any benefits or costs of the separation, including the tax treatment of the separation;
- our post-separation relationships with bluebird bio, third parties, collaborators and our employees;
- our and BMS' plans for the commercialization of ABECMA;
- our ability to operate as a stand-alone company and execute our strategic priorities;
- our ability to finance our operations and business initiatives and obtain funding for such activities;
- the timing, investment and associated activities involved in developing, obtaining regulatory approval for, launching, and commercializing our product candidates;
- our plans with respect to the development, manufacture or sale of our product candidates and the associated timing thereof, including the design and results of pre-clinical and clinical studies;
- the safety profile and related adverse events of our product candidates;
- the perceived therapeutic benefits of our product candidates and the potential indications and market opportunities therefor;
- U.S. and foreign regulatory requirements for our product candidates, including any post-approval development and regulatory requirements, and the ability of our product candidates to meet such requirements;
- our ability to attract and retain key employees needed to execute our business plans and strategies and our expectations regarding our ability to manage the impact of any loss of key employees;
- our ability to obtain and maintain intellectual property protection for our product candidates and the strength thereof;
- our future financial performance, revenues, expense levels, payments, cash flows, profitability, tax obligations, capital raising and liquidity sources, real estate needs and concentration of voting control, as well as the timing and drivers thereof, and internal control over financial reporting;
- our ability to compete with other companies that are or may be developing or selling products that are competitive with our product candidates;
- the status of government regulation in the life sciences industry, particularly with respect to healthcare reform;
- potential indemnification liabilities we may owe to bluebird bio after the separation;
- the tax treatment of the distribution and the limitations imposed on us under the tax matters agreement that we entered into with bluebird bio; and
- trends and challenges in our potential markets.

In some cases, you can identify forward-looking statements by terminology such as “may,” “should,” “expects,” “intends,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “potential,” “continue” or the negative of these terms or other comparable terminology. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the section titled “Risk Factors” in our Annual Report on Form 10-K for the year ended December 31, 2021, as filed with the SEC on March 22, 2022, and elsewhere in this prospectus. The impact of these risks or uncertainties may cause actual events or results to vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance. You should read this prospectus and the documents that we reference in this prospectus and have filed with the Securities and Exchange Commission as exhibits to the registration statement, of which this prospectus forms a part, completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements.

Subsequent events and developments may impact matters implied by these forward looking statements and cause our expectations to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law.

This prospectus also contains estimates, projections and other information concerning our industry, our business and the markets for our product candidates. 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. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from our own internal estimates and research as well as from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. While we are not aware of any misstatements regarding any third-party information presented in this prospectus, their estimates, in particular, as they relate to projections, involve numerous assumptions, are subject to risks and uncertainties and are subject to change based on various factors, including those discussed under the section titled “Risk Factors” and elsewhere in this prospectus.

#### **THE PRIVATE PLACEMENT**

On March 17, 2022, we completed a private placement in which we issued and sold an aggregate of 13,934,427 shares of our common stock to the selling stockholders for a purchase price of \$12.20 per share, for aggregate gross proceeds to us of approximately \$170 million, before deducting offering commissions and estimated offering expenses payable by us, which shares of common stock are being registered hereunder (the “Private Placement”). The shares were purchased pursuant to agreements (the “Purchase Agreements”) with each of the selling stockholders. At, and as a condition to, the closing of the Private Placement, the Company and the purchasers entered into a registration rights agreement (the “PIPE Registration Rights Agreement”). We have prepared this registration statement pursuant to the PIPE Registration Rights Agreement.

Additionally, at, and as a condition to, the closing of the Private Placement, our directors and executive officers entered into lock-up agreements not to dispose of any shares of common stock and other securities of the Company that they own during the lock-up period, subject to customary exceptions.

### **USE OF PROCEEDS**

We will not receive any proceeds from the sale of the shares of common stock offered by the selling stockholders. The proceeds from the offering are solely for the account of the selling stockholders. See “Selling Stockholders.”

We have also agreed to bear all fees and expenses incident to our obligation to register the shares of our common stock being offered by this prospectus.

### **MARKET FOR COMMON STOCK AND DIVIDEND POLICY**

Our common stock is traded on the Nasdaq Global Select Market under the symbol "TSVT." The last reported sale price of our common stock on May 5, 2022 on the Nasdaq Global Select Market was \$14.00 per share. As of April 26, 2022, there were 30 stockholders of record of our common stock.

We have never declared or paid any cash dividend on our common stock. We intend to retain any future earnings and do not expect to pay dividends in the foreseeable future.

## SELLING STOCKHOLDERS

The shares of common stock being offered by the selling stockholders are shares of common stock acquired from us in a private offering pursuant to exemptions from registration under Section 4(a)(2) of the Securities Act and Regulation D promulgated thereunder. Pursuant to the PIPE Registration Rights Agreement, we agreed to file a registration statement with the SEC for the purposes of registering for resale from time to time the shares of common stock issued to the selling stockholders pursuant to the Purchase Agreements. We are registering the shares of common stock in order to permit the selling stockholders to offer the shares for resale or other disposition from time to time. In addition to the ownership of the shares of our common stock that are the subject of this prospectus, certain of the selling stockholders have had material relationships with us within the past three years as disclosed in this prospectus and described below under “Relationships with Certain Selling Stockholders.”

Except as set forth in the footnotes below, the following table lists the selling stockholders and certain information, based on written representations from the selling stockholders, as of March 17, 2022 regarding the ownership of the shares of common stock by each of the selling stockholders. The second column lists the number of shares of common stock owned by each selling stockholder, based on its ownership of the shares of common stock, as of March 17, 2022.

The third column lists the shares of common stock being offered by this prospectus by the selling stockholders.

In accordance with the terms of the PIPE Registration Rights Agreement and the Purchase Agreements, as described above under “The Private Placement,” this prospectus generally covers the resale of at least the number of shares of common stock issued pursuant to the Purchase Agreements. The fourth column assumes the sale of all of the shares offered by the selling stockholders pursuant to this prospectus, and the fifth column sets forth the applicable percentages, based on approximately 37,618,103 shares of common stock outstanding as of April 22, 2022 assuming such sale. The selling stockholders may offer and sell some, all or none of their shares of common stock. See “Plan of Distribution.”

Unless otherwise noted below, the address of each selling stockholder listed on the table is c/o 2seventy bio, Inc., 60 Binney Street, Cambridge, Massachusetts 02142.

Name of Selling Stockholder	Number of Shares of Common Stock Owned Prior to Offering	Maximum Number of Shares of Common Stock to be Sold Pursuant to this Prospectus	Number of Shares of Common Stock Owned After Offering	Percent of Shares of Common Stock Owned After Offering
683 Capital Partners, LP (1)	491,803	491,803	—	— %
Armistice Capital Master Fund Ltd. (2)	2,000,000	819,672	1,180,328	3.14 %
Entities affiliated with Baker Bros. Advisors LP (3)	3,136,944	1,229,508	1,907,436	5.07 %
BCLS II Equity Opportunities, LP (4)	1,408,901	1,229,508	179,393	*
Boxer Capital, LLC (5)	459,836	409,836	50,000	*
Burn3 LLC (6)	81,967	81,967	—	— %
CaaS Capital Master Fund LP (7)	1,539,407	1,393,442	145,965	*
Casdin Partners Master Fund, L.P. (8)	1,229,508	614,754	614,754	1.63 %
CHI IV Public Investments LP (9)	819,672	819,672	—	— %
CVI Investments, Inc. (10)	819,672	819,672	—	— %
Entities affiliated with EcoR1 Capital (11)	3,495,943	2,049,180	1,446,763	3.85 %
Jan Leschly (12)	81,967	81,967	—	— %
Janus Henderson Biotech Innovation Master Fund Limited (13)	655,737	655,737	—	— %
Madison Avenue International LP (14)	896,972	819,672	77,300	*
Entities affiliated with Newtyn Management, LLC (15)	1,802,805	819,672	983,133	2.61 %
Nick Leschly (16)	556,888	368,857	188,031	*
Entities affiliated with RTW Investments, LP (17)	2,459,016	1,229,508	1,229,508	3.27 %

\* Less than 1%

- (1) Includes 491,803 shares of common stock purchased in the Private Placement and directly held by 683 Capital Partners, LP. The address of 683 Capital Partners is 1700 Broadway, Suite 4200, New York, NY 10019.
- (2) Includes 819,672 shares of common stock purchased in the Private Placement and directly held by Armistice Capital Master Fund Ltd. and may be deemed to be indirectly beneficially owned by (i) Armistice Capital, as the investment manager of the Master Fund; and (ii) Steven Boyd, as the Managing Member of Armistice Capital. Armistice Capital and Steven Boyd disclaim beneficial ownership of the securities except to the extent of their respective pecuniary interests therein. The address of Master Fund is c/o Armistice Capital, LLC, 510 Madison Ave, 7th Floor, New York, NY 10022.
- (3) Includes (i) 1,135,960 shares of common stock purchased in the Private Placement and directly held by Baker Brothers Life Sciences, L.P. (“BBLs”) and (ii) 93,548 shares of common stock purchased in the Private Placement and directly held by 667, L.P. (“667”), and together with BBLs, the “BBA Funds”). Baker Bros. Advisors LP (“BBA”), is the investment adviser to the BBA Funds and has sole voting and investment power with respect to the securities held by the BBA Funds and thus may be deemed to beneficially own such securities. Baker Bros. Advisors (GP) LLC (“BBA-GP”), is the sole general partner of BBA and thus may be deemed to beneficially own the securities held by the BBA Funds. The managing members of BBA-GP are Julian C. Baker and Felix J. Baker. The address for BBA, BBA-GP, Julian C. Baker and Felix J. Baker and the BBA Funds is 860 Washington Street, 3rd Floor, New York, NY 10014.
- (4) Includes 1,229,508 shares of common stock purchased in the Private Placement and directly held by BCLS II Equity Opportunities, LP (“BCLS II Equity”). Bain Capital Life Sciences Investors, LLC (“BCLSI”) is the ultimate general partner of BCLS II Equity. As a result, BCLSI may be deemed to share voting and dispositive power over the shares of common stock held by BCLS II Equity. The address of each of BCLSI and BCLS II Equity is c/o Bain Capital Life Sciences, LP, 200 Clarendon Street, Boston, MA 02116.
- (5) Includes 409, 836 shares of common stock purchased in the Private Placement and directly held by Boxer Capital, LLC. Boxer Asset Management, Inc. and Joseph Lewis hold shared voting and dispositive power over the shares held by Boxer Capital, LLC. Each individual and entity above disclaims beneficial ownership over the shares owned by Boxer Capital, LLC except to the extent of its or their pecuniary interest therein. The address of Boxer Asset Management, Inc. and Joseph Lewis is c/o Cay House, EP Taylor Drive N7776 Lyford Cay, New Providence, Bahamas. The address of Boxer Capital, LLC is 12860 El Camino Real, Ste 300, San Diego, CA 92130.
- (6) Includes 81,967 shares of common stock purchased in the Private Placement and directly held by Burn3 LLC. The address of Burn3 LLC is P.O. Box 748, Forked River, NJ 08731.
- (7) Includes 1,393,442 shares of common stock purchased in the Private Placement and directly held by CaaS Capital Master Fund LP. The address for CaaS Capital Master Fund L.P. is 800 Third Avenue, 26th Floor, New York, NY 10022.
- (8) Includes 614,754 shares of common stock purchased in the Private Placement and directly held by Casdin Partners Master Fund, L.P. The address for the Casdin entities is 1350 Avenue of the Americas, Suite 2600, New York, NY 10019.
- (9) Includes 819,672 shares of common stock purchased in the Private Placement and directly held by CHI IV Public Investments LP (“CHI IV”). CHI Advisors LLC, the investment adviser of CHI IV has sole voting and investment power with respect to the shares owned by CHI IV. The address for CHI Advisors, LLC and CHI IV is 599 Lexington Avenue, 19th Floor, New York, NY 10022.

- (10) Consists of 819,672 shares of common stock purchased in the Private Placement and directly held by CVI Investments, Inc. The address for CVI Investments, Inc. is c/o Heights Capital Management, Inc., 101 California, Street, Suite 3250, San Francisco, CA 94111.
- (11) Includes shares (i) 1,906,960 shares of common stock purchased in the Private Placement and directly held by EcoR1 Capital Fund Qualified, LP (“EcoR1 Qualified”) and (ii) 142,220 shares of common stock purchased in the Private Placement and directly held by EcoR1 Capital Fund, L.P. (“Ecor1 Capital”, and together with Ecor1 Qualified, the “EcoR1 Funds”). EcoR1 Capital, LLC is controlled Mr. Oleg Nodelman who has voting and investment control of the shares held by the EcoR1 Funds. The address for the EcoR1 Funds is 357 Tehama Street, Suite 3, San Francisco, California 94103.
- (12) Includes 81,967 shares of common stock purchased in the Private Placement and directly held by Jan Leschly. The address for Mr. Leschly is PO Box 276, Avon by the Sea, New Jersey, 07717.
- (13) Includes 655,737 shares of common stock purchased in the Private Placement and directly held by Janus Henderson Biotech Innovation Master Fund Limited. Janus Henderson Investors US LLC, 151 Detroit Street, Denver, CO 80206.
- (14) Includes 819,672 shares of common stock purchased in the Private Placement and directly held by Madison Avenue International LP. The address for Madison Avenue International LP is 150 East 58th St, Suite 1403, New York, NY 10155.
- (15) Includes (i) 351,639 shares of common stock purchased in the Private Placement and directly held by Newtyn Partners, LP (“Newtyn Partners”) and (ii) 468,033 shares of common stock purchased in the Private Placement and directly held by Newtyn TE Partners, LP (“Newtyn TE”, and together with Newtyn Partners the “Newtyn Funds”). The address of the Newtyn Funds is 60 East 42nd Street, Suite 960, New York, NY 10165.
- (16) Includes 368,857 shares of common stock purchased in the Private Placement and directly held by Nick Leschly.
- (17) Includes (i) 782,367 shares of common stock purchased in the Private Placement and directly held by RTW Master Fund, LTD (“RTW Master”), (ii) 425,552 shares of common stock purchased in the Private Placement and directly held by RTW Innovation Master Fund, Ltd. (“RTW Innovation”), and (iii) 21,589 shares of common stock purchased in the Private Placement and directly held by RTW Venture Fund Limited (“RTW Venture”, and together with RTW Master and RTW Innovation, the “RTW Funds”). RTW Investments, LP is the investment adviser to the RTW Funds. Mr. Roderick Wong is the Managing Partner and Chief Investment Officer of RTW Investments, L.P. Each of the RTW Funds and Mr. Wong disclaims any beneficial ownership of the shares directly held by the RTW Funds, except to the extent of its or his pecuniary interest therein. The address for each of these entities and individuals is 40 10th Avenue, Floor 7, New York, New York 10014.

### Relationship with Certain Selling Stockholders

Certain affiliates of 2seventy bio purchased shares of common stock on the same terms and conditions of the other investors in the Private Placement. The following table sets forth the number of shares of our common stock purchased by directors, executive officers and 5% stockholders and their affiliates and the aggregate purchase price paid for such shares.

Name	Shares of Common Stock Purchased	Aggregate Cash Purchase Price
Entities affiliated with EcoR1 Capital, LLC (1)	2,049,180	\$ 24,999,996.00
Baker Bros Advisors LP (2)	1,229,508	\$ 14,999,997.60
Nick Leschly (3)	368,857	\$ 4,500,055.40
Total:	3,647,545	\$ 44,500,049.00

- (1) EcoR1 Capital LLC is a holder of greater than five percent of our common stock.
- (2) Consists of 1,135,960 shares of common stock purchased and received by Baker Brothers Life Sciences, L.P., (“BBLs”) and 93,548 shares of common stock purchased and received by 667, L.P. (“667” and together with BBLs, the “ BBA Funds”). Baker Bros. Advisors LP, or BBA, is the investment adviser to the BBA Funds and has sole voting and investment power with respect to the securities held by the BBA Funds and thus may be deemed to beneficially own such securities. Baker Bros. Advisors (GP) LLC, or BBA-GP, is the sole general partner of BBA and thus may be deemed to beneficially own the securities held by the BBA Funds. The BBA Funds are holders of greater than five percent of our common stock.
- (3) Nick Leschly is our chief executive officer and a member of our Board. Mr. Leschly’s acquisition of shares in the Private Placement was approved by our Board of Directors and is exempted from the “short-swing” liability provisions of Section 16(b) of the Exchange Act pursuant to Rule 16b-3 promulgated thereunder.



## DESCRIPTION OF COMMON STOCK

The following descriptions are summaries of the material terms of our amended and restated certificate of incorporation and our amended and restated bylaws. We refer in this section to our amended and restated certificate of incorporation as our certificate of incorporation, and we refer to our amended and restated bylaws as our bylaws.

### **General**

Our authorized capital stock consists of 200,000,000 shares of common stock, par value \$0.0001 per share, and 10,000,000 shares of preferred stock, par value \$0.0001 per share, all of which shares of preferred stock are undesignated.

As of April 26, 2022, 37,618,103 shares of our common stock were outstanding and held by 30 stockholders of record.

### **Common Stock**

The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock.

### **Preferred Stock**

Our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our Company or other corporate action. Immediately after consummation of this offering, no shares of preferred stock will be outstanding, and we have no present plan to issue any shares of preferred stock.

### **Registration Rights**

Certain holders of our common stock are entitled to rights with respect to the registration of these securities under the Securities Act. These rights are provided under the terms of the PIPE Registration Rights Agreement. Pursuant to the PIPE Registration Rights Agreement, we have prepared and filed this registration statement with the SEC within 45 calendar days following the closing of the Private Placement, and we will use reasonable best efforts to cause this registration statement to be declared effective by the SEC within 30 calendar days thereafter (or within 45 calendar days thereafter if the SEC reviews the registration statement). All fees, costs and expenses of underwritten registrations under the PIPE Registration Rights Agreement will be borne by us.

### **Anti-Takeover Effects of our Certificate of Incorporation and Bylaws and Delaware Law**

Our certificate of incorporation and bylaws include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

### ***Board Composition and Filling Vacancies***

Our certificate of incorporation provides for the division of our board of directors into three classes serving staggered three-year terms, with one class being elected each year. Our certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of two-thirds or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum. The classification of directors, together with the limitations on removal of directors and treatment of vacancies, has the effect of making it more difficult for stockholders to change the composition of our board of directors.

### **No Written Consent of Stockholders**

Our certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our bylaws or removal of directors by our stockholders without holding a meeting of stockholders.

### **Meetings of Stockholders**

Our certificate of incorporation and bylaws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

### **Advance Notice Requirements**

Our bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. Our bylaws specify the requirements as to form and content of all stockholders' notices. These requirements may preclude stockholders from bringing matters before the stockholders at an annual or special meeting.

### **Anti-Takeover Effects of Provisions of Our Charter Documents**

Any amendment of our certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our certificate of incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, board composition, and limitation of liability must be approved by not less than two-thirds of the outstanding shares entitled to vote on the amendment, and not less than two-thirds of the outstanding shares of each class entitled to vote thereon as a class. Our bylaws may be amended or repealed by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the bylaws; and may also be amended or repealed by the affirmative vote of at least seventy-five percent of the outstanding shares entitled to vote on the amendment or repeal, voting together as a single class, or, if our board of directors recommends that the stockholders approve or repeal the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment or repeal, in each case voting together as a single class.

### **Undesignated Preferred Stock**

Our certificate of incorporation provides for 10,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to discourage an attempt to

obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

### **Choice of Forum**

Our bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware, or the Chancery Court, will be the sole and exclusive forum for state law claims for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of, or a claim based on, a breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (iii) any action asserting a claim pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or our bylaws, (iv) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws, or (v) any action asserting a claim governed by the internal affairs doctrine, or the Delaware Forum Provision. The Delaware Forum Provision does not apply to any causes of action arising under the Securities Act of 1933, as amended, or the Securities Act, or the Exchange Act. Our bylaws further provide that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America will be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, or the Federal Forum Provision. Our bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock is deemed to have notice of and consented to the foregoing Delaware Forum Provision and the Federal Forum Provision; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

### **Section 203 of the Delaware General Corporation Law**

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a “business combination” with an “interested stockholder” for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or;
- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder;

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder; or

- any sale, transfer, lease, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; and
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; and
- receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges, or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

#### **Stock Exchange Listing**

Our common stock is listed on The Nasdaq Global Select Market under the trading symbol “TSVT.”

#### **Transfer Agent and Registrar**

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC.

#### **Limitations of Liability and Indemnification Matters**

For a discussion of liability and indemnification, see “Executive Compensation” in our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 26, 2022.

## MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS

The following is a discussion of certain material U.S. federal income tax consequences of the acquisition, ownership and disposition of our shares of common stock. This discussion applies only to shares of common stock that are held as capital assets for U.S. federal income tax purposes and is applicable only to holders who are receiving our shares of common stock in this offering.

This discussion is a summary only and does not describe all of the tax consequences that may be relevant to you in light of your particular circumstances, including but not limited to the alternative minimum tax, the Medicare tax on certain investment income and the different consequences (such as the effects of Section 451 of the Code) that may apply if you are subject to special rules that apply to certain types of investors, including but not limited to:

- financial institutions or financial services entities;
- broker-dealers;
- governments or agencies or instrumentalities thereof;
- regulated investment companies;
- real estate investment trusts;
- expatriates or former long-term residents of the U.S.;
- persons that actually or constructively own five percent or more of our voting shares;
- insurance companies;
- dealers or traders subject to a mark-to-market method of accounting with respect to the common stock;
- persons holding the common stock as part of a “straddle,” hedge, integrated transaction or similar transaction;
- U.S. holders (as defined below) whose functional currency is not the U.S. dollar;
- partnerships or other pass-through entities for U.S. federal income tax purposes and any beneficial owners of such entities; and
- tax-exempt entities.

This discussion is based on the Code, and administrative pronouncements, judicial decisions and final, temporary and proposed Treasury regulations as of the date hereof, which are subject to change, possibly on a retroactive basis, and changes to any of which subsequent to the date of this prospectus may affect the tax consequences described herein. This discussion does not address any aspect of state, local or non-U.S. taxation, or any U.S. federal taxes other than income taxes (such as gift and estate taxes).

We have not sought, and will not seek, a ruling from the IRS as to any U.S. federal income tax consequence described herein. The IRS may disagree with the discussion herein, and its determination may be upheld by a court. Moreover, there can be no assurance that future legislation, regulations, administrative rulings or court decisions will not adversely affect the accuracy of the statements in this discussion. You are urged to consult your tax advisor with respect to the application of U.S. federal tax laws to your particular situation, as well as any tax consequences arising under the laws of any state, local or foreign jurisdiction.

This discussion does not consider the tax treatment of partnerships or other pass-through entities or persons who hold our common stock through such entities. If a partnership (or other entity or arrangement classified as a partnership or other pass-through entity for United States federal income tax purposes) is the beneficial owner of our common stock, the United States federal income tax treatment of a partner or member in the partnership or other pass-through entity generally will depend on the status of the partner or member and the activities of the partnership

or other pass-through entity. If you are a partner or member of a partnership or other pass-through entity holding our common stock, we urge you to consult your own tax advisor.

THIS DISCUSSION IS ONLY A SUMMARY OF CERTAIN UNITED STATES FEDERAL INCOME TAX CONSIDERATIONS ASSOCIATED WITH THE ACQUISITION, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK. EACH PROSPECTIVE INVESTOR IN OUR COMMON STOCK IS URGED TO CONSULT ITS OWN TAX ADVISOR WITH RESPECT TO THE PARTICULAR TAX CONSEQUENCES TO SUCH INVESTOR OF THE ACQUISITION, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK, INCLUDING THE APPLICABILITY AND EFFECT OF ANY UNITED STATES FEDERAL NON-INCOME, STATE, LOCAL, AND NON-U.S. TAX LAWS.

#### **U.S. holders**

This section applies to you if you are a “U.S. holder.” A U.S. holder is a beneficial owner of our shares of common stock who or that is, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation (or other entity taxable as a corporation) organized in or under the laws of the United States, any state thereof or the District of Columbia;
- an estate the income of which is includible in gross income for U.S. federal income tax purposes regardless of its source; or
- a trust, if (i) a court within the United States is able to exercise primary supervision over the administration of the trust and one or more U.S. persons (as defined in the Code) have authority to control all substantial decisions of the trust or (ii) it has a valid election in effect under Treasury Regulations to be treated as a U.S. person.

*Taxation of Distributions.* If we pay distributions in cash or other property (other than certain distributions of our stock or rights to acquire our stock) to U.S. holders of shares of our common stock, such distributions 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. Distributions in excess of current and accumulated earnings and profits will constitute a return of capital that will be applied against and reduce (but not below zero) the U.S. holder’s adjusted tax basis in our common stock. Any remaining excess will be treated as gain realized on the sale or other disposition of the common stock and will be treated as described under “*U.S. Holders—Gain or Loss on Sale, Taxable Exchange or Other Taxable Disposition of common stock*” below.

Dividends we pay to a U.S. holder that is a taxable corporation generally will qualify for the dividends received deduction if the requisite holding period is satisfied. With certain exceptions (including, but not limited to, dividends treated as investment income for purposes of investment interest deduction limitations), and provided certain holding period requirements are met, dividends we pay to a non-corporate U.S. holder may constitute “qualified dividends” that will be subject to tax at the maximum tax rate accorded to long-term capital gains. If the holding period requirements are not satisfied, then a corporation may not be able to qualify for the dividends received deduction and would have taxable income equal to the entire dividend amount, and non-corporate holders may be subject to tax on such dividend at regular ordinary income tax rates instead of the preferential rate that applies to qualified dividend income.

*Gain or Loss on Sale, Taxable Exchange or Other Taxable Disposition of common stock.* Upon a sale or other taxable disposition of our common stock, a U.S. holder generally will recognize capital gain or loss in an amount equal to the difference between the amount realized and the U.S. holder’s adjusted tax basis in the common stock. Any such capital gain or loss generally will be long-term capital gain or loss if the U.S. holder’s holding period for the common stock so disposed of exceeds one year. If the holding period requirements are not satisfied, any gain on a sale or taxable disposition of the shares would be subject to short-term capital gain treatment and would be taxed at regular ordinary income tax rates. Long-term capital gains recognized by non-corporate U.S. holders will be eligible to be taxed at reduced rates. The deductibility of capital losses is subject to limitations.

Generally, the amount of gain or loss recognized by a U.S. holder is an amount equal to the difference between (i) the sum of the amount of cash and the fair market value of any property received in such disposition and (ii) the U.S. holder's adjusted tax basis in its common stock so disposed of. A U.S. holder's adjusted tax basis in its common stock generally will equal the U.S. holder's acquisition cost for the common stock or less, in the case of a share of common stock, any prior distributions treated as a return of capital. In the case of any shares of common stock originally acquired as part of an investment unit, the acquisition cost for the share of common stock that were part of such unit would equal an allocable portion of the acquisition cost of the unit based on the relative fair market values of the components of the unit at the time of acquisition.

*Information Reporting and Backup Withholding.* In general, information reporting requirements may apply to dividends paid to a U.S. holder and to the proceeds of the sale or other disposition of our shares of common stock, unless the U.S. holder is an exempt recipient. Backup withholding may apply to such payments if the U.S. holder fails to provide a taxpayer identification number, a certification of exempt status or has been notified by the IRS that it is subject to backup withholding (and such notification has not been withdrawn).

Any amounts withheld under the backup withholding rules generally should be allowed as a refund or a credit against a U.S. holder's U.S. federal income tax liability provided the required information is timely furnished to the IRS.

### **Non-U.S. holders**

This section applies to you if you are a "Non-U.S. holder." As used herein, the term "Non-U.S. holder" means a beneficial owner of our common stock who or that is for U.S. federal income tax purposes:

- a non-resident alien individual (other than certain former citizens and residents of the U.S. subject to U.S. tax as expatriates);
- a foreign corporation or
- an estate or trust that is not a U.S. holder;

but generally does not include an individual who is present in the U.S. for 183 days or more in the taxable year of disposition. If you are such an individual, you should consult your tax advisor regarding the U.S. federal income tax consequences of the acquisition, ownership or sale or other disposition of our common stock.

*Taxation of Distributions.* In general, any distributions we make to a Non-U.S. holder of shares of our common stock, to the extent paid out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles), will constitute dividends for U.S. federal income tax purposes and, provided such dividends are not effectively connected with the Non-U.S. holder's conduct of a trade or business within the United States, we will be required to withhold tax from the gross amount of the dividend at a rate of 30%, unless such Non-U.S. holder is eligible for a reduced rate of withholding tax under an applicable income tax treaty and provides proper certification of its eligibility for such reduced rate (usually on an IRS Form W-8BEN or W-8BEN-E). Any distribution not constituting a dividend will be treated first as reducing (but not below zero) the Non-U.S. holder's adjusted tax basis in its shares of our common stock and, to the extent such distribution exceeds the Non-U.S. holder's adjusted tax basis, as gain realized from the sale or other disposition of the common stock, which will be treated as described under "*Non-U.S. Holders—Gain on Sale, Taxable Exchange or Other Taxable Disposition of common stock*" below.

The withholding tax does not apply to dividends paid to a Non-U.S. holder who provides a Form W-8ECI, certifying that the dividends are effectively connected with the Non-U.S. holder's conduct of a trade or business within the United States. Instead, the effectively connected dividends will be subject to regular U.S. income tax as if the Non-U.S. holder were a U.S. resident, subject to an applicable income tax treaty providing otherwise. A Non-U.S. corporation receiving effectively connected dividends may also be subject to an additional "branch profits tax" imposed at a rate of 30% (or a lower treaty rate).

*Gain on Sale, Taxable Exchange or Other Taxable Disposition of common stock.* A Non-U.S. holder generally will not be subject to U.S. federal income or withholding tax in respect of gain recognized on a sale, taxable exchange or other taxable disposition of our common stock, unless:

- the gain is effectively connected with the conduct of a trade or business by the Non-U.S. holder within the United States (and, under certain income tax treaties, is attributable to a United States permanent establishment or fixed base maintained by the Non-U.S. holder); or
- we are or have been a “U.S. real property holding corporation” for U.S. federal income tax purposes at any time during the shorter of the five-year period ending on the date of disposition or the period that the Non-U.S. holder held our common stock, and, in the case where shares of our common stock are regularly traded on an established securities market, the Non-U.S. holder has owned, directly or constructively, more than 5% of our common stock at any time within the shorter of the five-year period preceding the disposition or such Non-U.S. holder’s holding period for the shares of our common stock. There can be no assurance that our common stock will be treated as regularly traded on an established securities market for this purpose.

Unless an applicable treaty provides otherwise, gain described in the first bullet point above will be subject to tax at generally applicable U.S. federal income tax rates as if the Non-U.S. holder were a U.S. resident. Any gains described in the first bullet point above of a Non-U.S. holder that is a foreign corporation may also be subject to an additional “branch profits tax” at a 30% rate (or lower treaty rate).

If the second bullet point above applies to a Non-U.S. holder, gain recognized by such holder on the sale, exchange or other disposition of shares of our common stock will be subject to tax at generally applicable U.S. federal income tax rates, and a buyer of such shares may be required to withhold U.S. federal income tax at a rate of 15% of the amount realized upon the disposition. We expect not to be classified as a “U.S. real property holding corporation” for U.S. federal income tax purposes. However, such determination is factual in nature and subject to change and no assurance can be provided as to whether we will be a “U.S. real property holding corporation” for U.S. federal income tax purposes in the future.

*Information Reporting and Backup Withholding.* Information returns will be filed with the IRS in connection with payments of dividends and the proceeds from a sale or other disposition of our shares of common stock. A Non-U.S. holder may have to comply with certification procedures to establish that it is not a United States person in order to avoid information reporting and backup withholding requirements. The certification procedures required to claim a reduced rate of withholding under a treaty will generally satisfy the certification requirements necessary to avoid the backup withholding as well. The amount of any backup withholding from a payment to a Non-U.S. holder will be allowed as a credit against such holder’s U.S. federal income tax liability and may entitle such holder to a refund, provided that the required information is timely furnished to the IRS.

*FATCA Withholding Taxes.* Sections 1471 through 1474 of the Code and the Treasury Regulations and administrative guidance promulgated thereunder (commonly referred as the “Foreign Account Tax Compliance Act” or “FATCA”) generally impose withholding at a rate of 30% in certain circumstances on dividends in respect of, and (subject to the proposed Treasury Regulations discussed below) gross proceeds from the sale or other disposition of, securities (including shares of our common stock) which are held by or through certain foreign financial institutions (including investment funds), unless any such institution (i) enters into, and complies with, an agreement with the IRS to report, on an annual basis, information with respect to interests in, and accounts maintained by, the institution that are owned by certain U.S. persons and by certain non-U.S. entities that are wholly or partially owned by U.S. persons and to withhold on certain payments, or (ii) if required under an intergovernmental agreement between the United States and an applicable foreign country, reports such information to its local tax authority, which will exchange such information with the U.S. authorities. An intergovernmental agreement between the United States and an applicable foreign country may modify these requirements. Accordingly, the entity through which shares of our common stock are held will affect the determination of whether such withholding is required. Similarly, dividends in respect of, and (subject to the proposed Treasury Regulations discussed below) gross proceeds from the sale or other disposition of, our common stock held by an investor that is a non-financial non-U.S. entity that does not qualify under certain exceptions will generally be subject to withholding at a rate of 30%, unless such entity either (i) certifies to the applicable withholding agent that such entity does not have any “substantial United States



owners” or (ii) provides certain information regarding the entity’s “substantial United States owners,” which will in turn be provided to the U.S. Department of Treasury.

Under the applicable Treasury Regulations and administrative guidance, withholding under FATCA generally applies to payments of dividends in respect of our common stock. While withholding under FATCA generally would also apply to payments of gross proceeds from the sale or other disposition of securities (including shares of our common stock), proposed Treasury Regulations eliminate FATCA withholding on payments of gross proceeds entirely. Taxpayers generally may rely on these proposed Treasury Regulations until final Treasury Regulations are issued. All holders should consult their tax advisors regarding the possible implications of FATCA on their investment in shares of our common stock.

## PLAN OF DISTRIBUTION

Each selling stockholder of the securities and any of their donees, pledgees, assignees, transferees and other successors-in-interest may, from time to time, sell any or all of their securities covered hereby on the principal trading market or any other stock exchange, market or trading facility on which the securities are traded or in private transactions. These sales may be at fixed or negotiated prices. A selling stockholder may use any one or more of the following methods when selling securities:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the securities as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- settlement of short sales;
- in transactions through broker-dealers that agree with the selling stockholders to sell a specified number of such securities at a stipulated price per security;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- a combination of any such methods of sale; or
- any other method permitted pursuant to applicable law.

The selling stockholders may also sell securities under Rule 144 or any other exemption from registration under the Securities Act of 1933, as amended (the "Securities Act"), if available, rather than under this prospectus.

Broker-dealers engaged by the selling stockholders may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the Selling Stockholders (or, if any broker-dealer acts as agent for the purchaser of securities, from the purchaser) in amounts to be negotiated, but, except as set forth in a supplement to this prospectus, in the case of an agency transaction not in excess of a customary brokerage commission in compliance with FINRA Rule 2121; and in the case of a principal transaction a markup or markdown in compliance with FINRA Rule 2121.

The selling stockholders may, from time to time, pledge or grant a security interest in some or all of the securities owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the securities, from time to time, under this prospectus, or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act, amending the selling stockholder list to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus. The selling stockholders also may transfer the securities in other circumstances, in which case the transferees, pledgees, donees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

In connection with the sale of the securities or interests therein, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the securities in the course of hedging the positions they assume. The selling stockholders may also sell securities short and deliver these securities to close out their short positions, or loan or pledge the securities to broker-dealers that in turn may sell these securities. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or create one or more derivative securities which require the delivery to such broker-dealer or other financial institution of securities offered by this prospectus, which securities such broker-

dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The aggregate proceeds to the selling stockholders from the sale of the securities offered by them will be the purchase price of the securities less discounts or commissions, if any. Each of the selling stockholders reserves the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of securities to be made directly or through agents. We will not receive any of the proceeds from this offering.

The selling stockholders and any broker-dealers or agents that are involved in selling the securities may be deemed to be “underwriters” within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the securities purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. Each selling stockholder has informed the Company that it does not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the securities.

The Company is required to pay certain fees and expenses incurred by the Company incident to the registration of the securities. The Company has agreed to indemnify the selling stockholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

We agreed to keep this prospectus effective until the earliest of (i) the date on which the securities may be resold by the selling stockholders without registration and without regard to any volume or manner-of-sale limitations by reason of Rule 144, without the requirement for the Company to be in compliance with the current public information under Rule 144 under the Securities Act or any other rule of similar effect, (ii) the date on which all of the securities have been sold pursuant to this prospectus or Rule 144 under the Securities Act or any other rule of similar effect and (iii) the date that is one year following the date of effectiveness of this registration statement. The resale securities will be sold only through registered or licensed brokers or dealers if required under applicable state securities laws. In addition, in certain states, the resale securities covered hereby may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

Under applicable rules and regulations under the Exchange Act, any person engaged in the distribution of the resale securities may not simultaneously engage in market making activities with respect to the common stock for the applicable restricted period, as defined in Regulation M, prior to the commencement of the distribution. In addition, the selling stockholders will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including Regulation M, which may limit the timing of purchases and sales of the common stock by the selling stockholders or any other person. We will make copies of this prospectus available to the selling stockholders and have informed them of the need to deliver a copy of this prospectus to each purchaser at or prior to the time of the sale (including by compliance with Rule 172 under the Securities Act).

## LEGAL MATTERS

The validity of the securities being offered by this prospectus will be passed upon by Goodwin Procter LLP, Boston, MA. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in an applicable prospectus supplement.

## EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated and combined financial statements included in our Annual Report on [Form 10-K](#) for the year ended December 31, 2021, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

## WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the common stock offered by this prospectus. This prospectus, which constitutes part of the registration statement, does not contain all of the information included in the registration statement. For further information pertaining to us and our common stock, you should refer to the registration statement and to its exhibits. Whenever we make reference in this prospectus to any of our contracts, agreements or other documents, the references are not necessarily complete, and you should refer to the exhibits attached to the registration statement for copies of the actual contract, agreement or other document.

We are subject to the informational requirements of the Exchange Act and file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, at the SEC's website at [www.sec.gov](http://www.sec.gov). We also maintain a website at [www.2seventybio.com](http://www.2seventybio.com). The information contained in or accessible from our website is not incorporated into this prospectus, and you should not consider it part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

## INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" information that we file with it into this prospectus, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is an important part of this prospectus. The information incorporated by reference is considered to be a part of this prospectus, and information that we file later with the SEC will automatically update and supersede information contained in this prospectus and any accompanying prospectus supplement.

We incorporate by reference the documents listed below that we have previously filed with the SEC:

- Our [Annual Report on Form 10-K](#) for the year ended December 31, 2021, filed on March 22, 2022;
- Our [Definitive Proxy Statement on Schedule 14A](#) (to the extent incorporated by reference into our Annual Report on Form 10-K), filed with the SEC on April 26, 2022;
- Our Current Reports on Form 8-K filed with the SEC on [January 6, 2022](#), [January 11, 2022](#), [March 16, 2022](#), [April 8, 2022](#) and [April 29, 2022](#) (in each case, except for information contained therein which is furnished rather than filed); and
- The description of our common stock contained in the Information Statement filed with the SEC on October 8, 2021 as [Exhibit 99.1 to the Form 10](#), including any further amendments thereto or reports filed for the purposes of updating such description.
- Any statement contained in a document incorporated by reference in this prospectus or any prospectus supplement shall be deemed to be modified or superseded to the extent that a statement contained herein, therein or in any other subsequently filed document that also is incorporated by reference herein or therein

modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus or any prospectus supplement. Under no circumstances will any information filed under current items 2.02 or 7.01 of Form 8-K be deemed incorporated herein by reference unless such Form 8-K expressly provides to the contrary.

Upon request, we will provide, without charge, to each person, including any beneficial owner, to whom a copy of this prospectus is delivered, a copy of the documents incorporated by reference into this prospectus but not delivered with the prospectus. You may make a request for copies of these filings, and any exhibits we have specifically incorporated by reference as an exhibit in this prospectus, at no cost by writing or by telephone. Requests should be directed to:

2seventy bio, Inc.  
60 Binney Street, Cambridge, Massachusetts 02142  
Attn: Corporate Secretary  
617-675-7270

You may also access these documents, free of charge on the SEC's website at [www.sec.gov](http://www.sec.gov) or on our website at [www.2seventybio.com](http://www.2seventybio.com). Information contained on our website is not incorporated by reference into this prospectus, and you should not consider any information on, or that can be accessed from, our website as part of this prospectus or any accompanying prospectus supplement.

**13,934,427 Shares**



**PROSPECTUS**

**May 6, 2022**