Prospectus Supplement No. 5 (to Prospectus dated May 6, 2022)



Up to 13,934,427 Shares of Common Stock

This prospectus supplement updates and supplements the prospectus dated May 6, 2022 (the "Prospectus"), which forms a part of our Registration Statement on Form S-1 (333-264544). This prospectus supplement is being filed to update and supplement the information in the Prospectus with the information contained in our Current Report on Form 8-K, filed with the Securities and Exchange Commission on September 7, 2022 (the "Current Report on Form 8-K"). Accordingly, we have attached the Current Report on Form 8-K to this prospectus supplement.

The Prospectus and this prospectus supplement relate to the offer and sale, from time to time, by the selling stockholders named in the Prospectus, or the Selling Stockholders, or any of their pledgees, donees, assignees and successors-in-interest, or collectively, the permitted transferees, of up to 13,934,427 shares of our common stock that were issued to certain investors in a private placement.

This prospectus supplement should be read in conjunction with the Prospectus. This prospectus supplement updates and supplements the information in the Prospectus. If there is any inconsistency between the information in the Prospectus and this prospectus supplement, you should rely on the information in this prospectus supplement.

Our common stock is listed on the Nasdaq Capital Market under the symbol "TSVT." On September 6, 2022, the closing price of our common stock was \$13.90 per share.

We are an "emerging growth company" as that term is defined under the federal securities laws and, as such, are subject to certain reduced public company reporting requirements.

Investing in our securities involves risks that are described in the "Risk Factors" section beginning on page 6 of the Prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of the securities to be issued under this prospectus or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus supplement is September 7, 2022.

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): September 7, 2022

2seventy bio, Inc.

(Exact name of Registrant as Specified in Its Charter)

Delaware (State or other jurisdiction of incorporation)

001-40791 (Commission File Number) 86-3658454

(IRS Employer Identification No.)

60 Binney Street, Cambridge, MA (Address of principal executive offices)

02142 (Zip Code)

Registrant's telephone number, including area code: (339) 499-9300

Not Applicable

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instructions A.2. below):

Ш	Written communications	pursuant to F	Kule 425	under the S	Securities Ac	t (1/	CFR 230.425)

- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, \$0.0001 par value per share	TSVT	The NASDAQ Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company x

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. 0

Item 8.01 Other Events.

On September 7, 2022, 2seventy bio, Inc. announced plans to initiate the KarMMa-9 study to evaluate ABECMA (idecabtagene vicleucel) in newly diagnosed multiple myeloma patients who have suboptimal response to transplant. A copy of the press release is being filed as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated by reference herein.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits

Exhibit No.	Description
<u>99.1</u>	Press release issued by 2seventy bio, Inc. on September 7, 2022.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document and incorporated as Exhibit 101)

SIGNATURESPursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Dated: September 7, 2022 2seventy bio, Inc.

/s/ Chip Baird

Chip Baird

Chief Financial Officer

(Principal Financial and Accounting Officer)