UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

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

Date of Report (Date of earliest event reported): January 9, 2023

2seventy bio, Inc.

(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-40791**	**86-3658454**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**
60 Binney Street, Cambridge, MA		**02142**
(Address of principal executive offices)		**(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):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 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 ☒

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. ☐

Item 2.02 Results of Operation and Financial Condition.

2seventy bio, Inc. (the "Company") intends to share with investors the amount of cash, cash equivalents and marketable securities it had on hand as of December 31, 2022 and the revenue received from sales of ABECMA in the U.S. for the year ended December 31, 2022. Although the Company has not finalized its financial results for the twelve months ended December 31, 2022, the Company currently anticipates that its cash, cash equivalents and marketable securities were approximately $268 million as of December 31, 2022 and that revenue from sales of ABECMA in the U.S. in 2022 equaled approximately $250 to $300 million, which is shared equally with Bristol-Myers Squibb. This information is unaudited and does not present all information necessary for an understanding of the Company's financial condition as of December 31, 2022 and its results of operations for the twelve months ended December 31, 2022. The Company expects to announce its full results for the twelve months ended December 31, 2022 on or before March 31, 2023.

Item 7.01 Regulation FD Disclosure.

The Company from time to time presents and distributes to investors slide presentations to provide updates and summaries of its business. A copy of its current presentation is being furnished as Exhibit 99.1, which is incorporated herein by reference.

The information in this Current Report on Form 8-K pursuant to Item 7.01 is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section. It may only be incorporated by reference in another filing under the Exchange Act or the Securities Act of 1933, as amended, if such subsequent filing specifically references the information furnished pursuant to Item 7.01 of this Current Report.

Item 8.01 Other Events.

On January 9, 2023, the Company issued a press release announcing key milestone updates and providing other business highlights.

The full text of the press release regarding the announcement is filed as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits

Exhibit No.	Description
99.1	Slide presentation of 2seventy bio, Inc. furnished herewith.
99.2	Press release issued by 2seventy bio, Inc. on January 9, 2023.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document and incorporated as Exhibit 101)

SIGNATURES

Pursuant 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: January 9, 2023

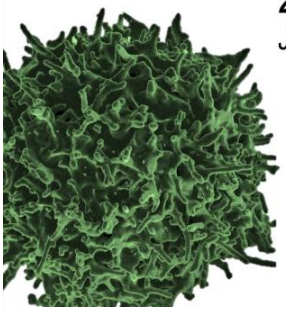
2seventy bio, Inc.

By: /s/ Chip Baird
Chip Baird
Chief Financial Officer
(Principal Financial and Accounting Officer)

Unleash Time

2seventy bio company presentation

January 2023



2seventybio

Cautionary note regarding forward-looking statements

These slides and the accompanying oral presentation may contain "forward-looking statements". These statements include, but are not limited to: statements about our plans, strategies, timelines and expectations with respect to the development, manufacture or sale of our product candidates, including the design, initiation, enrollment and completion of pre-clinical and clinical studies; timelines for the results of ongoing and planned clinical trials for our product candidates and for ABECMA (ide-cel) in additional indications; the timing or likelihood of regulatory filings and acceptances and approvals thereof; expectations as to the market size for ABECMA and any other approved product we may successfully develop; the progress and results of our commercialization of ABECMA, including our goal of increasing manufacturing capacity and improving the manufacturing process and the number of patients that are expected to be treated with ABECMA in the commercial setting and potential late line global revenue for ABECMA; anticipated revenues resulting from sales of ABECMA; statements about the efficacy and perceived therapeutic benefits of our product candidates and the potential indications and market opportunities therefor; statements about the strategic plans for 2seventy bio and potential corporate development opportunities, including manufacturing expectations and benefits received from collaborations; statements about our ability to operate as a stand-alone company and execute our strategic priorities; and expectations regarding our use of capital, expenses and other future financial results, including our net cash spend, cash runway and U.S. net revenue for ABECMA in 2023. Any forward-looking statements in this presentation are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this presentation, including, without limitation, the risk that the market opportunities for our approved product or any future approved product are smaller than we believe they are; the risk that BMS, upon whom we rely for the successful development and commercialization of ABECMA does not devote sufficient resources thereto, is unsuccessful in its efforts, or chooses to terminate its agreements with us; the risk that we and/or BMS or our third party vendors will be unable to increase manufacturing and supply capacity for ABECMA; the risk that our BLAs, sBLAs and INDs will not be accepted for filing by the FDA on the timeline that we expect, or at all; the risk that our plans with respect to the preclinical and clinical development and regulatory approval of our product candidates may not be successfully achieved on the planned timeline, or at all; the risk that ABECMA will not be as commercially successful as we may anticipate; and the risk that we are unable to manage our operating expenses or cash use for operations. For a discussion of other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in the information statement contained in our most recent Form 10-Q and most recent quarterly reports any other filings that we have made or will make with the Securities and Exchange Commission in the future. All information in this press release is as of the date of the release, and 2seventy bio undertakes no duty to update this information unless required by law. This presentation has been prepared by 2seventy bio for the exclusive use of the party to whom the Company delivers this presentation. This presentation does not constitute an offer to sell or the solicitation of an offer to buy any securities of the Company. The information contained herein is for informational purpose, and may not be relied upon in connection with the purchase or sale of any security. Neither the Company nor any of its affiliates or representatives makes any representation or warranty, expressed or implied, as to the accuracy or completeness of this presentation or any of the information contained herein, or any other written or oral communication transmitted or made available to the you or your affiliates or representatives. The Company and its affiliates and representatives expressly disclaim to the fullest extent permitted by law any and all liability based, in whole or in part, on the presentation or any information contained herein or any other written or oral communication transmitted or made available to you or your affiliates or representatives, including, without limitation, with respect to errors therein or omissions therefrom. This presentation shall not constitute an offer to sell or the solicitation of an offer to buy any securities, nor shall there be any sale of any securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or jurisdiction.

The sole mission of 2seventy is to **“unleash the curative potential of the T cell”**

Our experience in drug development and deep execution capabilities in cell therapy allow us to design & deliver multi-layered, multi-modality T cell-based solutions that address and overcome the immunologically evasive and suppressive properties of tumors.

2seventybio

Purpose-built strategy to unleash the curative potential of the T cell

STRATEGIC PRINCIPLES

- **Unleash the T cell.** We focus on autologous T cell therapies: proven modality with curative potential
- **Advanced engineering, broad scope.** We apply cell engineering across both heme and solid tumors – bespoke therapies to optimize performance against biological challenges
- **Ask and Answer.** We can rapidly design, manufacture, and study cell therapies – then iterate to build best-in-class treatments

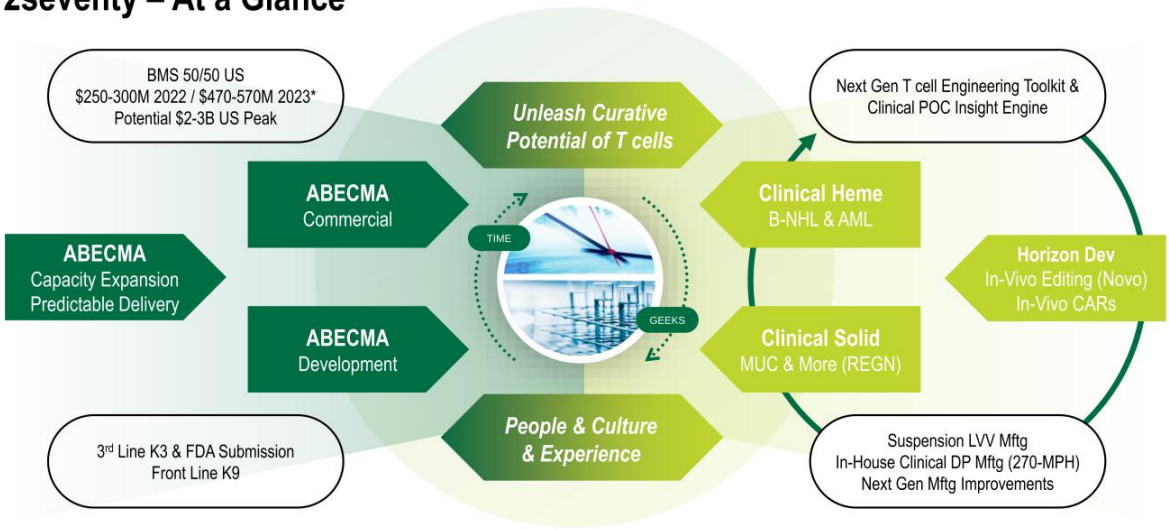
COMMERCIAL PRODUCT & ROBUST PIPELINE

- **ABECMA,** the first approved CAR T therapy for multiple myeloma; own 50/50 US rights in partnership with BMS; on track for upper end of $250-$300M 2022 topline & growing to $470-570M anticipated revenue in 2023
- **Next Gen clinical programs:** bbT369 (B-NHL) and SC-DARIC33 (AML)
- **Strong early pipeline** targeting heme and solid tumors (MUC and more with REGN)

CLASS-LEADING CAPABILITIES

- **Multiple T cell engineering technologies** power research engine to design differentiated products – with meaningful clinical validation emerging
- **In-house clinical drug product manufacturing facility** enables continuous innovation, & facile delivery
- **Best in class vector suspension product** to enable product engine

2seventy – At a Glance



ABECMA profitable in 2023** | **Cash runway into 2025** | **410 employees**

*Anticipated revenue, US topline revenue, profit and loss shared 50/50 with BMS
**Based on current operating plan and anticipated revenue

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2022 – 2seventy's Foundational First Year

Company/Platform

Reset & rebalanced company size, shape & burn

Launched **"Unleash T cell"** vision, culture & core values

Built in-house DP capability to support product engine

End of year runway into 2025

ABECMA

- U.S. topline revenue tracking at upper end of $250-300 million range
- Increased manufacturing capacity and reduced COGS
- Positive KarMMa-3 data & announced KarMMa-9 NDMM study

Pipeline

- Initiated enrollment of bbT369/B-NHL & SC-DARIC33/AML studies
- Established strategic relationship with JW Therapeutics for clinical dev of our enhanced MAGE-A4 TCR in China
- Signed expanded translational partnership with Regeneron enabling combinations of engineered T cells with mAbs/bi-specs
- Selected NG-AML candidate for pre-clinical dev based on novel RESET architecture (2022 Horizon X Program)
- Progressed F8 / Novo Nordisk megaTAL gene editing program to large animal studies

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2023 Goals and Long-Term Drivers

Longer-Term Drivers

- Drive toward $2-3B ABECMA U.S. peak sales potential
- Path to profitability and sustainability
- Enabling partnerships
- Lever end-to-end cell therapy platform and capabilities
- Hire and retain the best & brightest

2023 Goals

ABECMA

- Total US revenue $470-570M shared with BMS
- Present and publish KarMMa-3 data
- U.S. Approval in 3rd line
- Initiate KarMMa-9

Pipeline

- Data update for DARIC33 Mid 2023
- Data update for bbT369 EOY 2023
- MUC16 IND EOY 2023
- MAGE-A4 IIT EOY 2023 (JW)

Net cash spend of $180-220M

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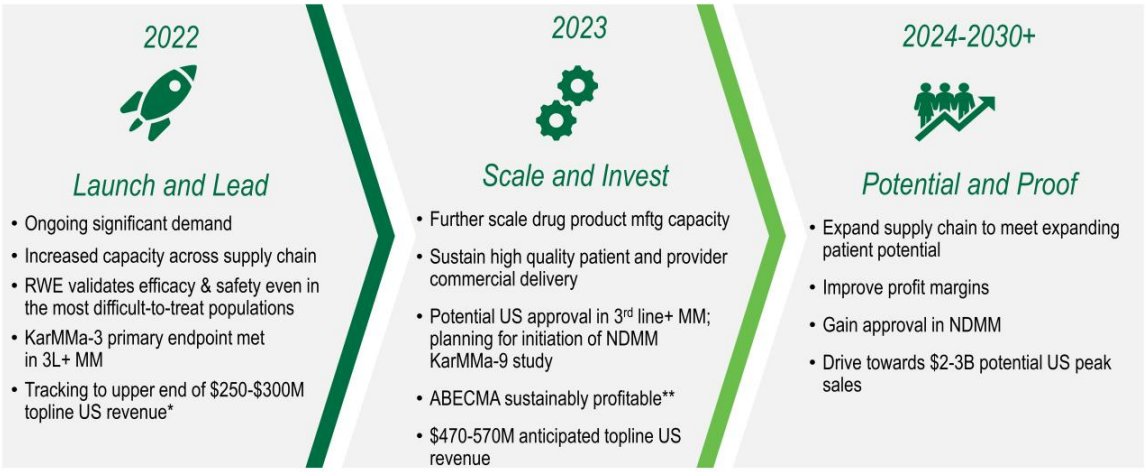
ABECMA® potential to be $2-3B market opportunity in US driven by label expansion, increased capacity and double-digit market growth



*US ABECMA profit and loss shared 50/50 between 2seventy and BMS as part of the collaboration agreement; unaudited, based on information currently available and subject to change; **Based on current operating plan and anticipated revenue

Real-world MM treatment decisions are practical and patient-driven

Select ABECMA Launch Metrics
Through Dec 2022

- Over 1,100 US commercial patients treated since launch
- ~70 treatment centers online in the U.S.
- 85-90% average in-spec manufacturing success since launch
- ~30-day average turn-around-time

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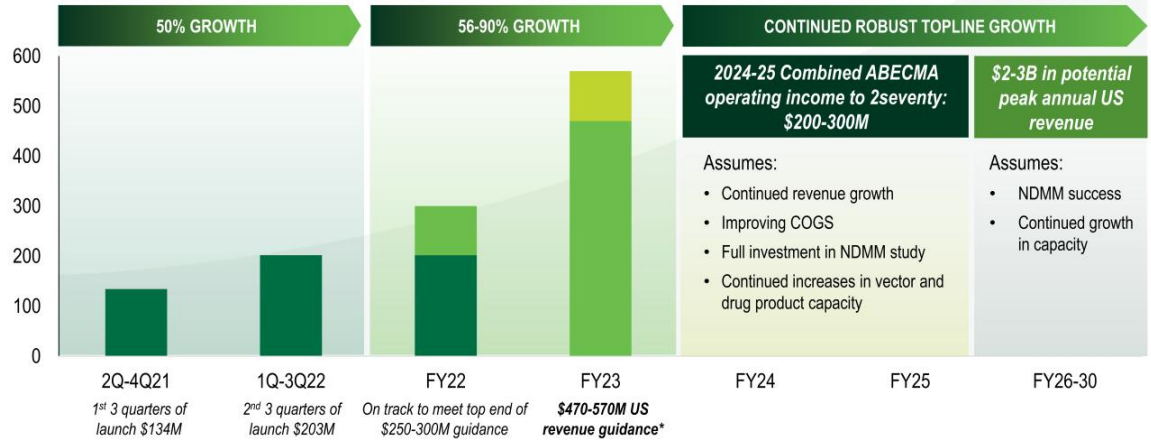
ABECMA Financial Outlook

Strong US revenue growth. Blockbuster potential.
2024-25 cashflow significantly reduces future capital needs



*Anticipated revenue based on current operating plan

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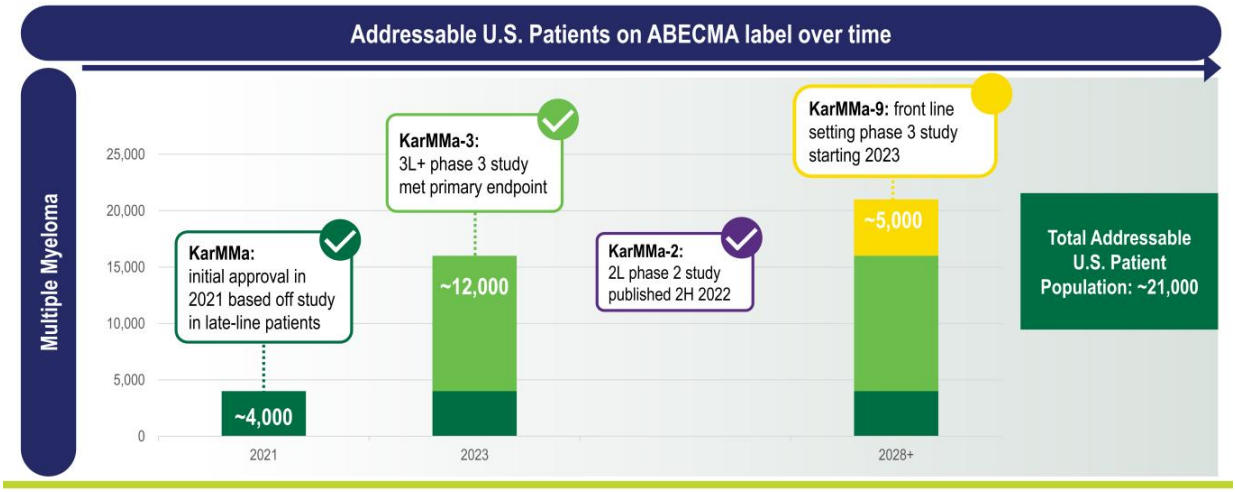
KarMMa-3 results and KarMMa-9 front-line study drive label expansion into broad U.S. market opportunity



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KarMMa-2 and KarMMa-3 data support conviction in transformative potential of ABECMA in front-line setting

KarMMa-3: significantly improves PFS in earlier line

- RRMM after 2-4 prior lines of therapy and refractory to the last regimens
- Planned BLA submission early 2023
- Full data to be presented at EBMT-EHA meeting Feb. 10, 2023

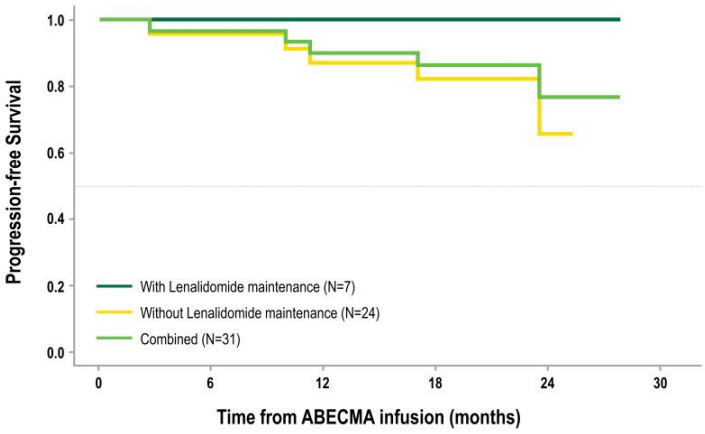
KarMMa-2: promising data in suboptimal ASCT responders support KarMMa-9 design

- Cohort 2c in suboptimal responders (<VGPR) post transplant **shows promising ORR of 87% and CRR of 74%**
- PFS at 12m = 90.1%; 24m = 83.1%
- No progressive disease (PD) events occurred in patients who received maintenance
- Toxicities are consistent with established and favorable ide-cel safety profile

KarMMa-9: improving upon the SoC in transplant eligible NDMM with high POS

- ASCT is SoC in NDMM transplant eligible patients, however high unmet need of up to **50-60% patients <CR after transplant**
- **KarMMa-9 addresses a unique NDMM segment by adding on to transplant**
- Planned study start in 2023

KarMMa-2 data give confidence of ABECMA in NDMM – suboptimal responders post transplant



KarMMa-2 cohort 2c in <VGPR post transplant demonstrate promising efficacy in 31 patients

- **Patients *without lenalidomide* maintenance (n=24):** ORR=87%, CRR=74%, PD=5/24, mDOR=29.8 months, mPFS: not reached
- **Patients *with lenalidomide* maintenance (n=7):** ORR=100%, CRR=57%, PD=0/7
- **Consistent, predictable and well manageable safety profile**

Data cut: Feb 2022

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Expanding ABECMA manufacturing footprint

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Innovative cell therapy candidates across broad indications

INDICATION [DRUG]	TARGET	TECHNOLOGY	DISCOVERY STAGE R&D	IND-ENABLING PRECLINICAL STUDIES	CLINICAL STUDIES	APPROVED PRODUCTS
Multiple Myeloma [ABECMA]	BCMA	CAR T cell	BMS Partnership			Abecma
Multiple Myeloma [ABECMA]	BCMA	CAR T cell	BMS Partnership; Earlier Line Studies			3L+ potential approval 2023 NDMM study initiation 2023
AML-Pediatric [SC-DARIC33]	CD33	Drug-Regulated; CAR T cell (DARIC)	TSVT Owned; SCRI Collaboration		Patients Enrolling; Update mid 2023	
B-NHL [bbT369]	Dual B cell targets	Dual-Targeted CAR T cell Signal Enhanced Gene Edited	TSVT Owned		Patients Enrolling; Update in 2023	
Ovarian Cancer	MUC16	CAR T cell Pharmacologic Enhancements	REGN Collaboration		IND EOY 2023	
Solid Tumors	MAGE-A4	TCR T cell Potency Enhanced	REGN/JW Collaboration		IIT EOY 2023 (JW / China)	
AML-Adult [SC-DARIC33 Next-Gen]	CD33 + Undisclosed	Drug-Regulated CAR T cell Dual-Targeted Potency Enhanced	TSVT Owned			
Solid Tumors	Multiple	CAR / TCR T cell Potency Enhanced	Multiple TSVT Owned; Plus Regeneron Collab.		Product engine generating ~1+ INDs per year	
Multiple Myeloma	Multiple	Multi-Targeted CAR T cell Potency Enhanced	TSVT Owned			
Additional Indications	Undisclosed	Multiple	Multiple TSVT Owned; Plus Novo Nordisk Collab.			

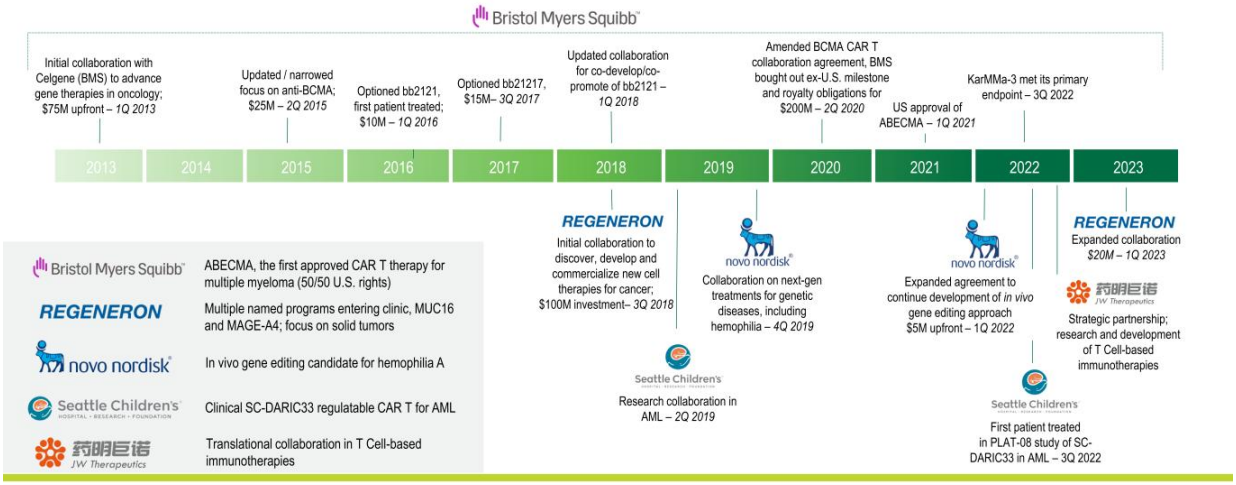
Collaboration program

TSVT-owned program

*Investigational New Drug application – IND; Investigator Initiated Trial – IIT; Newly Diagnosed Multiple Myeloma – NDMM

Long-term partnership track record

New collaborations are a key focus over next three years



REGN Collaboration 2.0: The Combinatorial Potential of Engineered T cells

Leverages 2seventy's CAR/TCR Platform with Regeneron mAbs and Bi-specifics for Solid Tumors

August 6, 2018

bluebird bio and Regeneron Announce Collaboration to Discover, Develop and Commercialize New Cell Therapies for Cancer

- $100M equity investment by Regeneron
- 2seventy retains significant (50-100%) product rights
- For 50/50 collaboration products, costs shared equally
- Five-year research collaboration

January 6, 2023

2seventybio

2seventy bio Announces Expanded Translational Collaboration with Regeneron to Develop New Cell Therapy-Based Combinations for Solid Tumors

Collaboration Leverages 2seventy's Platform for T Cell Therapy Research and Development with Regeneron Antibodies and Bispecifics to Explore Multiplex Combination Approaches

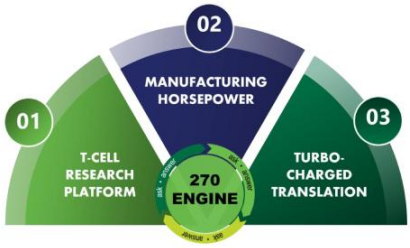
Regeneron Investing $20 million in 2seventy Equity; Regeneron to Fund 100% of Clinical Development Costs for Regeneron-Based Combination Clinical Trial Arms Through Approval

- Builds on **several previously identified product candidates** advancing toward the clinic including MUC16
- Combines **engineered T cells with biologics** to attack the challenge of treating solid tumors
- **Enables multi-arm clinical studies to triple the "shots on goal"** and lessons learned in the clinic vs each CAR/TCR T cell alone
- Leverages 2seventy's **newly built in-house clinical cell therapy manufacturing facility** (270-MPH)
- **Significant Funding** through Regeneron investment of $20 million in 2seventy equity at 50% premium; Regeneron paying 100% of Regeneron-based translational development costs through approval
- Original deal **product and picking rights remain unchanged**

2seventy's end-to-end capabilities in place to unleash the cure

Manufacturing Horsepower (270-MPH)
to increase speed, control costs, and improve learning/iteration

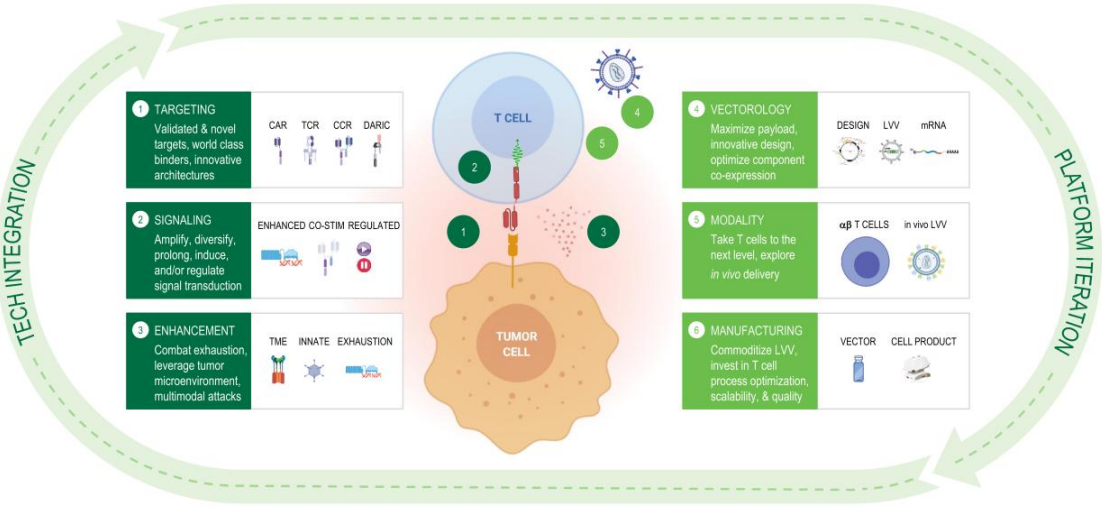
Research Platform
with transformative toolkit



Translational Engine
to run multiple parallel studies, integrating knowledge across all aspects of the Insight Engine

Our mission is to unlock the curative potential of the T cell by developing tumor-tailored, multi-layered autologous T cell products

T cell research platform built to rapidly design, test, learn, & iterate



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2seventy bio's NEW in-house manufacturing facility (270-MPH)

The heart of our translational cell therapy engine

Enables Fully Integrated Translational Cell Therapy Platform

- Enables manufacture and release of drug product for multiple Phase I clinical trials
- Co-located @60Binney with research, PD and analytics
- Provides ~300 patients/year capacity
- Accelerates product development learnings and iteration

Enhances Clinical Study Quality, Flexibility and Speed

- Provides clinical slot flexibility and faster patient data turnaround/analysis
- Shortens DP turnaround time and enables efficient monitoring/trouble shooting
- Significant costs savings through Phase 1 compared to CDMO costs

Anticipated to be Operational By Mid 2023

Despite transforming the treatment paradigm of B-NHL, the majority of patients ultimately fail CAR T therapy

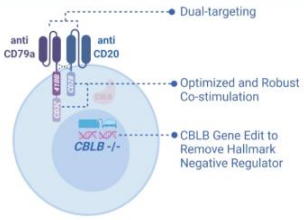
We identified four key challenges in current CAR T therapies

Challenges in B-NHL CAR T

1 CD19 Loss	~30% of CD19 CAR T relapse has CD19 negative disease
2 Target-Antigen Downregulation	CD19-Low tumors have been shown to escape CAR T detection and killing
3 Loss of Tumor cell co-stimulatory ligands	CD58 loss/mutation results in loss of CAR T activity
4 Bulky and extranodal disease	Potentially more "hostile" TME and may require a greater need for "serial killing"

bbT369: Novel CAR T candidate purpose-built to address needs in B-NHL

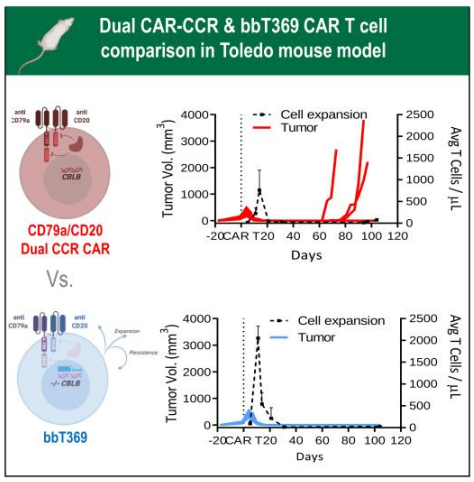
bbT369

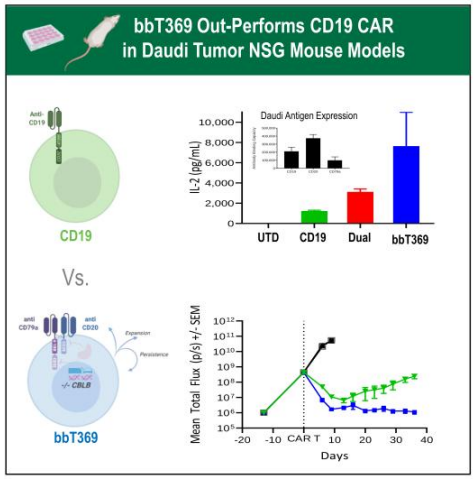


TARGET(S)	Dual target: CD20, CD79a
TECH	• Chimeric costimulatory architecture with split 41BB and CD28 • *CBLB* gene edit for expansion, antigen sensitivity, performance
INDICATION	B-NHL
STATUS	Ph1 Trial enrolling
PARTNER	2seventy owned

- **Designed to address outstanding need in B-NHL** by increasing response rate and durability of response to a larger fraction of patients.
- **Novel combination of antigens to address antigen escape:** Targets CD79a and CD20 – B cell restricted antigens strongly co-expressed on B cell lymphomas
- **Synergistic antigen receptor signaling domains to augment T cell activation:** Dual CAR design featuring split 41BB and CD28 co-stimulation (CCR) ensures robust and more complete cell stimulation against single or dual expressing tumor cells
- **Gene edit to enhance potency and reduce T cell exhaustion** *CBLB* gene edit removes a hallmark negative regulator of T cell function to increases cell expansion, antigen sensitivity, and performance in hostile microenvironments

bbT369: Complete and durable tumor control in lymphoma mouse models





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CRC-403 study in B-NHL open and enrolling

CRC-403: A Phase 1/2 Study of bbT369 in Relapsed and/or Refractory B-Cell Non-Hodgkin Lymphoma (B-NHL)

bbT369 Dose Levels for CRC-403 BOIN dose escalation

STUDY STATUS

- **First cohort of dose escalation (50 x 10^6) complete; no DLTs to date**
- **High manufacturing success rate, TAT in-line with auto CAR T**
- Target enrollment: n=50; 4 study sites
- RR B-NHL after autologous SCT or ≥ 2 prior lines of therapy
- Prior CD19 CAR T therapy is permitted

Key Questions / Features

QUESTIONS

- Is the safety and tolerability of bbT369 in line with prior CAR Ts?
- Does bbT369 show anti-B cell activity in R/R B-NHL patients?
- Does bbT369 treatment result in deep and durable responses?
- Does the dual-targeting CAR architecture limit antigen escape?
- Do *CBLB* edited T cells expand and persist?

FEATURES

- First in human application of three 2seventy bio innovations:
  - Dual targeted T cell
  - Split-costimulation signaling architecture
  - MegaTAL gene editing to remove *CBLB*
- All 3 are believed to have application across our research pipeline, including enhanced liquid tumor settings and solid tumors

CRC-403 Ph1 dose escalation in B-NHL is open and enrolling, initial data expected in 2023

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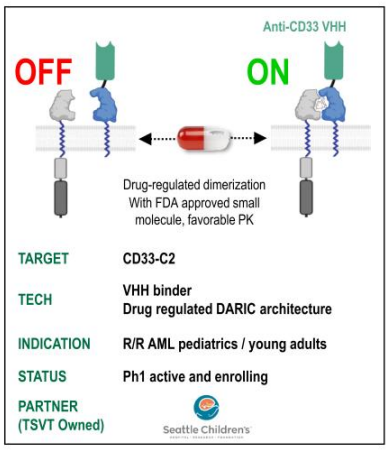
Engineered cell therapies have the potential to overcome key challenges in AML

Challenges in AML	Description of issue
1 Aplasia Risk	AML targets are expressed on healthy myeloid lineage & progenitor cells; Aplasia related toxicities are likely to emerge if targeted robustly & constitutively
2 Disease Heterogeneity	AML originates from myeloid progenitors that have intrinsic genetic diversity and developmental plasticity
3 T cell Persistence	AML cell therapies have shown low response durability without consolidation with SCT
4 Achieving Robust Efficacy	Preliminary cell therapy efficacy data in AML has been underwhelming relative to other heme malignancies
5 Rapid Progression	mOS <6 months for R/R AML patients, challenging for products requiring lengthy manufacturing time

AML = worst survival rates of any blood cancer … ~80% of patients relapse, life expectancy <1 year

SC-DARIC33: CD33 targeted CAR T cell with drug-regulated ON/OFF states



TARGET	CD33-C2
TECH	VHH binder Drug regulated DARIC architecture
INDICATION	R/R AML pediatrics / young adults
STATUS	Ph1 active and enrolling
PARTNER (TSVT Owned)	Seattle Children's

DARIC: a switchable CAR architecture that potentially solves fundamental AML challenges…

- Architecture enables T cell activity to be turned ON and OFF
- ON state occurs at *non-immunosuppressive* rapamycin dose levels
- OFF state allows for hematopoietic recovery
- OFF state prevents T cell exhaustion and promotes T cell memory formation
- Switchable T cells can be reactivated upon relapse or intermittently to drive persistence

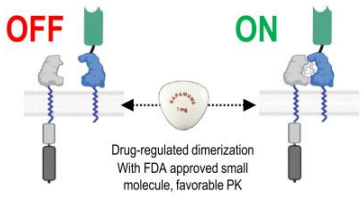
CD33: a clinically validated AML target

- Uniform, high expression on most/all AML blasts (>95%)
- Normal expression restricted to myeloid lineage; absent from early HSCs
- Targeting C2-domain, present on all CD33 isoforms independent of genotype

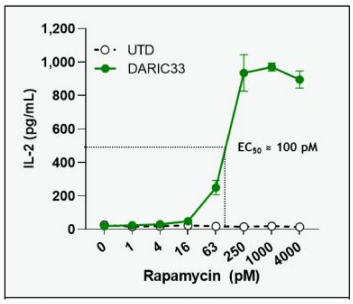
SC-DARIC33 in AML: Sensitive, drug-regulated tumor control achieved

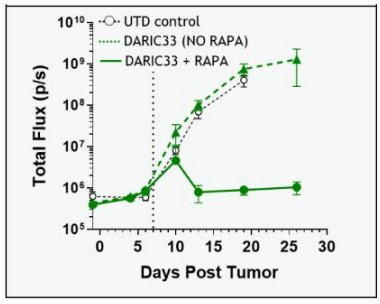
SC-DARIC33

DARIC = Dimerizing Agent Regulated Immunoreceptor Complex



TARGET(S)	CD33-C2
TECH	VHH binder Drug-regulated DARIC architecture
INDICATION	R/R AML pediatrics / young adults
STATUS	Ph1 Trial Enrolling
PARTNER	2seventybio, Seattle Children's





- Aggressively targeting AML requires pharmacologically-controlled CAR architecture that works under clinically feasible drug dosing
- Next generation AML asset leverages clinical experience & includes layered technologies that enhance potency and address potential mechanisms of resistance

Phase I study (PLAT-08) open and enrolling

Study Design: A Study Of SC-DARIC33 In Pediatric And Young Adults With Relapsed Or Refractory CD33+ AML

STUDY STATUS

- **Nearing completion of mandatory adult dosing phase; anticipate to begin treating pediatric patients in Q1 2023**
- **Totality of initial data suggests SC-DARIC33 activation by rapamycin**
- Single-center, academic study
- Target enrollment: N=18; Age ≤ 28 years
- Relapsed or refractory CD33+ AML
- Prior allogeneic stem cell transplant permitted
- Stem cell donor source identified

Key Questions / Features

QUESTONS

- Do SC-DARIC33 T cells engraft & show activity vs CD33+ve cells?
- Is SC-DARIC33 safe and does it drive a clinical response?
- Can SC-DARIC33 deactivation enable myeloid recovery?

FEATURES

- First in human application of 2seventy bio's regulatable CAR T cell technology (DARIC)
- First application of a licensed INHIBRX VHH binder in CAR T format targeting a conserved domain of CD33
- Myeloid disease learnings
- Provides platform for NextGen multiplex CAR T cells
- Establishes CD33 targeting supporting other applications
- Potential DARIC technology extension to solid tumor targets

PLAT-08 Ph1 is open and enrolling; initial data expected mid 2023

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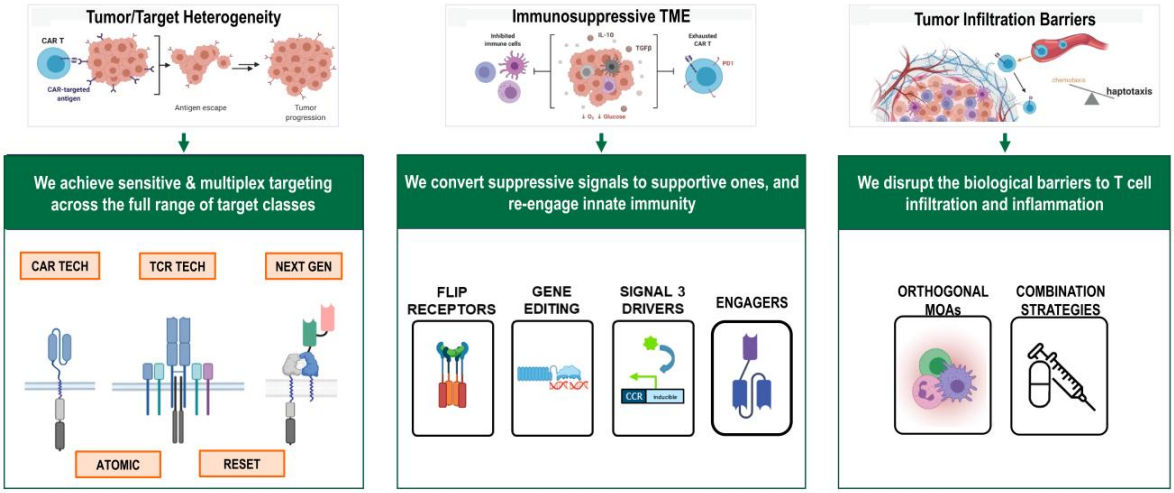
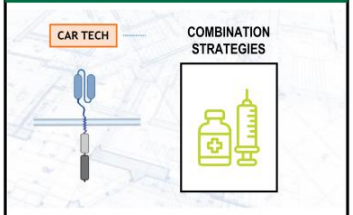
2seventy's differentiated toolbox enables attack on solid tumors by addressing key barriers to success



Created with BioRender.com

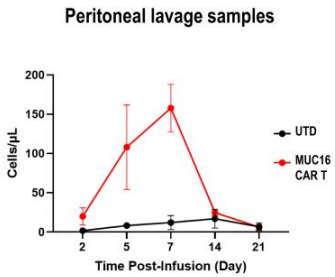
MUC16 / Ovarian cancer program: designed to exploit the power of CAR T + pharmaceutical combination strategies to unlock deep responses

Ovarian Cancer MUC16 CAR T Combo

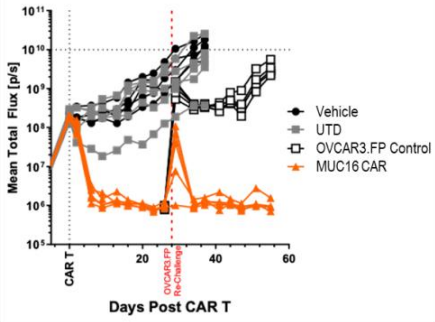


TARGET(S)	MUC16
TECH	CAR targeting prevalent MUC16 membrane-retained fragment
INDICATION	Solid Tumor (Ovarian)
STATUS	2023 IND Submission
PARTNER	REGENERON

MUC16 CAR T traffics to and expands at the tumor site



MUC16 CAR T displays robust activity in tumor rechallenge model



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Exploring the potential of combinations to unlock solid tumors

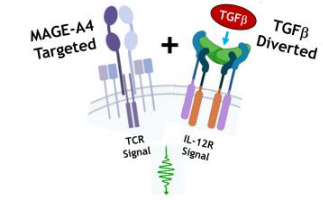
Deepened Regeneron collaboration enables clinical testing of MUC16 CAR T + mAbs and/or bi-specifics

MUC16 Know-how	Novel Co-stimulatory Bi-specific Combinations	Checkpoint Inhibitor Combinations
Mouse models, huAbs & pre-clinical data	Tumor targeted co-stimulation	*PD-1 inhibitor demonstrating promising results in solid tumors*
VELOCIMOUSE® Humanized mouse models VELOCIMMUNE® Fully human antibodies SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE CANCER **A Mucin 16 bispecific T cell–engaging antibody for the treatment of ovarian cancer** Alison Crawford*, Lauric Haber, Marcus P. Kelly, Kristin Vazzana, Lauren Canova, Priyanka Ram, Arpita Pawashe, Jennifer Finney, Sumreen Jalal, Danica Chiu, Curtis A. Colleton, Elena Garnova, Sosina Makonnen, Carlos Hickey, Pamela Krueger, Frank DelFino, Terra Potocky, Jessica Kuhnert, Stephen Godin, Marc W. Retter, Paurene Duramad, Douglas MacDonald, William C. Olson, Jeanette Fairhurst, Tammy Huang, Joel Martin, John C. Lin, Eric Smith, Gavin Thurston, Jessica R. Kirshner **SCIENCE TRANSLATIONAL MEDICINE Jun 2019**	Multiple CD28 bi-specifics in pre-clinical and clinical development  ***Drive a more potent CAR T cell response through signal 2 activation***	Cemiplimab (anti-PD-1 antibody) plus novel CPIs in development  ***Unleash the full power of CAR T cells by blocking the immunosuppressive PD-1 signaling axis***

Robust toolbox with the potential to unlock deep responses in Ovarian Cancer

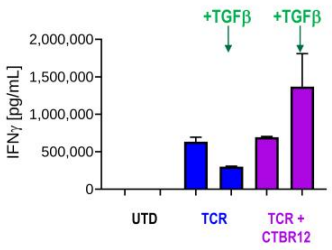
MAGE-A4 Expressing Solid Tumor Program: A powerful MAGE-A4 TCR potency enhanced with a "flip" receptor to neutralize TGFβ

Solid Tumor MAGE-A4 TCR-T Cell Therapy

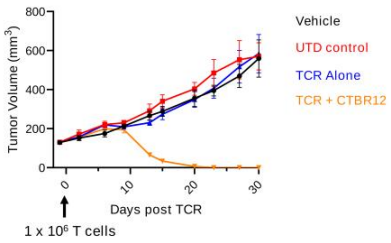


TARGET(S)	MAGE-A4 (HLA-A*02)
TECH	• MAGE-A4 directed TCR • CTBR12 TGFβ flip receptor
INDICATION	Solid tumors
STATUS	Preclinical
PARTNER	REGENERON medigene 药明巨诺

CTBR12 converts TGFβ into an activation signal



CTBR12 enhances MAGEA4 TCR anti-tumor activity



- Lead candidate demonstrates TGFβ signal conversion and potent tumor control in a lung xenograft model
- Potential IIT in China (JW Therapeutics) by end of 2023

Journal for ImmunoTherapy of Cancer 2021;9:e002035 (25 March 2021)

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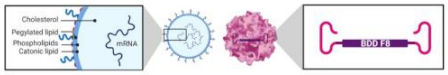
F8-GE: Novo Nordisk Partnered Program to Leverage Gene Editing Capabilities Directly in vivo for Durable Hemophilia A Gene Therapy

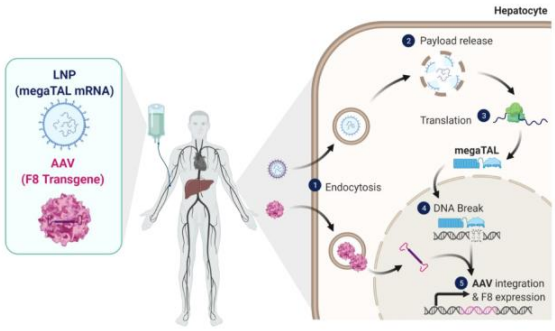
MegaTAL Gene Editing for Hemophilia A / FVIII

Lipid nanoparticle (LNP)
megaTAL mRNA

Adeno-associated virus (AAV)
Therapeutic transgene



TARGET(S)	Endogenous gene promoter trap knock-in of F8 transgene
TECH	• TSVT megaTAL gene edit • TSVT in vivo grade mRNA production / purification platform • AAV for transgene delivery • Genevant LNPs for hepatocyte delivery
INDICATION	Hemophilia A
STATUS	Pre-clinical
PARTNER	novo nordisk® GENEVANT



- Direct *in vivo* application of megaTAL technology using TSVT developed clinical grade mRNA production/purification process
- Novo Nordisk partnership ongoing
- Enables expansion of the megaTAL technology into additional ex vivo and in vivo applications

2seventy team

Leadership

Susan Abu-Absi, Ph.D.
Chief Technology & Mfg Officer

Chip Baird
Chief Financial Officer

Steve Bernstein, M.D.
Chief Medical Officer

Nicola Heffron
Chief Operating Officer

Teresa Jurgensen, J.D.
General Counsel

Nick Leschly
Chief Kairos Officer*

Melissa Price
Head of Program Strategy

Philip Gregory, D. Phil.
Chief Scientific Officer

Jenn Snyder
Head of Corporate Affairs

Kathy Wilkinson
Head of People & Culture

Board of Directors

Sarah Glickman
Criteo

Ramy Ibrahim, M.D.
BIT.BIO

Michael Jensen, M.D.**
Seattle Children's

Nick Leschly
Chief Kairos Officer

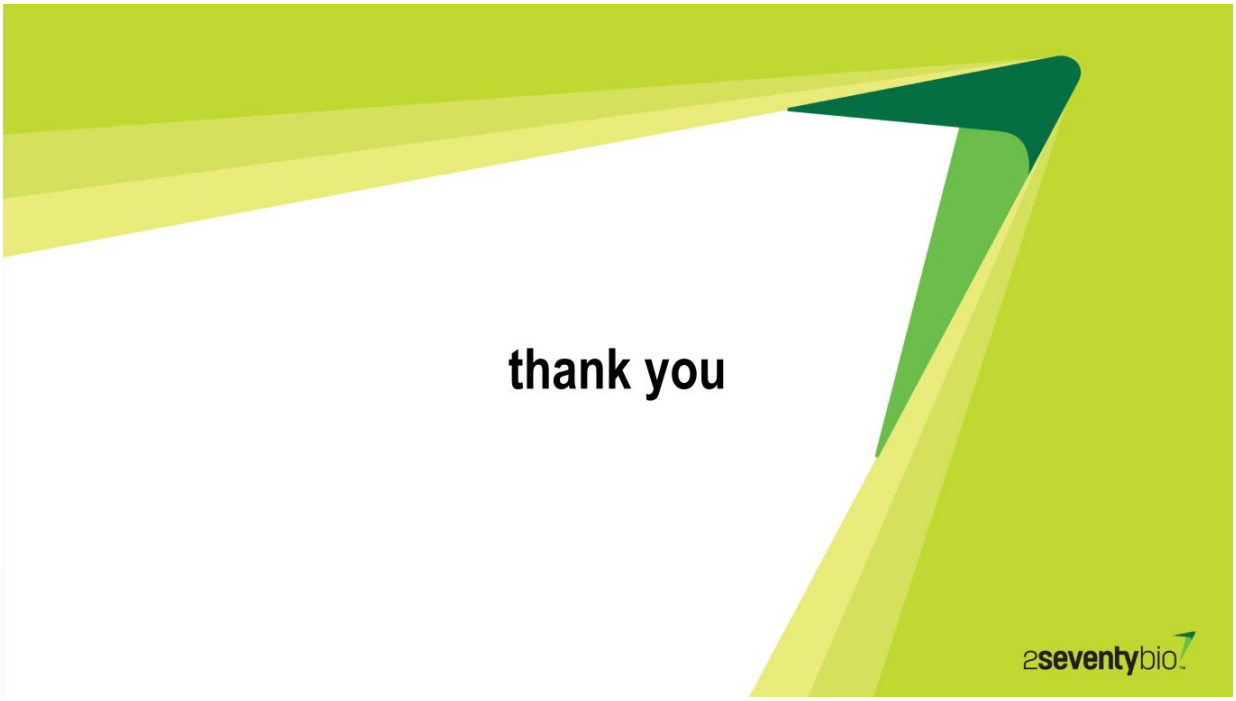
Dan Lynch
Board Chair

Marcela Maus, M.D., Ph.D.
Massachusetts General Hospital (MGH) Cancer Center

Denice Torres, J.D.
From Johnson & Johnson

+ ~410 awesome timekeepers

*Kairos: is an Ancient Greek word meaning the right, critical, or opportune moment; **Board Observer


thank you
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2seventy bio Provides Company Outlook for 2023

Anticipate $470-$570M topline U.S. revenue Abecma *(idecabtagene vicleucel) in 2023, shared equally with Bristol Myers Squibb (BMS)*

KarMMa-3 data to be presented at EBMT-EHA 5th European CAR T-cell Meeting on February 10, 2023; 3L+ sBLA submission for Abecma *targeted completion in Q1*

Expanded translational collaboration with Regeneron to explore and fund cell therapy combinations in solid tumors

Enrollment progress across clinical-stage programs – on track for data readouts in 2023

Cash runway into 2025 and path to financial sustainability

CAMBRIDGE, Mass.—January 9, 2023—2seventy bio, Inc. (Nasdaq: TSVT) announced today key corporate milestones and financial outlook for 2023.

"2022 was the launch year of 2seventy bio and we made important progress establishing the fundamentals of our business," said Nick Leschly, chief kairos officer. "We focused on bringing *Abecma*, our first-in-class BCMA CAR T for multiple myeloma, to as many patients in need as possible. Together with BMS, we made significant progress in scaling our manufacturing capacity as well as delivering positive data from our KarMMa-3 study almost one year ahead of schedule. In 2023, our goals include expanding the *Abecma* label, launching a study of *Abecma* in newly diagnosed patients, and continuing to increase our manufacturing capacity to drive toward the potential $2-3B U.S. peak sales opportunity. In 2022, we also were able to double down on our differentiated cell therapy science and translational platform to more fully unleash the curative potential of the T cell. On this dimension, we initiated enrollment on two first of kind clinical studies in B-NHL and AML with data expected throughout 2023. We also advanced several solid tumor programs toward the clinic and expanded our translational plans with Regeneron. Importantly, we are nearing completion of our 270-MPH in-house clinical drug product manufacturing site adding to our relationship with JW Therapeutics to accelerate clinical product development in China and more effectively support our growing U.S. clinical needs. Finally, we set a strong people and culture foundation that is passionately committed to finding a way to give back priceless time to the patients and families we serve."

***Abecma* Outlook**

Commercial Performance and Manufacturing Progress

Commercial demand for *Abecma* (idecabtagene vicleucel) remained strong throughout 2022. 2seventy bio and BMS increased manufacturing capacity and made important progress on key supply chain metrics, including delivering drug product at an average in-spec rate of 85-90% with a turnaround time (time from patient apheresis to delivery of *Abecma*) of approximately 30 days. As previously stated, 2seventy bio anticipates reaching the upper end of $250-$300M for topline U.S. revenue in 2022.

In 2023, the Company anticipates continued increases in vector and drug product manufacturing capacity, including an additional adherent vector manufacturing suite, enabling topline U.S. revenue of $470-$570M. Looking out into 2024-25, 2seventy bio expects further commercial growth with an anticipated label expansion. With this growth, 2seventy bio expects *Abecma* to generate $200-300M in operating income for 2seventy bio in the 2024-25 period.

KarMMa-3 Results and Regulatory Plans

In August 2022, BMS and 2seventy bio disclosed that KarMMa-3, a Phase 3 study comparing *Abecma* to standard combination regimens in adults with multiple myeloma that is relapsed and refractory after two to four prior lines of therapy and refractory to the last regimen, had met its primary endpoint.

Results of a pre-specified interim analysis showed that KarMMa-3 met its primary endpoint of demonstrating a statistically significant improvement in progression-free survival. Treatment with *Abecma* also showed an improvement in the key secondary endpoint of overall response rate compared to standard regimens. Follow-up for overall survival, a key secondary endpoint, remains ongoing.

The full data from this study will be presented at the EBMT-EHA 5th European CAR T-cell meeting in Rotterdam (Netherlands) on February 10, 2023. Abstracts for this meeting are currently available on the conference website. Based on the positive data, the companies anticipate submitting a supplemental Biologics Licensing Application (sBLA) to the U.S. FDA in Q1 2023, with potential approval also in 2023.

KarMMa-2 Results and Planned Study in Newly Diagnosed Multiple Myeloma
At ASH 2022, BMS and 2seventy bio presented data from two arms of the KarMMa-2 study. These data suggest that *Abecma* can provide significant clinical benefit to patients with suboptimal response to transplant and support further evaluation of *Abecma* in newly diagnosed patients in the KarMMa-9 study, with planned study initiation in 2023.

The KarMMa-9 study is anticipated to enroll patients with newly diagnosed multiple myeloma who have suboptimal response to transplant, which represents a patient population with an unfavorable outcome. Of the approximately 70% of newly diagnosed multiple myeloma patients who are eligible and chose to receive transplant, up to 50% do not achieve complete response post-transplant, underscoring the high unmet need in this population.

Next-Gen Cell Therapy Product Engine and Pipeline
Pipeline Programs Update

- **bbT369**: In 2022, 2seventy bio made meaningful progress in enrolling patients with relapsed and/or refractory B cell non-Hodgkin lymphoma (B-NHL) in its Phase I CRC-403 study of bbT369, an investigational novel CD79a/CD20 dual-targeting *CBLB* gene edited CAR T cell therapy. At the end of 2022, 2seventy bio completed the first cohort of dose-escalation. There were no dose-limiting toxicities observed to-date. The manufacturing success rate was high and turnaround time was in line with other autologous CAR Ts despite the additional complexity of this product. Patient enrollment in CRC-403 continues at the second dose level, and 2seventy bio anticipates sharing a data update in 2023.
- **SC-DARIC33:** 2seventy bio and Seattle Children's Research Institute (SCRI) is nearing completion of the mandatory adult dosing phase of a Phase 1 study evaluating our rapamycin-regulated CAR T cell therapy in patients with acute myeloid leukemia (AML); the totality of the initial data to-date suggests SC-DARIC33 activation by rapamycin. Patient enrollment in PLAT-08 continues, and, with SCRI, we expect to present initial clinical data in 2023. Additionally, a next-generation AML product concept has been selected and will enter non-clinical development in 2023. This new candidate is built off of our new RESET receptor architecture and incorporates dual targeting along with a potency enhancement while retaining the DARIC-like drug-regulation.
- **MUC16:** In collaboration with Regeneron, we anticipate an Investigational New Drug application in 2023 for our CAR T targeting MUC16 in patients with relapsed/refractory ovarian cancer. This first-in-human study will prospectively include combination agents, including those in Regeneron's pipeline, and will be the first program to utilize 2seventy bio's new in-house drug product manufacturing facility.
- **MAGE-A4:** In 2022, 2seventy bio entered into an agreement with JW Therapeutics to clinically evaluate 2seventy bio's potency enhanced MAGE-A4 TCR program in solid tumors which is being developed as part of a collaboration with Regeneron. MAGE-A4 is a member of the MAGE family of cancer-testis antigens expressed in a number of solid tumor types. JW Therapeutics plans an investigator-initiated trial in China in 2023, initially focused on esophageal carcinoma.

Regeneron Collaboration Amendment
Last week, 2seventy bio announced an expanded translational collaboration with Regeneron to facilitate the acceleration of novel cell therapy-based combinations for solid tumors. The collaboration will leverage 2seventy bio's unique cell therapy engineering and early-stage development capabilities, including the newly built in-house clinical cell therapy manufacturing facility, with Regeneron's differentiated antibodies and bispecifics.

To support this expanded clinical development plan Regeneron made a $20 million equity investment in 2seventy bio at a 50% premium and has committed to another $20 million in near-term pre-clinical and clinical milestones. The parties will continue sharing costs for these activities in a manner largely consistent with the existing agreement, with Regeneron covering 75% of certain preclinical costs necessary to study combinations and 100% of the costs for the arms of the clinical studies that include Regeneron agents through regulatory approval. For other programs, cost-sharing will follow the existing 50/50 cost sharing agreement.

Preliminary 2023 Financial Outlook
2seventy bio entered 2023 with approximately $268M in cash, cash equivalents and marketable securities and incurred net cash spend of approximately $260M in 2022, driven in part by upfront investments in *Abecma* manufacturing. In early January 2023, the Company received a $20M equity investment as part of its expanded Regeneron collaboration resulting in a cash balance of approximately $288M at the start of 2023. Based on its current operating plan, 2seventy bio anticipates net cash spend of $180 – 220M in 2023 and expects net cash spend to be meaningfully lower in 2024 due to the projected continued U.S. *Abecma* commercial ramp and improving profitability. The range on *Abecma* revenue guidance for 2023 and *Abecma* cash flow in 2024 and 2025 reflects the variability in timing of regulatory approvals for vector and drug product capacity increases. Our base case operating plan assumes continued success in vector and drug product scale up for *Abecma* and under this plan, the Company anticipates that its cash will be sufficient to fund current planned operations into early 2025.

“In addition to scientific innovation and patient focus, we are 2x focused on building a cell therapy company that is fit for purpose with a path to financial sustainability,” said Chip Baird, chief financial officer. “Our 2022 net cash spend of approximately $260M was impacted by significant upfront investments in *Abecma* manufacturing that made the year our high-water mark in terms of our annual net cash spend. Looking forward, we see *Abecma* contributing cash back to the business in 2023, with significant growth in *Abecma* cash flow in 2024-25. Over the next three years, we plan to maximize the cash flow from the *Abecma* business, carefully manage expenses, and look to continue to be active on the corporate development front to deliver transformative medicines to the patients we serve while generating value for our shareholders.”

Updated Corporate Presentation
These updates and additional information can be found in the company’s updated corporate presentation, which can be found in the investor section of www.2seventybio.com.

About bbT369
bbT369 is an investigational dual-targeting CAR T cell therapy with a gene edit being evaluated for the treatment of patients with relapsed and/or refractory B-NHL. In the 3L+ relapsed and/or refractory B-NHL setting, 60-70% of patients treated with commercially available CAR T cell therapies do not achieve a long-term remission, highlighting a significant unmet clinical need.

To address this unmet need, bbT369 has been designed with three layers of innovation that aim to address several potential mechanisms of anti-CD19 CAR T cell therapy failure: dual targeting (CD79a/CD20), split co-stimulation signaling technology, and a gene edit to remove the function of CBLB.

In December 2021, the FDA cleared the Investigational New Drug (IND) application for bbT369.

The clinical development program for bbT369 includes the Phase 1/2 CRC-403 study (NCT05169489). Safety and potential efficacy of bbT369 in patients with specific subtypes of relapsed and/or refractory B-NHL will be assessed, including patients who relapsed after CD19 CAR T cell therapy as well as patients who are CAR-naïve.

bbT369 is not approved for any indication in any geography.

About SC-DARIC33
SC-DARIC33 is an investigational CD33-specific cell therapy that utilizes 2seventy bio’s proprietary Dimerizing Agent Regulated Immunoreceptor Complex (DARIC) T cell platform. SC-DARIC33 is designed as a regulatable, potentially first-in-class autologous T cell therapy and is now being studied at Seattle

Children's in a Phase 1 trial, PLAT-08 (NCT05105152), as a first-in-human investigation of the DARIC T cell platform in relapsed/refractory pediatric and young adult AML.

DARIC separates the antigen binding and signaling functions of a CAR, with the intent that these two components are brought together by the small molecule rapamycin (RAPA), resulting in a functional CAR construct. In preclinical studies, SC-DARIC33 has shown robust drug-dependent anti-tumor activity (similar to CD19 CAR T controls). Importantly, SC-DARIC33 has been shown to be activated by low non-immunosuppressive concentrations of RAPA in the blood and, when RAPA is removed, DARIC returns to an inactive state. SC-DARIC33 tests the hypothesis that a pharmacologically regulated CAR can enable potent AML targeting while limiting toxicities associated with normal myeloid and myeloid progenitor cell targeting.
The investigation of SC-DARIC33 in the Phase 1 PLAT-08 study of pediatric and young adult AML patients and the scientific translation of these data are intended to establish the safety profile of SC-DARIC33 and evaluate feasibility of the reversable modulation (OFF-ON-OFF) of SC-DARIC33.

About KarMMa-3
KarMMa-3 (NCT03651128) is a pivotal, Phase 3, global, randomized, multicenter trial evaluating *Abecma* compared to standard regimens in patients with multiple myeloma that is relapsed and refractory after two to four prior lines of treatment and refractory to the last treatment regimen. Patients were randomized to receive *Abecma* or standard regimens that consisted of combinations that included daratumumab, pomalidomide, dexamethasone, bortezomib, ixazomib, lenalidomide, carfilzomib or elotuzumab. The primary endpoint evaluated in this study is progression-free survival, defined as time from randomization to the first documentation of progressive disease or death due to any cause, whichever occurs first. Key secondary endpoints include overall response rate and overall survival.

About *Abecma*
Abecma is the first-in-class B-cell maturation antigen (BCMA)-directed chimeric antigen receptor (CAR) T cell immunotherapy approved in the U.S. for the treatment of adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody. *Abecma* recognizes and binds to BCMA on the surface of multiple myeloma cells leading to CAR T cell proliferation, cytokine secretion, and subsequent cytolytic killing of BCMA-expressing cells.

Abecma was approved by the U.S. Food and Drug Administration (FDA) in March 2021 for the treatment of adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody. Please see the Important Safety Information section below, including **Boxed WARNINGS** for *Abecma* regarding cytokine release syndrome, neurologic toxicities, Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome and Prolonged Cytopenia. *Abecma* is being jointly developed and commercialized in the U.S. as part of a Co-Development, Co-Promotion, and Profit Share Agreement between Bristol Myers Squibb and 2seventy bio.

The companies' broad clinical development program for *Abecma* includes clinical studies (KarMMa-2, KarMMa-3, KarMMa-7, KarMMa-9) in earlier lines of treatment for patients with multiple myeloma. For more information visit clinicaltrials.gov.

Important Safety Information
BOXED WARNING: CYTOKINE RELEASE SYNDROME, NEUROLOGIC TOXICITIES, HLH/MAS, AND PROLONGED CYTOPENIA

- Cytokine Release Syndrome (CRS), including fatal or life-threatening reactions, occurred in patients following treatment with ABECMA. Do not administer ABECMA to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids.
- Neurologic Toxicities, which may be severe or life-threatening, occurred following treatment with ABECMA, including concurrently with CRS, after CRS resolution, or in the absence of CRS. Monitor for neurologic events after treatment with ABECMA. Provide supportive care and/or corticosteroids as needed.

- Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS) including fatal and life-threatening reactions, occurred in patients following treatment with ABECMA. HLH/MAS can occur with CRS or neurologic toxicities.
- Prolonged Cytopenia with bleeding and infection, including fatal outcomes following stem cell transplantation for hematopoietic recovery, occurred following treatment with ABECMA.
- ABECMA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the ABECMA REMS.

Cytokine Release Syndrome (CRS): CRS, including fatal or life-threatening reactions, occurred following treatment with ABECMA. CRS occurred in 85% (108/127) of patients receiving ABECMA. Grade 3 or higher CRS (Lee grading system) occurred in 9% (12/127) of patients, with Grade 5 CRS reported in one (0.8%) patient. The median time to onset of CRS, any grade, was 1 day (range: 1 - 23 days) and the median duration of CRS was 7 days (range: 1 - 63 days) in all patients including the patient who died. The most common manifestations of CRS included pyrexia (98%), hypotension (41%), tachycardia (35%), chills (31%), hypoxia (20%), fatigue (12%), and headache (10%). Grade 3 or higher events that may be associated with CRS include hypotension, hypoxia, hyperbilirubinemia, hypofibrinogenemia, acute respiratory distress syndrome (ARDS), atrial fibrillation, hepatocellular injury, metabolic acidosis, pulmonary edema, multiple organ dysfunction syndrome and HLH/MAS.
Identify CRS based on clinical presentation. Evaluate for and treat other causes of fever, hypoxia, and hypotension. CRS has been reported to be associated with findings of HLH/MAS, and the physiology of the syndromes may overlap. HLH/MAS is a potentially life-threatening condition. In patients with progressive symptoms of CRS or refractory CRS despite treatment, evaluate for evidence of HLH/MAS.
Fifty four percent (68/127) of patients received tocilizumab; 35% (45/127) received a single dose while 18% (23/127) received more than 1 dose of tocilizumab. Overall, across the dose levels, 15% (19/127) of patients received at least 1 dose of corticosteroids for treatment of CRS. All patients that received corticosteroids for CRS received tocilizumab.

Overall rate of CRS was 79% and rate of Grade 2 CRS was 23% in patients treated in the 300 x 10^6 CAR+ T cell dose cohort. For patients treated in the 450 x 10^6 CAR+ T cell dose cohort, the overall rate of CRS was 96% and rate of Grade 2 CRS was 40%. Rate of Grade 3 or higher CRS was similar across the dose range. The median duration of CRS for the 450 x 10^6 CAR+ T cell dose cohort was 7 days (range: 1-63 days) and for the 300 x 10^6 CAR+ T cell dose cohort was 6 days (range: 2-28 days). In the 450 x 10^6 CAR+ T cell dose cohort, 68% (36/53) of patients received tocilizumab and 23% (12/53) received at least 1 dose of corticosteroids for treatment of CRS. In the 300 x 10^6 CAR+ T cell dose cohort, 44% (31/70) of patients received tocilizumab and 10% (7/70) received corticosteroids. All patients that received corticosteroids for CRS also received tocilizumab. Ensure that a minimum of 2 doses of tocilizumab are available prior to infusion of ABECMA.

Monitor patients at least daily for 7 days following ABECMA infusion at the REMS-certified healthcare facility for signs and symptoms of CRS. Monitor patients for signs or symptoms of CRS for at least 4 weeks after infusion. At the first sign of CRS, institute treatment with supportive care, tocilizumab and/or corticosteroids as indicated.

Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time.

Neurologic Toxicities: Neurologic toxicities, which may be severe or life-threatening, occurred following treatment with ABECMA, including concurrently with CRS, after CRS resolution, or in the absence of CRS. CAR T cell-associated neurotoxicity occurred in 28% (36/127) of patients receiving ABECMA, including Grade 3 in 4% (5/127) of patients. One patient had ongoing Grade 2 neurotoxicity at the time of death. Two patients had ongoing Grade 1 tremor at the time of data cutoff. The median time to onset of neurotoxicity was 2 days (range: 1 - 42 days). CAR T cell-associated neurotoxicity resolved in 92% (33/36) of patients with a median duration of neurotoxicity was 5 days (range: 1 - 61 days). The median duration of neurotoxicity was 6 days (range: 1 - 578) in all patients including those with ongoing neurotoxicity at the time of death or data cut off. Thirty-four patients with neurotoxicity had CRS. Neurotoxicity had onset in 3 patients before, 29 patients during, and 2 patients after CRS. The rate of Grade 3 neurotoxicity was 8% in the 450 x 10^6 CAR+ T cell dose cohort and 1.4% in the 300 x 10^6 CAR+ T cell dose cohort. The most frequently reported (greater than or equal to 5%) manifestations of CAR T cell-associated

neurotoxicity include encephalopathy (20%), tremor (9%), aphasia (7%), and delirium (6%). Grade 4 neurotoxicity and cerebral edema in 1 patient has been reported with ABECMA in another study in multiple myeloma. Grade 3 myelitis and Grade 3 parkinsonism have been reported after treatment with ABECMA in another study in multiple myeloma.

Monitor patients at least daily for 7 days following ABECMA infusion at the REMS-certified healthcare facility for signs and symptoms of neurologic toxicities. Rule out other causes of neurologic symptoms. Monitor patients for signs or symptoms of neurologic toxicities for at least 4 weeks after infusion and treat promptly. Neurologic toxicity should be managed with supportive care and/or corticosteroids as needed.

Counsel patients to seek immediate medical attention should signs or symptoms of neurologic toxicity occur at any time.

Hemophagocytic Lymphohistiocytosis (HLH)/Macrophage Activation Syndrome (MAS): HLH/MAS occurred in 4% (5/127) of patients receiving ABECMA. One patient treated in the 300 x 10^6 CAR+ T cell dose cohort developed fatal multi-organ HLH/MAS with CRS. In another patient with fatal bronchopulmonary aspergillosis, HLH/MAS was contributory to the fatal outcome. Three cases of Grade 2 HLH/MAS resolved. The rate of HLH/MAS was 8% in the 450 x 10^6 CAR+ T cell dose cohort and 1% in the 300 x 10^6 CAR+ T cell dose cohort. All events of HLH/MAS had onset within 10 days of receiving ABECMA with a median onset of 7 days (range: 4-9 days) and occurred in the setting of ongoing or worsening CRS. Two patients with HLH/MAS had overlapping neurotoxicity. The manifestations of HLH/MAS include hypotension, hypoxia, multiple organ dysfunction, renal dysfunction, and cytopenia. HLH/MAS is a potentially life-threatening condition with a high mortality rate if not recognized early and treated. Treatment of HLH/MAS should be administered per institutional standards.

ABECMA REMS: Due to the risk of CRS and neurologic toxicities, ABECMA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the ABECMA REMS. Further information is available at www.AbecmaREMS.com or 1-888-423-5436.

Hypersensitivity Reactions: Allergic reactions may occur with the infusion of ABECMA. Serious hypersensitivity reactions, including anaphylaxis, may be due to dimethyl sulfoxide (DMSO) in ABECMA.

Infections: ABECMA should not be administered to patients with active infections or inflammatory disorders. Severe, life-threatening, or fatal infections occurred in patients after ABECMA infusion. Infections (all grades) occurred in 70% of patients. Grade 3 or 4 infections occurred in 23% of patients. Overall, 4 patients had Grade 5 infections (3%); 2 patients (1.6%) had Grade 5 events of pneumonia, 1 patient (0.8%) had Grade 5 bronchopulmonary aspergillosis, and 1 patient (0.8%) had cytomegalovirus (CMV) pneumonia associated with Pneumocystis jirovecii. Monitor patients for signs and symptoms of infection before and after ABECMA infusion and treat appropriately. Administer prophylactic, preemptive, and/or therapeutic antimicrobials according to standard institutional guidelines.
Febrile neutropenia was observed in 16% (20/127) of patients after ABECMA infusion and may be concurrent with CRS. In the event of febrile neutropenia, evaluate for infection and manage with broad spectrum antibiotics, fluids, and other supportive care as medically indicated.
Viral Reactivation: Cytomegalovirus (CMV) infection resulting in pneumonia and death has occurred following ABECMA administration. Monitor and treat for CMV reactivation in accordance with clinical guidelines. Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death, can occur in patients treated with drugs directed against plasma cells. Perform screening for CMV, HBV, hepatitis C virus (HCV), and human immunodeficiency virus (HIV) in accordance with clinical guidelines before collection of cells for manufacturing.

Prolonged Cytopenias: Patients may exhibit prolonged cytopenias following lymphodepleting chemotherapy and ABECMA infusion. In the KarMMa study, 41% of patients (52/127) experienced prolonged Grade 3 or 4 neutropenia and 49% (62/127) experienced prolonged Grade 3 or 4 thrombocytopenia that had not resolved by Month 1 following ABECMA infusion. Rate of prolonged neutropenia was 49% in the 450 x 10^6 CAR+ T cell dose cohort and 34% in the 300 x 10^6 CAR+ T cell dose cohort. In 83% (43/52) of patients who recovered from Grade 3 or 4 neutropenia after Month 1, the median time to recovery from ABECMA infusion was 1.9 months. In 65% (40/62) of patients who

recovered from Grade 3 or 4 thrombocytopenia, the median time to recovery was 2.1 months. Median time to cytopenia recovery was similar across the 300 and 450 x 10^6 dose cohort.
Three patients underwent stem cell therapy for hematopoietic reconstitution due to prolonged cytopenia. Two of the three patients died from complications of prolonged cytopenia. Monitor blood counts prior to and after ABECMA infusion. Manage cytopenia with myeloid growth factor and blood product transfusion support according to institutional guidelines.

Hypogammaglobulinemia: Plasma cell aplasia and hypogammaglobulinemia can occur in patients receiving treatment with ABECMA. Hypogammaglobulinemia was reported as an adverse event in 21% (27/127) of patients; laboratory IgG levels fell below 500 mg/dl after infusion in 25% (32/127) of patients treated with ABECMA.

Monitor immunoglobulin levels after treatment with ABECMA and administer IVIG for IgG <400 mg/dl. Manage per local institutional guidelines, including infection precautions and antibiotic or antiviral prophylaxis.

The safety of immunization with live viral vaccines during or following ABECMA treatment has not been studied. Vaccination with live virus vaccines is not recommended for at least 6 weeks prior to the start of lymphodepleting chemotherapy, during ABECMA treatment, and until immune recovery following treatment with ABECMA.

Secondary Malignancies: Patients treated with ABECMA may develop secondary malignancies. Monitor life-long for secondary malignancies. If a secondary malignancy occurs, contact Bristol Myers Squibb at 1-888-805-4555 to obtain instructions on patient samples to collect for testing of secondary malignancy of T cell origin.

Effects on Ability to Drive and Operate Machinery: Due to the potential for neurologic events, including altered mental status or seizures, patients receiving ABECMA are at risk for altered or decreased consciousness or coordination in the 8 weeks following ABECMA infusion. Advise patients to refrain from driving and engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery, during this initial period.

Adverse Reactions: The most common nonlaboratory adverse reactions (incidence greater than or equal to 20%) include CRS, infections – pathogen unspecified, fatigue, musculoskeletal pain, hypogammaglobulinemia, diarrhea, upper respiratory tract infection, nausea, viral infections, encephalopathy, edema, pyrexia, cough, headache, and decreased appetite.
Please see full Prescribing Information, including **Boxed WARNINGS** and Medication Guide.

About 2seventy bio
Our name, 2seventy bio, reflects why we do what we do - TIME. Cancer rips time away, and our goal is to work at the maximum speed of translating human thought into action – 270 miles per hour – to give the people we serve more time. We are building the leading immuno-oncology cell therapy company, focused on discovering and developing new therapies that truly disrupt the cancer treatment landscape With a deep understanding of the human body's immune response to tumor cells and how to translate cell therapies into practice, we're applying this knowledge to deliver next generation cellular therapies that focus on a broad range of hematologic malignancies, including the first FDA-approved CAR T cell therapy for multiple myeloma, as well as solid tumors. Our research and development is focused on delivering therapies that are designed with the goal to "think" smarter and faster than the disease. Importantly, we remain focused on accomplishing these goals by staying genuine and authentic to our "why" and keeping our people and culture top of mind every day.
For more information, visit www.2seventybio.com.
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2seventy bio Cautionary Note Regarding Forward-Looking Statements
This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. All statements that are not statements of historical facts are, or may be deemed to be, forward-looking statements. Such forward-looking statements are based on historical

performance and current expectations and projections about our future financial results, goals, plans and objectives and involve inherent risks, assumptions and uncertainties, including internal or external factors that could delay, divert or change any of them in the next several years, that are difficult to predict, may be beyond our control and could cause our future financial results, goals, plans and objectives to differ materially from those expressed in, or implied by, the statements. These statements include, but are not limited to, statements about: the research, development, and commercialization of Abecma; our plans, strategies, timelines and expectations with respect to the development, manufacture or sale of our product candidates, including the initiation and completion of pre-clinical and clinical studies; ; anticipated revenues and operating income resulting from sales of Abecma and related financial contribution and cash flow; the potential expansion of the Abecma label; launching a study in newly diagnosed patents; expected increases in vector and drug product manufacturing; the potential U.S. peak sales opportunity for Abecma; the timing or likelihood of regulatory filings and acceptances and approvals thereof; timelines for the initiation and results of ongoing and planned clinical trials for our product candidates; expectations regarding Abecma financial expectations regarding our use of capital, expenses and other future financial results, including our net cash spend in 2023 and 2024 and cash runway. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation,; the risk that interim, "topline," and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to confirmation, audit, and verification procedures that could result in material changes in the final data; the risk that we may fail to demonstrate the safety and efficacy of our product candidates to the satisfaction of applicable regulatory authorities; the risk that the market opportunities for our approved product or any future approved product are smaller than we believe they are; the risk that BMS, upon whom we rely for the successful development and commercialization of Abecma does not devote sufficient resources thereto, is unsuccessful in its efforts, or chooses to terminate its agreements with us; the risk that we and/or BMS will be unable to increase manufacturing and supply capacity for Abecma; the risk that our BLAs and INDs will not be accepted for filing by the FDA on the timeline that we expect, or at all; the risk that our plans with respect to the preclinical and clinical development and regulatory approval of our product candidates may not be successfully achieved on the planned timeline, or at all; the risk that Abecma will not be as commercially successful as we may anticipate; and the risk that we are unable to manage our operating expenses or cash use for operations. No forward-looking statement can be guaranteed. Forward-looking statements in this press release should be evaluated together with the many risks and uncertainties that affect 2seventy bio's business, particularly those identified in the risk factors discussion in 2seventy bio's Annual Report on Form 10-K, as updated by our subsequent Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other filings with the Securities and Exchange Commission. The forward-looking statements included in this document are made only as of the date of this document and except as otherwise required by applicable law, 2seventy bio undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events, changed circumstances or otherwise.

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