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): June 14, 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, par value $0.0001 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. o

Item 7.01 Regulation FD Disclosure.

2seventy bio, Inc. (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.

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 June 14, 2023, the Company issued a press releasing announcing that the Phase 1 trial of the PLAT-08 study of SC-DARIC33 in Acute Myeloid Leukemia has been paused by Seattle Children's, the Company's partner and the regulatory sponsor of the study. A copy of the press release is being filed as Exhibit 99.2 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
99.1	Presentation prepared by 2seventy bio, Inc.
99.2	Press release issued by 2seventy bio, Inc. on June 14, 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: June 14, 2023

2seventy bio, Inc.

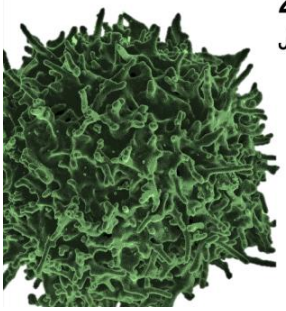
By: /s/ Chip Baird

Chip Baird
Chief Financial Officer
(Principal Financial and Accounting Officer)

Unleash Time

2seventy bio company presentation

June 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-K 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 presentation 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 have the potential to address and overcome the immunologically evasive and suppressive properties of tumors.

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 as we seek to build best-in-class treatments

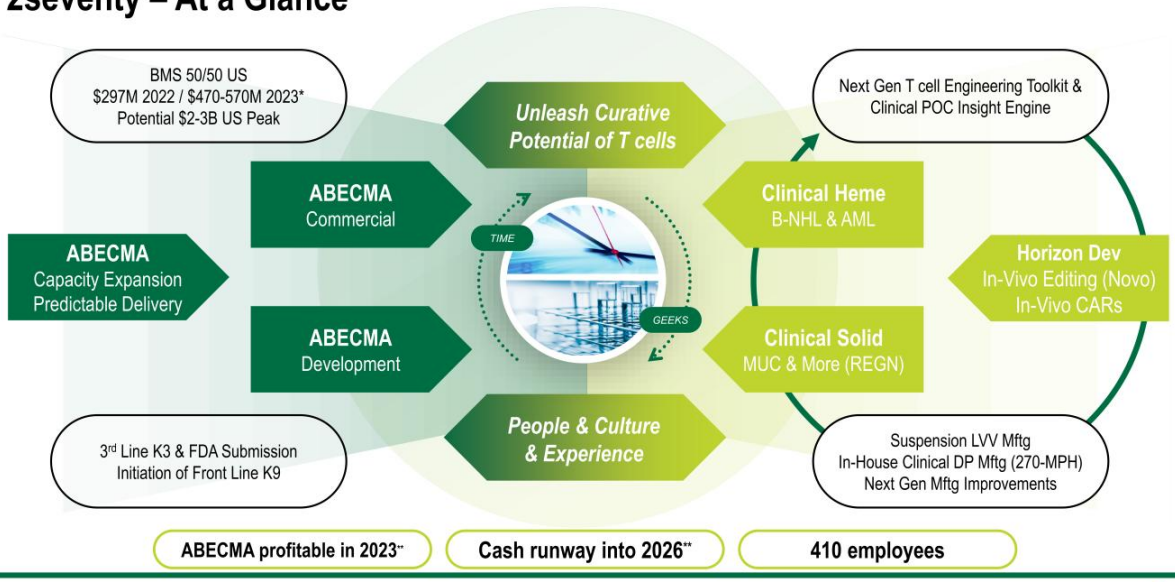
COMMERCIAL PRODUCT & ROBUST PIPELINE

- **ABECMA,** the first approved CAR T therapy for multiple myeloma; own 50/50 US rights in partnership with BMS; $297M 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** will enable continuous innovation, & facile delivery
- **Vector suspension product** to enable product engine

2seventy – At a Glance



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

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 – **now extended to 2026****

ABECMA

- $297M U.S. topline revenue*
- Increased manufacturing capacity and reduced COGS
- Positive KarMMa-3 data & announced plans for 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
- Progressed F8 / Novo Nordisk megaTAL gene editing program to large animal studies

*US topline revenue, profit and loss shared 50/50 with BMS
**Projected; based on current operating plan and anticipated revenue

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

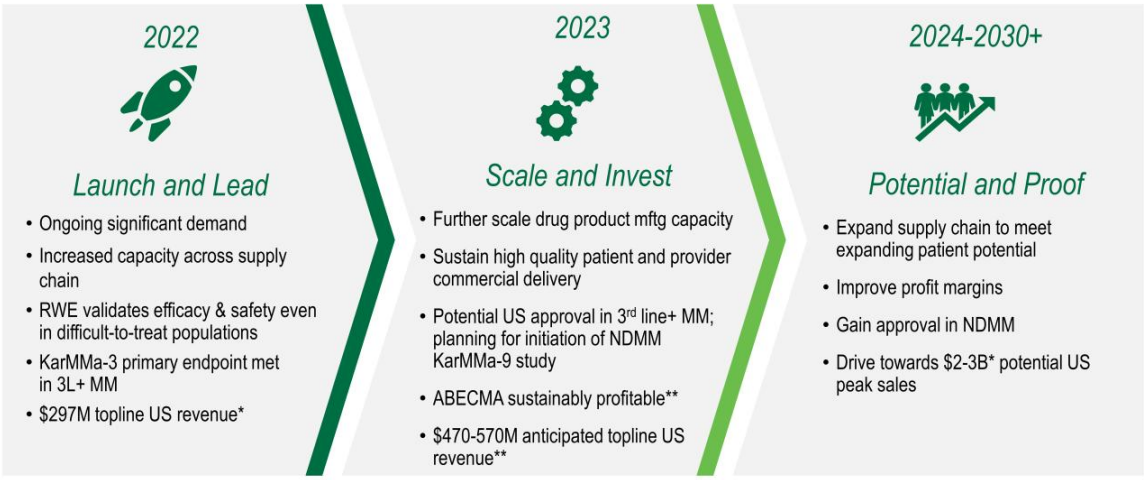
Pipeline

- 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***

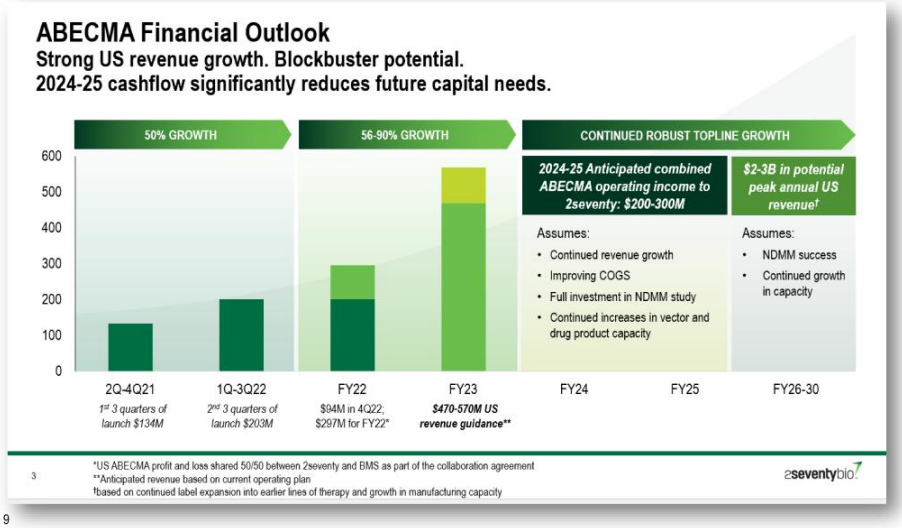
*US topline revenue, profit and loss shared 50/50 with BMS
**Projected, based on current operating plan and anticipated revenue
***Net cash spend is the change in cash between the beginning of the year and the end of the year, excluding any financing proceeds

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

Strong start to 2023 for ABECMA



May 2023 update

- **Cash flow positive in 1Q23**
- On track to achieve upper end of $470-570M* revenue guidance
- Second aLVV suite approved; on track for sLVV approval in 1H24
- Successful DP step-up complete; additional step-ups on track for 2023
- **$200-300M of operating income expected for the 2024-25 timeframe****

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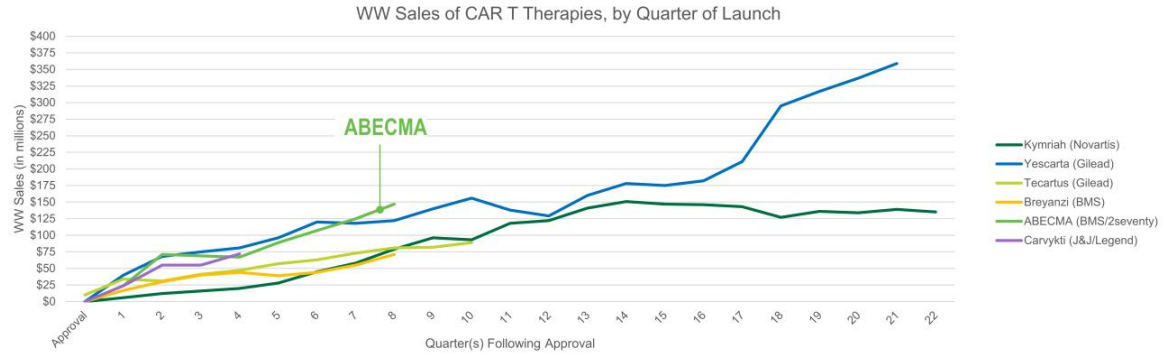
ABECMA launch growth trajectory driven by efficacy profile, strong patient demand, and manufacturing step-ups



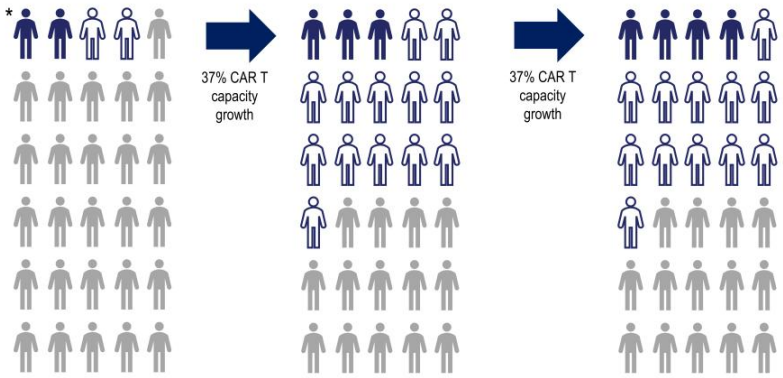
Average Annual Growth Rate	Year 2	Year 3	Year 4	Year 5
	94%	49%	29%	33%

Class CAGR for years 3-5: 37%

Source: Company filings

Assuming capacity growth in-line with CD-19 experience, more than half of eligible patients will not have access to a CAR T in 2025

Illustrative US Multiple Myeloma CAR T Capacity Growth Scenario



Assumptions and Methodology

- 30,000 US MM patients
- 2023 patients treated based on analyst estimates for commercially approved BCMA CAR Ts
- 2024 & 2025 patients treated based on 37% annual growth from 2023 levels
- Assumes commercially approved BCMA CAR Ts achieve 3L+ label by end of 2023

2023 (5L+)	2024 (3L+)	2025 (3L+)	2026-30 (label expansion)

*Each figure = ~1,000 patients

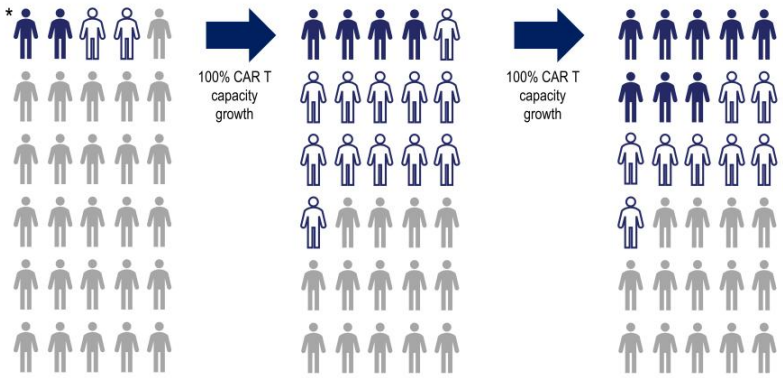
= RRMM patients treated with CAR T

= RRMM patients eligible for CAR T but cannot be served due to capacity constraint

= not eligible for CAR T

Even with 100% annual growth in commercial capacity, 50% of eligible patients will not be able to receive a CAR T in 2025

Illustrative US Multiple Myeloma CAR T Capacity Growth Scenario



Assumptions and Methodology

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= RRMM patients treated with CAR T

= RRMM patients eligible for CAR T but cannot be served due to capacity constraint

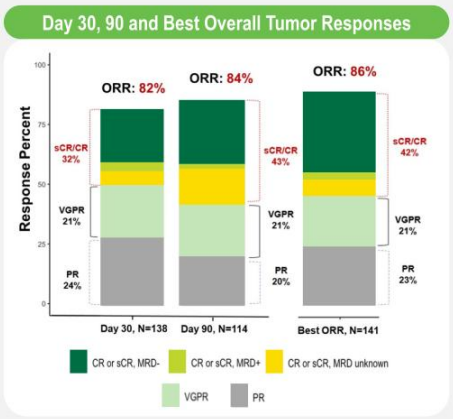
= not eligible for CAR T

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

ABECMA real world experience reinforces paradigm-changing efficacy



- **ASCO 2022 physician poster on real world experience at 11 sites:** safety and efficacy in the real world is consistent with KarMMa study
- **77% of patients in real world study** would not have met the eligibility criteria for KarMMa
- **Very low rate of manufacturing failure** (2.5%) in the real world

Hansen et al, Abstract 8042 ASCO 2022

*7 treated patients had manufacturing failures on first attempt, but a 2nd attempt was successful.

KarMMa-3 Summary

KarMMa-3 is the first randomized phase 3 clinical study to directly compare a CAR T cell therapy with standard regimens in triple-class–exposed RRMM

In this **high-risk triple-class–exposed and highly refractory population, a single infusion** of ide-cel treatment demonstrated significant and clinically meaningful improvement in PFS and ORR versus standard regimens

- **Risk of disease progression or death with ide-cel was 51% lower** than with standard regimens ($P < 0.0001$)
- **Ide-cel significantly increased the ORR versus standard regimens** (odds ratio, 3.47; $P < 0.0001$)
  - A higher proportion of patients achieved CR and MRD-negative status than with standard regimens
- Ide-cel treatment benefit was consistent across highly refractory and difficult-to-treat populations
- OS data were immature at the time of analysis and remain blinded

The **toxicity profile of ide-cel was manageable and consistent with previous studies,**[1,2] and **no Parkinsonism was reported**

- **Data supports sBLA filing accepted in 1Q 2023**

These results support the use of ide-cel in patients with earlier-line relapse and triple-class–exposed RRMM, a patient population with poor survival outcomes

1. Munshi NC, et al. *N Engl J Med* 2021;384:705–716; 2. Raje N, et al. *N Engl J Med* 2019;380:1726–1737.

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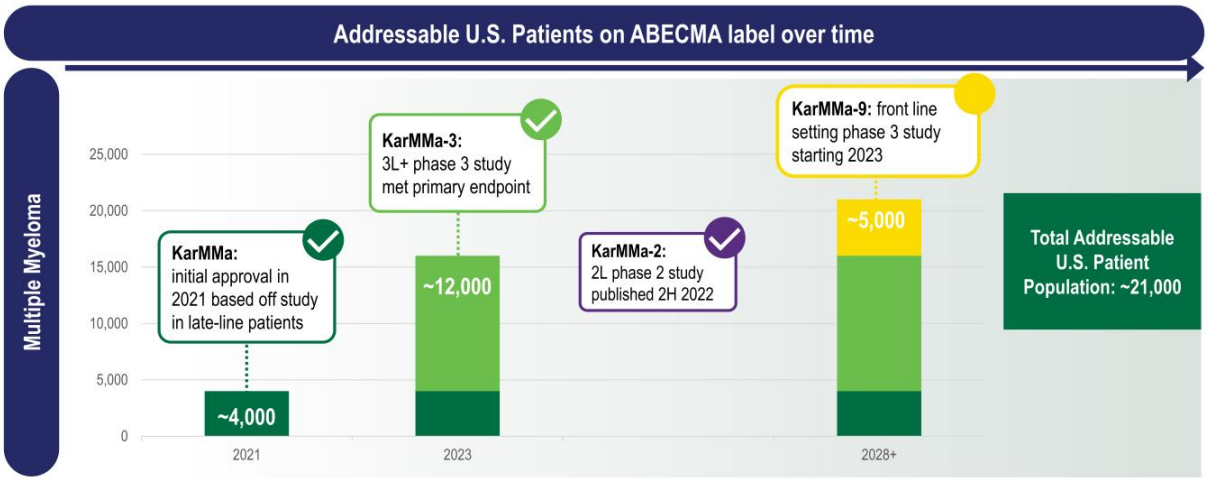
KarMMa-3 results and planned KarMMa-9 front-line study have the potential to drive label expansion into broad U.S. market opportunity



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

KarMMa-3: significant improvement in PFS in 3rd line

- RRMM after 2-4 prior lines of therapy and refractory to the last regimens); **clinically meaningful and statistically significant improvement in PFS compared with standard regimens**
- Median PFS of 13.3 months vs. 4.4 months (HR:0.49)
- FDA accepted sBLA submission; PDUFA date of December 16, 2023

KarMMa-2: encouraging 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: seeks to improve 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 will address a unique NDMM segment by adding on to transplant**
- Planned study start in 2023

KarMMa-3 Progression-free survival (ITT population)

	Ide-cel	Standard
Median PFS	13.3 months (11.8-16.1)	4.4 months (3.4-5.9)
ORR	71%	42%
CR	39%	5%

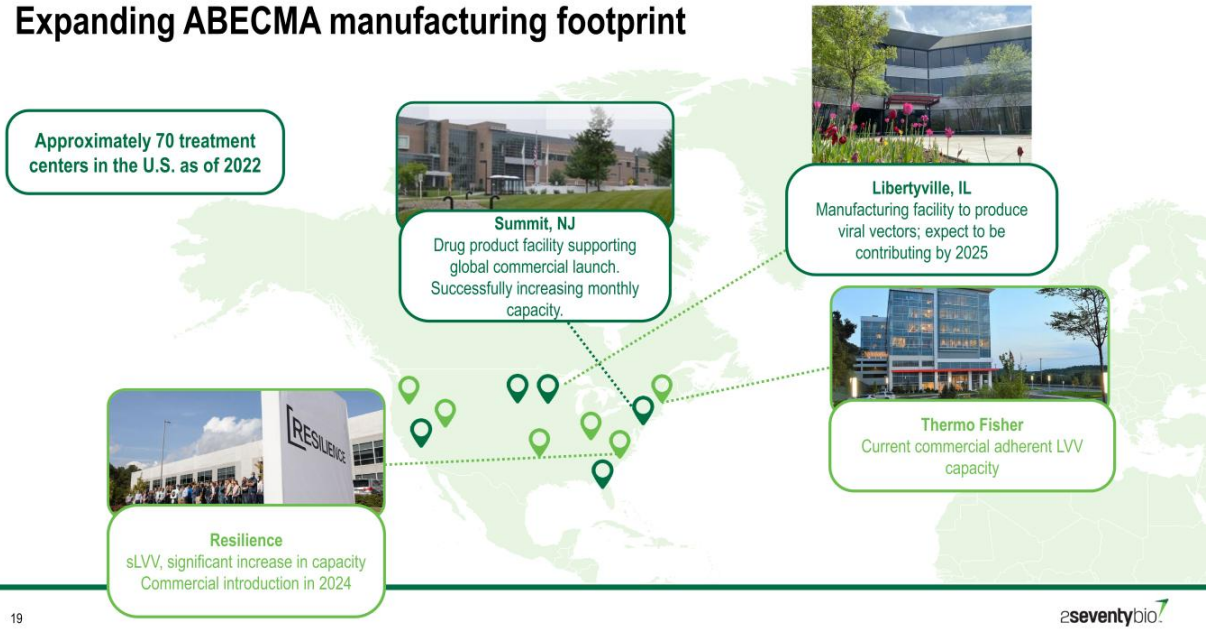
Patients at risk

Ide-cel	254	206	178	149	110	62	40	22	14	4	2	0
Standard regimens	132	75	42	32	25	13	10	7	6	2	1	0

Treatment with ide-cel resulted in a significantly longer PFS than standard regimens, with a 51% lower risk of disease progression or death (Hazard Ratio: 0.49)

PFS based on IMWG criteria per IRC.
[a]Based on stratified log-rank test.
IMWG, International Myeloma Working Group.

Expanding ABECMA manufacturing footprint



Approximately 70 treatment centers in the U.S. as of 2022

Summit, NJ
Drug product facility supporting global commercial launch. Successfully increasing monthly capacity.

Libertyville, IL
Manufacturing facility to produce viral vectors; expect to be contributing by 2025

Thermo Fisher
Current commercial adherent LVV capacity

Resilience
sLVV, significant increase in capacity
Commercial introduction in 2024

Innovative cell therapy candidates targeting broad potential indications

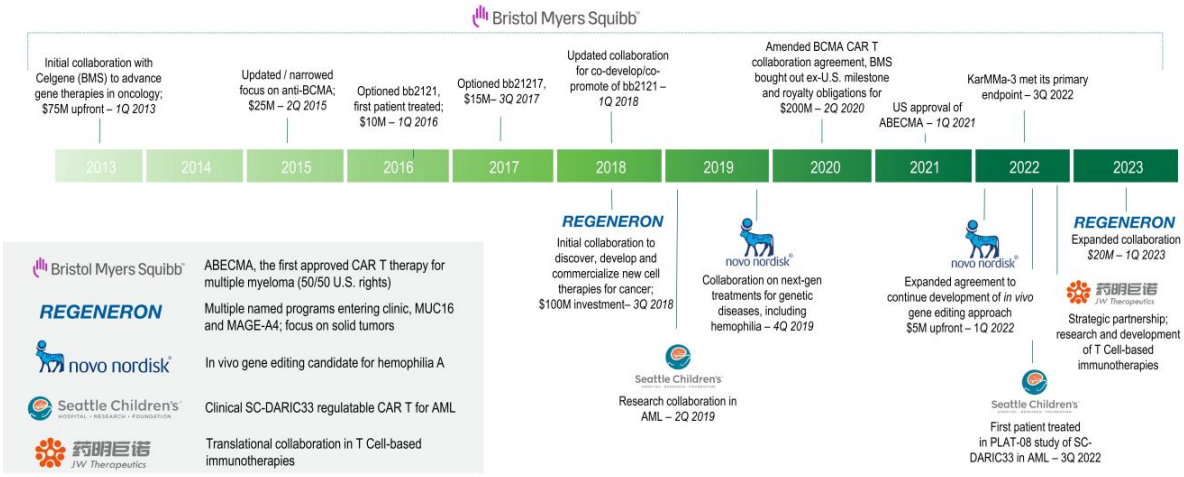
INDICATION [DRUG]	TARGET	TECHNOLOGY	DISCOVERY STAGE R&D	IND-ENABLING PRECLINICAL STUDIES	CLINICAL STUDIES	APPROVED PRODUCTS
Multiple Myeloma [ABECMA]	BCMA	CAR T cell	BMS Partnership; Approved in 5L+			Abecma
Multiple Myeloma [ABECMA]	BCMA	CAR T cell	BMS Partnership; Earlier Line Studies			3L+ potential approval 2023 NDMM study initiation 2023
AML-Pediatric [SC-DARIC33]	CD33	Drug-Regulated; CAR T cell (DARIC)	TSVT Owned; SCRI Collaboration			Paused as of June 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 [RESET Next-Gen]	CD33 + CLL-1	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.			

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

Collaboration program
TSVT-owned program

Long-term partnership track record

New collaborations are a key focus over next three years



Bristol Myers Squibb	ABECMA, the first approved CAR T therapy for multiple myeloma (50/50 U.S. rights)
REGENERON	Multiple named programs entering clinic, MUC16 and MAGE-A4; focus on solid tumors
novo nordisk	In vivo gene editing candidate for hemophilia A
Seattle Children's HOSPITAL · RESEARCH · FOUNDATION	Clinical SC-DARIC33 regulatable CAR T for AML
药明巨诺 JW Therapeutics	Translational collaboration in T Cell-based immunotherapies

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

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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

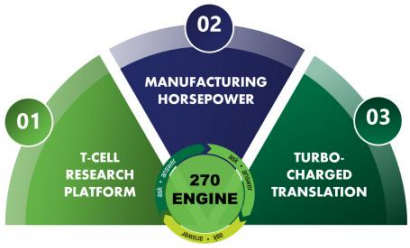
Regeneron Investing $20 million in 2seventy Equity; Regeneron to Fund 100% of Clinical Development Costs for Regeneron-Based Combination Clinical Trial Arms Through Approval

- 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
- Intended to leverage 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 designed to unleash the cure

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

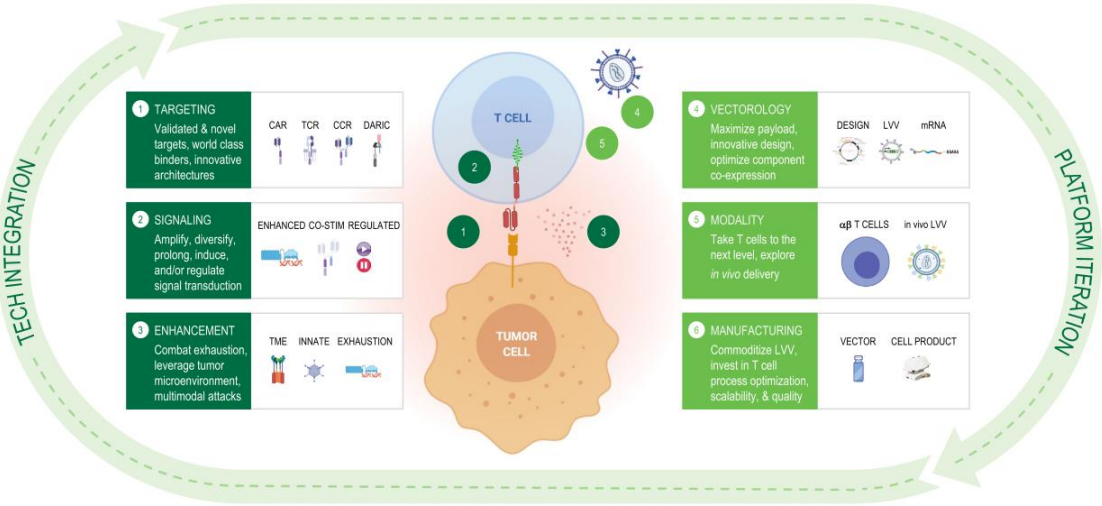
Research Platform
with transformative toolkit



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



2seventy bio's NEW in-house manufacturing facility (270-MPH)
The heart of our translational cell therapy engine

Enable Fully Integrated Translational Cell Therapy Platform

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

Enhance Clinical Study Flexibility, Speed and Efficiency

- 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

Facility qualification nearing completion and we expect to be fully GMP operational by summer 2023

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

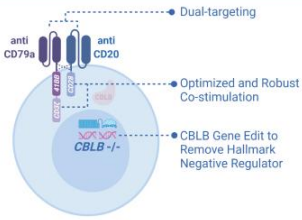
We identified four key challenges in current CAR T therapies

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

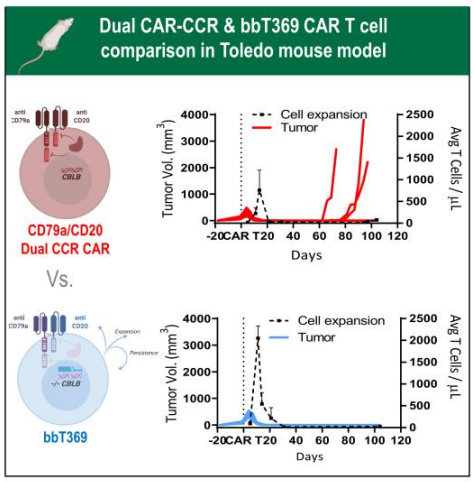
bbT369

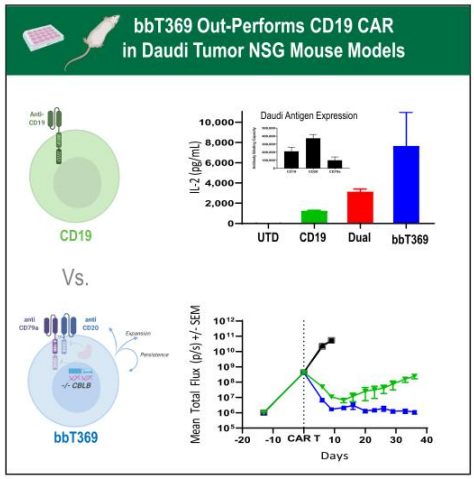


TARGET(S)	Dual target: CD20, CD79a
TECH	• Chimeric costimulatory architecture with split 41BB and CD28 • *CBLB* gene edit for expansion, antigen sensitivity, performance
TARGET INDICATION	B-NHL
STATUS	Ph1 Trial enrolling
PARTNER	2seventy owned

- **Designed to address outstanding need in B-NHL –** we believe bbT369 has the potential to increase response rate and durability of response for 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





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

Update from Phase I CRC-403 study anticipated by the end of 2023

PLAT-08 Trial of SC-DARIC33 in AML on Pause

- As a result of a recent Grade 5 serious adverse event (SAE), the PLAT-08 study has been placed on pause by Seattle Children's, the study sponsor and 2seventy bio collaborator
- The pause was instituted as part of the clinical study protocol stopping rules in response to the SAE and was followed by the required notification to the U.S. Food & Drug Administration (FDA)
- 2seventy bio and Seattle Children's are investigating the root cause of the SAE, including any potential relationship to study drug (SC-DARIC33)
- The company will share additional information once this assessment is completed

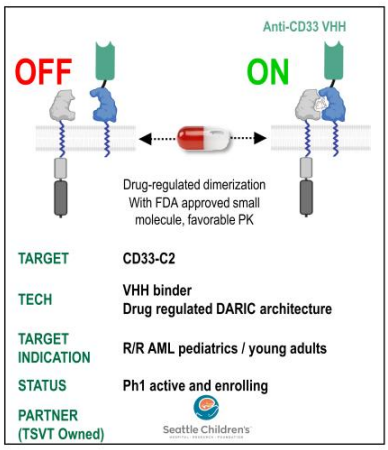
PLAT-08 is the dose escalation Phase 1 study of SC-DARIC33 in relapsed/refractory pediatric AML, led by SCRI, and couples 2seventy bio's drug-regulated DARIC T cell platform with SCRI's expertise in oncology cell therapies.

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

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



TARGET	CD33-C2
TECH	VHH binder Drug regulated DARIC architecture
TARGET 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 addresses 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

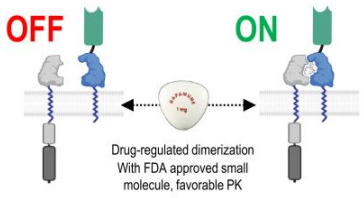
➢ ***CD33: a clinically validated AML target***

- 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

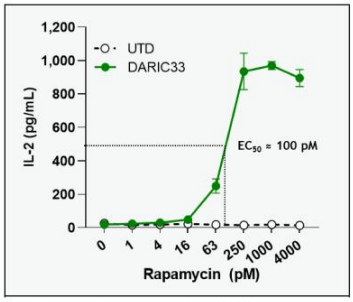
SC-DARIC33 in AML: Sensitive, drug-regulated tumor control achieved in preclinical studies

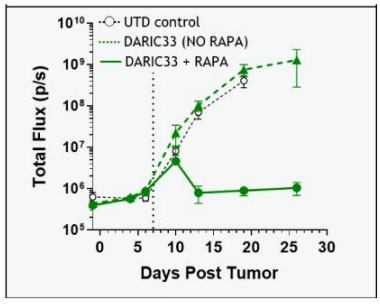
SC-DARIC33

DARIC = Dimerizing Agent Regulated Immunoreceptor Complex



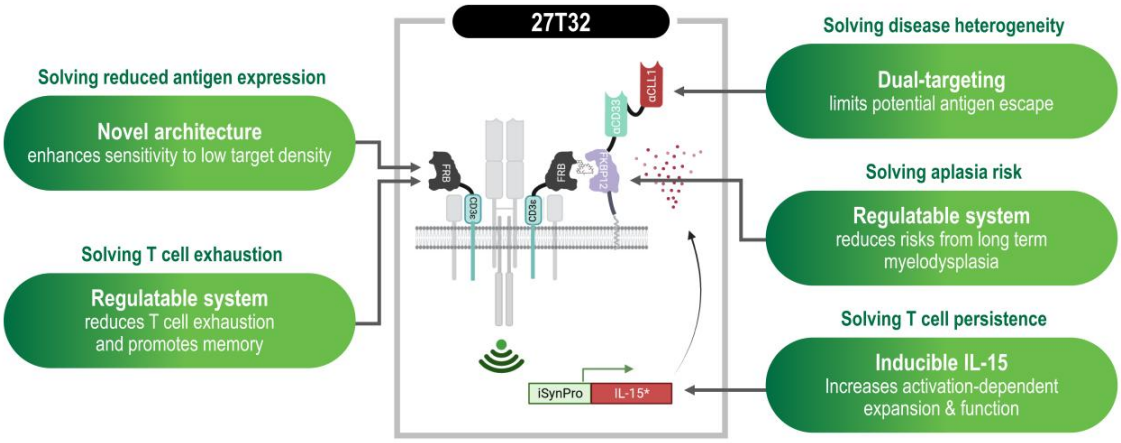
TARGET(S)	CD33-C2
TECH	VHH binder Drug-regulated DARIC architecture
TARGET INDICATION	R/R AML pediatrics / young adults
STATUS	Ph1 Trial Enrolling
PARTNER	2seventybio, Seattle Children's



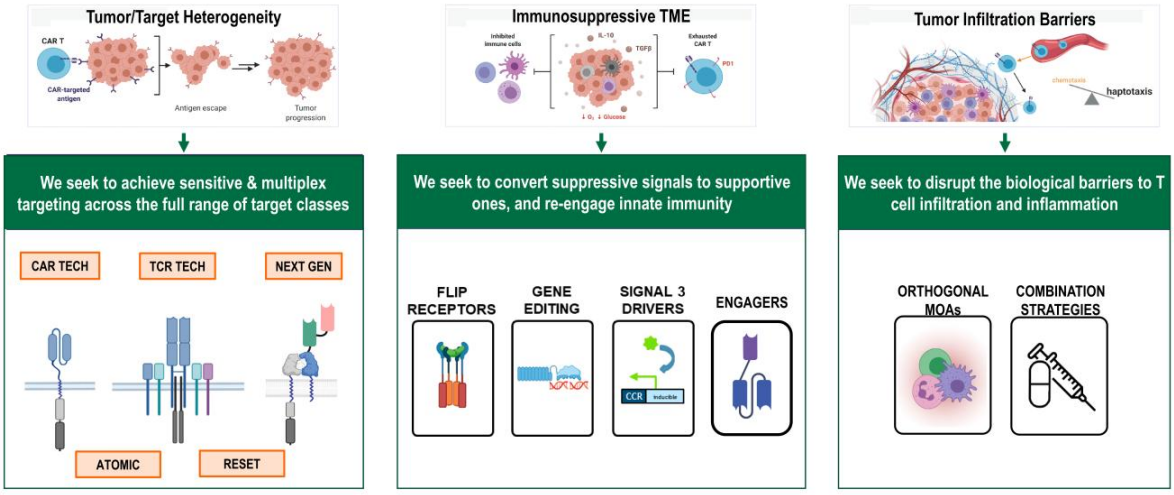


- Aggressively targeting AML requires pharmacologically-controlled CAR architecture that works under clinically feasible drug dosing
- Next generation AML asset leverages clinical experience & includes layered technologies that enhance potency and address potential mechanisms of resistance

27T32 Our Next-Gen CAR T for AML: Bold and packed with innovations



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



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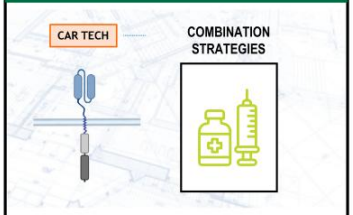
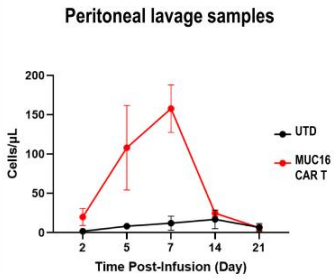
MUC16 / Ovarian cancer program: designed to exploit the power of CAR T + pharmaceutical combination strategies to unlock deep responses

Ovarian Cancer MUC16 CAR T Combo

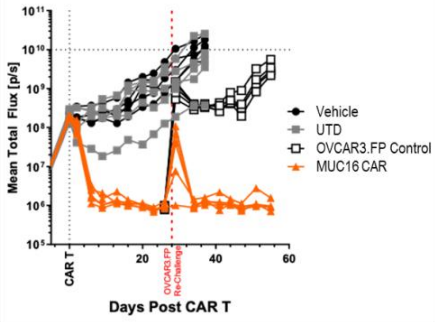


TARGET(S)	MUC16
TECH	CAR targeting prevalent MUC16 membrane-retained fragment
TARGET INDICATION	Solid Tumor (Ovarian)
STATUS	2023 IND Submission
PARTNER	REGENERON

MUC16 CAR T traffics to and expands at the tumor site



MUC16 CAR T displays robust activity in tumor rechallenge mouse model



Exploring the potential of combinations to unlock solid tumors

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

MUC16 Know-how

Mouse models, huAbs & pre-clinical data

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

Novel Co-stimulatory Bi-specific Combinations

Tumor targeted co-stimulation

Multiple CD28 bi-specifics in pre-clinical and clinical development

Drive a more potent CAR T cell response through signal 2 activation

Checkpoint Inhibitor Combinations

PD-1 inhibitor demonstrating encouraging results in solid tumors

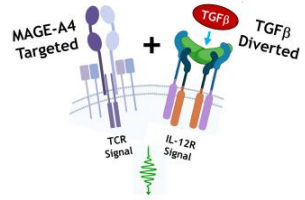
Cemiplimab (anti-PD-1 antibody) plus novel CPIs in development

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

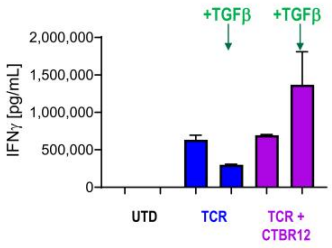
Solid Tumor MAGE-A4 TCR-T Cell Therapy



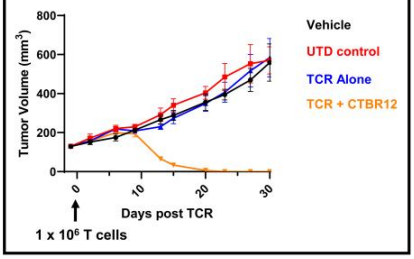
Enhanced Potency

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

CTBR12 converts TGFβ into an activation signal



CTBR12 enhances MAGEA4 TCR anti-tumor activity



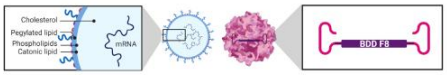
- Lead candidate demonstrates TGFβ signal conversion and potent tumor control in a lung xenograft mouse model
- Potential IIT in China (JW Therapeutics) by end of 2023

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

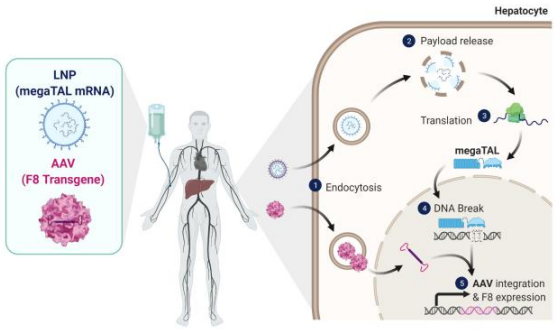
MegaTAL Gene Editing for Hemophilia A / FVIII

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
TARGET INDICATION	Hemophilia A
STATUS	Pre-clinical
PARTNERS	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 & Manufacturing Officer

Chip Baird
Chief Financial Officer

Steve Bernstein, M.D.
Chief Medical Officer

Teresa Jurgensen, J.D.
General Counsel

Nick Leschly
Chief Kairos Officer*

Melissa Price
SVP, Development Operations & Portfolio Strategy

Philip Gregory, D. Phil.
Chief Scientific Officer

Jenn Snyder
SVP, Corporate Communications

Kathy Wilkinson
Chief People Officer

Board of Directors

Sarah Glickman
Criteo

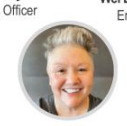
Dan Lynch
Board Chair

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

Nick Leschly
Chief Kairos Officer

Wei Lin, M.D.
Erasca

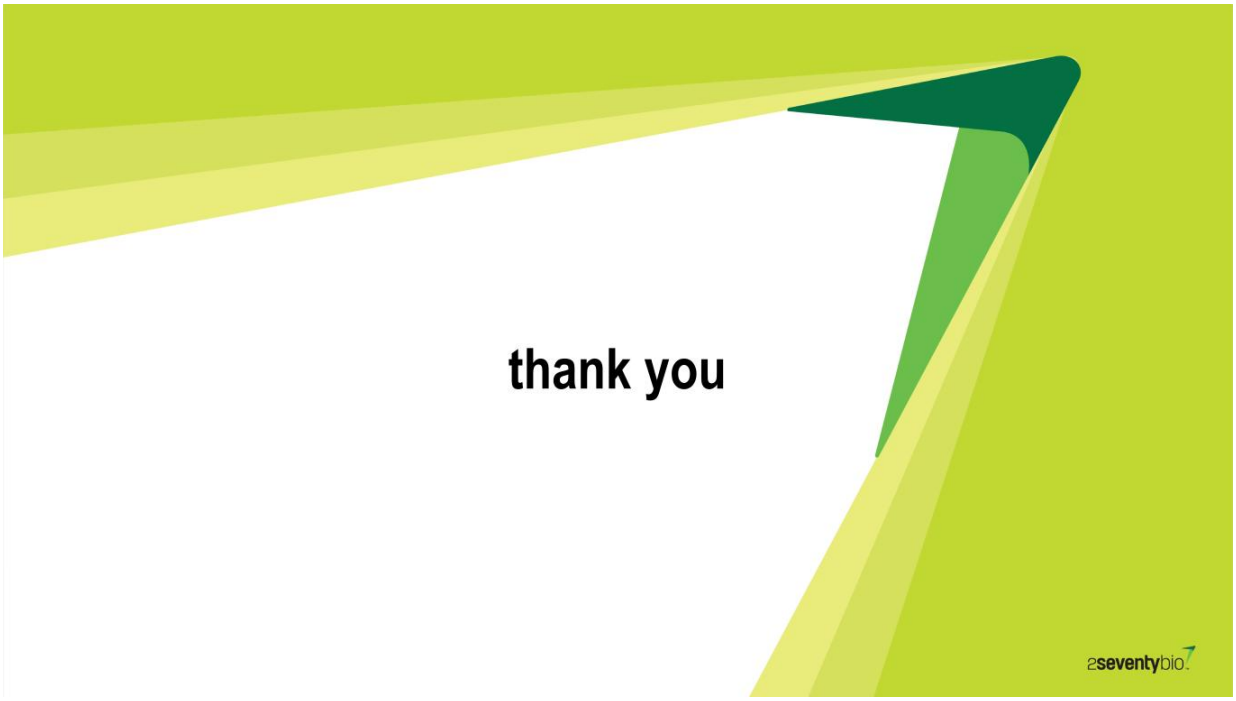
Marcela Maus, M.D., Ph.D.
Massachusetts General Hospital (MGH) Cancer Center



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
2seventybio

2seventy bio Announces Clinical Study Pause of PLAT-08 Trial of SC-DARIC33 in Acute Myeloid Leukemia

CAMBRIDGE, Mass. — (BUSINESS WIRE)—June 14, 2023—2seventy bio, Inc. (Nasdaq: TSVT), a leading immuno-oncology cell therapy company, today announced that the Phase 1 trial of the PLAT-08 study of SC-DARIC33 in Acute Myeloid Leukemia (AML) has been paused by Seattle Children's, the Company's partner and the regulatory sponsor of the study. The pause was instituted as part of the clinical study protocol stopping rules in response to a recent Grade 5 (fatal) serious adverse event (SAE) and was followed by the required notification to the U.S. Food & Drug Administration (FDA). The root cause of this SAE and its potential relationship to the study drug is currently under investigation.
PLAT-08 is the Phase 1 study of SC-DARIC33 in relapsed/refractory pediatric AML, conducted by Seattle Children's, and couples 2seventy bio's DARIC T cell platform with Seattle Children's expertise in oncology cell therapies. This study is a first-in-human investigation of the DARIC T cell platform. The SAE occurred in the first patient treated at the second dose level in the Phase 1 trial.

"Importantly, I'd like to offer that our thoughts are with the family during this time. The safety of every patient who participates in our studies or is treated with our therapies is the utmost priority for us, and we are in communication with FDA while we assess the data surrounding this SAE, and the potential next steps for the study," said Steve Bernstein, M.D., chief medical officer, 2seventy bio.

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.

Follow 2seventy bio on social media: Twitter and LinkedIn.

Cautionary Note Regarding Forward-Looking Statements
This release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to: statements about the Grade 5 SAE in the PLAT-08 study, the root cause of this toxicity and its relationship to the study drug, and the implication of this SAE on our other clinical programs. 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. 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 our annual report on Form 10-K for the year ended December 31, 2022, as

supplemented and/or modified by our most recent Quarterly Report on Form 10-Q and 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.

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