**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): September 13, 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 9.01 Financial Statements and Exhibits**

(d) Exhibits

| Exhibit No. | Description |
|---|---|
| 99.1 | Presentation prepared by 2seventy bio, Inc. |
| 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: September 13, 2023

**2seventy bio, Inc.**

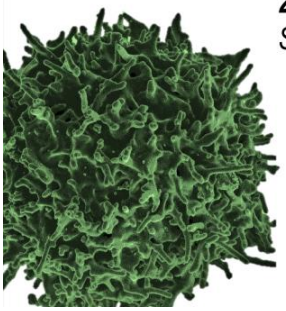
By: /s/ Chip Baird

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

# Unleash Time

## 2seventy bio company presentation

*September 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**

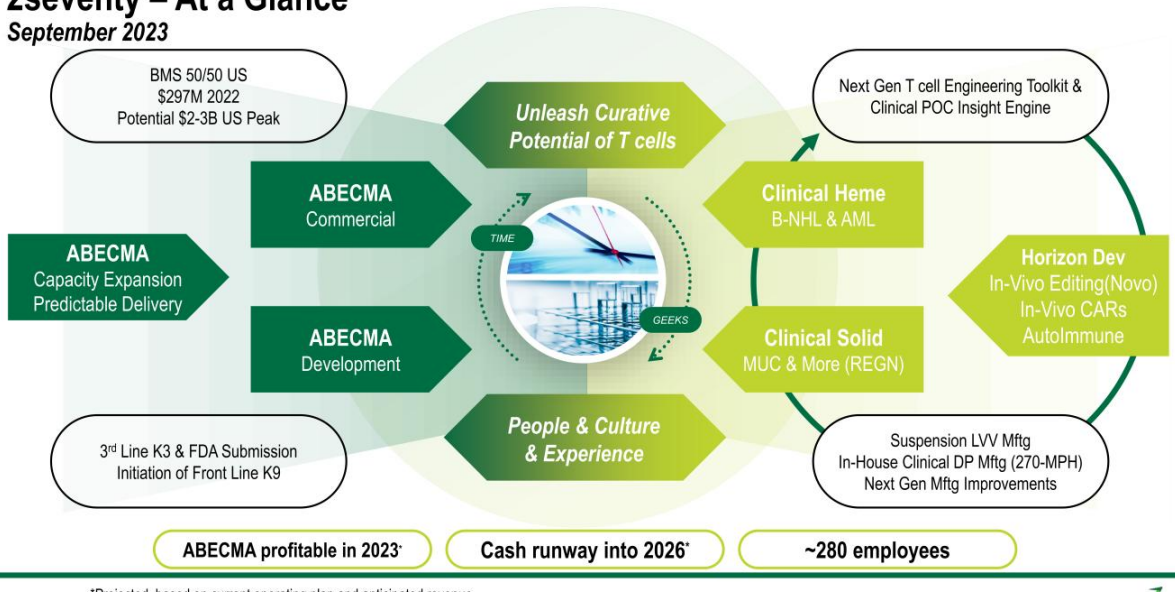
- **ABECMA,** the first approved CAR T therapy for multiple myeloma; own 50/50 US rights in partnership with BMS; $297M 2022 topline & growing in 2023
- **Partnered pipeline** targeting heme, solid tumors and autoimmune (MUC and more with REGN, JW in China)
- **Next Gen clinical programs:** bbT369 (B-NHL) and SC-DARIC33 (AML)

**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

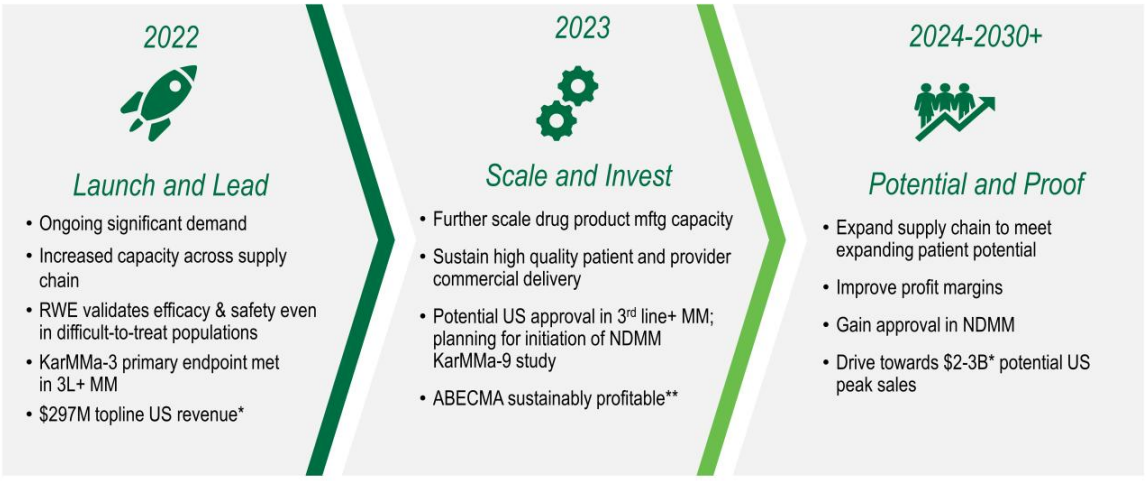
# 2seventy – At a Glance

***September 2023***




*Projected, based on current operating plan and anticipated revenue

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





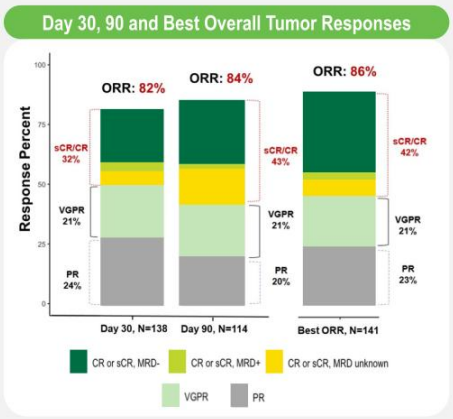

*US ABECMA profit and loss shared 50/50 between 2seventy and BMS as part of the collaboration agreement; unaudited, based on information currently available and subject to change; **Based on current operating plan and anticipated revenue

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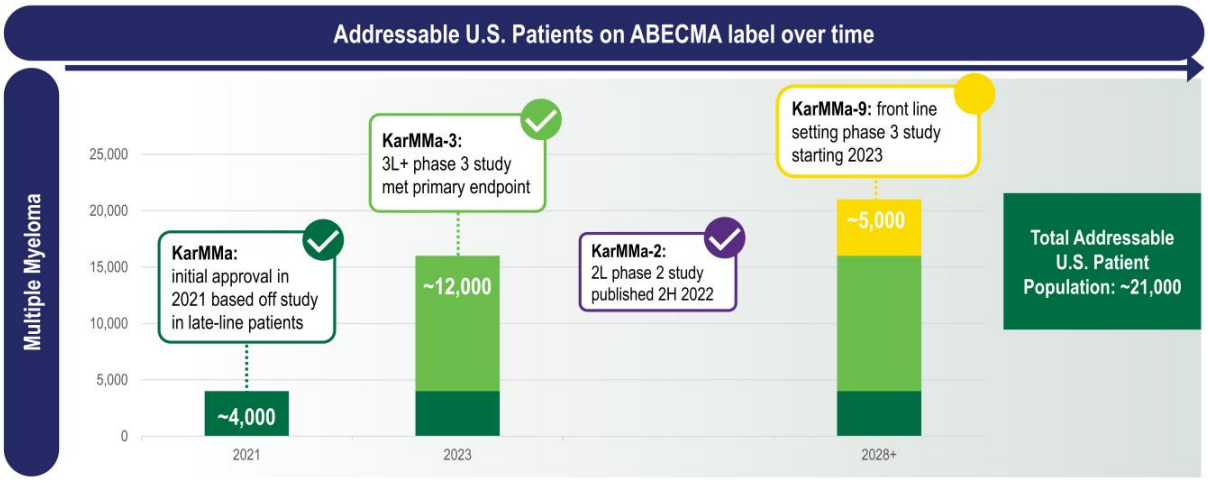
# KarMMa-3 results and planned KarMMa-9 front-line study have the potential to drive label expansion into broad U.S. market opportunity



# 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

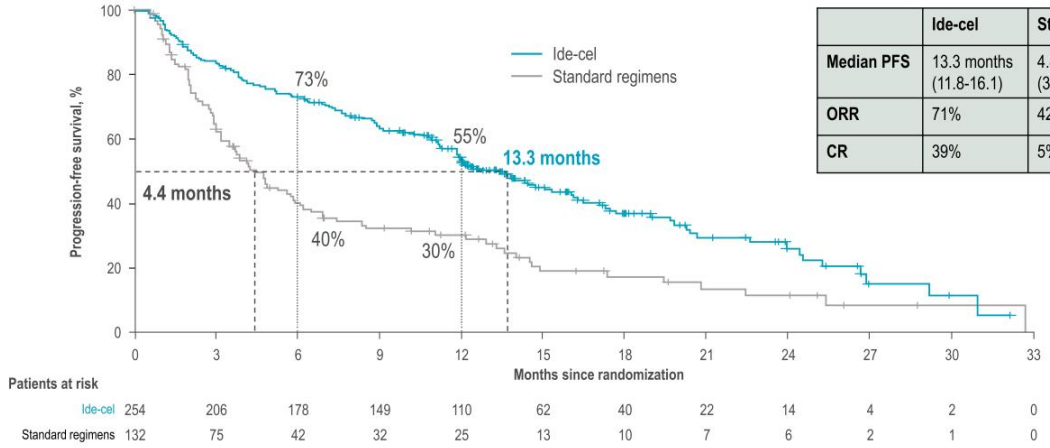
**KarMMa-2:** encouraging data in suboptimal ASCT responders support KarMMa-9 design

- 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**

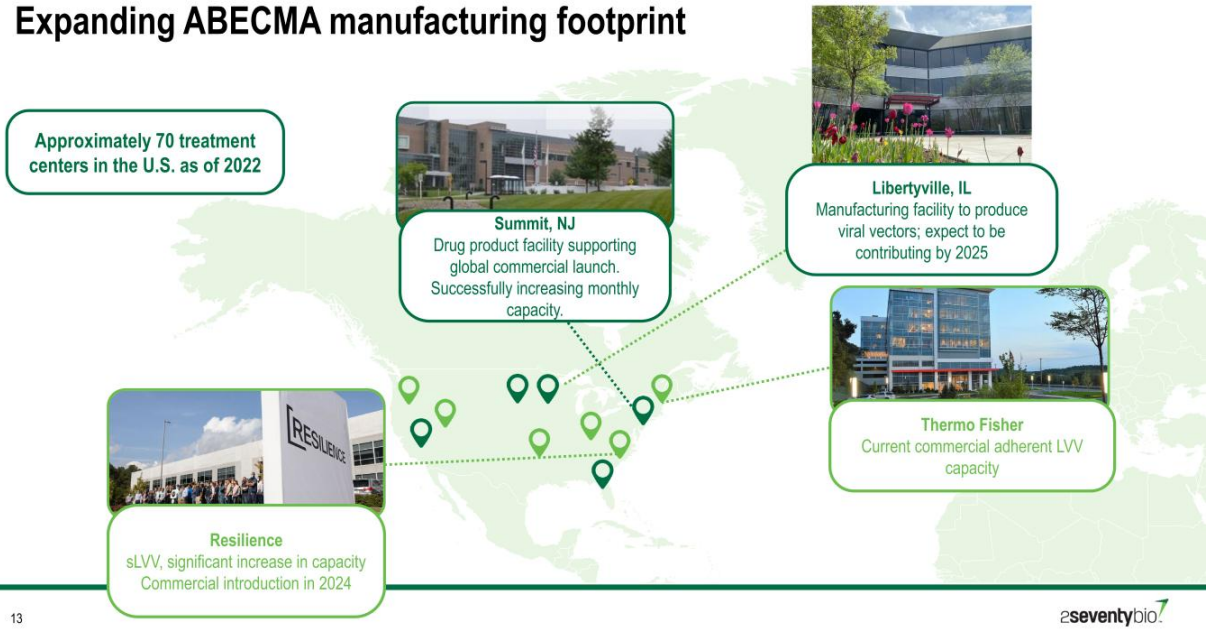
| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ide-cel | 254 | 206 | 178 | 149 | 110 | 62 | 40 | 22 | 14 | 4 | 2 | 0 |
| Standard regimens | 132 | 75 | 42 | 32 | 25 | 13 | 10 | 7 | 6 | 2 | 1 | 0 |

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 |
| | | | BMS Partnership; Earlier Line Studies | | | 3L+ potential approval 2023<br>NDMM study initiation 2023 |
| B-NHL [bbT369] | Dual B cell targets | Dual-Targeted CAR T cell Signal Enhanced Gene Edited | TSVT Owned | | | Patients Enrolling; Update in 2024 |
| AML-Pediatric [SC-DARIC33] | CD33 | Drug-Regulated; CAR T cell (DARIC) | TSVT Owned, SCRI Collaboration | | | Update Estimated early 2025** |
| 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) | |
| Solid Tumors | Undisclosed | TCR T cell Pharmacologic Enhancements | REGN/JW Collaboration | | | |
| Auto-Immune Disease | Dual targets | CAR T cells | JW Collaboration | | | |
| Hem A | FVIII | In Vivo MegaTAL Gene Editing Targeted Gene Insertion | Novo Nordisk Collaboration | | | |

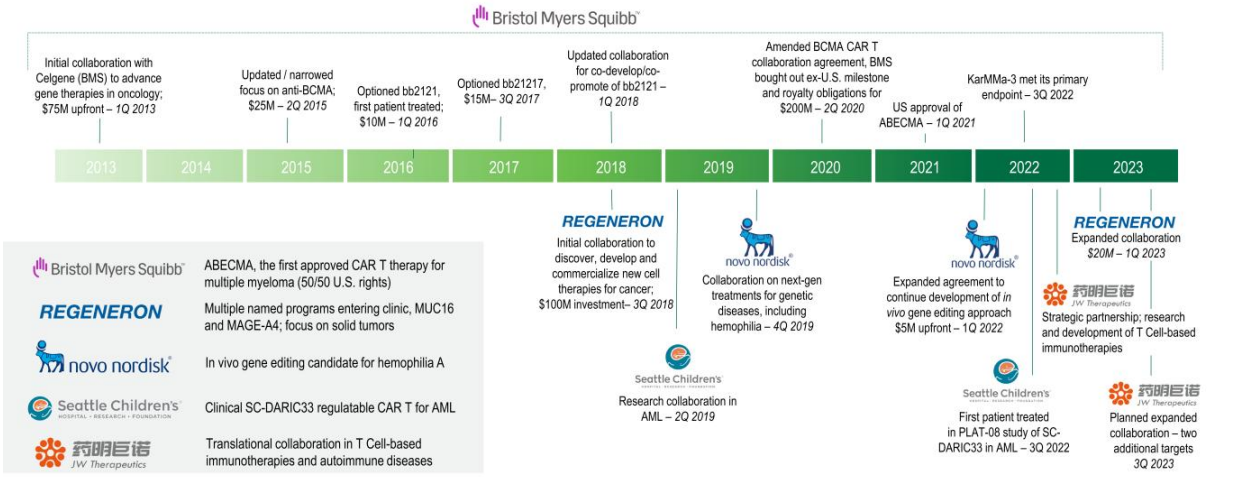
Collaboration program
TSVT-owned program



*Investigational New Drug application – IND; Investigator Initiated Trial – IIT; Newly Diagnosed Multiple Myeloma – NDMM
**Study currently on clinical hold

# 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

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

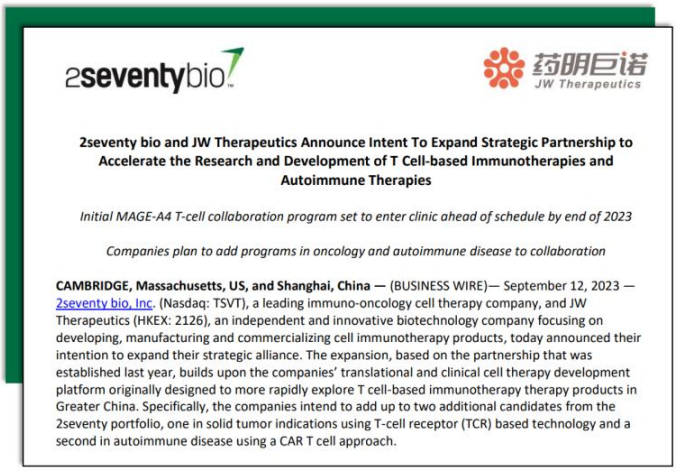
*Collaboration Leverages 2seventy's Platform for T Cell Therapy Research and Development with Regeneron Antibodies and Bispecifics to Explore Multiplex Combination Approaches*

*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**

# Planned Partnership Expansion with JW Therapeutics

*Accelerate Clinical POC at Significantly Reduced Cost*



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药明巨诺 JW Therapeutics

**2seventy bio and JW Therapeutics Announce Intent To Expand Strategic Partnership to Accelerate the Research and Development of T Cell-based Immunotherapies and Autoimmune Therapies**

*Initial MAGE-A4 T-cell collaboration program set to enter clinic ahead of schedule by end of 2023*

*Companies plan to add programs in oncology and autoimmune disease to collaboration*

**CAMBRIDGE, Massachusetts, US, and Shanghai, China —** (BUSINESS WIRE)— September 12, 2023 — 2seventy bio, Inc. (Nasdaq: TSVT), a leading immuno-oncology cell therapy company, and JW Therapeutics (HKEX: 2126), an independent and innovative biotechnology company focusing on developing, manufacturing and commercializing cell immunotherapy products, today announced their intention to expand their strategic alliance. The expansion, based on the partnership that was established last year, builds upon the companies' translational and clinical cell therapy development platform originally designed to more rapidly explore T cell-based immunotherapy therapy products in Greater China. Specifically, the companies intend to add up to two additional candidates from the 2seventy portfolio, one in solid tumor indications using T-cell receptor (TCR) based technology and a second in autoimmune disease using a CAR T cell approach.

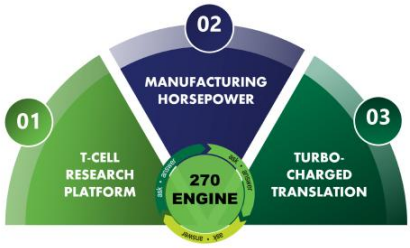
## Key Takeaways

- Moving two programs from the 2seventy pipeline into our expanded JW collaboration:
  - A solid tumor program, and a novel CAR T based autoimmune cell therapy
- On track to initiate the investigator-initiated study in China for MAGE-A4 by end of 2023 – well ahead of its original timeline
- Based on our MAGE-A4 experience, we believe alliance expansion allows us to accelerate clinical POC at a significantly reduced cost structure

# 2seventy's end-to-end capabilities designed to unleash the cure

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

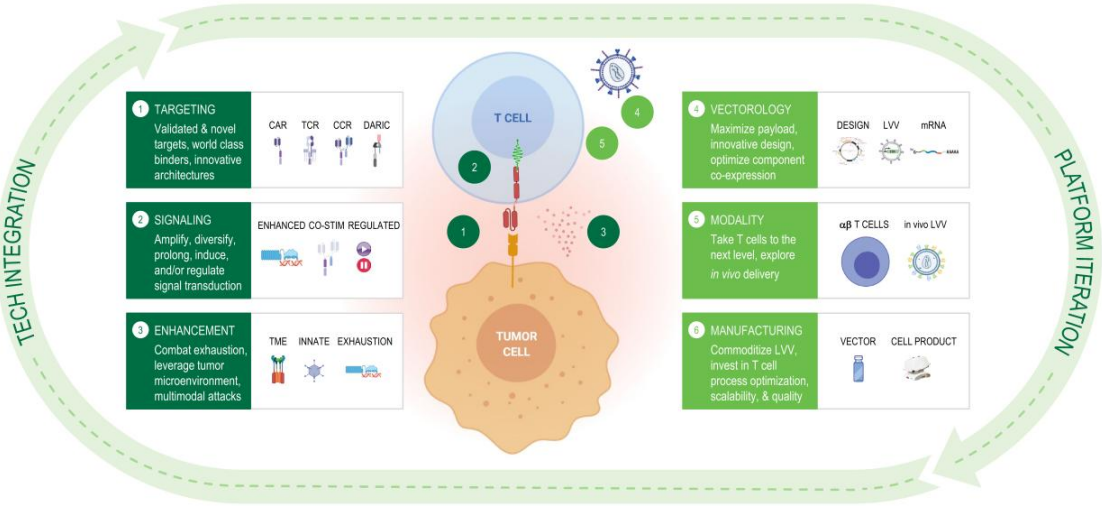
**Research Platform**
with transformative toolkit




**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

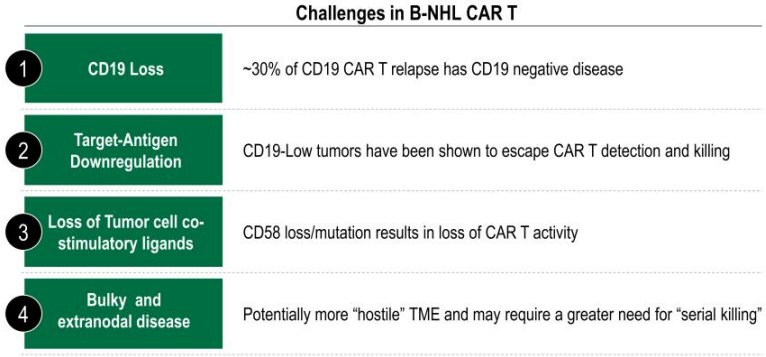
### Enhance Clinical Study Flexibility, Speed and Efficiency

- 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***

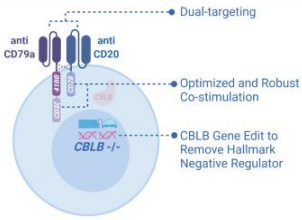
# Majority of patients with B-NHL ultimately fail CAR T therapy

## *We identified four key challenges in current CAR T therapies*



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

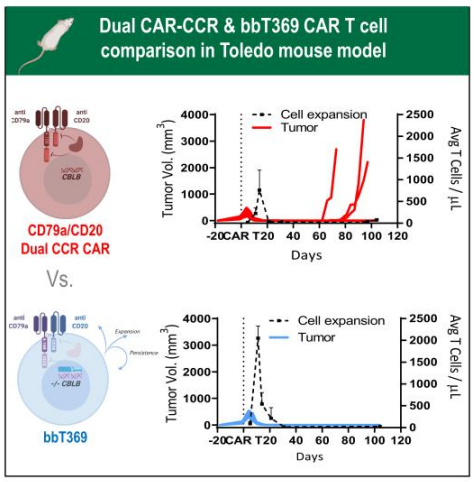
**bbT369**

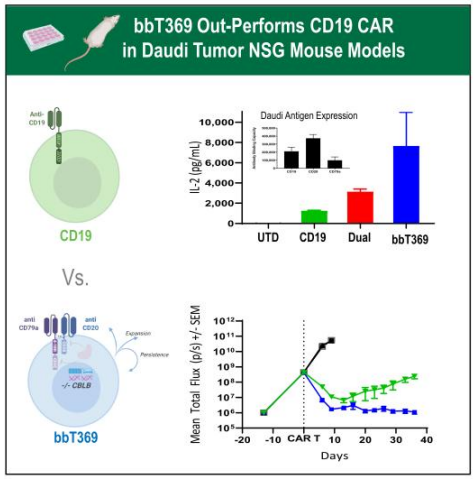



| | |
|---|---|
| TARGET(S) | Dual target: CD20, CD79a |
| TECH | • Chimeric costimulatory architecture with split 41BB and CD28<br>• *CBLB* gene edit for expansion, antigen sensitivity, performance |
| TARGET INDICATION | B-NHL |
| STATUS | Ph1 Trial enrolling |
| PARTNER | 2seventy owned |

- **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

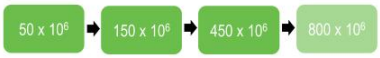


# CRC-403 study in B-NHL open and enrolling

## 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**

- **CAR expansion kinetics, including the potential role of the CBL-B gene edit, and clinical efficacy data, including complete responses in some patients support continuation of Phase I.**
- 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

**Data presentation in 2024**

# PLAT-08 Trial of SC-DARIC33 in AML on Clinical Hold

- As a result of a recent Grade 5 serious adverse event (SAE), the PLAT-08 study has been placed on clinical hold
- The company and its collaborators at SCRI are working with the FDA to enable restart of the Phase 1 study which is currently on clinical hold.
- 2seventy plans to limit financial commitment solely to the completion of the dose escalation phase. Consistent with the Company's streamlined pipeline activities, the Company has elected to pause its next-generation AML program.
- The Company will provide the next update on the PLAT-08 study upon completion of the Phase I.

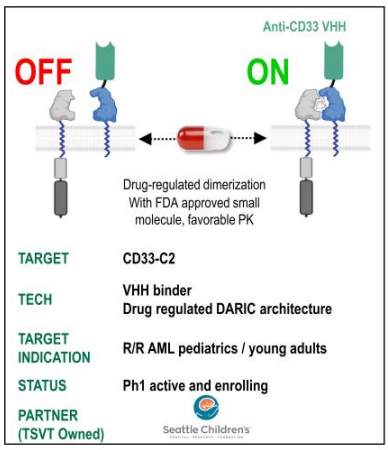
**PLAT-08 is the dose escalation Phase 1 study of SC-DARIC33 in relapsed/refractory pediatric AML, led by SCRI, and couples 2seventy bio's drug-regulated DARIC T cell platform with SCRI's expertise in oncology cell therapies.**

# 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<br>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

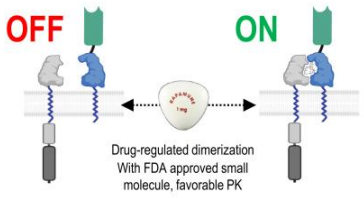
➢ ***CD33: a clinically validated AML target***

- 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

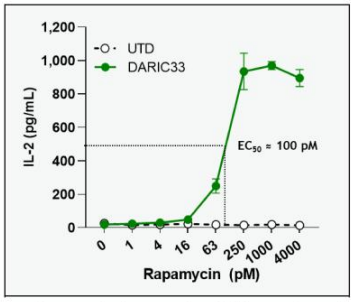
# SC-DARIC33 in AML: Sensitive, drug-regulated tumor control achieved in preclinical studies

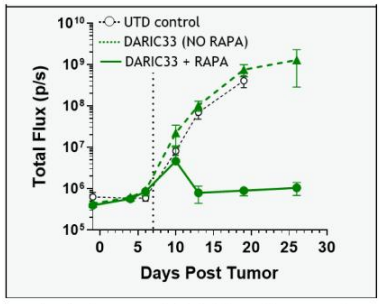
**SC-DARIC33**

DARIC = Dimerizing Agent Regulated Immunoreceptor Complex



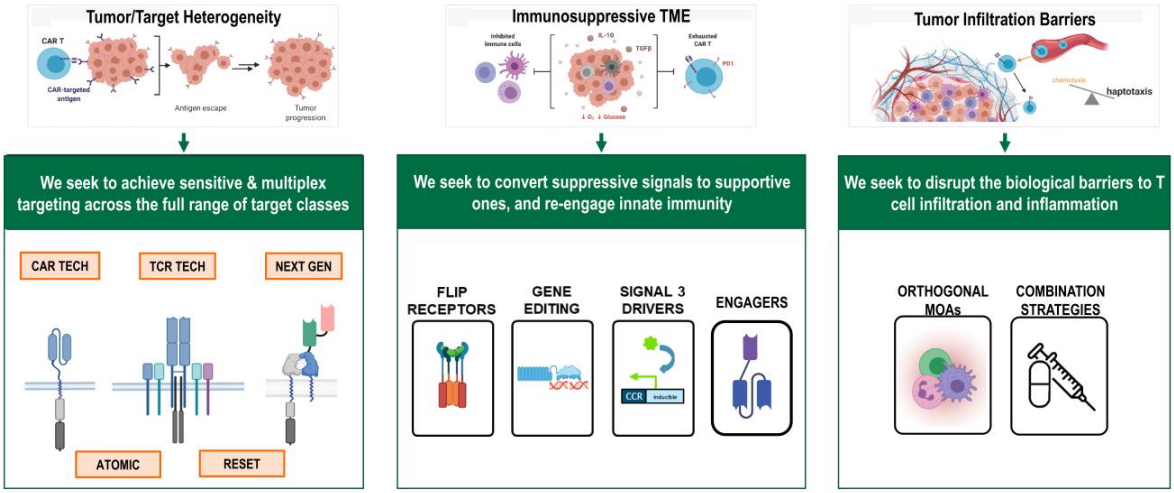

| | |
|---|---|
| TARGET(S) | CD33-C2 |
| TECH | VHH binder<br>Drug-regulated DARIC architecture |
| TARGET INDICATION | R/R AML pediatrics / young adults |
| STATUS | Ph1 Trial Enrolling |
| PARTNER | 2seventybio, Seattle Children's |




- 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

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

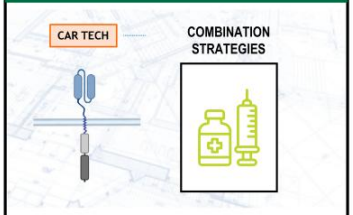





Created with BioRender.com

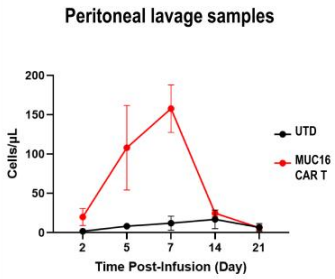
# MUC16 / Ovarian cancer program: designed to exploit the power of CAR T + pharmaceutical combination strategies to unlock deep responses

## Ovarian Cancer MUC16 CAR T Combo

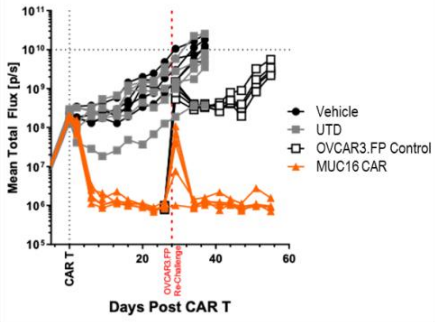



| | |
|---|---|
| TARGET(S) | MUC16 |
| TECH | CAR targeting prevalent MUC16 membrane-retained fragment |
| TARGET INDICATION | Solid Tumor (Ovarian) |
| STATUS | 2023 IND Submission |
| PARTNER | REGENERON |

## 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*

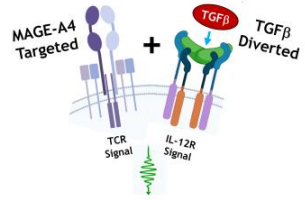
Cemiplimab (anti-PD-1 antibody) plus novel CPIs in development


***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

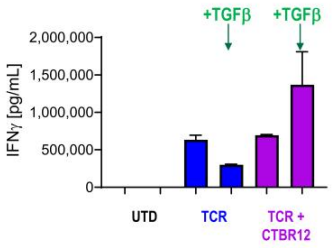
## Solid Tumor MAGE-A4 TCR-T Cell Therapy



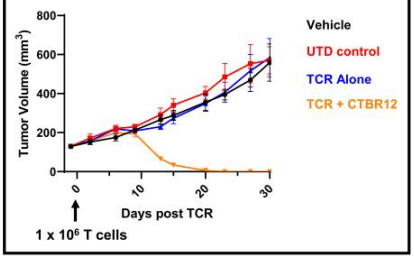

Enhanced Potency

| | |
|---|---|
| TARGET(S) | MAGE-A4 (HLA-A*02) |
| TECH | • MAGE-A4 directed TCR<br>• 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



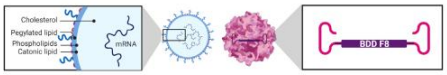

- Lead candidate demonstrates TGFβ signal conversion and potent tumor control in a lung xenograft mouse model
- Potential IIT in China (JW Therapeutics) by end of 2023

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

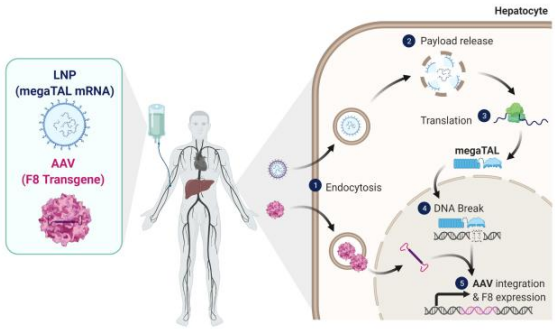
## MegaTAL Gene Editing for Hemophilia A / FVIII

**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<br>• TSVT in vivo grade mRNA production / purification platform<br>• AAV for transgene delivery<br>• 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 Officer

**Chip Baird**
Chief Operating Officer

**Steve Bernstein, M.D.**
Chief Medical Officer

**Kerri Jensen**
Head of People & Culture

**Teresa Jurgensen, J.D.**
General Counsel

**Nick Leschly**
Chief Kairos Officer*

**Philip Gregory, D. Phil.**
Chief Scientific Officer

**Jenn Snyder**
SVP, Corporate Communications

## 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.**
Revolution Medicines

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

**Denice Torres, J.D.**
From Johnson & Johnson

*+ ~280 awesome timekeepers*



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