Join the Patient Mission

Company Presentation

August 2022

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 2022. 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 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. 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 Registration Statement on Form 10, 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. This presentation has been prepared by 2seventy bio, Inc., a Delaware corporation, (together with its subsidiaries, the “Company”) for the exclusive use of the party to whom the Company delivers this presentation. 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It’s about time™

The most committed and passionate geeks driving next gen oncology cell therapeutics

2seventybio™

Key “launch” ingredients and plans

12 years
in the making

People
+
Culture
+
Experience

Product Engine Double Down

Science, translation, capabilities

ABECMA®

Deliver to patients and scale to demand

NextGen Potential Proof-of-Concept

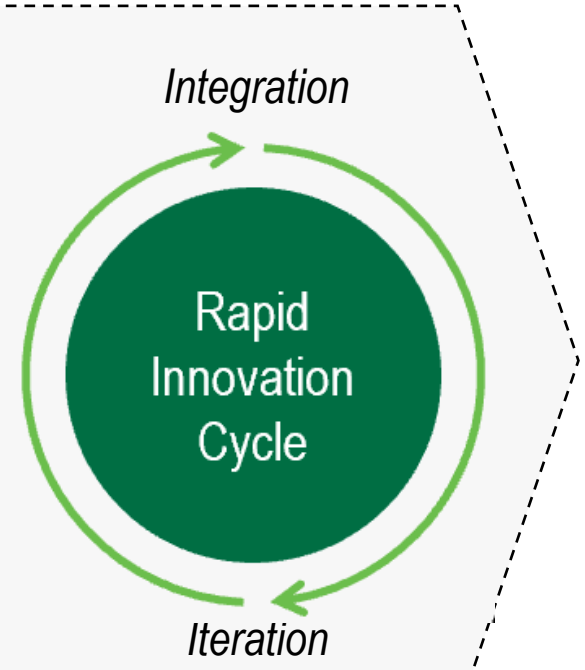
Test, learn & iterate in the clinic

Disrupt

Relentless innovation – science, medicine & manufacturing

Horizons focused on long term learning and disruption

Horizon 0: Launch Company	Spin & Double Down	Focus Team & Burn
Horizon 1: ABECMA®	Launch & Scale	3rd Line & Beyond
Horizon 2: Clinical Pipeline	Liquid Tumors: B-NHL & AML	Solid Tumors: MUC16, MAGE-A4 & Beyond
Horizon X: Disrupt	Deep Deep Auto (Very Angry T cell)	In-Vivo Editing (Novo)



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2022 Goals – Transformative build & deliver year

Deliver ABECMA®

Anticipated $250-$300M U.S. revenue in 2022

Amp Up Product Engine

B-NHL & AML; advance in solid tumors

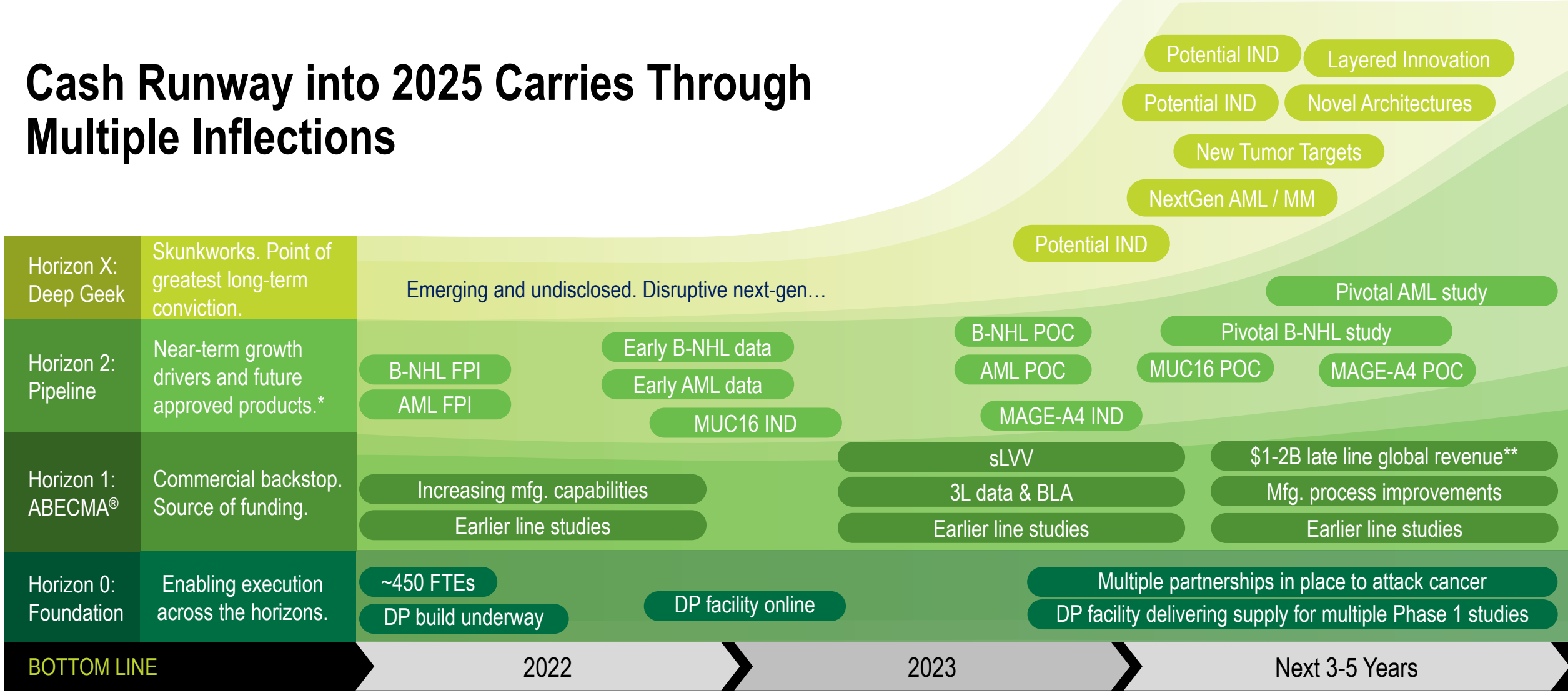
Tune Burn + Capabilities

Anticipated $245-265M net cash spend; goal to complete drug product facility build

Cash Runway into 2025

B-NHL: B-cell non-Hodgkin lymphoma
AML: acute myeloid leukemia

Cash Runway into 2025 Carries Through Multiple Inflections



Potential Patients Treated* **	High hundreds	>1,000	Thousands across indications
Financial	$170M private placement $245-265M net cash spend	ABECMA contributing cash back to business	Path to financial sustainability

*subject to FDA approval
**based on management projections
***across 2seventy portfolio

B-NHL: B-cell non-Hodgkin lymphoma; AML: acute myeloid leukemia;
POC: Proof-of-Concept; IND: Investigational New Drug Application; DP: Drug Product

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ABECMA® expected to be $1-2B late line global market opportunity

2021 Launch

- Approved on March 26, 2021
- Significant demand to date from patients and physicians
- Unaudited US product net revenue of approximately $150M*

2022 Outlook

- Anticipated $250-300M US product net revenue; tracking to upper end of range
- Increasing capacity across supply chain; U.S. business will fully utilize capacity as it becomes available
- Growing body of clinical data from earlier line studies
- Topline data from KarMMa-3 in 2-4L MM

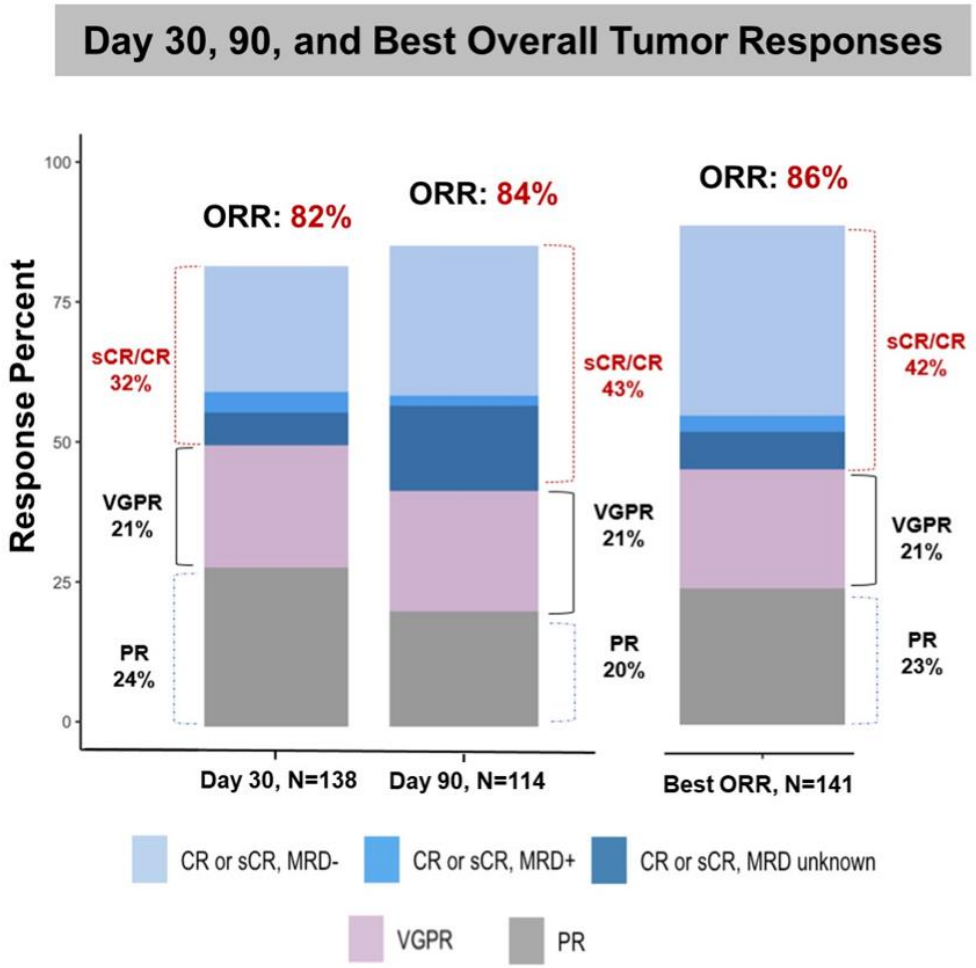
2023 and Beyond

- 3L potential BLA submission
- Growing profitability
- Continued capacity expansion
- Next-gen development underway

Ongoing commercial learnings from ABECMA can benefit the 2seventy pipeline and provide financial backstop from a value and funding perspective

*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

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
- KarMMa-3 study met primary endpoint of progression-free survival at interim analysis
- KarMMa-2 data to be presented in 2H 2022; additional KarMMa-3 data in 2023

Hansen et al, Abstract 8042 ASCO 2022

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

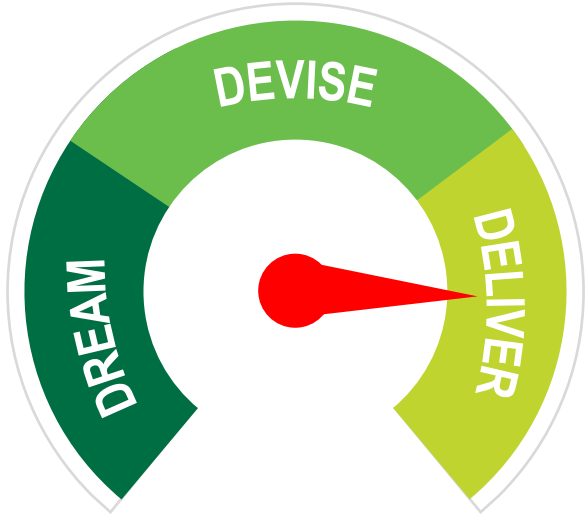
2seventy's R&D philosophy - accelerating innovation

Autologous CAR T cells work, but their full potential has not yet been realized

Multiple approved autologous CAR T products establish a powerful platform on which to build.

We have **yet to scratch the surface** with ways to embellish engineered T cells to truly capture the potential of cell therapy.

2seventy bio has the toolbox to do this **better than anyone.**



Accelerate innovation through cycles of TSVT's ASK/ANSWER engine

DREAM	• Identify fundamental problems • Look beyond the horizon • Explore new biology
DEVISE	• Define clear hypotheses • Invent compelling solutions • Bridge gaps through partnerships
DELIVER	• Define prospective data inflections • Forge clear development path • Invest in manufacturing 2.0

Our mission is to develop sophisticated and tumor-tailored autologous CAR/TCR T cell products to realize the potential of personalized, cell-based oncology therapeutics.

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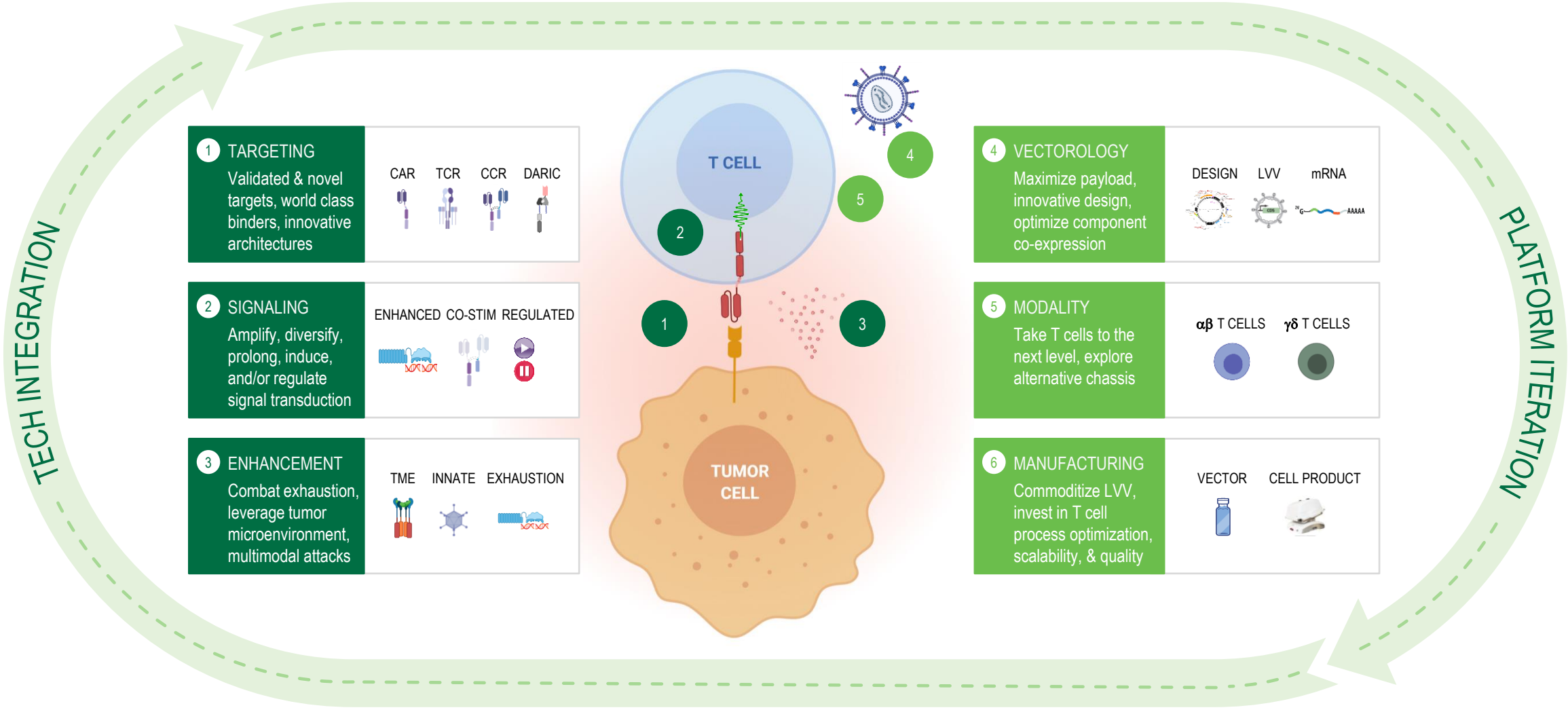
R&D engine built to rapidly design, test, learn, & iterate



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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		**Label Expansion**	
AML-Pediatric [DARIC33]	CD33	Drug-Regulated CAR T cell (DARIC)	SCRI Collaboration		**Phase 1 Open**	
B-NHL [bbT369]	Dual B cell targets	Dual-Targeted CAR T cell Signal Enhanced Gene Edited	TSVT Owned		**Phase 1 Open**	
AML-Adult [DARIC33 Next-Gen]	CD33 + Undisclosed	Drug-Regulated CAR T cell Dual-Targeted Potency Enhanced	SCRI Collaboration			
Ovarian Cancer	MUC16	CAR T cell Pharmacologic Enhancements	REGN Collaboration		**2023 IND Submission**	
Solid Tumors	MAGE-A4	TCR T cell Potency Enhanced	REGN / MEDG Collaboration		**Product engine generating ~1+ INDs per year**	
Solid Tumors	Multiple	CAR / TCR T cell Potency Enhanced	Multiple			
Multiple Myeloma	Multiple	Multi-Targeted CAR T cell Potency Enhanced	TSVT Owned			
Additional Indications	Undisclosed	Multiple	Multiple; Including Collab. with Novo Nordisk			

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bbT369: Designed with purpose. Study underway.

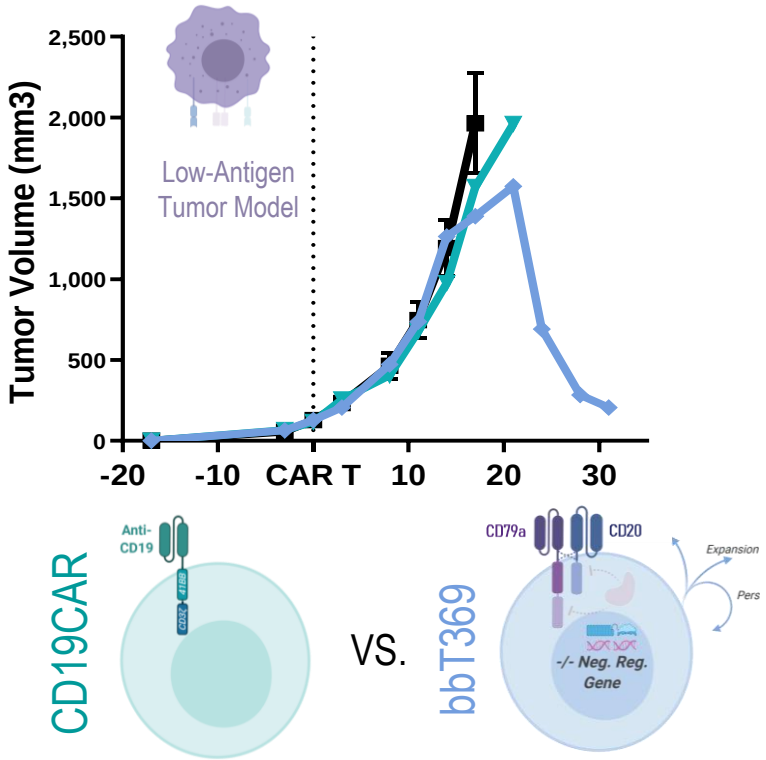
DEVISE

How to get there:

- Devise a sophisticated and disruptive cell therapy: a dual-targeting, potency-enhanced candidate that could solve failure modes of CD19 CAR-Ts
  - Novel combination of antigens to address antigen escape.
  - Synergistic antigen receptor signaling domains to augment T cell activation.
  - Gene edit to enhance potency and reduce T cell exhaustion.

bbT369 eliminates challenging tumors

Execution



- bbT369 outperformed model CD19 CAR in challenging low antigen expressing tumors in vivo
- Data supports potential to overcome resistance and elongate durability of response
- Phase I trial permits both CD19 CAR relapsed and naïve patients
- Trial intended to be enriched for patients with high risk factors as a proving ground to demonstrate improved patient outcomes

Patients enrolled 1H 2022

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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)

STUDY DESIGN

- Target enrollment: n=50
- 4 study sites
- Relapsed/Refractory B-cell NHL after autologous SCT or ≥ 2 prior lines of therapy
- B-cell NHL according to WHO 2017 classification
- 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 show 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 4 2seventy bio innovations:
  - Dual targeted T cell
  - Split-costimulation signaling architecture
  - MegaTAL gene editing tech
  - CBLB edited T cell
- All 4 are believed to have application across our research pipeline, including enhanced liquid tumor settings and solid tumors

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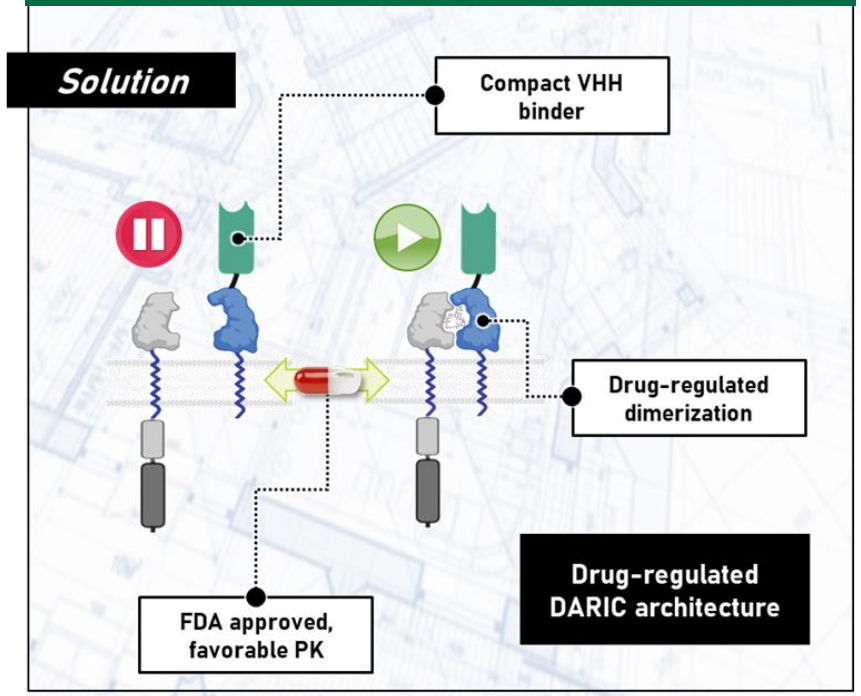
SC-DARIC33: Engineered to kickstart CAR T cell therapy in AML

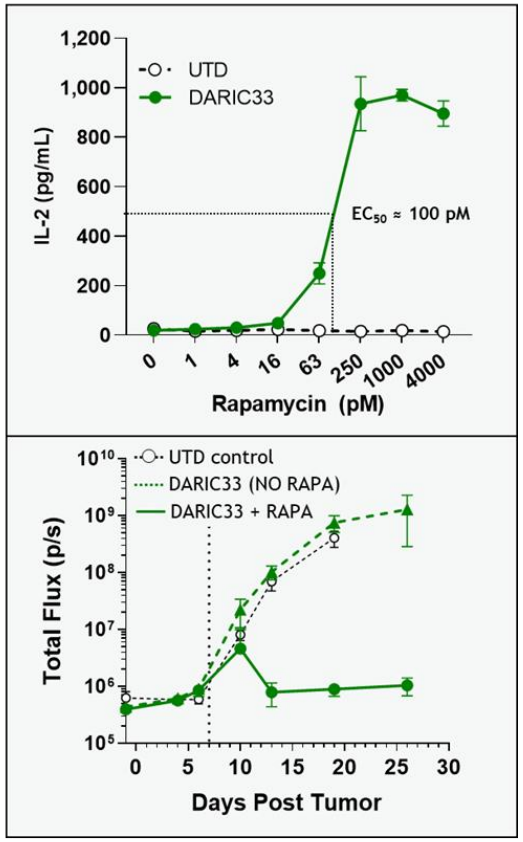
DEVISE

How to get there:

- Drug regulated CAR Ts overcome the underlying aplasia risk of targeting myeloid cells
- Enhance CAR T cell persistence by reducing exhaustive effect of continuous antigen stimulation
- Targeting the C2 domain of CD33 designed to deliver target abundance across genotypes limiting antigen escape

A drug-controlled CAR T cell to enable sequential AML targeting & myeloid recovery





Aggressively targeting AML requires pharmacologically-controlled CAR architecture that works under clinically feasible drug dosing

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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 DESIGN

- 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

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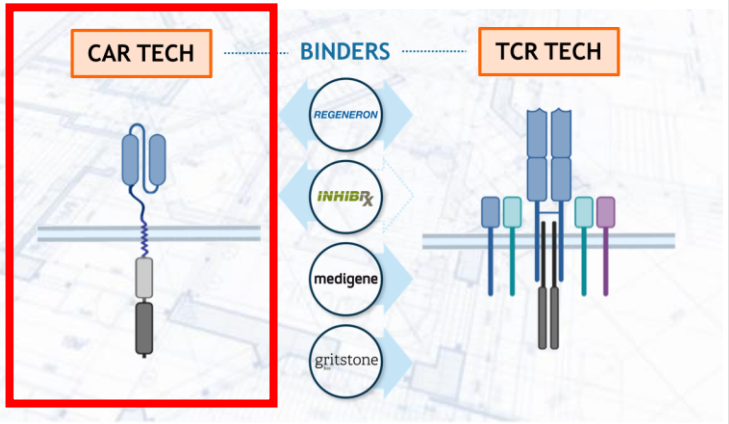
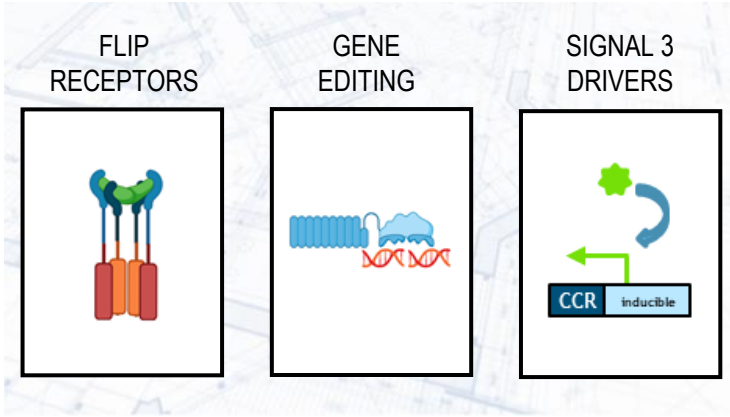
2seventy's attack on solid tumors designed to address the key barriers to success

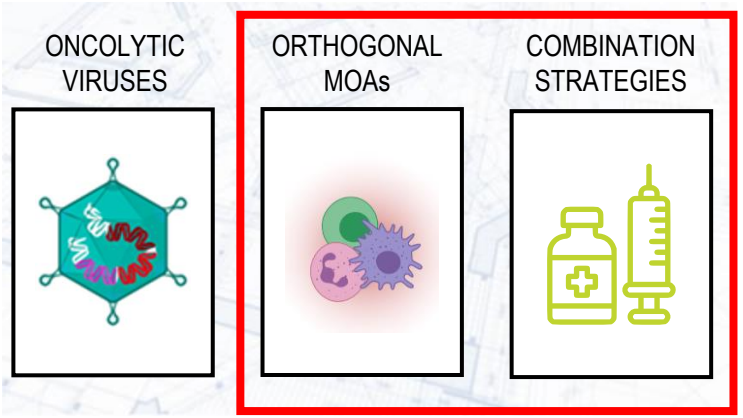
Can we achieve sensitive & multiplex targeting across the full range of target classes?



Can we convert suppressive signals to supportive ones, and re-engage innate immunity?



Can we disrupt the physical & biological barriers to T cell infiltration and inflammation?



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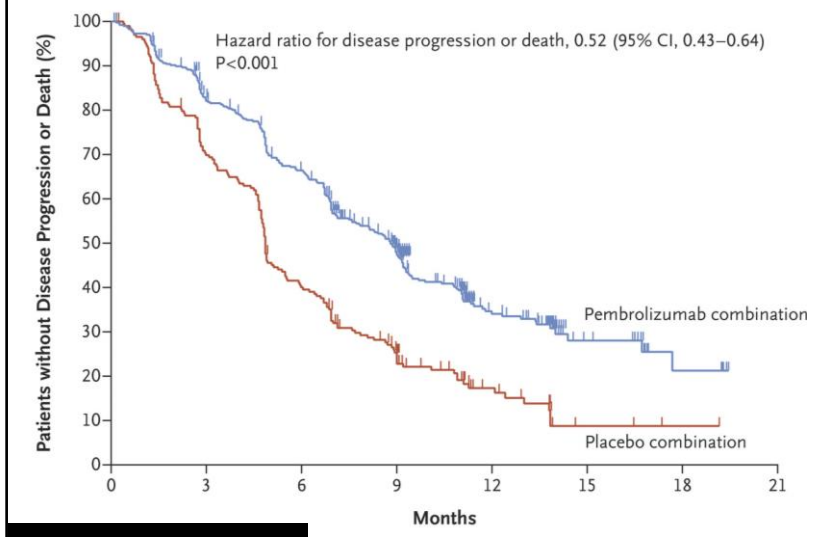
MAGEA4-CTBR12: Solid tumors

What if T cells can deliver heme cancer-like outcomes for patients?

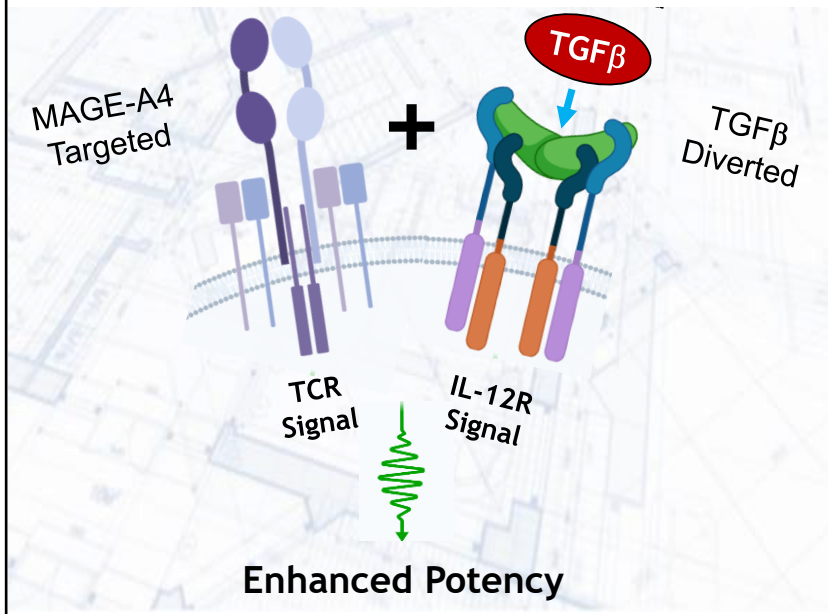


Problem

- Limited ability to access deep responses
- Some profoundly immunosuppressive pathways are difficult to target systemically

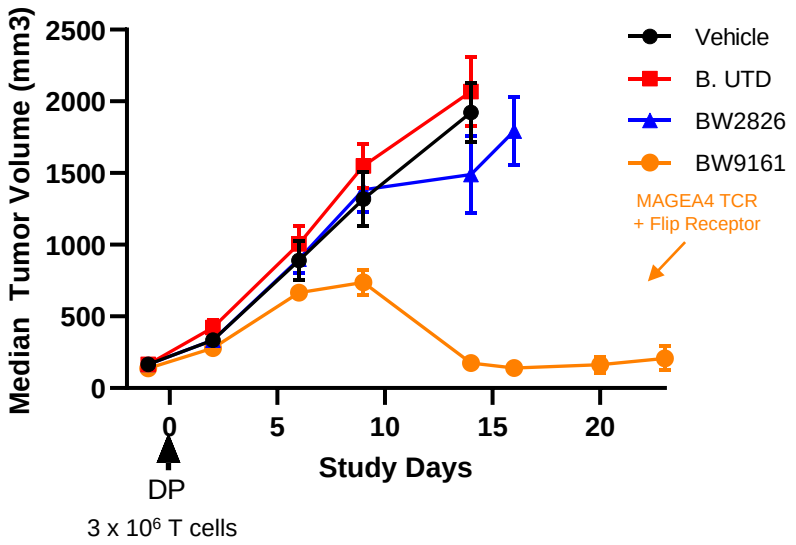
Can we substantially enhance the potency of a TCR T cell using a TME signal conversion technology?

We have engineered a potent MAGE-A4 TCR with a flip receptor to neutralize TGFb and potentiate T cell activity



Lead integrated candidate selected, demonstrates signal conversion & potent tumor control

Tumor regression achieved with MAGEA4 TCR + TGFb flip receptor in a melanoma xenograft model



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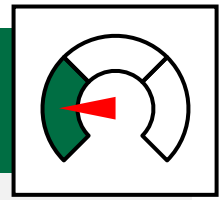
Our MUC16/ovarian cancer program aims to exploit CAR T + pharmaceutical combination strategies to unlock solid tumors

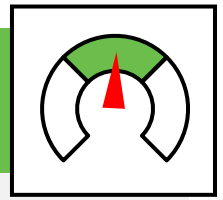
DREAM



Strive to create a product that:

- Targets MUC16-positive solid tumors (expressed in ~80% of ovarian cancers)
- Unleashes the potential of T cells in solid tumors by synergizing with transformative pharmaceutical agents
- Addresses the challenges of the tumor microenvironment (TME), target heterogeneity and on target / off tumor activity

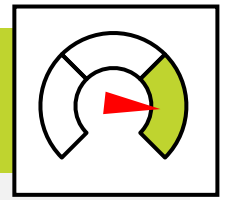
DEVISE



How to get there:

- A bold product concept combining an engineered T cell and a potent pharmacologic agent:
  - CAR targeting a highly prevalent membrane-retained fragment of MUC16 (uses REGN binder)
  - A titratable pharmacologic agent to counteract the tumor microenvironment while mitigating off-tumor activity

DELIVER



Progress on execution:

- Encouraging pre-clinical data: T cells expressing MUC16-targeted CAR Ts clear tumors in a tumor rechallenge model
- Program being co-researched as part of TSVT-REGN strategic collaboration: leverage experience of REGN's investigational MUC16 targeting therapies in ovarian cancer to develop best-in-class cell therapy
- Potential 2023 IND

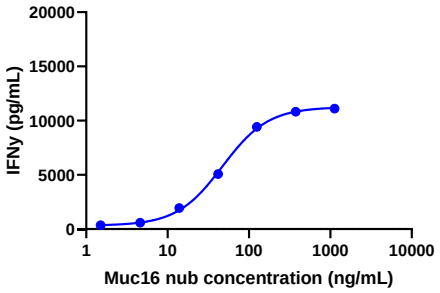
MUC16 expression data in OvCa: – Chauhan et. al., Modern Pathology, 2006; Cervical – Wang et. al., 2020, Exp Ther Med

Ovarian Cancer [DEVISE]: Pre-clinical data demonstrate deep responses

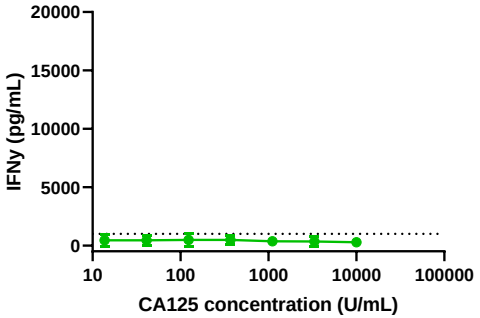
MUC16 CAR exhibits MUC16 ectodomain ("nub") specificity – does not bind shed CA125

Solution

CAR vs "nub" [surface retained]



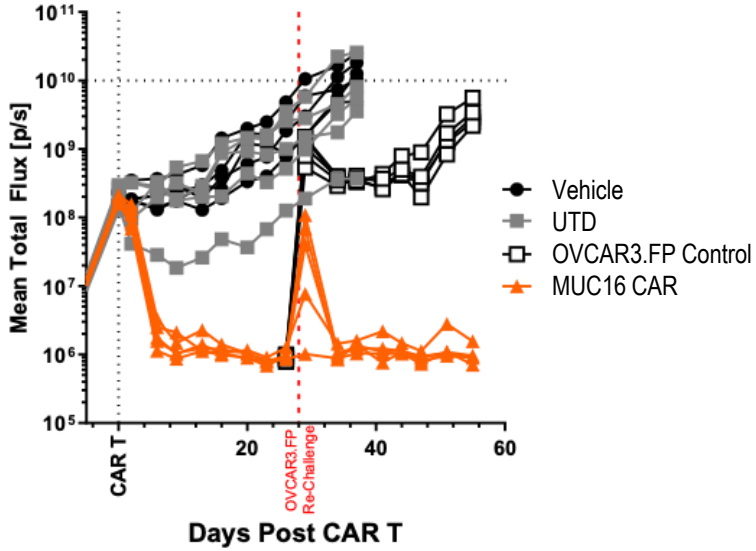
CAR vs CA125 [shed]



MUC16 CAR shows robust single agent activity in tumor rechallenge model

Solution

OVCAR3 Ovarian Cancer Xenograft Model



Our MUC16 CAR T provides in vivo tumor clearance and can prevent re-growth in a stringent tumor rechallenge model

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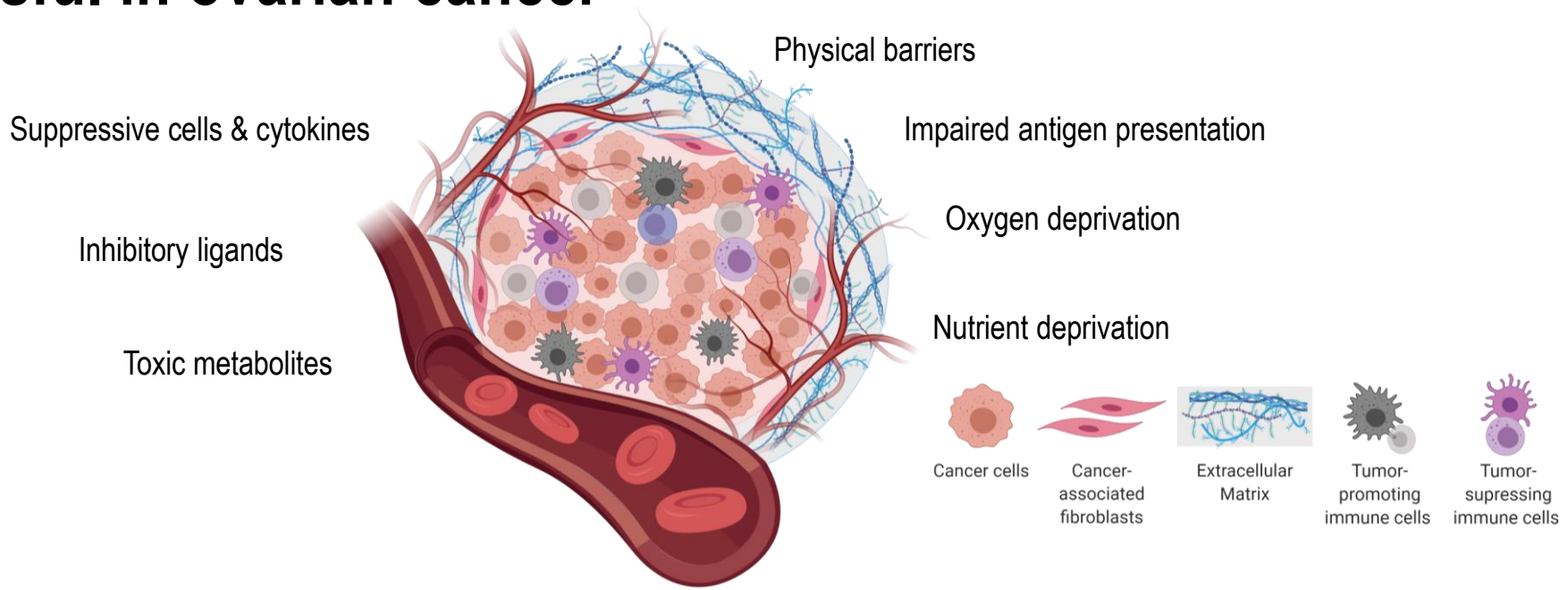
A MUC16 CAR T cell therapy must overcome several challenges to be successful in ovarian cancer



Key challenges

- ❑ Hostile/immunosuppressive tumor microenvironment (TME)
- ❑ Target expression heterogeneity and antigen negative relapse
- ❑ T cell expansion, persistence & penetration
- ❑ Healthy tissue liabilities

Potential Solutions

- ✓ Immune checkpoint neutralization, e.g., PD1
- ✓ Oncolytic virus-induction of an inflamed TME
- ✓ Costimulatory enhancement of CAR activity in combo with CD28 bispecifics
- ✓ Titratable enhancement tools engaging orthogonal targets

Image adapted from Molecular Therapy (2020): 28, 2320 using BioRender.com.

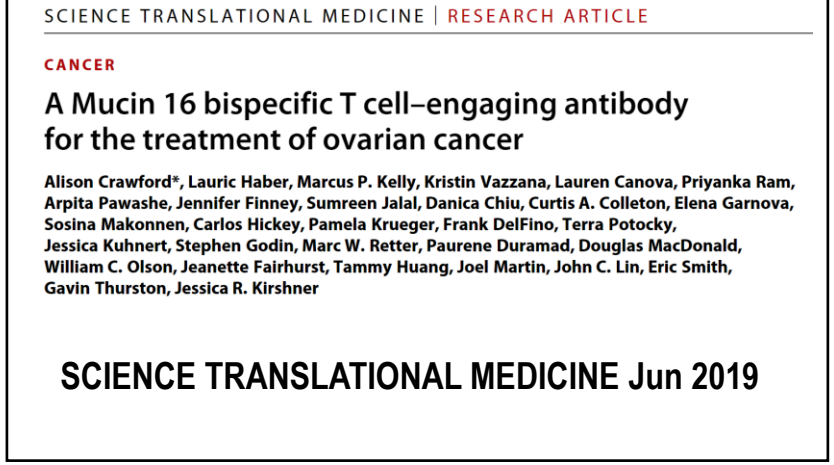
Our MUC16 program realizes the scientific power of collaboration with Regeneron

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

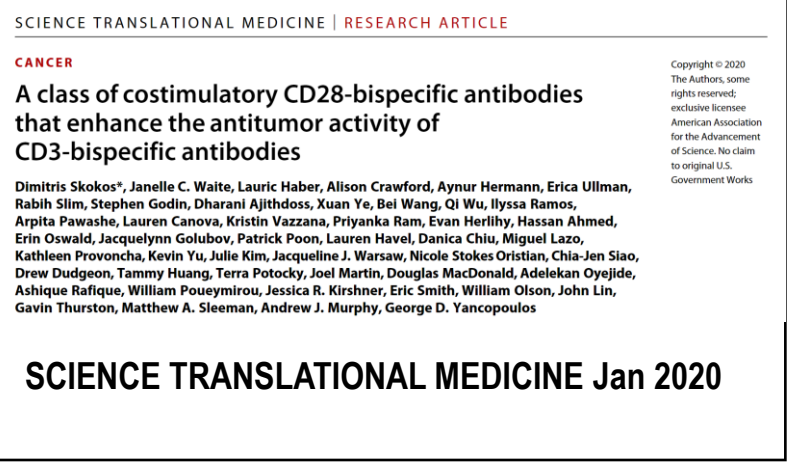
Alison Crawford*, Lauric Haber, Marcus P. Kelly, Kristin Vazzana, Lauren Canova, Priyanka Ram, Arpita Pawashe, Jennifer Finney, Sumreen Jalal, Danica Chiu, Curtis A. Colleton, Elena Garnova, Sosina Makonnen, Carlos Hickey, Pamela Krueger, Frank DelFino, Terra Potocky, Jessica Kuhnert, Stephen Godin, 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 bispecifics in pre-clinical and clinical development



SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

CANCER

A class of costimulatory CD28-bispecific antibodies that enhance the antitumor activity of CD3-bispecific antibodies

Dimitris Skokos*, Janelle C. Waite, Lauric Haber, Alison Crawford, Aynur Hermann, Erica Ullman, Rabih Slim, Stephen Godin, Dharani Ajithdoss, Xuan Ye, Bei Wang, Qi Wu, Ilyssa Ramos, Arpita Pawashe, Lauren Canova, Kristin Vazzana, Priyanka Ram, Evan Herlihy, Hassan Ahmed, Erin Oswald, Jacquelynn Golubov, Patrick Poon, Lauren Havel, Danica Chiu, Miguel Lazo, Kathleen Provoncha, Kevin Yu, Julie Kim, Jacqueline J. Warsaw, Nicole Stokes Oristian, Chia-Jen Siao, Drew Dudgeon, Tammy Huang, Terra Potocky, Joel Martin, Douglas MacDonald, Adelekan Oyejide, Ashique Rafique, William Poueymirou, Jessica R. Kirshner, Eric Smith, William Olson, John Lin, Gavin Thurston, Matthew A. Sleeman, Andrew J. Murphy, George D. Yancopoulos

SCIENCE TRANSLATIONAL MEDICINE Jan 2020

Checkpoint Inhibitor Combinations

PD-1 inhibitor demonstrating promising results in solid tumors

CEMIPLIMAB

PD-1 Antibody

Plus novel CPIs in development

MOLECULAR CANCER THERAPEUTICS

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Large Molecule Therapeutics

Preclinical Development of the Anti-LAG-3 Antibody REGN3767: Characterization and Activity in Combination with the Anti-PD-1 Antibody Cemiplimab in Human *PD-1xLAG-3*–Knockin Mice

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

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Innovative cell therapy candidates across broad indications

INDICATION [DRUG]	TARGET	TECHNOLOGY	DISCOVERY STAGE R&D	IND-ENABLING PRECLIN. 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		**Label Expansion**	
AML-Pediatric [DARIC33]	CD33	Drug-Regulated CAR T cell (DARIC)	SCRI Collaboration		**Phase 1 Open**	
B-NHL [bbT369]	Dual B cell targets	Dual-Targeted CAR T cell Signal Enhanced Gene Edited	TSVT Owned		**Phase 1 Open**	
AML-Adult [DARIC33 Next-Gen]	CD33 + Undisclosed	Drug-Regulated CAR T cell Dual-Targeted Potency Enhanced	SCRI Collaboration			
Ovarian Cancer	MUC16	CAR T cell Pharmacologic Enhancements	REGN Collaboration		**2023 IND Submission**	
Solid Tumors	MAGE-A4	TCR T cell Potency Enhanced	REGN / MEDG Collaboration		**Product engine generating ~1+ INDs per year**	
Solid Tumors	Multiple	CAR / TCR T cell Potency Enhanced	Multiple			
Multiple Myeloma	Multiple	Multi-Targeted CAR T cell Potency Enhanced	TSVT Owned			
Additional Indications	Undisclosed	Multiple	Multiple; Including Collab. with Novo Nordisk			

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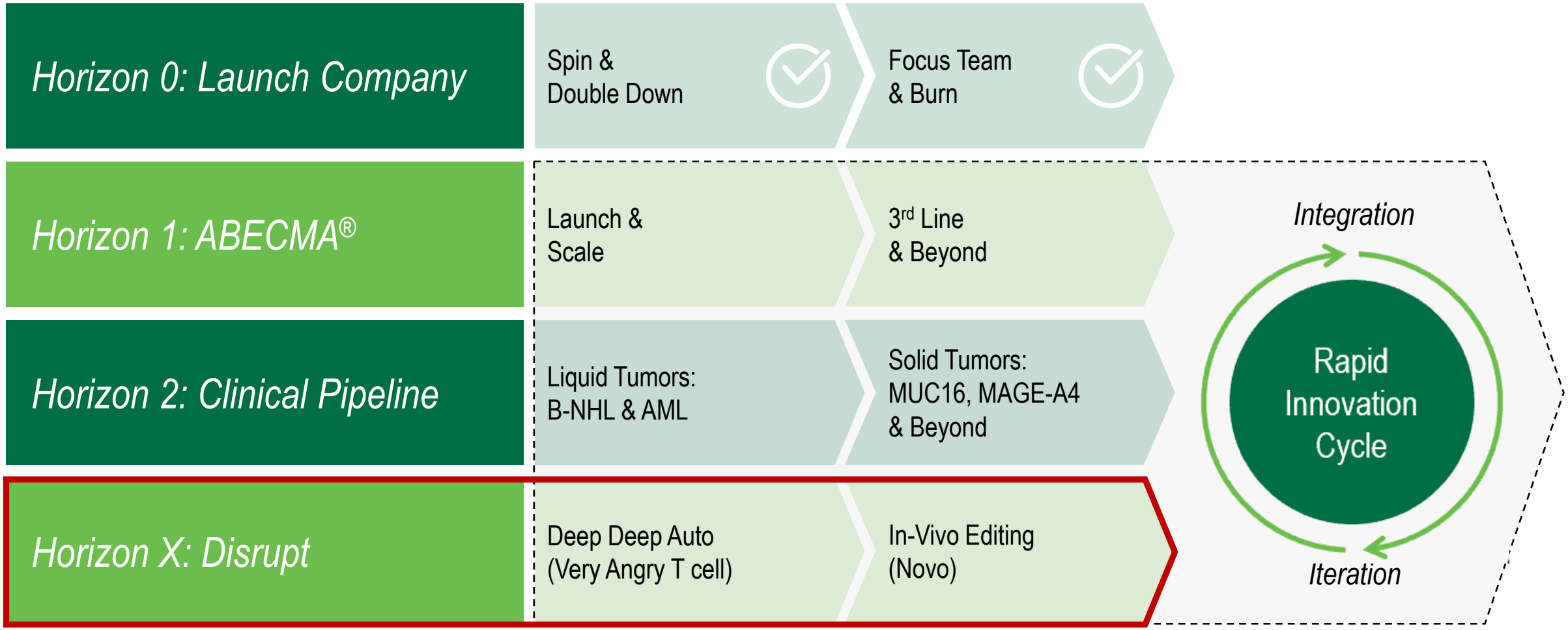
Horizons focused on long term learning and disruption



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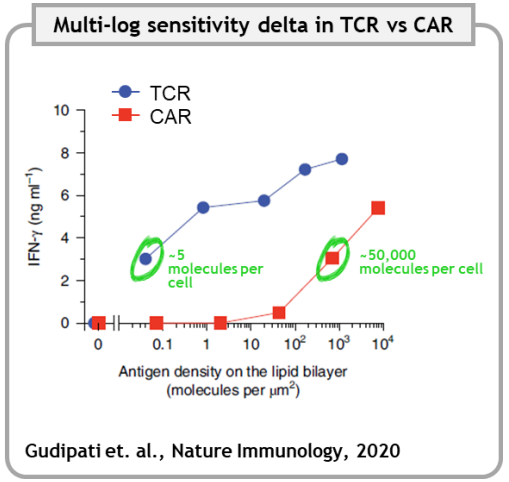
What are the biological barriers to achieving deep and durable responses?

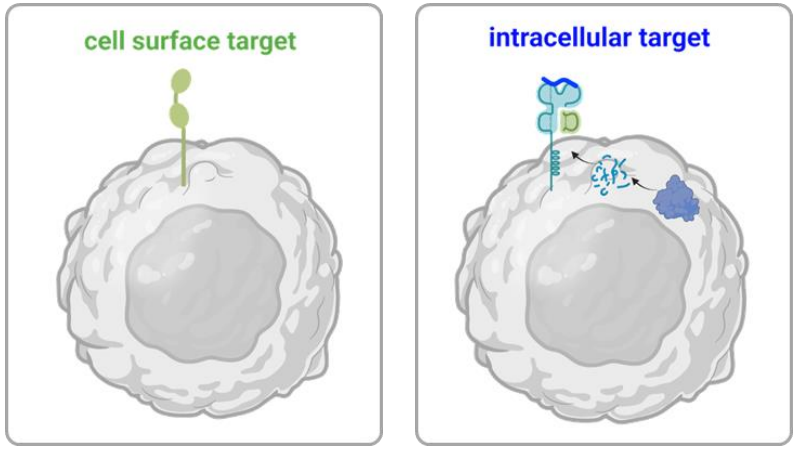
- *Low or reduced target abundance*
- *Target loss & heterogeneous expression*
- *Poor T cell engraftment and persistence*
- *Immunosuppressive microenvironment*
- *Cancer immune cycle breakdown*

TCRs >> CARs



Need to improve sensitivity

TARGET CLASS



Need to multiplex across target classes

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2seventy's novel receptor architecture: a new platform for tumor targeting

We have overhauled antigen receptor design and significantly advanced our targeting capabilities…

An orthogonal approach to improved T cell signaling and tumor target engagement

- TCRs have 2- to 3-log higher sensitivity to antigen density
- New architecture achieves TCR-like sensitivity to surface expressed antigens
  - May deepen responses in hematological tumors
  - May improve functional T cell responses in solid tumors

Enables simultaneous targeting of BOTH cell surface AND intracellular targets

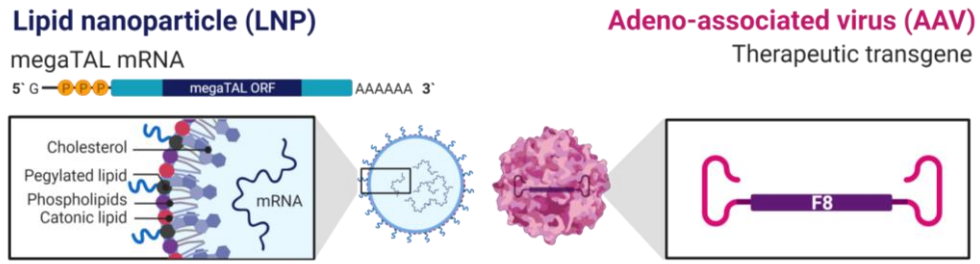
- New architecture enables facile targeting of both target classes
- For solid tumor targets in particular
  - Targets are limiting
  - They are heterogeneous in expression level and heterogeneous in expression pattern

Compact, readily engineered, and vectorized facilitating rapid adoption

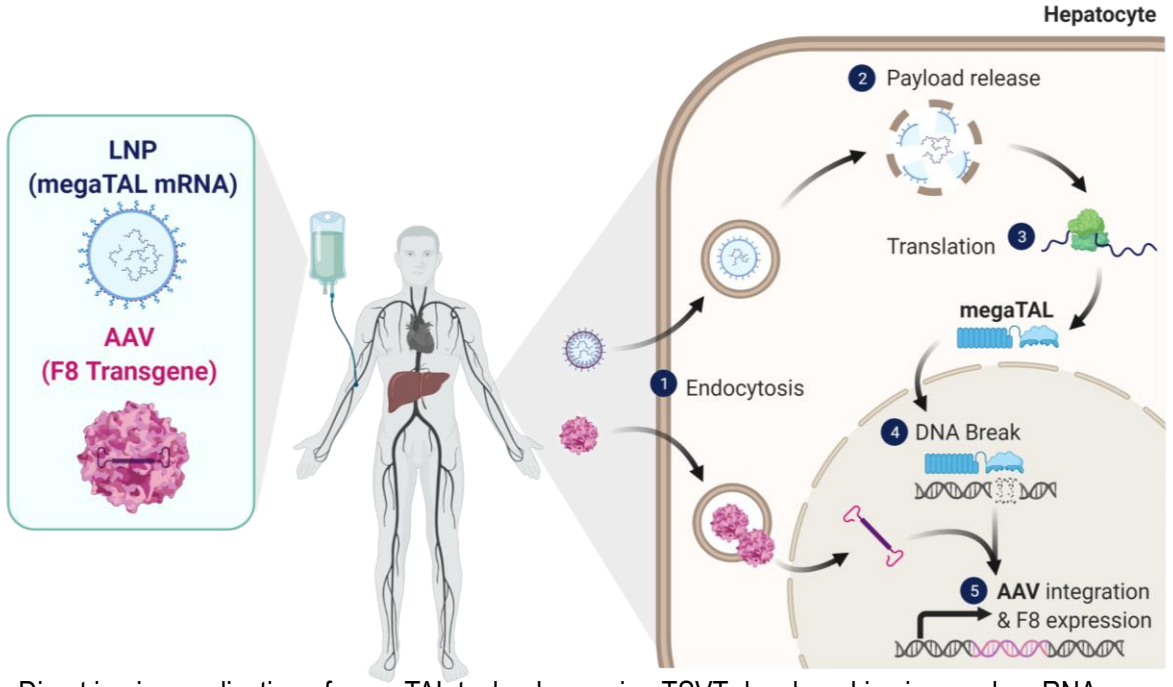
- Constructs are compact, readily engineered and vectorized
- New receptor architecture is compatible with 2seventy bio's binder and platform technologies

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

HemeA



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 in vivo grade mRNA production/purification process
- Recent expansion of collaboration with Novo Nordisk including $5M upfront + research costs, $35M of available near-term milestones + downstream sales royalties/milestones.
- Validates megaTAL platform and provides support for further expansion into ex-vivo and in vivo applications within the oncology portfolio

2seventy's manufacturing network: Poised to deliver

VELOCITY
Enable pipeline speed & decision making to proof-of-concept

Secure best-in-class academic partnerships for exploratory programs

- Outlets for high-risk programs for clinical validation while preserving flexibility & 2seventy resources
- Access to external innovation and programs, network

INNOVATION
Multiply our reach, capacity & ability to innovate

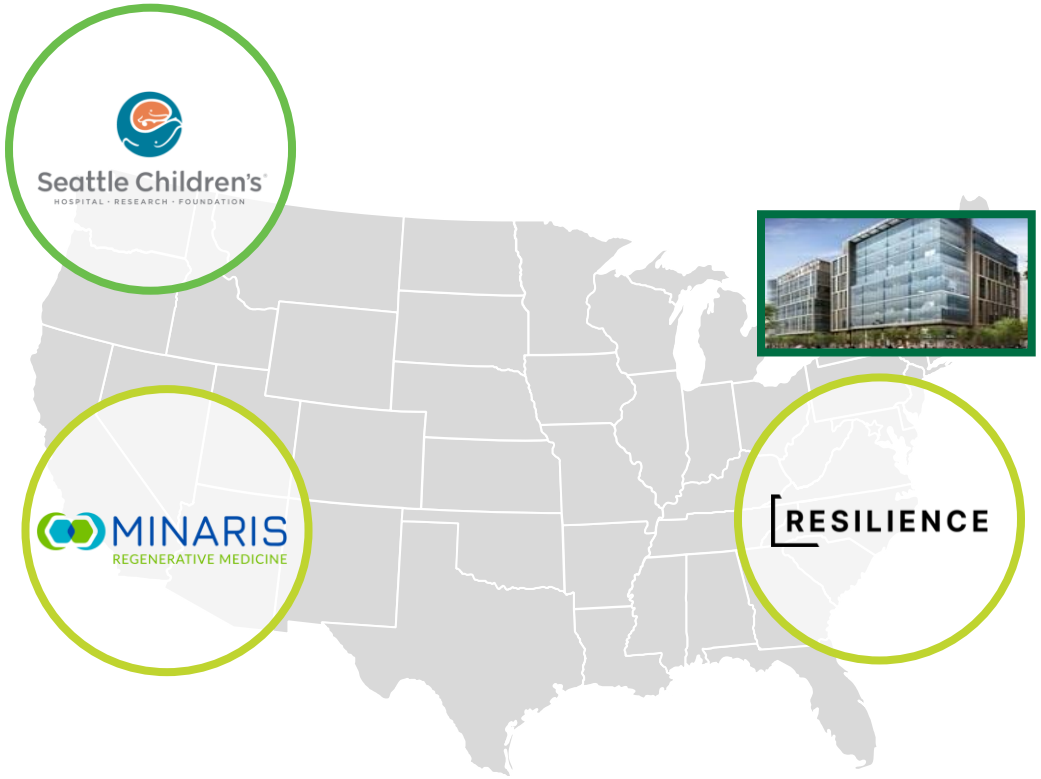
Establish an in-house clinical drug product manufacturing facility in Cambridge, MA

- Aimed to ensure ownership of the process, analytics, execution, value creation
- Enables deep integration of CMC with research and correlative sciences plus, flexibility to iterate

CAPABILITY
Manufacturing partnerships defined by identical goals

Leverage industry partnerships

- Risk-reward partnership with Resilience- new model for access to CDMO capabilities, aligning incentives & promoting agility



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Our seasoned team is ready

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Chief Kairos Officer*

Chip Baird
Chief Financial Officer

Nicola Heffron
Chief Operating Officer

Philip Gregory, D. Phil.
Chief Scientific Officer

Kathy Wilkinson
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Steve Bernstein, M.D.
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Susan Abu-Absi, Ph.D.
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+450 Awesome 270ers

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

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The most committed and passionate geeks driving next gen oncology cell therapeutics

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thank you