Deep Dive Session 2: B-NHL and solid tumors

September 2021

Agenda

- **2seventy's Paradigm & Pipeline | Dream Devise Deliver**
  - Nick Leschly, Chief Kairos Officer
  - Philip Gregory, Chief Scientific Officer
- **bbT369 Program in bNHL | Next-Gen now**
  - Mike Certo, Sr. Director, Genome Editing
  - Kevin Chin, SVP, Oncology Clinical Development
- **Our approach in Solid Tumors | MAGE A4**
  - Steve Shamah, SVP, Oncology Research
- **Manufacturing & Collaborations | The Foundation and the Future**
  - Susan Abu-Absi, SVP, Oncology TD&O

forward-looking statements

These slides and the accompanying oral presentation contain forward-looking statements and information. The use of words such as “may,” “might,” “will,” “should,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “intend,” “future,” “potential,” or “continue,” and other similar expressions are intended to identify forward-looking statements. For example, all statements we make regarding the initiation, timing, progress and results of our preclinical and clinical studies and our research and development programs, our financial guidance, our ability to advance product candidates into, and successfully complete, clinical studies, the timing or likelihood of regulatory filings and approvals, and our financial projections are forward looking. All forward-looking statements are based on estimates and assumptions by our management that, although we believe to be reasonable, are inherently uncertain. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that we expected. These statements are also subject to a number of material risks and uncertainties that are described in our most recent quarterly report on Form 10-Q, as well as our subsequent filings with the Securities and Exchange Commission. Any forward-looking statement speaks only as of the date on which it was made. We undertake no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

Time is Life

CARE DEEPLY

The Why

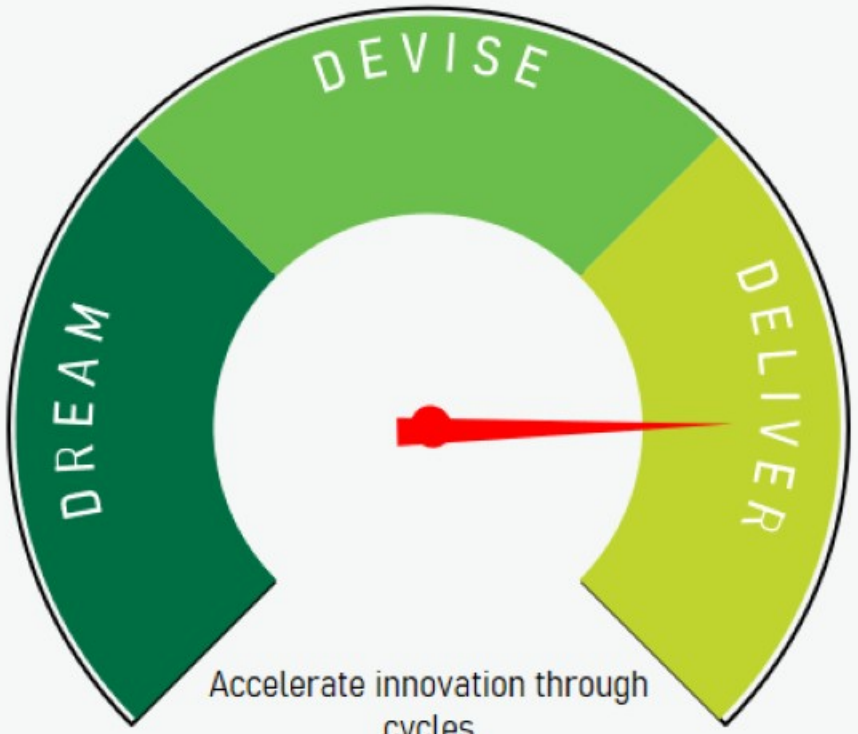
The How

BE HUMAN

2seventy bio – Time to Launch

1. Most experienced team in cell therapy. Done it. Want to do it again and again
2. Tuned to 100% oncology cell therapy focus – do it smarter and faster
3. Most advanced and sophisticated scientific toolkit and engine in cell therapy
4. Capabilities, partners & funding in place to deliver – know what it takes
5. Delivering on next-gen oncology cell therapy products TODAY

2seventy's R&D philosophy - accelerating innovation



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

DREAM

Identify fundamental problems
Look beyond the horizon
Explore new biology

What opportunities have the greatest potential impact?

DEVISE

Define clear hypotheses
Invent compelling solutions
Bridge gaps through partnership

What solutions can we conceive to unlock that potential?

DELIVER

Prospective data inflections
Defined development path
Invest in manufacturing v2.0

What development strategy robustly tests the hypothesis?

Recoding R&D engine built to rapidly build, test, learn, & improve

1 TARGETING
Validated & novel targets, world class binders, innovative architectures

CAR TCR CCR DARIC

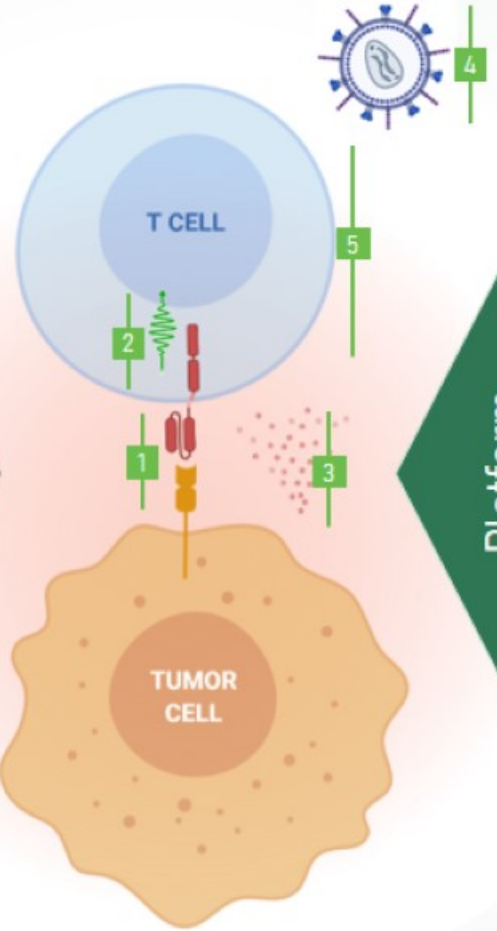
2 SIGNALING
Amplify, diversify, prolong, induce, and/or regulate signal transduction

ENHANCED CO-STIM REGULATED

3 ENHANCEMENT
Combat exhaustion, leverage tumor microenvironment, multimodal attacks

TME INNATE EXHAUSTION

Tech



Platform

4 VECTOROLOGY
Maximize payload, innovative design, optimize component co-expression

DESIGN LVV mRNA

5 MODALITY
Take T cells to the next level, explore alternative chassis

αβ T CELLS γδ T CELLS

6 MANUFACTURING
Commoditize LVV, invest in T cell process optimization, scalability, & quality

VECTOR CELL PRODUCT

2seventy Pipeline – Innovative cell therapy candidates across broad indications

INDICATION [DRUG]	TARGET	TECHNOLOGY	DREAM	DEVISE	DELIVER
Multiple Myeloma [ABECMA]	BCMA	CAR T cell	BMS Partnership		Abecma
Multiple Myeloma [bb21217]	BCMA	CAR T cell PI3K Enhanced Manufacturing	BMS Partnership		Data at ASH'21
AML-Pediatric [DARIC33]	CD33	Drug-Regulated CAR T cell (DARIC)	SCRI Collaboration		IND 2H 2021
B-NHL [bbT369]	Dual B cell targets	Dual-Targeted CAR T cell Signal Enhanced Gene Edited	TSVT owned		IND 2H 2021
AML-Adult [DARIC33 Next-Gen]	CD33 + Undisclosed	Drug-Regulated CAR T cell Dual-Targeted Potency Enhanced	SCRI Collaboration		
Solid Tumors	MAGE-A4	TCR T cell Potency Enhanced	REGN / MEDG Partnership		
Solid Tumors	Multiple	CAR / TCR T cell Potency Enhanced	TSVT & UNC		
Multiple Myeloma	Multiple	Multi-Targeted CAR T cell Potency Enhanced	TSVT		
Additional Indications	Undisclosed	Multiple	Multiple		

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Today's focus

2seventybio

bNHL | bbT369

Despite recent progress, there is still outstanding need in aggressive lymphoma

Disease Overview

Non-Hodgkin's Lymphoma (NHL) is the **#1** MOST common blood cancer[1]

Annual NHL Incidence: **~78k** in the US[2]; **~544k** Worldwide[1]

DLBCL[2] is an aggressive form of NHL that accounts for **~1/3rd of all NHL**

Significant Unmet Need

40% of DLBCL patients do not survive beyond 5 years[5]

Outcomes are poor especially for patients who are in later lines of therapy

90% of DLBCL patients will relapse or be refractory to 3rd line of therapy[2]

Despite improved outcomes from CAR-T in 3rd line, **~60% of patients relapse** after CAR-T[5]

Source: (1) Globocan Database, (2) Kantar CancerMPact 2021, (3) American Cancer Society – Survival Rates, (4) NCCN Guidelines 2021, (5) Vercellino et. al., Blood Advances 2020
Note: "Other Options" is a fragmented mix of treatments including but not limited to chemotherapy +/- Rituxan, monoclonal antibodies and, anti-body drug conjugates
Abbreviations: NHL = Non-Hodgkin's Lymphoma, R = Rituxan, SCT = Stem Cell Transplant

bbT369 is purpose-built to enhance depth and durability of response in B-NHL

DREAM

Strive to create a product that:

- Meets the significant need in bNHL
- Addresses shortcomings of existing therapies by increasing response rate and durability of response to a larger fraction of patients.

DEVISE

How to get there:

- Devise a sophisticated and disruptive cell therapy: a dual-targeting, potency-enhanced candidate that solves 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**.

DELIVER

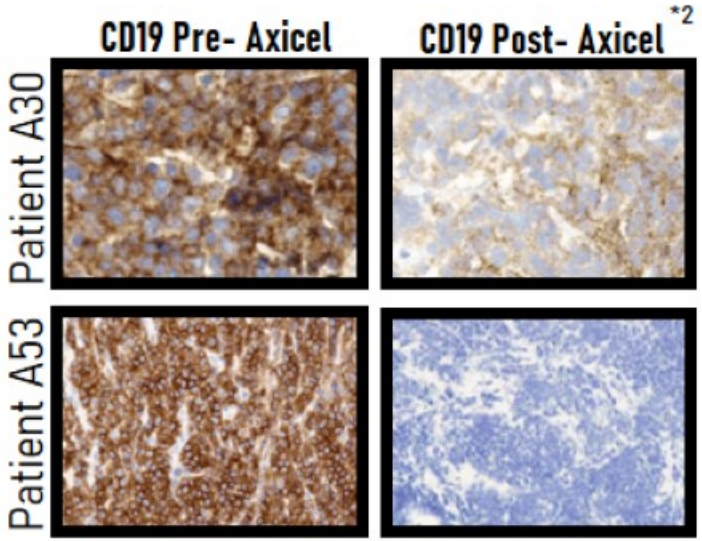
Progress on execution:

- Encouraging pre-clinical data: bbT369 clears single and low antigen tumors, and achieves deep, durable responses
- Clinical development plan poised to quickly determine if bbT369 can provide better outcomes for patients
- **IND anticipated in 2H21**

bNHL [DREAM]: Can we leverage emerging correlative data to guide next-gen product development?

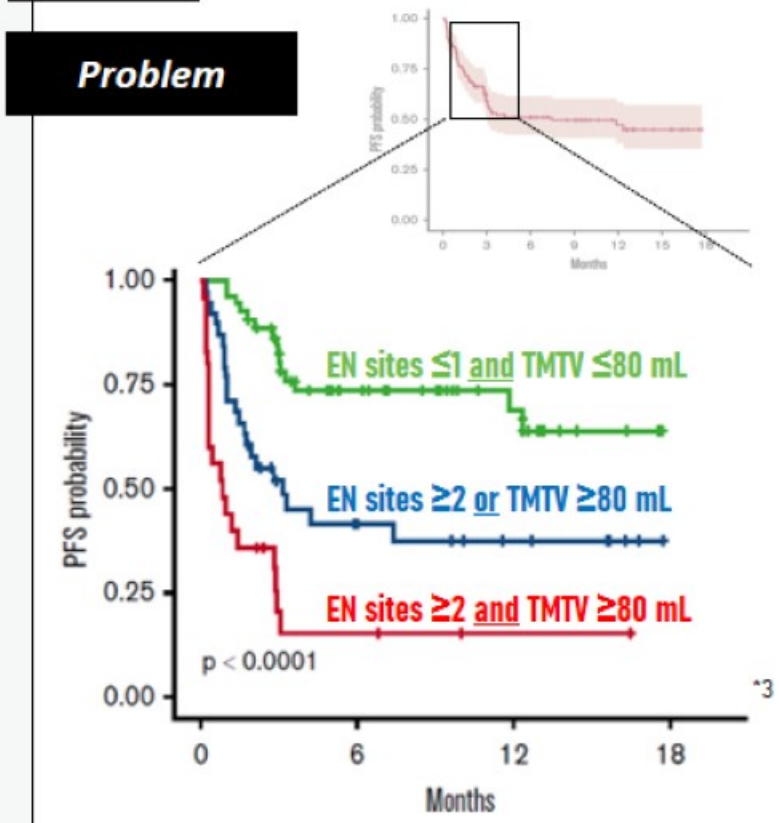
~30% of patients are relapsing with CD19 low/negative disease[1]

Problem



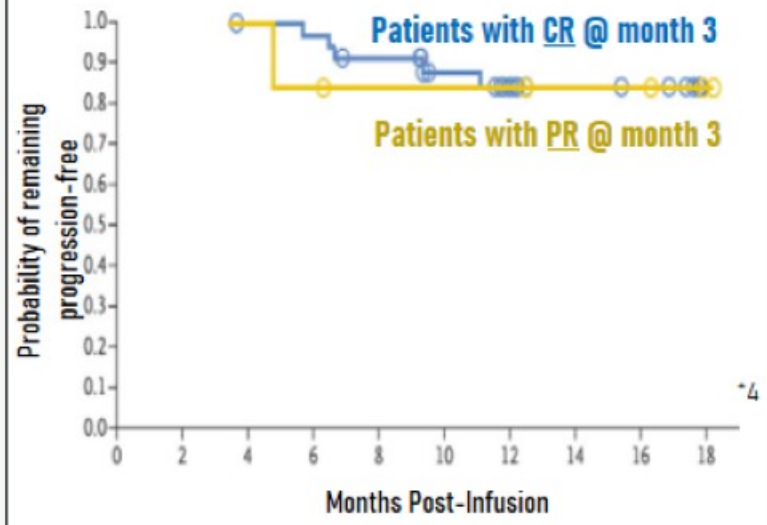
Poor outcomes associated with more aggressive tumors

Problem



~80% of patients have durable outcomes if response present at 3mo

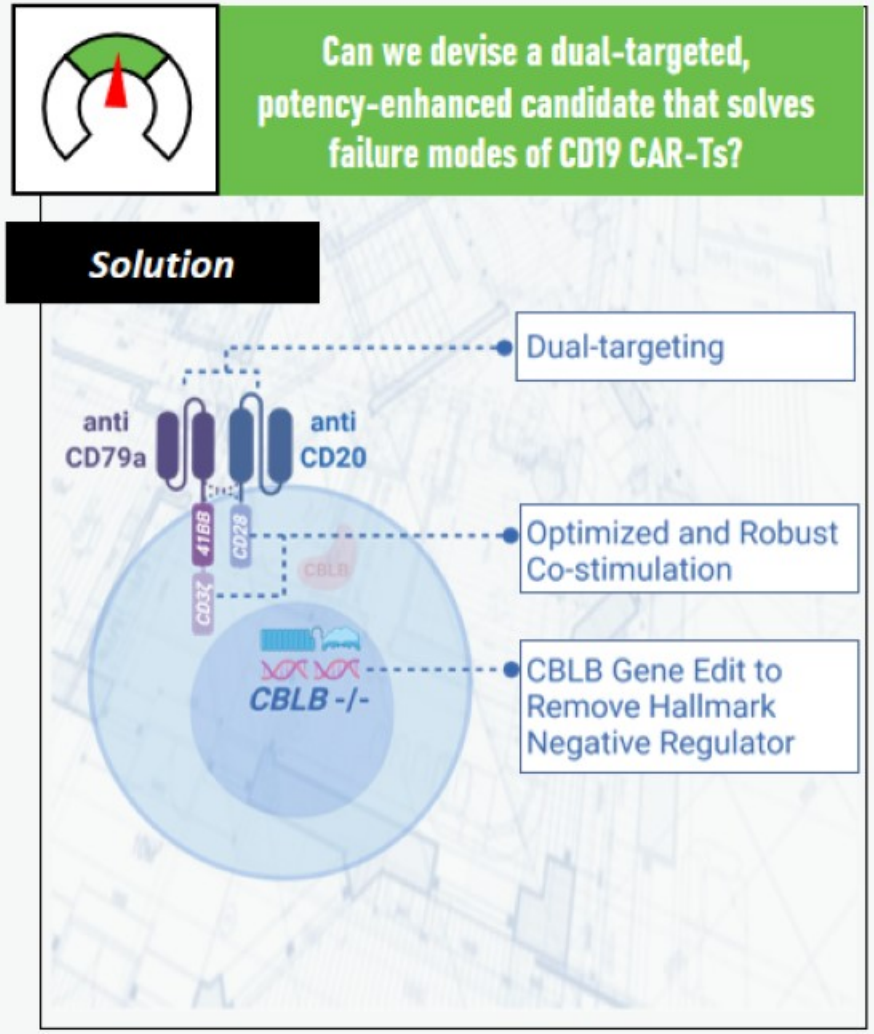
Observation



Novel approaches to overcome relapse/refractory mechanisms and induce deeper responses early are likely to result in more durable outcomes for a broader population of bNHL patients.

Source: (1) Neelapu et. al., Blood 2019; (2) Adapted from Spiegel et. al., Nature Medicine 2021; (3) Adapted from Vercellino et. al., Blood Advances 2020; (4) Adapted from Schuster et. al. NEJM 2019

bNHL [DEVISE]: bbT369 purpose-built to solve limitations of currently approved CD19 CAR T



- **Targets CD79a and CD20** – B cell restricted antigens strongly co-expressed on B cell lymphomas
- Dual CAR design featuring split 41BB and CD28 co-stimulation ensures robust and **more complete cell stimulation against single or dual expressing tumor cells**
- **CBLB gene edit removes a hallmark negative regulator of T cell function** to increases cell expansion, antigen sensitivity, and performance in hostile microenvironments

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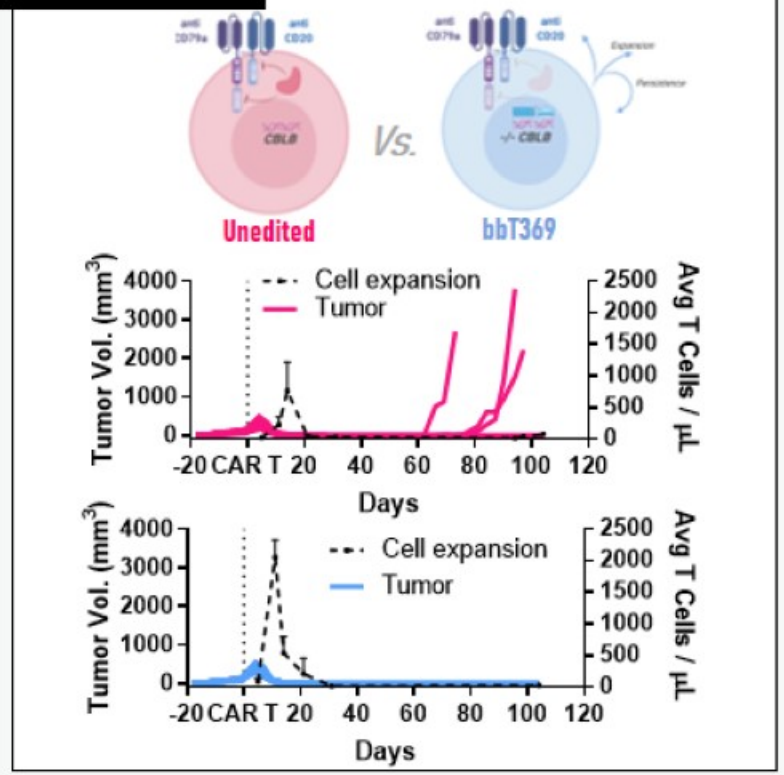
bNHL [DEVISE]: Pre-clinical data demonstrate bbT369 can deliver deep responses

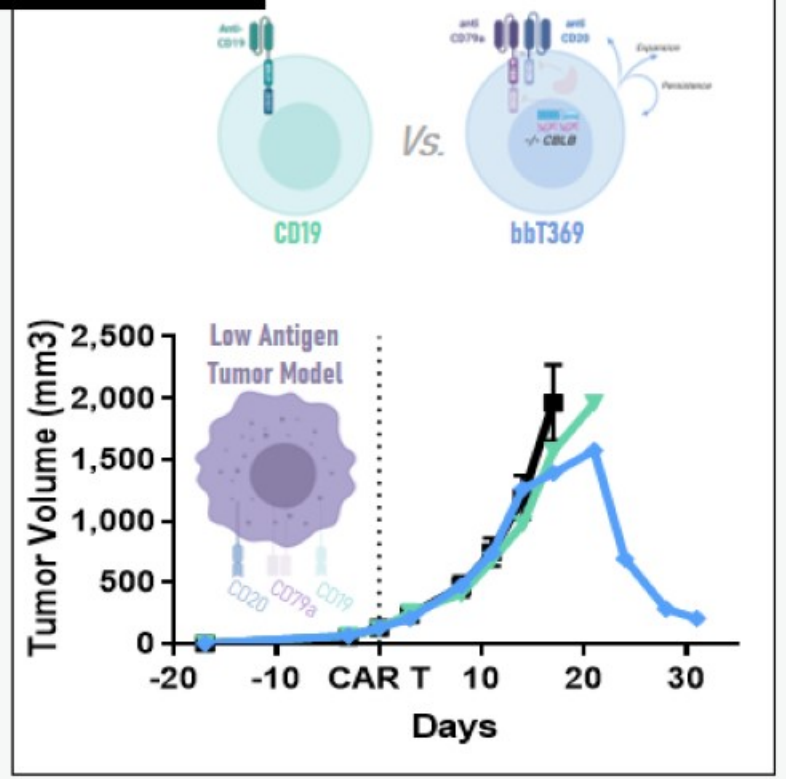
CBLB edit drives deep and sustained responses in *in vivo* models

Solution



bbT369 outcompetes CD19 in challenging low-antigen models

Solution



bbT369 provides greater expansion, deep responses, and increased antigen sensitivity that prevents tumor escape.

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DELIVER: Overview of provisional bbT369 phase I dose escalation study in R/R B-cell NHL

Phase I Patient Population

- Relapsed/Refractory B-cell NHL after autologous SCT or ≥2 prior lines incl. anti CD20 MoAb + anthracycline containing chemotherapy
- Diagnosis of B-cell NHL according to WHO 2017 classification

Objectives of Study

- Determine MTD and RP2D
- Evaluate safety of RP2D
- Provide preliminary data on the efficacy
- Evaluate bbT369 kinetics
- Evaluate additional pharmacodynamic or other exploratory assessments

Enrollment	Apheresis	Lymphodepletion	bbT369	DLT Period	Response Assessment
		day -5-2	day 0	day 0-30	day 30

→ SAFE?

Is the safety profile of bbT369 acceptable?

→ DOSE?

What is the recommended dose for phase II?

→ EFFECTIVE?

Does bbT369 show activity in CD-19 CAR-T exposed and CAR naïve patients?

→ EXPANSION?

Does the dual targeting gene edited bbT369 expand and persist to drive anti tumor activity?

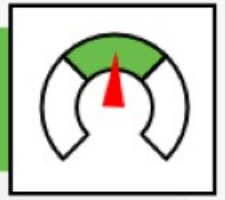
B-NHL [SUMMARY]: bbT369 is purpose-built to outsmart tumor resistance

DREAM

Unmet need in B-NHL is to solve for CAR T resistance

- ~60% relapse after CAR T
- 40% of DLBCL patients do not survive beyond 5 years
- Mechanisms of CAR T cell resistance emerging

DEVISE



Innovative triple-play CAR T cell approach

- CD79a and CD20 dual-targeting
  - Reduces escape potential
  - Independent of CD19 loss
- Improved co-stimulatory signaling
  - Minimize escape via low antigen levels
- Gene edited to enhance potency and reduce T cell exhaustion

DELIVER

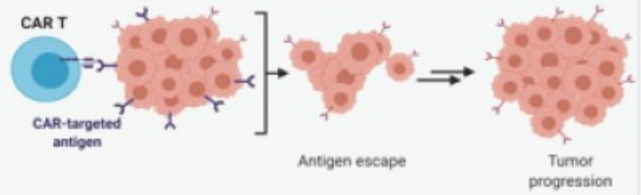
Progress on execution

- Pre-clinical data surpasses CD19 benchmarks with 2021 IND on track
- Clinical development plan poised to quickly determine if bbT369 can provide better outcomes for patients
- Archetype for TSVTs innovation through integration approach
- PoC for gene edit, dual target platform and CCR technology ALL with broad applications

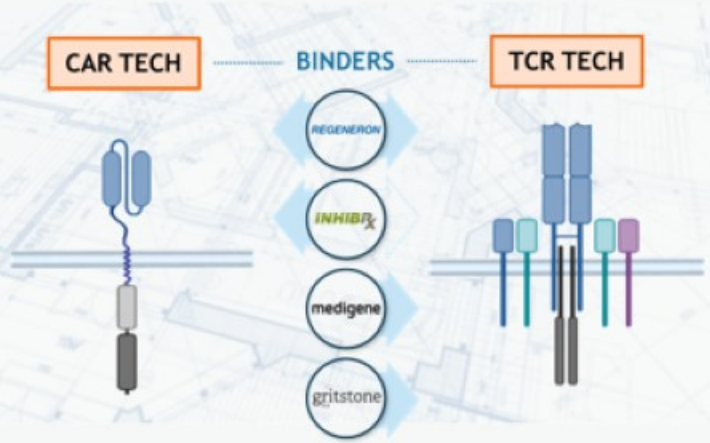
Solid Tumors | MAGE A4

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

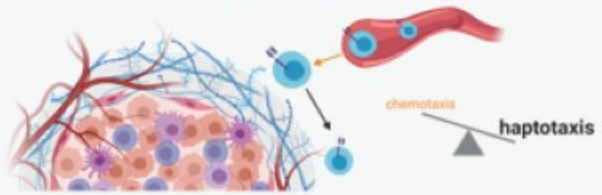
Tumor/Target Heterogeneity



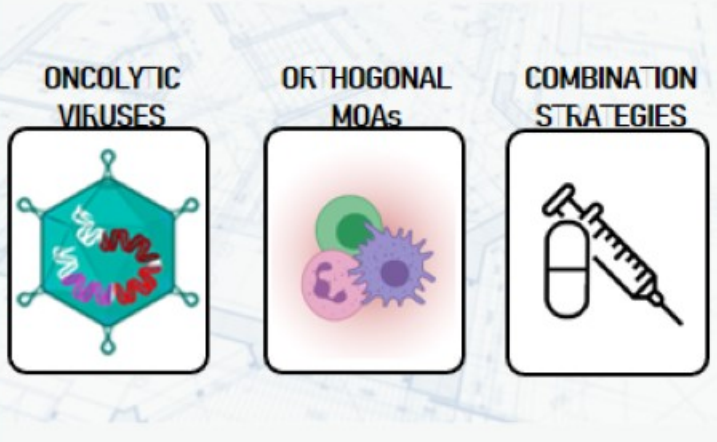
We achieve sensitive & multiplex targeting across the full range of target classes



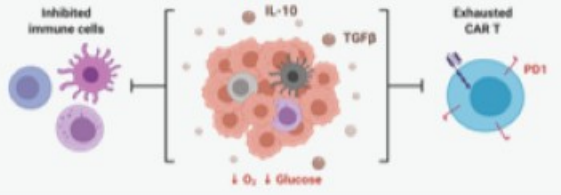
Tumor Infiltration Barriers



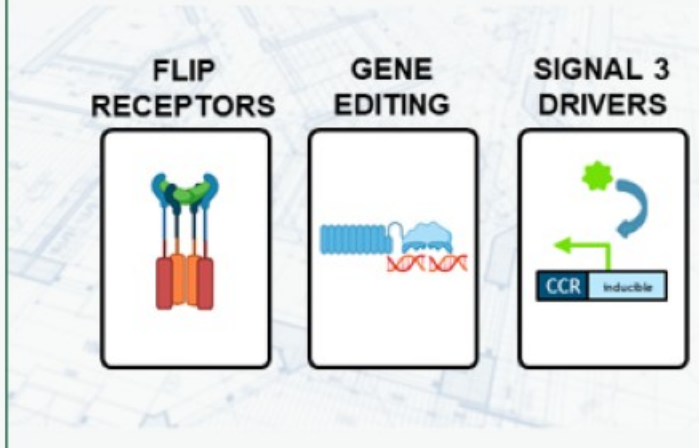
We disrupt the biological barriers to T cell infiltration and inflammation



Immunosuppressive TME



We convert suppressive signals to supportive ones, and re-engage innate immunity



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Our MAGEA4 solid tumor program is designed to empower TCR-engineered T cells by overpowering the suppressive TME

DREAM

Strive to create a product that:

- Targets MAGEA4-positive solid tumors with the intent to provide these patients with complete responses
- Empowers T cells to overcome a prominent defense mechanism within the immunosuppressive TME

DEVISE

How to get there:

- Devise a powerful cell therapy product designed to drive meaningful clinical responses
  - A TCR engineered to be highly potent for targeting solid tumor cells expressing HLA-MAGEA4 peptides
  - A flip receptor (CTBR12) that converts the immuno-suppressive effects of TGFβ into a potent stimulatory T cell signal

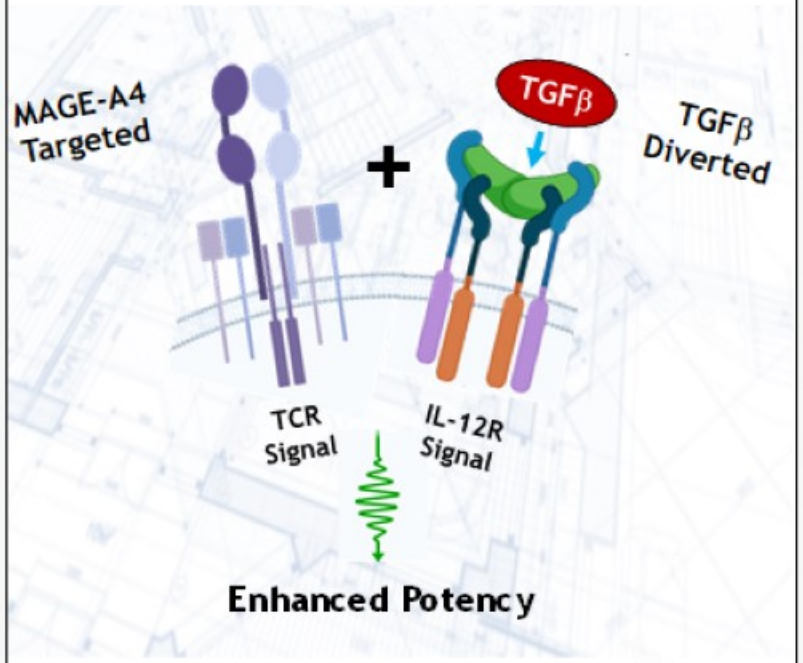
DELIVER

Progress on execution:

- Encouraging pre-clinical data: T cells expressing MAGEA4 TCR_CTBR12 clear tumors in an aggressive melanoma xenograft model
- PoC for CTBR12 flip receptor technology with broad applications across both CAR and TCR based solid tumors applications.

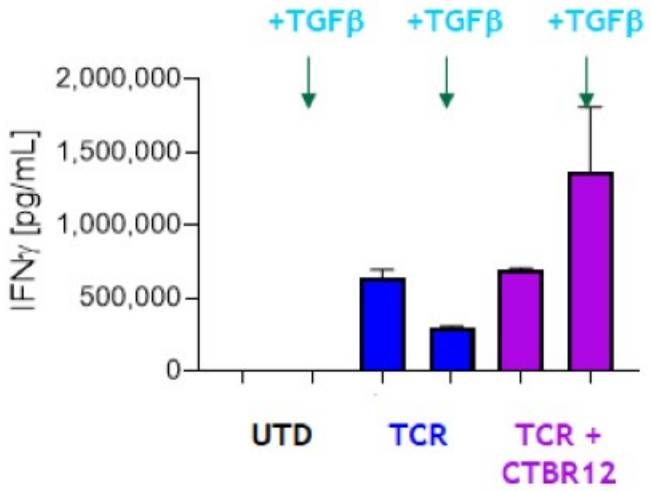
MAGEA4-CTBR12: Solid Tumors

Couple a potent MAGEA4 TCR with a TME signal conversion technology



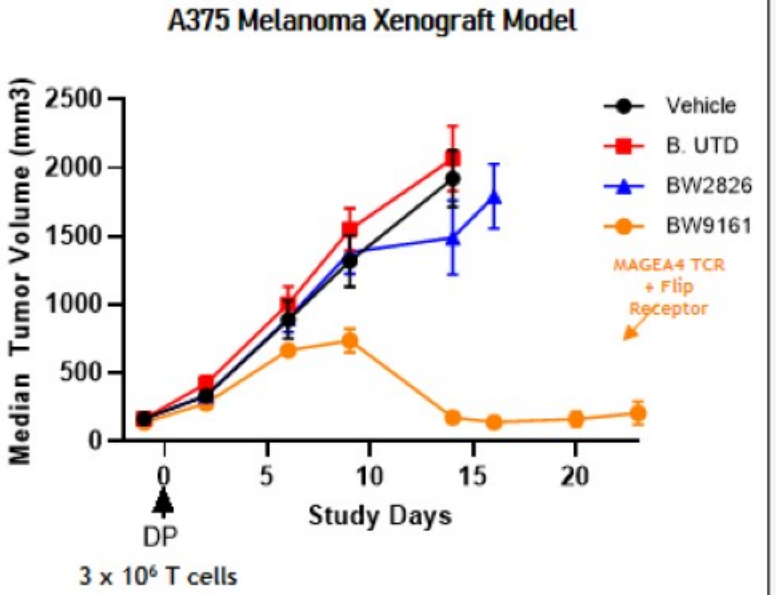
Can we enhance the potency of a TCR T cell using a TME signal conversion technology?

Our flip receptor technology converts the suppressive effect of TGFβ into a potent T cell activation signal



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

Complete tumor regression achieved with MAGEA4 TCR + TGFβ flip receptor

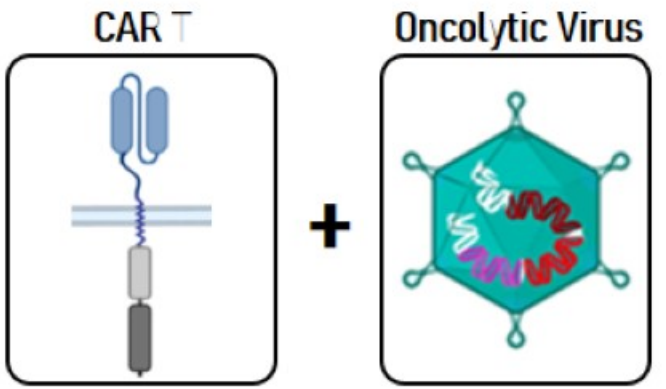


Winner of the 2021 *Journal for ImmunoTherapy of Cancer* Best Immune Cell Therapies and Immune Cell Engineering Paper Award!

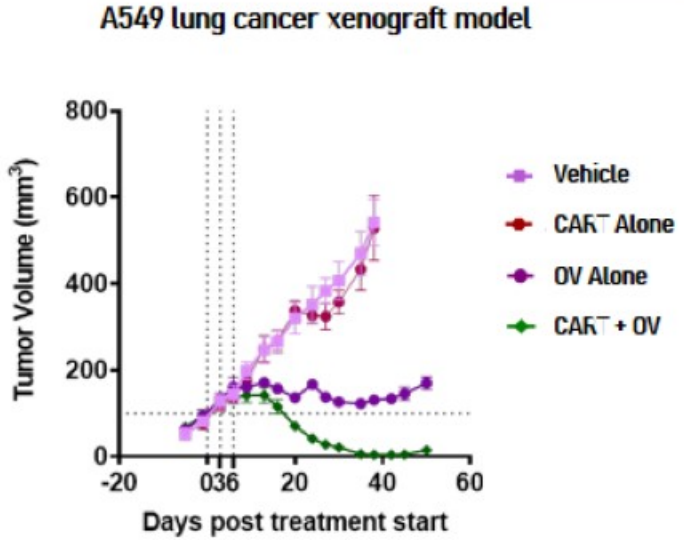
Systemic oncolytic virus delivery unleashes CAR T for solid tumor clearance

What if we could couple the power of CAR T technology with sustained reprogramming of the solid tumor microenvironment to overcome resistance to therapy?

CAR T cells combined with systemically delivered oncolytic viruses

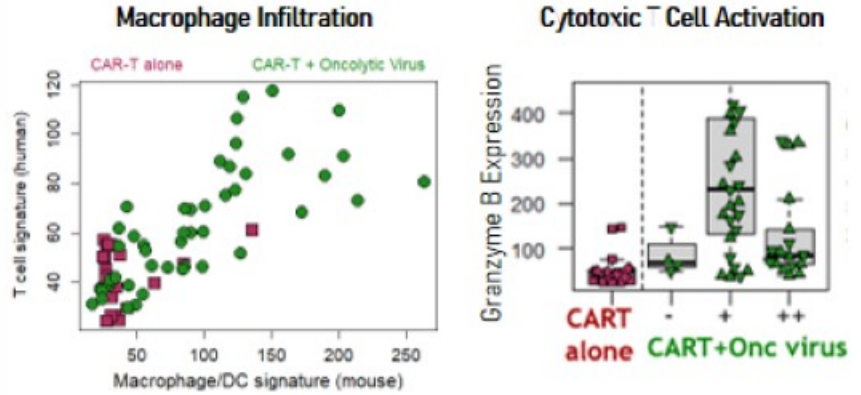


CAR T + oncolytic virus synergistically regress tumors

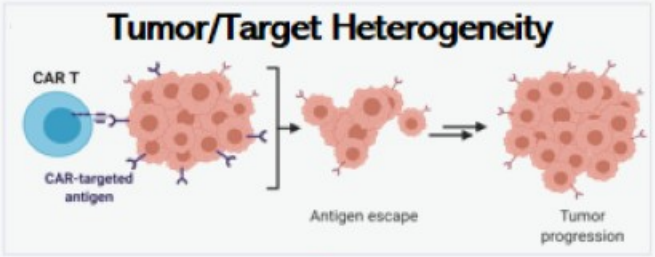


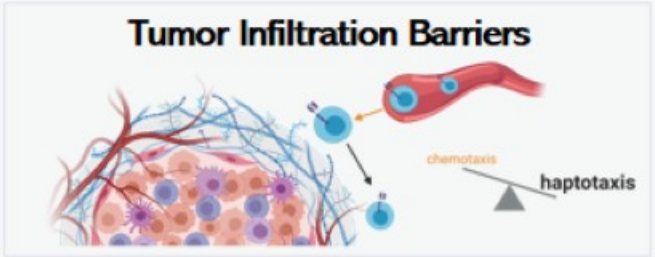
Oncolytic virus induces immune cell recruitment & activation into the TME

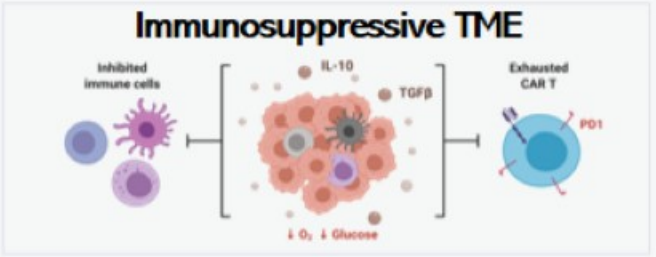
TME reprograming achieved



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







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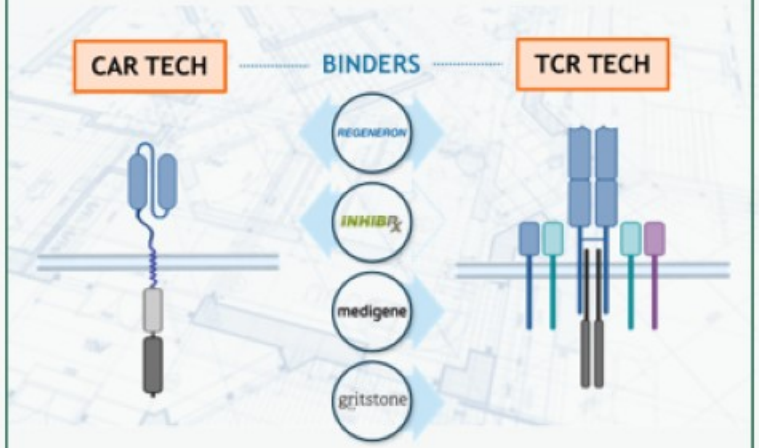

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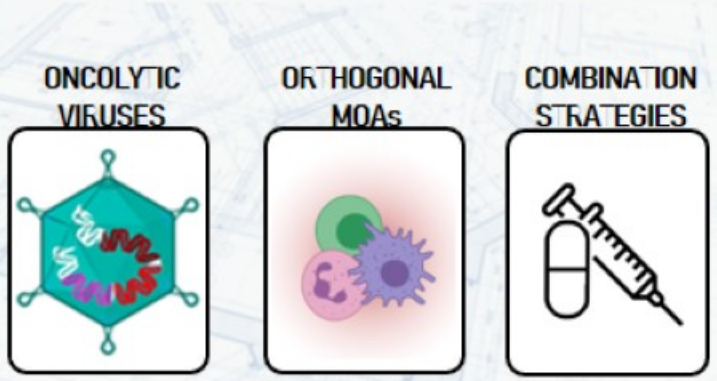

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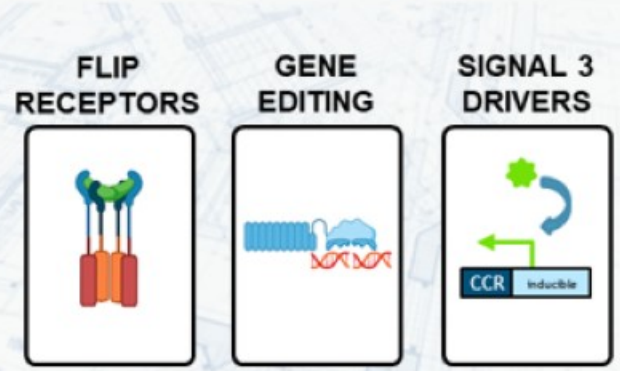

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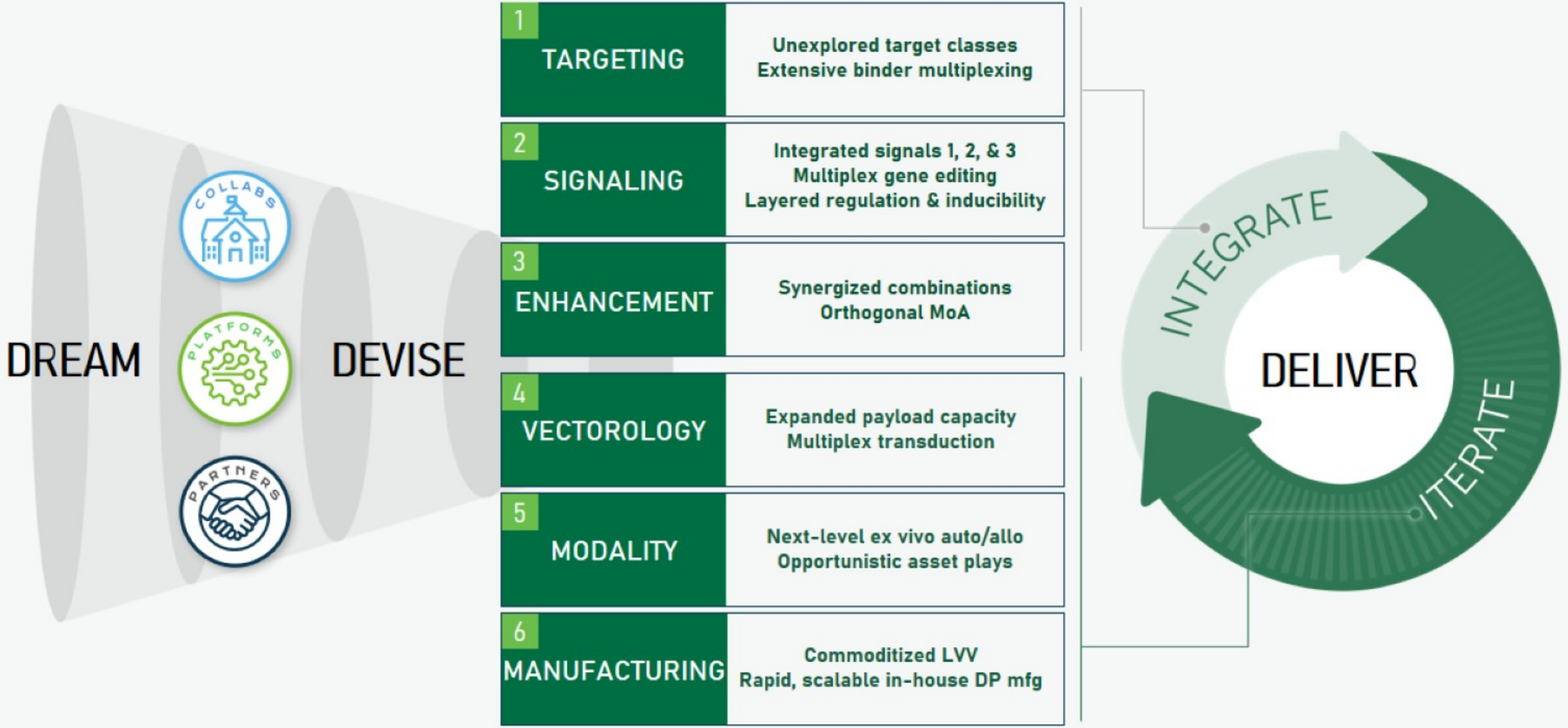
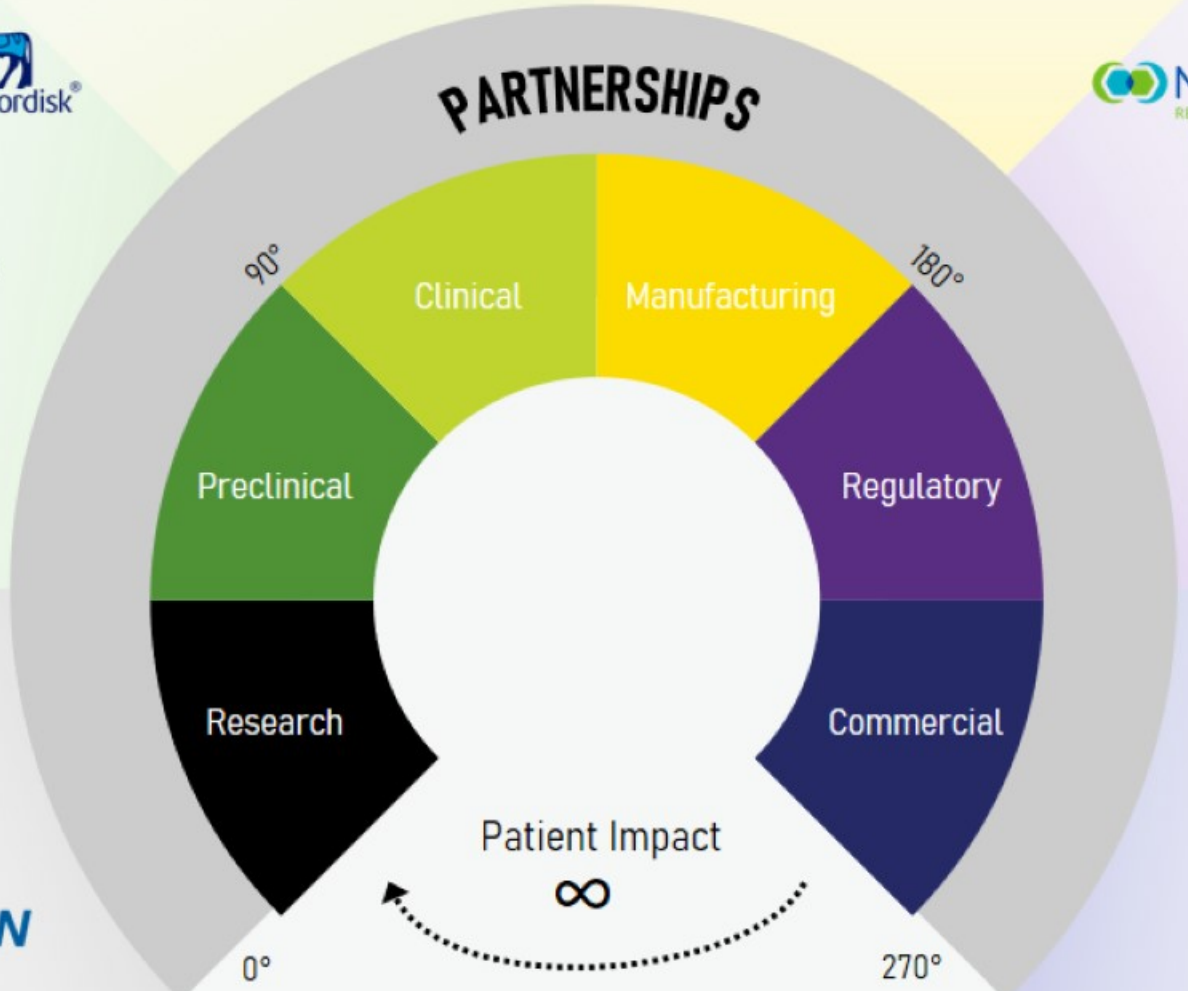
Manufacturing | Network

Dreaming, Devising, and Delivering on the future of cell therapy



Network effect: collaborating across the ecosystem to deliver for patients



2seventy's manufacturing network: poised to deliver

VELOCITY
Enable pipeline speed & decisions making to POC

INNOVATION
Multiply our reach, capacity & ability to innovate

CAPABILITY
Manufacturing partnerships defined by identical goals

Seattle Children's

TriLink BIOTECHNOLOGIES part of Maravai LifeSciences

Deliver an In-house clinical cell therapy manufacturing facility

- Under construction in our headquarters building, Cambridge, MA
- Ensures ownership of the process, analytics, execution, value creation
- Enables 'deep' integration of CMC with research and correlative sciences plus, flexibility to iterate

MINARIS REGENERATIVE MEDICINE

RESILIENCE

MOFFITT CANCER CENTER

Deliver "best-in-class" academic partnerships

- Robust academic relationships that allow us to advance our cutting-edge research into clinical development quickly
- Access to external innovation, programs, network

Deliver on game-changing industry partnerships

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

2seventy bio: a clear and differentiated strategy, well-funded to deliver

✓ *Strategy + Vision*

- Deliver ABECMA commercially and expand product opportunity
- Relentless innovation focus on product engine – ask/answer/learn & iterate

✓ *Products that Matter*

- ABECMA launch exceeding plan
- Innovative cell therapy candidates across broad indications
- 2 INDs 2021

✓ *Leadership + Team*

- New leadership team in place
- BOD retooling for oncology focus

✓ *Funding + Financial*

- $75M private stock offering (WholeCo)
- Resilience collaboration brings $110M upfront and $25M+ savings/year
- Anticipating approximately 24 months of runway at launch

Anticipate ~$975M Wholeco cash balance at time of split; 2seventy poised to launch with approximately 24 months of runway

Time is Life

CARE DEEPLY

The Why

The How

BE HUMAN

Q&A

Q&A Participants:

- Nick Leschly, Chief Kairos Officer
- Chip Baird, Chief Financial Officer
- Philip Gregory, Chief Scientific Officer
- Mike Certo, Senior Director, Genome Editing
- Kevin Chin, SVP, Oncology Clinical Development
- Susan Abu-Absi, SVP and Head of Technical Development & Operations
- Jordan Jarjour, VP, Oncology Research
- Cintia Piccina, SVP, Head of Commercial
- Steve Shamah, SVP, Oncology Research
- Melissa Price, SVP, Oncology Emerging Products