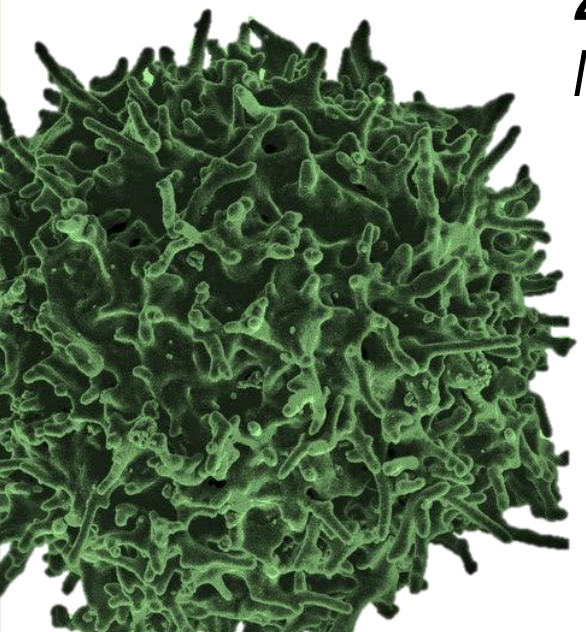
Unleash Time

2seventy bio company presentation

March 2023



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

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

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

STRATEGIC PRINCIPLES

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

COMMERCIAL PRODUCT & ROBUST PIPELINE

- **ABECMA,** the first approved CAR T therapy for multiple myeloma; own 50/50 US rights in partnership with BMS; $297M 2022 topline & growing to $470-570M anticipated revenue in 2023
- **Next Gen clinical programs:** bbT369 (B-NHL) and SC-DARIC33 (AML)
- **Strong early pipeline** targeting heme and solid tumors (MUC and more with REGN)

CLASS-LEADING CAPABILITIES

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

2seventy – At a Glance

BMS 50/50 US
$297M 2022 / $470-570M 2023*
Potential $2-3B US Peak

ABECMA
Commercial

ABECMA
Capacity Expansion
Predictable Delivery

ABECMA
Development

3rd Line K3 & FDA Submission
Initiation of Front Line K9

Unleash Curative Potential of T cells

People & Culture & Experience

Next Gen T cell Engineering Toolkit &
Clinical POC Insight Engine

Clinical Heme
B-NHL & AML

Horizon Dev
In-Vivo Editing (Novo)
In-Vivo CARs

Clinical Solid
MUC & More (REGN)

Suspension LVV Mftg
In-House Clinical DP Mftg (270-MPH)
Next Gen Mftg Improvements

ABECMA profitable in 2023**

Cash runway into 2026**

410 employees

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

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2022 – 2seventy's Foundational First Year

Company/Platform

Reset & rebalanced company size, shape & burn

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

Built in-house DP capability to support product engine

End of year runway into 2025 – **now extended to 2026****

ABECMA

- $297M U.S. topline revenue*
- Increased manufacturing capacity and reduced COGS
- Positive KarMMa-3 data & announced plans for KarMMa-9 NDMM study

Pipeline

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

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

2023 Goals and Long-Term Drivers

Longer-Term Drivers

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

2023 Goals

ABECMA

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

Pipeline

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

Net cash spend of $180-220M***

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

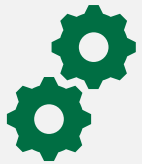
ABECMA® potential to be $2-3B* market opportunity in US driven by label expansion, increased capacity and double-digit market growth

2022

Launch and Lead

- Ongoing significant demand
- Increased capacity across supply chain
- RWE validates efficacy & safety even in difficult-to-treat populations
- KarMMa-3 primary endpoint met in 3L+ MM
- $297M topline US revenue*

2023



Scale and Invest

- Further scale drug product mftg capacity
- Sustain high quality patient and provider commercial delivery
- Potential US approval in 3rd line+ MM; planning for initiation of NDMM KarMMa-9 study
- ABECMA sustainably profitable**
- $470-570M anticipated topline US revenue**

2024-2030+

Potential and Proof

- Expand supply chain to meet expanding patient potential
- Improve profit margins
- Gain approval in NDMM
- Drive towards $2-3B* potential US peak sales

*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

Efficacy
Potential for deep and durable response

Availability
Slot availability in the relevant time frame

Safety
Predictable and manageable side-effect profile

Turn-around time
Speed to manufacturing and deliver patient cells

Real World Experience
Physician real-world experience with the product

Out of Spec Risk
Percentage of time cells are out of spec

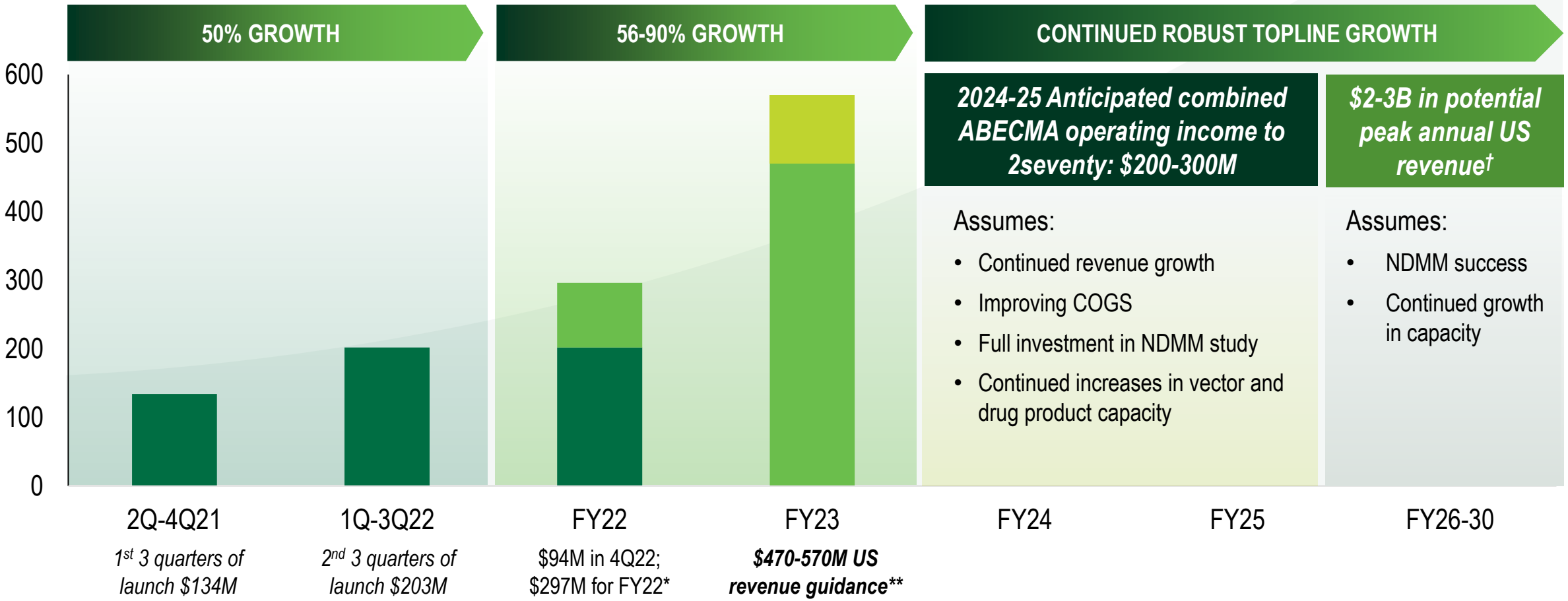
End-to-End Patient and Provider Experience

Select ABECMA Launch Metrics
Through Dec 2022

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

ABECMA Financial Outlook

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

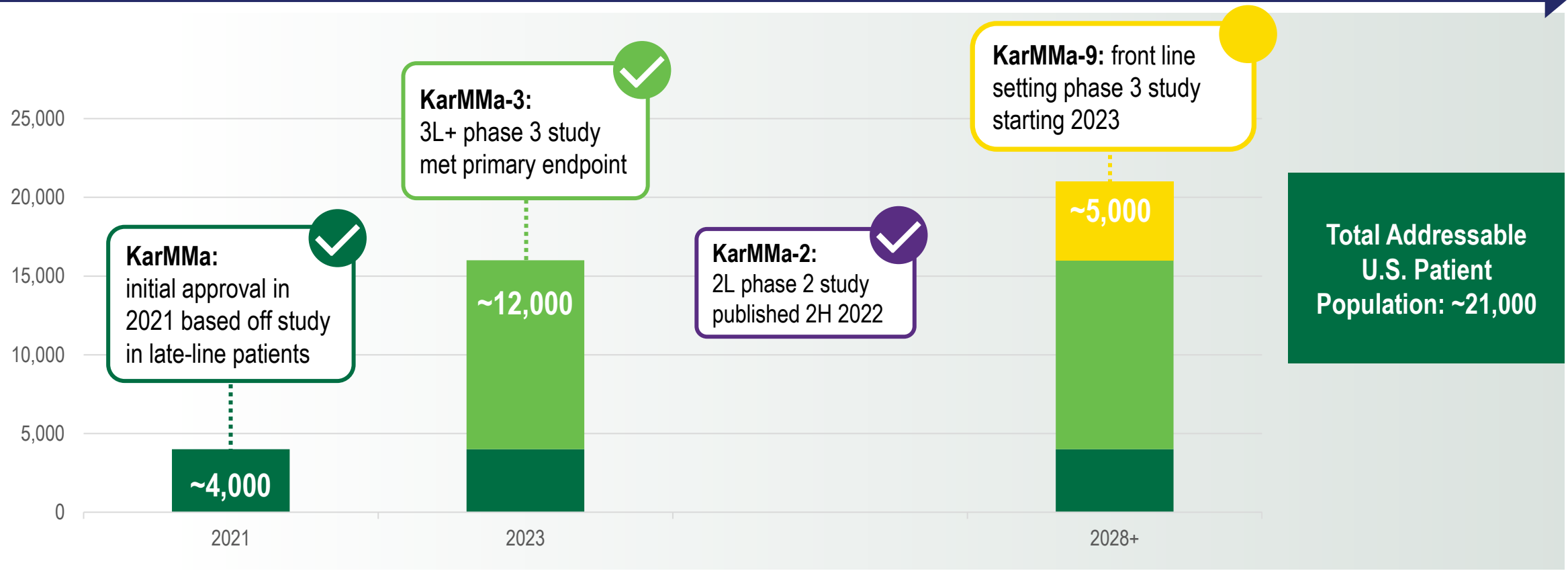


*US ABECMA profit and loss shared 50/50 between 2seventy and BMS as part of the collaboration agreement
**Anticipated revenue based on current operating plan
†based on continued label expansion into earlier lines of therapy and growth in manufacturing capacity

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

Addressable U.S. Patients on ABECMA label over time

Multiple Myeloma



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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)
- Planned BLA submission early 2023

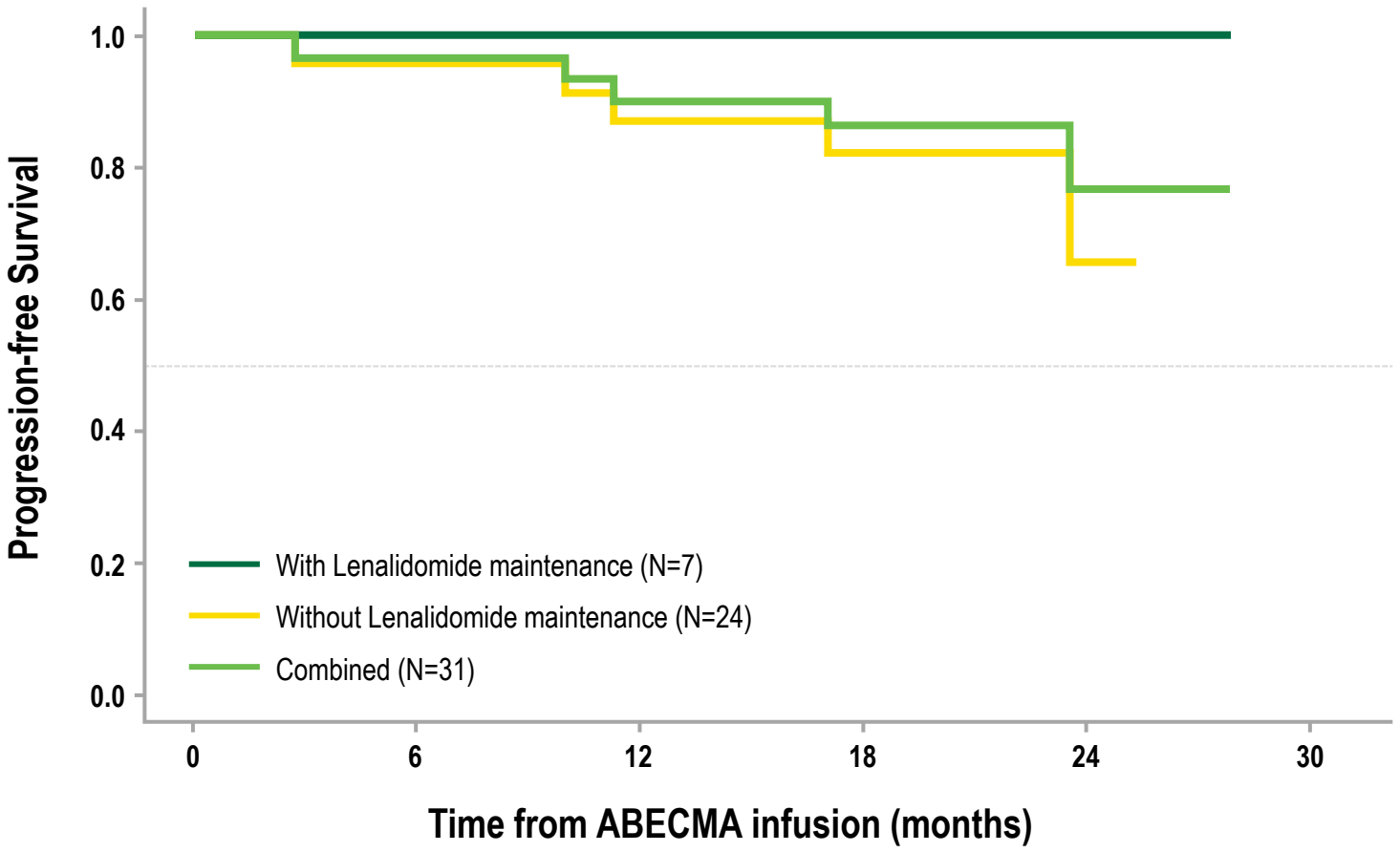
KarMMa-2: encouraging data in suboptimal ASCT responders support KarMMa-9 design

- 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-2 data supports potential of ABECMA in NDMM – suboptimal responders post transplant



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

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

Data cut: Feb. 2022

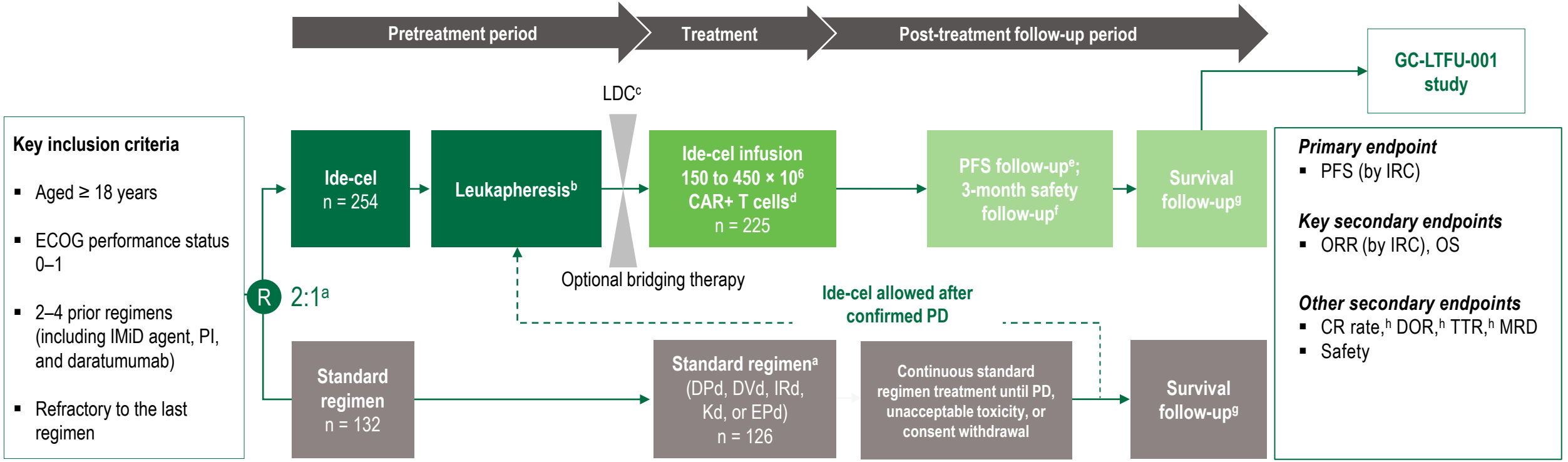
KarMMa-3 Summary

- 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 to support sBLA filing 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.

KarMMa-3 study design (NCT03651128)



Stratification factors

- Age (< 65 vs ≥ 65 years)
- Number of prior regimens (2 vs 3 or 4)
- High-risk cytogenetics (t[4;14], t[14;16], or del[17p]; yes vs absent/unknown)

Data cutoff: April 18, 2022

Median (range) duration of follow-up: 18.6 (0.4–35.4) months

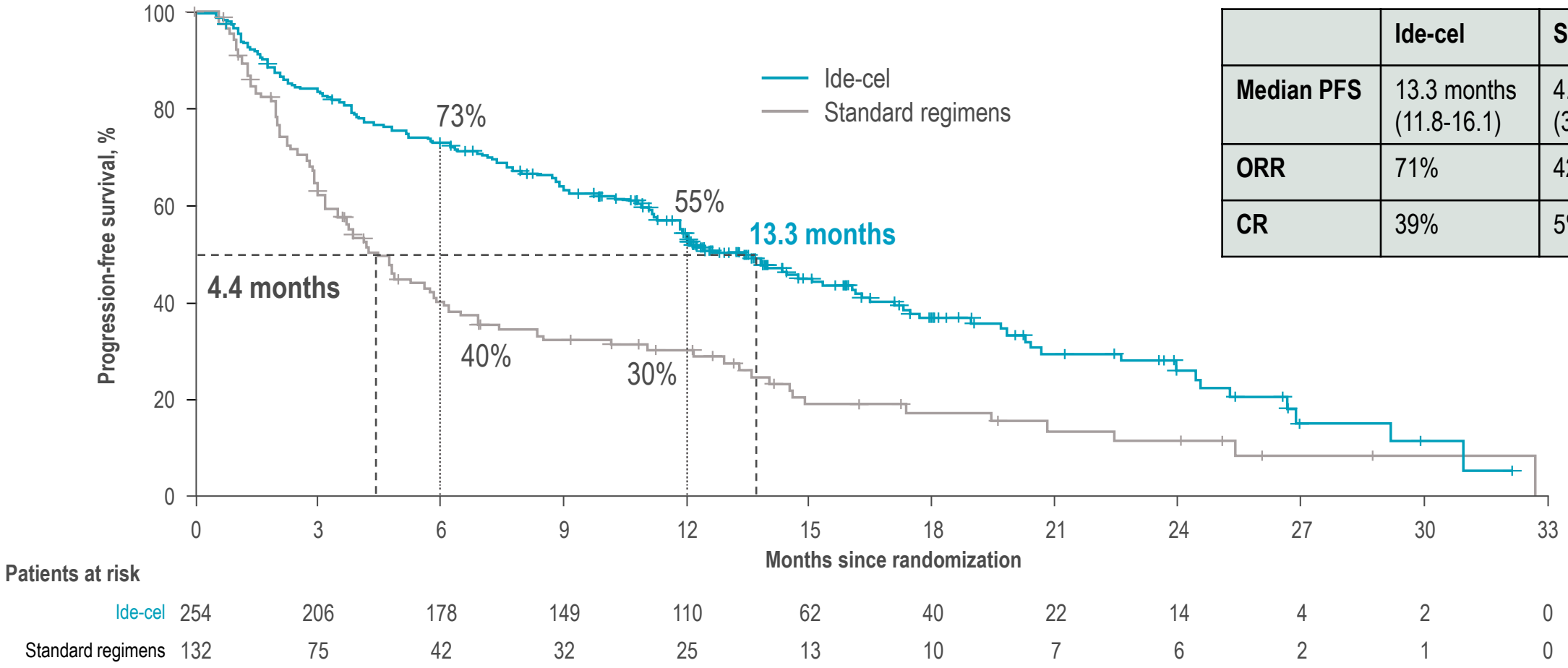
Ide-cel arm: treated population (patients who underwent either leukapheresis, bridging therapy, LDC, or ide-cel treatment) was used to assess AEs; safety population (patients who received ide-cel) was used to assess TRAEs, iiNT, and CRS; standard regimens arm: the treated and safety populations included those patients who received any treatment. [a]Based on most recent treatment regimen and investigator's discretion; [b]Up to 1 cycle of DPd, DVd, IRd, Kd, or EPd may be given as bridging therapy; [c]3 days fludarabine 30 mg/m^2 and cyclophosphamide 300 mg/m^2; [d]Doses ≤ 540 x 106 cells permitted; [e]Monthly for patients randomized to ide-cel for 24-months, then every 3 months until PD; [f]Patients randomized to standard regimens and received subsequent ide-cel therapy; [g]Every 3 months after PD until end of trial; 5 years after last patient randomized; [h]By IRC.
AE, adverse event; CR, complete response; CRS, cytokine release syndrome; DOR, duration of response; DPd, daratumumab/pomalidomide/dexamethasone; DVd, daratumumab/bortezomib/dexamethasone; EPd, elotuzumab/pomalidomide/dexamethasone; IRC, Independent Response Committee; IRd, ixazomib/lenalidomide/dexamethasone; Kd, carfilzomib/dexamethasone; LDC, lymphodepleting chemotherapy; MRD, minimal residual disease; PD, progressive disease; R, randomization; TRAE, treatment-related AE, TTR, time to response.

KarMMa-3 Baseline demographics and characteristics

Characteristic	Ide-cel (n = 254)	Standard regimens (n = 132)
Median (range) age, years	63 (30–81)	63 (42–83)
Sex, male, n (%)	156 (61)	79 (60)
Median (range) time from diagnosis to screening, years	4.1 (0.6[a]–21.8)	4.0 (0.7–17.7)
High tumor burden, n (%)[b]	71 (28)	34 (26)
Extramedullary disease, n (%)[c]	61 (24)	32 (24)
ECOG performance status score, n (%)[d]		
0	120 (47)	66 (50)
1	133 (52)	62 (47)
R-ISS disease stage, n (%)[e]		
I	50 (20)	26 (20)
II	150 (59)	82 (62)
III	31 (12)	14 (11)
Unknown	23 (9)	10 (8)
High-risk cytogenetics, n (%)[f]	107 (42)	61 (46)
del(17p)	66 (26)	42 (32)
t(4;14)	43 (17)	18 (14)
t(4;16)	8 (3)	4 (3)
1q gain/amplification, n (%)	125 (49)	51 (39)
Ultra-high risk cytogenetics, n (%)[g]	67 (26)	29 (22)
Previous autologous HSCT, n (%)	214 (84)	114 (86)

Baseline characteristics were generally balanced between treatment arms

KarMMa-3 Progression-free survival (ITT population)



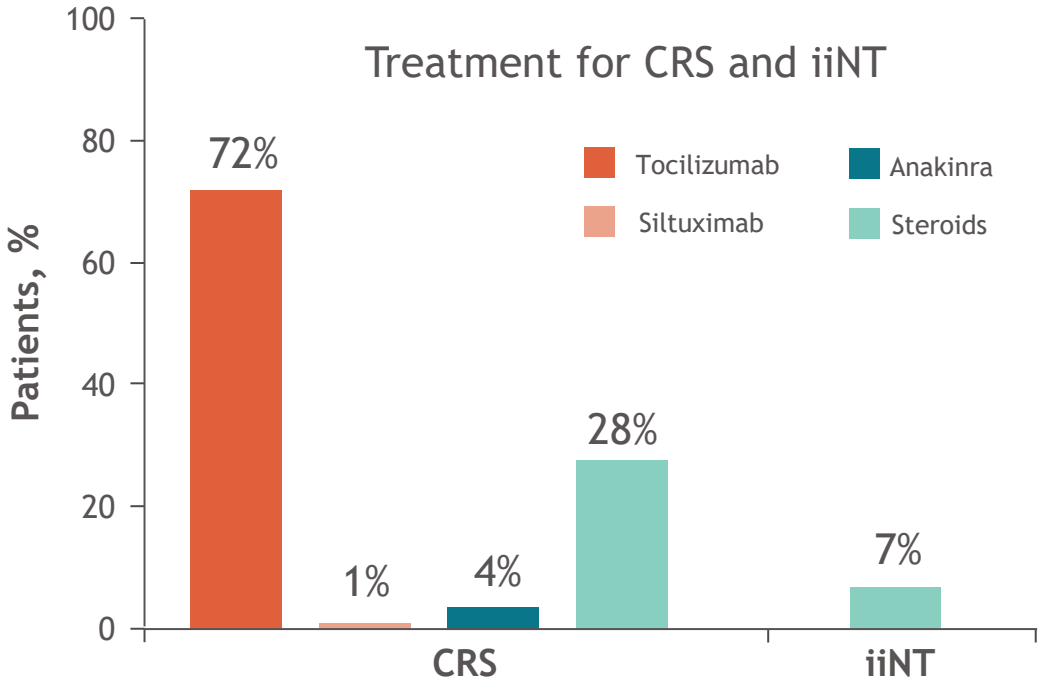
	Ide-cel	Standard
Median PFS	13.3 months (11.8-16.1)	4.4 months (3.4-5.9)
ORR	71%	42%
CR	39%	5%

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.

KarMMa-3 CRS and iiNT in patients treated with ide-cel (safety population)

	Ide-cel (n = 225)
CRS,[a] n (%)	
Any grade	197 (88)
Grade 3/4	9 (4)
Grade 5	2 (1)
Median (range) time to first onset, days[b]	1.0 (1.0–14.0)
Median (range) duration, days	3.5 (1.0–51.0)
iiNT,[c] n (%)	
Any grade	34 (15)
Grade 3/4	7 (3)
Grade 5	0
Median (range) time to first onset, days[b]	3.0 (1.0–317.0)
Median (range) duration, days	2.0 (1.0–37.0)



- No cases of CRS or iiNT were observed with standard regimen
- One of the grade 5 CRS events occurred after a decline in organ function[d] and 1 from concomitant grade 5 *Candida* sepsis
- Grade 2 encephalopathy, unrelated to ide-cel, was reported in 1 patient 317 days after ide-cel infusion, and was considered by the investigator to be related to worsening pneumonia and *C. difficile* colitis, not ide-cel
  - The next longest duration of onset to a neurotoxicity event was 46 days

The low incidence of high-grade (grade ≥ 3) CRS and iiNT was consistent with previous reports,[1,2] and resolved within a median of 3.5 and 2 days, respectively. No Parkinsonism was reported. Safety profile was consistent with previous studies.

iiNT, investigator-identified neurotoxicity; [a]CRS was graded according to modified Lee's criteria[3]; maximum-grade events are reported, patients could have > 1 event; [b]Time to first onset of CRS or neurotoxicity: first start date of CRS or neurotoxicity – infusion date + 1; [c]Includes immune effector cell-associated neurotoxicity syndrome reported by investigator as a neurological toxicity AE; [d]Acute myocardial infarction potentially related to anemia, and rapid atrial flutter, the patient died on day 6. ; 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

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.

Resilience
sLVV, significant increase in capacity
Commercial introduction in 2024

Thermo Fisher
Current commercial adherent LVV capacity

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 (idecabtagene vicleucel)
Multiple Myeloma [ABECMA]	BCMA	CAR T cell	BMS Partnership; Earlier Line Studies			3L+ potential approval 2023 NDMM study initiation 2023
AML-Pediatric [SC-DARIC33]	CD33	Drug-Regulated; CAR T cell (DARIC)	TSVT Owned; SCRI Collaboration			Patients Enrolling; Update mid 2023
B-NHL [bbT369]	Dual B cell targets	Dual-Targeted CAR T cell Signal Enhanced Gene Edited	TSVT Owned			Patients Enrolling; Update in 2023
Ovarian Cancer	MUC16	CAR T cell Pharmacologic Enhancements	REGN Collaboration		IND EOY 2023	
Solid Tumors	MAGE-A4	TCR T cell Potency Enhanced	REGN/JW Collaboration		IIT EOY 2023 (JW / China)	
AML-Adult [SC-DARIC33 Next-Gen]	CD33 + Undisclosed	Drug-Regulated CAR T cell Dual-Targeted Potency Enhanced	TSVT Owned			
Solid Tumors	Multiple	CAR / TCR T cell Potency Enhanced	Multiple TSVT Owned; Plus Regeneron Collab.			
Multiple Myeloma	Multiple	Multi-Targeted CAR T cell Potency Enhanced	TSVT Owned			
Additional Indications	Undisclosed	Multiple	Multiple TSVT Owned; Plus Novo Nordisk Collab.			

Product engine generating ~1+ INDs per year

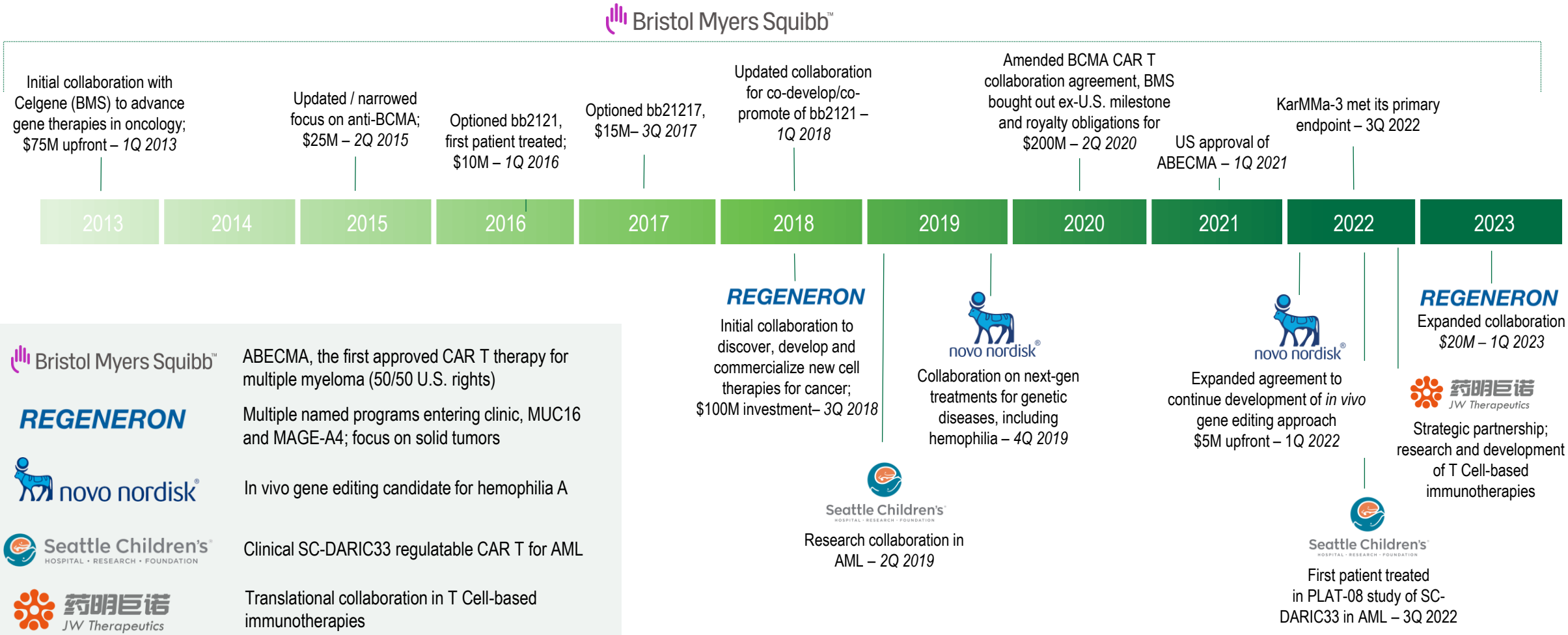
*Investigational New Drug application – IND;
Investigator Initiated Trial – IIT; Newly Diagnosed Multiple Myeloma – NDMM

Collaboration program

TSVT-owned program

Long-term partnership track record

New collaborations are a key focus over next three years



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

2seventybio

REGN Collaboration 2.0: The Combinatorial Potential of Engineered T cells

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

August 6, 2018

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

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

January 6, 2023

2seventybio

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

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

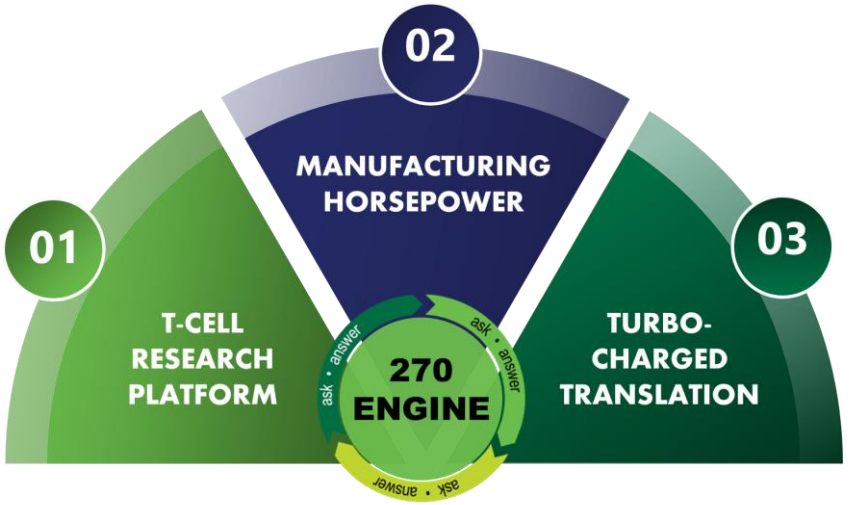
Regeneron Investing $20 million in 2seventy Equity; Regeneron to Fund 100% of Clinical Development Costs for Regeneron-Based Combination Clinical Trial Arms Through Approval

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

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

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

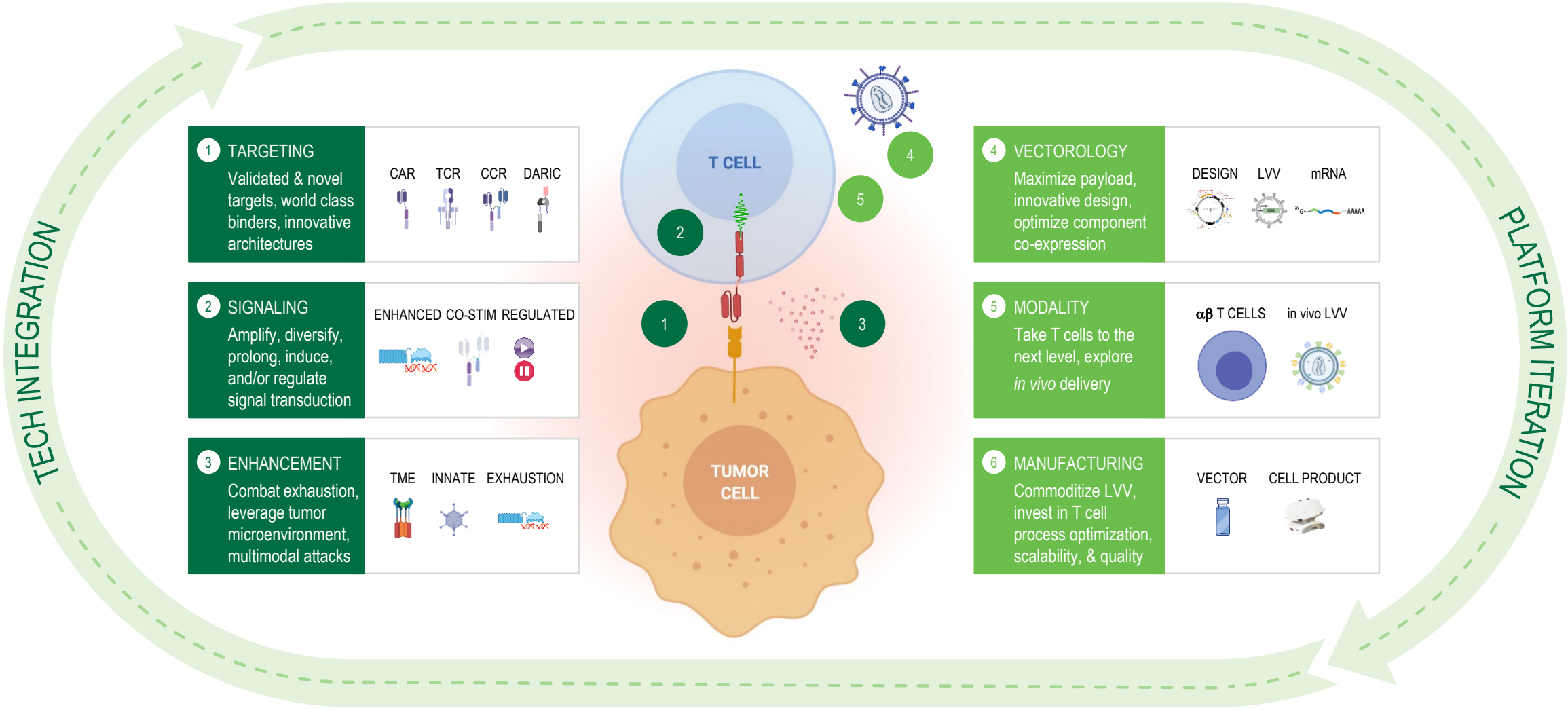
Research Platform
with transformative toolkit



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

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

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



2seventybio

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

Anticipated to be Operational By Mid 2023

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

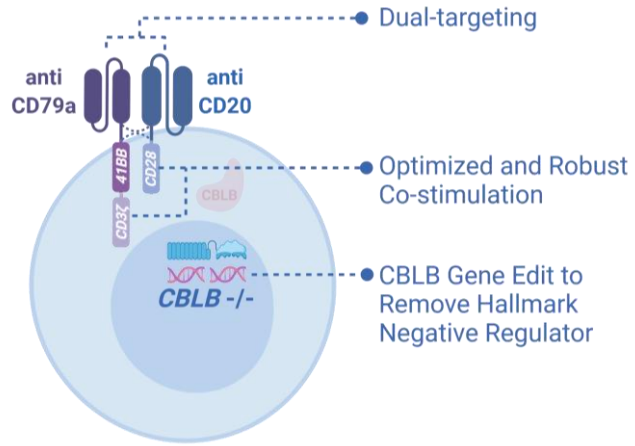
We identified four key challenges in current CAR T therapies

Challenges in B-NHL CAR T

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

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

bbT369

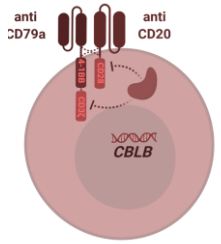


TARGET(S)	Dual target: CD20, CD79a
TECH	• Chimeric costimulatory architecture with split 41BB and CD28 • *CBLB* gene edit for expansion, antigen sensitivity, performance
TARGET INDICATION	B-NHL
STATUS	Ph1 Trial enrolling
PARTNER	2seventy owned

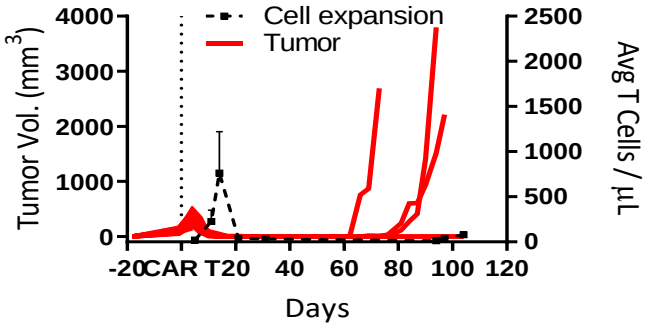
- **Designed to address outstanding need in B-NHL –** we believe bbT369 has the potential to increase response rate and durability of response for a larger fraction of patients.
- **Novel combination of antigens to address antigen escape:** Targets CD79a and CD20 – B cell restricted antigens strongly 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

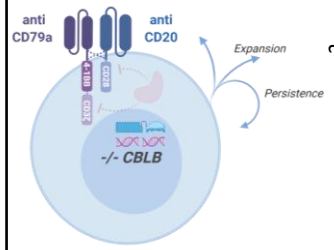
Dual CAR-CCR & bbT369 CAR T cell comparison in Toledo mouse model



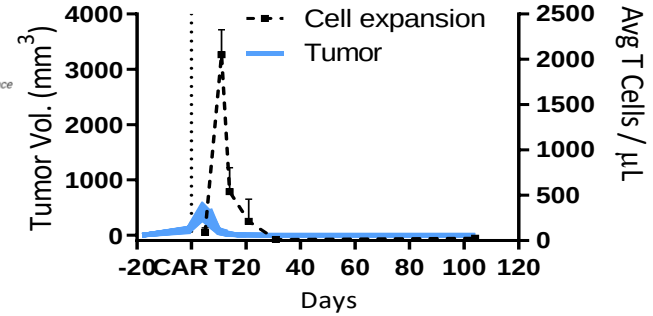
CD79a/CD20 Dual CCR CAR



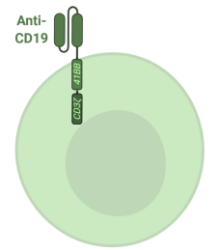
Vs.



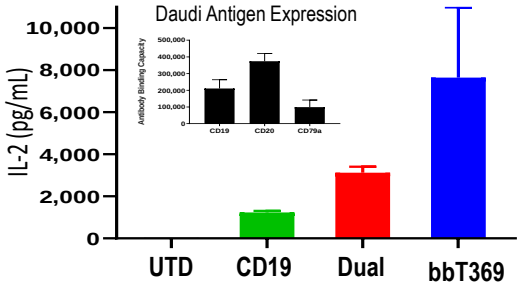
bbT369



bbT369 Out-Performs CD19 CAR in Daudi Tumor NSG Mouse Models



CD19



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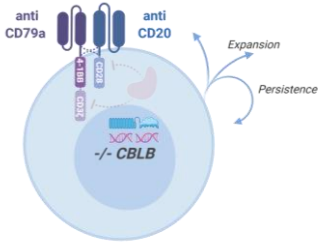
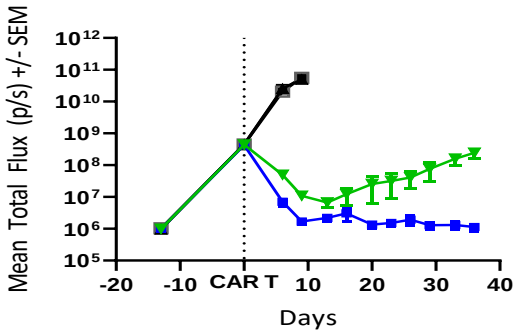


bbT369

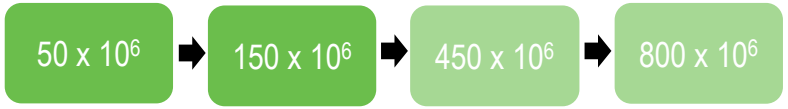


2seventybio

CRC-403 study in B-NHL open and enrolling

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

bbT369 Dose Levels for CRC-403 BOIN dose escalation



STUDY STATUS

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

Key Questions / Features

QUESTIONS

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

FEATURES

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

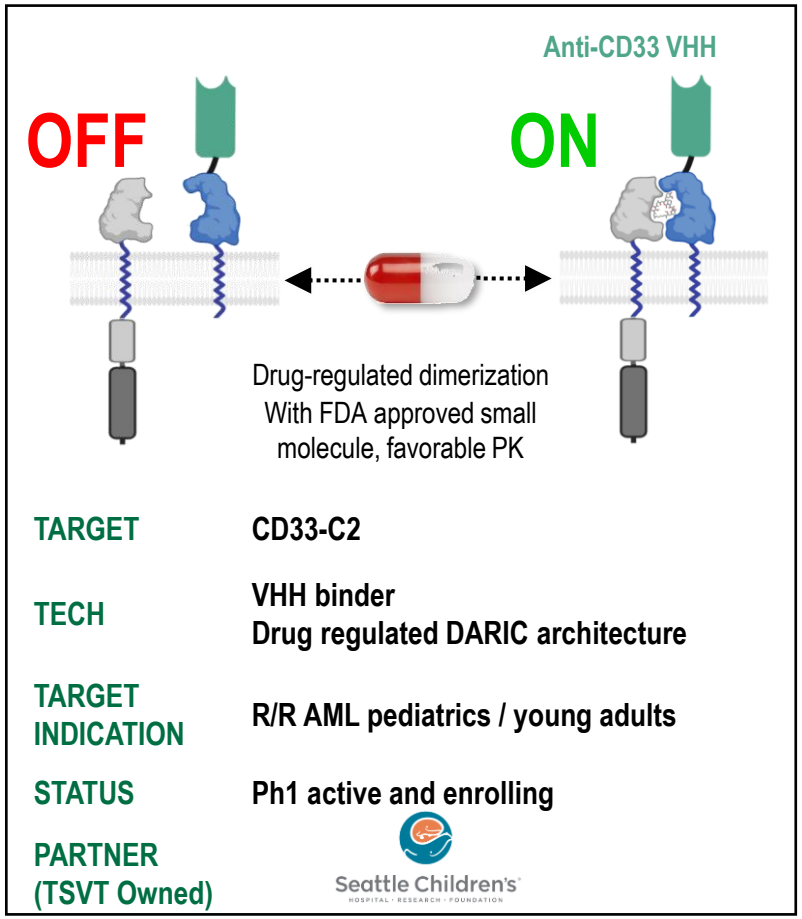
CRC-403 Ph1 dose escalation in B-NHL is open and enrolling, initial data expected in 2023

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

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

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

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



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

➢ ***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

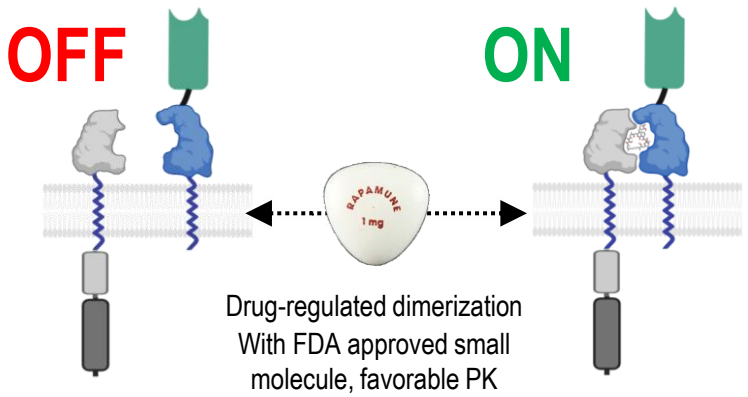
➢ ***CD33: a clinically validated AML target***

- 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

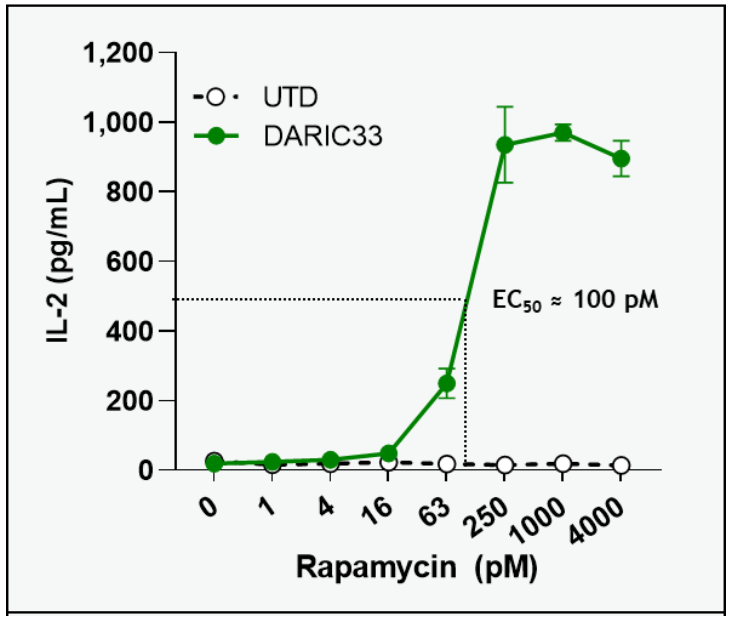
SC-DARIC33

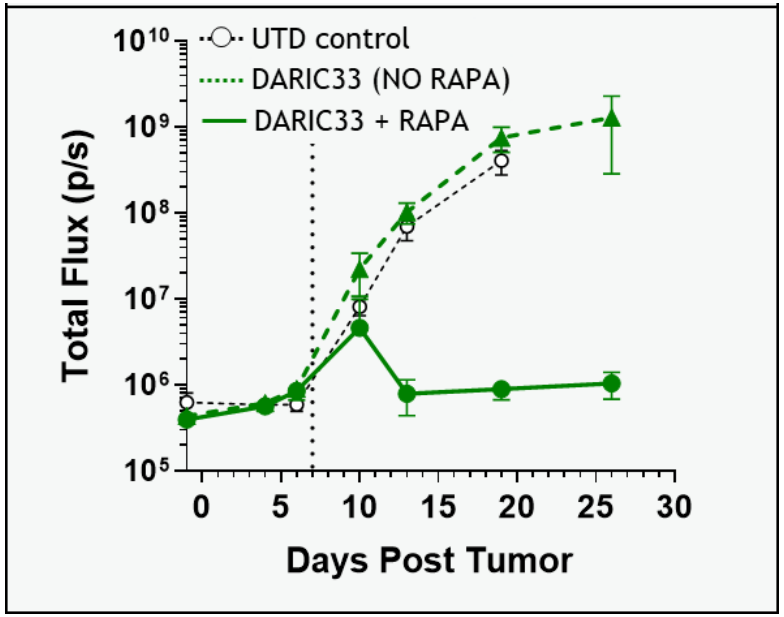
DARIC = Dimerizing Agent Regulated Immunoreceptor Complex



Drug-regulated dimerization
With FDA approved small molecule, favorable PK

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





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

Phase I study (PLAT-08) open and enrolling

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

STUDY STATUS

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

Key Questions / Features

QUESTONS

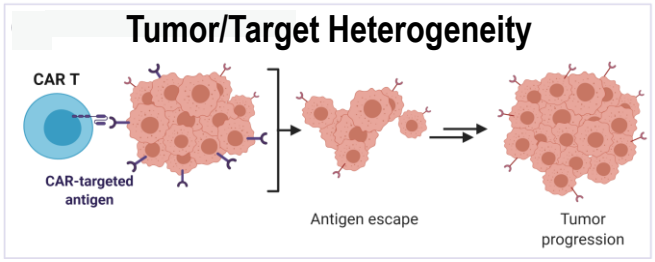
- Do SC-DARIC33 T cells engraft & show activity vs CD33+ve cells?
- Is SC-DARIC33 safe and does it drive a clinical response?
- Can SC-DARIC33 deactivation enable myeloid recovery?

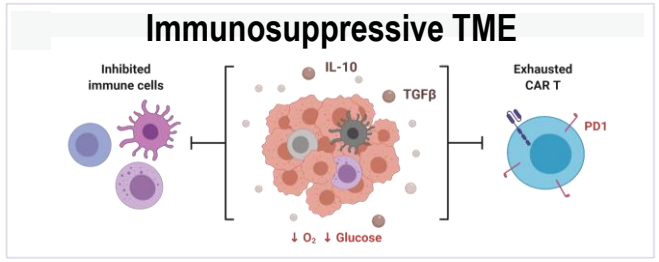
FEATURES

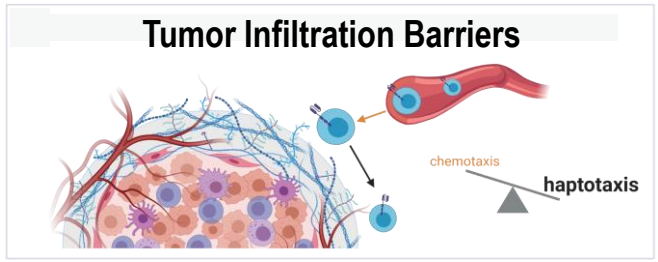
- First in human application of 2seventy bio's regulatable CAR T cell technology (DARIC)
- First application of a licensed INHIBRX VHH binder in CAR T format targeting a conserved domain of CD33
- Myeloid disease learnings
- Provides platform for NextGen multiplex CAR T cells
- Establishes CD33 targeting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

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

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

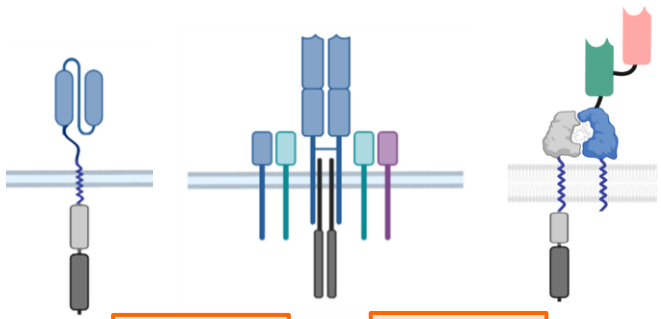






We seek to achieve sensitive & multiplex targeting across the full range of target classes

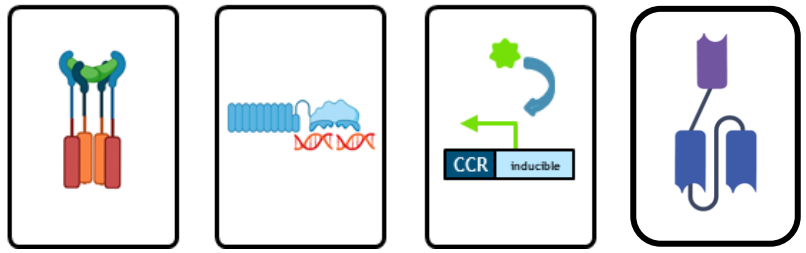
CAR TECH | TCR TECH | NEXT GEN



ATOMIC | RESET

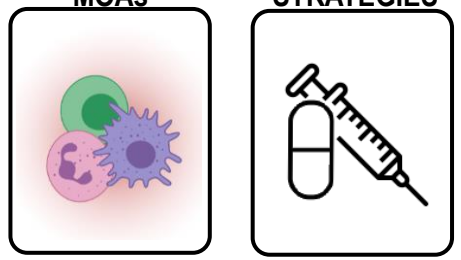
We seek to convert suppressive signals to supportive ones, and re-engage innate immunity

FLIP RECEPTORS | GENE EDITING | SIGNAL 3 DRIVERS | ENGAGERS



We seek to disrupt the biological barriers to T cell infiltration and inflammation

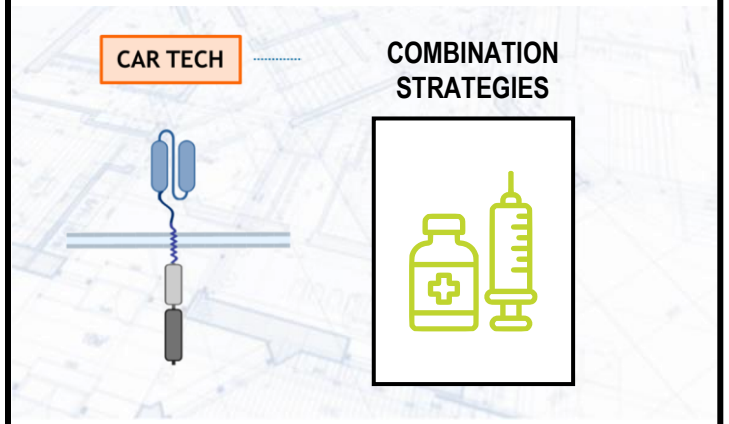
ORTHOGONAL MOAs | COMBINATION STRATEGIES



Created with BioRender.com

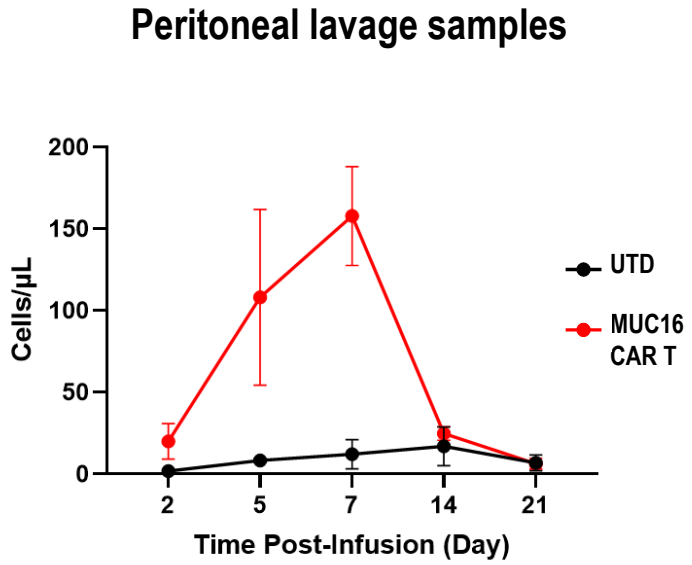
MUC16 / Ovarian cancer program: designed to exploit the power of CAR T + pharmaceutical combination strategies to unlock deep responses

Ovarian Cancer MUC16 CAR T Combo

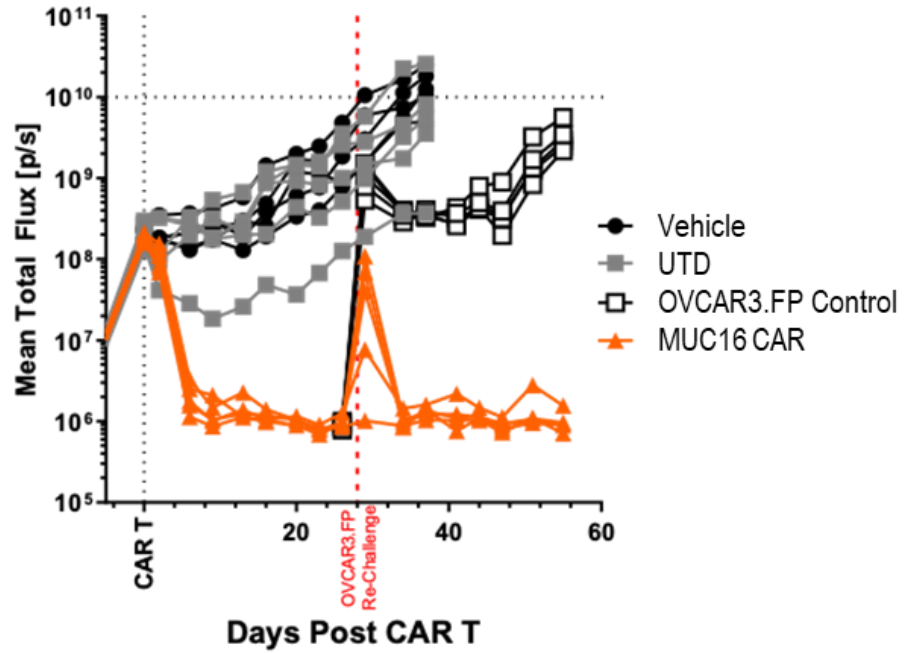


TARGET(S)	MUC16
TECH	CAR targeting prevalent MUC16 membrane-retained fragment
TARGET INDICATION	Solid Tumor (Ovarian)
STATUS	2023 IND Submission
PARTNER	REGENERON

MUC16 CAR T traffics to and expands at the tumor site



MUC16 CAR T displays robust activity in tumor rechallenge mouse model



2seventybio

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

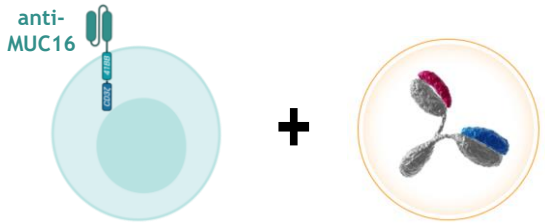
Alison Crawford*, Lauric Haber, Marcus P. Kelly, Kristin Vazzana, Lauren Canova, Priyanka Ram, Arpita Pawashe, Jennifer Finney, Sumreen Jalal, Danica Chiu, Curtis A. Colleton, Elena Garnova, Sosina Makonnen, Carlos Hickey, Pamela Krueger, Frank DelFino, Terra Potocky, Jessica Kuhnert, Stephen Godin,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

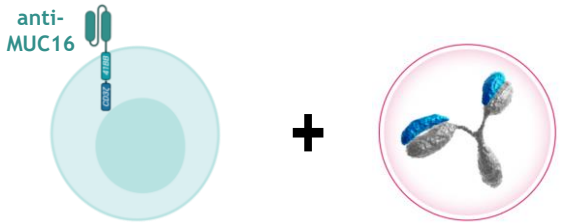


Drive a more potent CAR T cell response through signal 2 activation

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

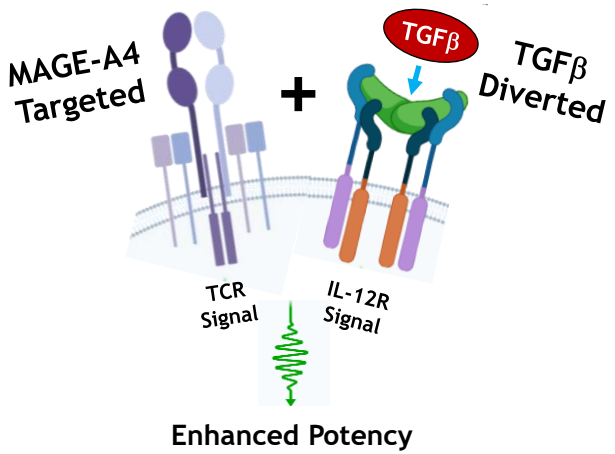
Robust toolbox with the potential to unlock deep responses in Ovarian Cancer

REGENERON

2seventybio

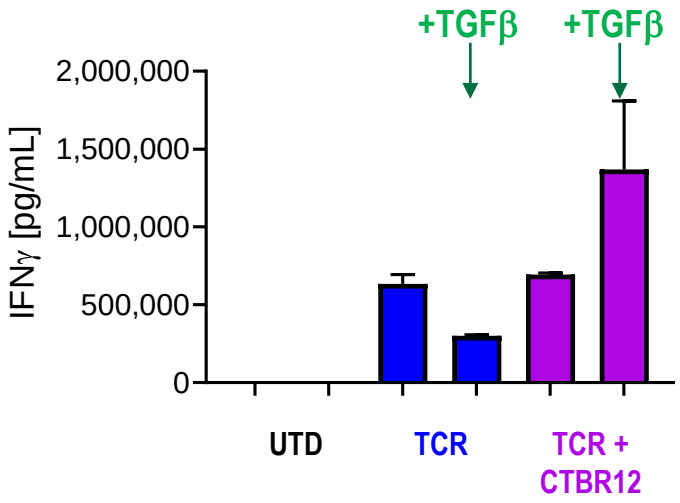
MAGE-A4 Expressing Solid Tumor Program: A powerful MAGE-A4 TCR potency enhanced with a "flip" receptor to neutralize TGFβ

Solid Tumor MAGE-A4 TCR-T Cell Therapy

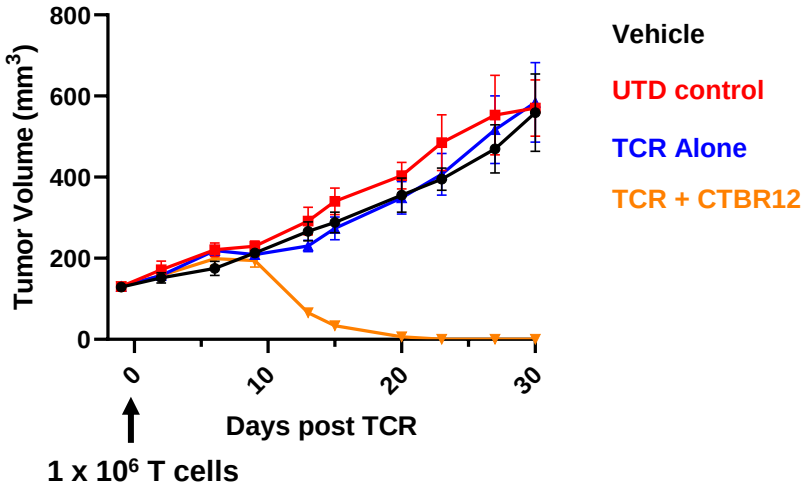


TARGET(S)	MAGE-A4 (HLA-A*02)
TECH	• MAGE-A4 directed TCR • CTBR12 TGFβ flip receptor
TARGET INDICATION	Solid tumors
STATUS	Preclinical
PARTNERS	REGENERON medigene 药明巨诺 JW Therapeutics

CTBR12 converts TGFβ into an activation signal



CTBR12 enhances MAGEA4 TCR anti-tumor activity

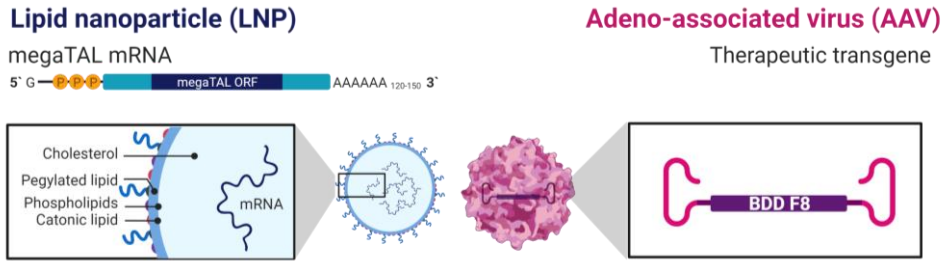


- Lead candidate demonstrates TGFβ signal conversion and potent tumor control in a lung xenograft mouse model
- Potential IIT in China (JW Therapeutics) by end of 2023

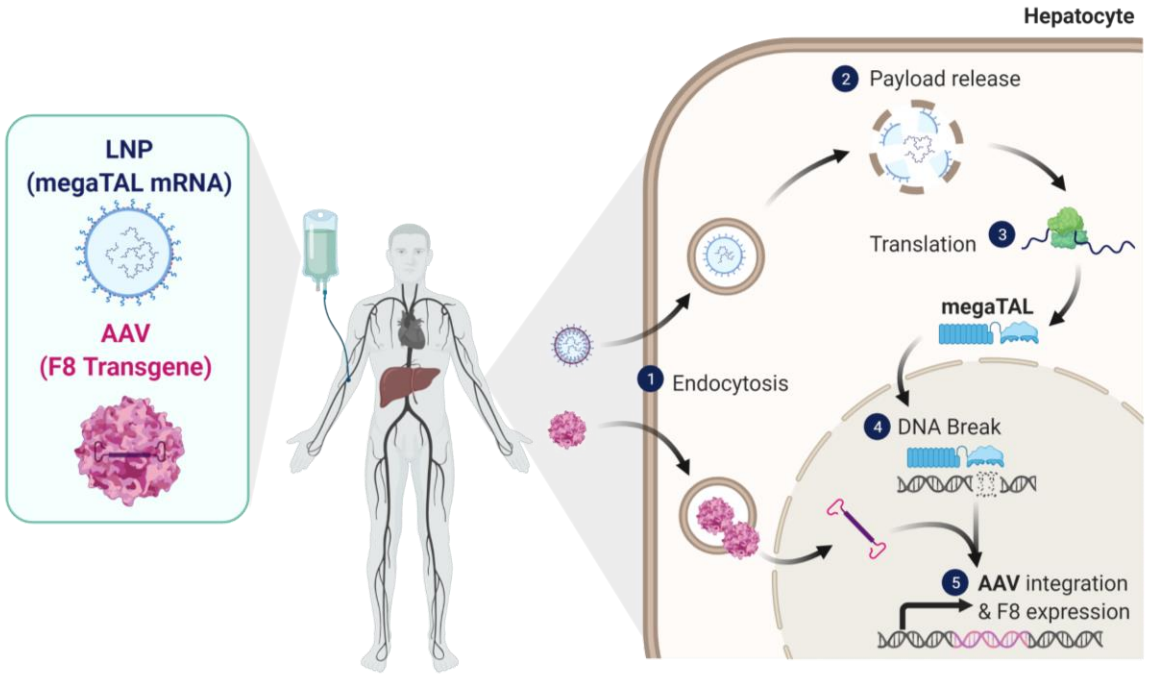
Journal for ImmunoTherapy of Cancer 2021;9:e002035 (25 March 2021)

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



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



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

2seventy team

Leadership

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

Chip Baird
Chief Financial Officer

Steve Bernstein, M.D.
Chief Medical Officer

Teresa Jurgensen, J.D.
SVP, General Counsel

Nick Leschly
Chief Kairos Officer*

Melissa Price
SVP, Development Operations & Portfolio Strategy

Philip Gregory, D. Phil.
Chief Scientific Officer

Jenn Snyder
SVP, Corporate Communications

Kathy Wilkinson
Chief People Officer

Board of Directors

Sarah Glickman
Criteo

Ramy Ibrahim, M.D.
BIT.BIO

Dan Lynch
Board Chair

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

Nick Leschly
Chief Kairos Officer

Wei Lin, M.D.
Erasca

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

Denice Torres, J.D.
From Johnson & Johnson

+ ~410 awesome timekeepers

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

thank you