23 de octubre de 2024

STAb-T19, a novel autologous T cell immunotherapy for the treatment of CD19 positive B-cell Acute Lymphoblastic Leukemia and B-cell Non-Hodgkin Lymphoma

STAb Therapeutics

Carolina Pola, PhD

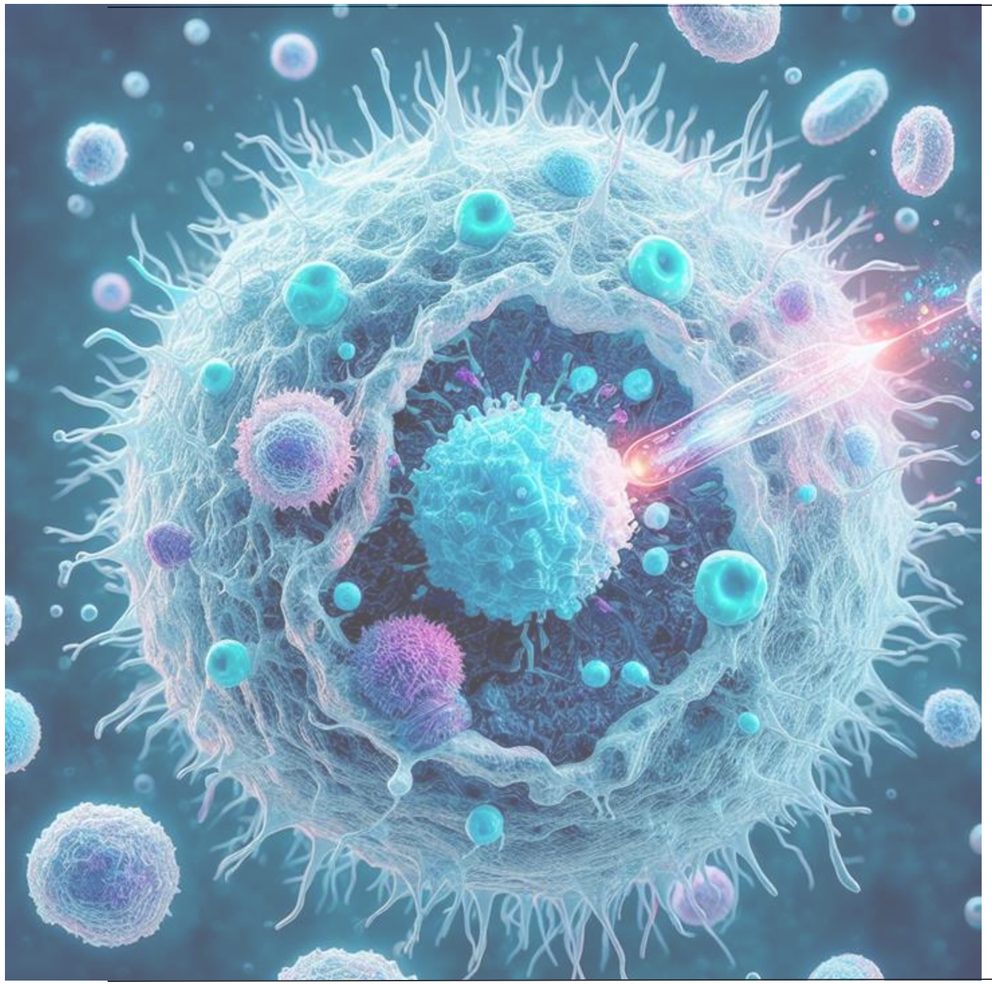
Content

RE-ARMING THE IMMUNE SYSTEM IN CANCER

STAb-T CELLS - a Next Generation T Cell Immunotherapy

STAb Therapeutics

MILESTONES



1. **Pre-seed 250K and non-dilutive funding** in 2023
2. **CEO hired** in December 2023
3. Exclusive **license for IP to cover STAb-T Products**
4. Preclinical validation of **STAb – T19 & STAb-TBCMA**
5. **Pipeline consolidation**
6. **680K € CPP non-dilutive grant to develop STAb-TS03 in solid tumor**
7. **2.4 Mill € in grants from ISCIII** for clinical trials
8. **Seed fundraising ongoing** in 2024
9. Launch of **phase 1 trial for STAb – T19** in Q1 2025
10. Launch of **phase 1 trial for STAb – TBCMA** in Q2 2025

STAb Therapeutics

ORGANIZATION 2024

CEO

Dr. Carolina Pola

Carolina is a PhD in molecular biology by NYU. She brings more than 15 years of experience in translational research, biotechnology and early stage-company development.

Co-founder & CSO

Dr. Belén Blanco

Belén brings more than 20 years of translational research in the immunotherapy field. She has developed the STAb platform and leads the scientific strategy.

CAM Research Assistant
Elena Barba

CAM Industrial PhD
Lucía Rivas

C0-founder & President of the SAB

Dr. Luis Álvarez-Vallina

Luis is a world-renowned leader in cancer immunotherapeutics. He leads a Unit focused on understanding the molecular and cellular mechanisms of cancer immune escape for designing next-generation cancer immunotherapies. He has developed STAb T cell as a novel cancer immunotherapy strategy.

SCIENTIFIC ADVISORY BOARD

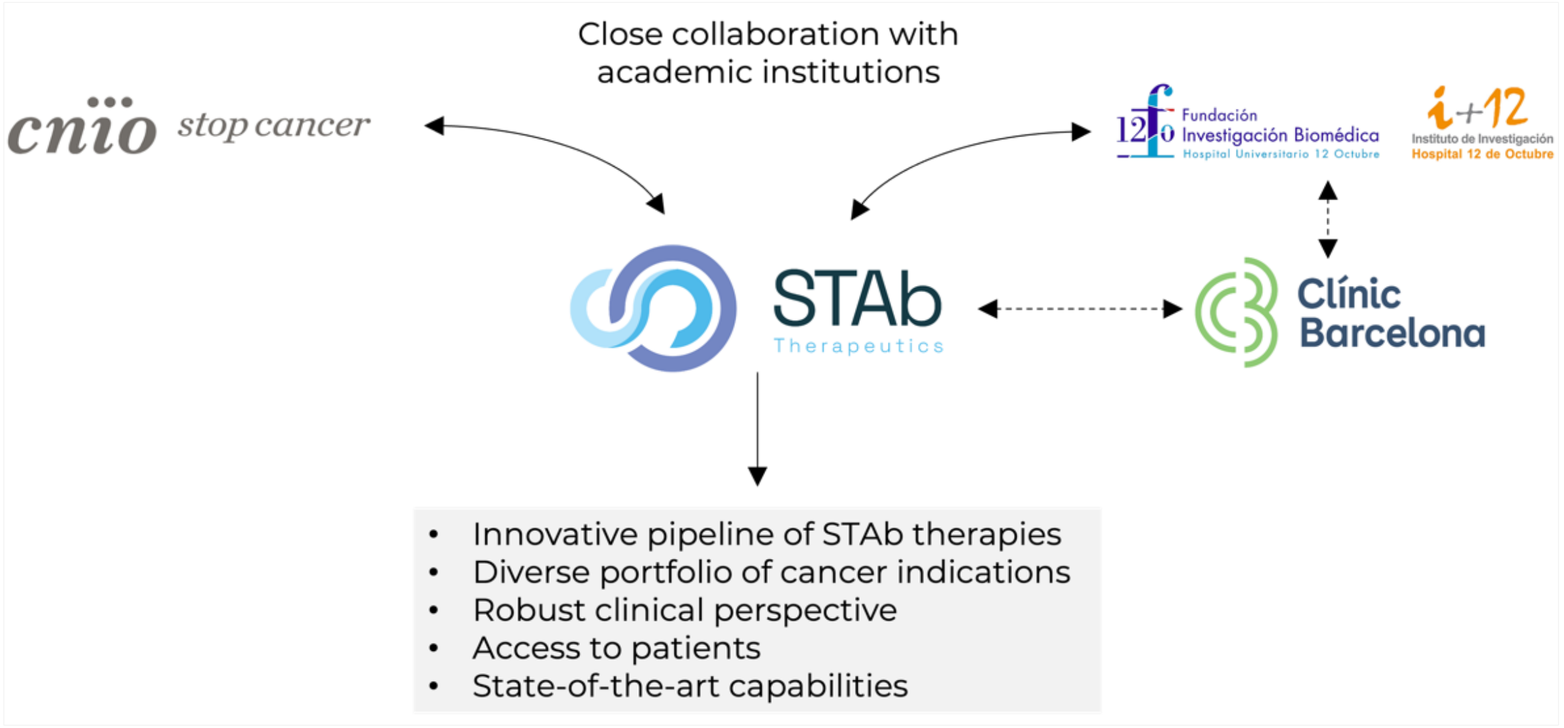
Dr. Joaquín Martínez
Co-founder & SAB member
Head of Hematological Oncology, H12O & PI at CNIO
Recognized MM clinical expert

Dr. Luis Paz-Ares
Co-founder & SAB member
Head of Medical Oncology, H12O & PI at CNIO
Recognized SCLC clinical expert

Dr. Richard Vile
SAB member
Professor of Immunology, Mayo Clinic

STAb Therapeutics

OUR SUPPORTERS & COLLABORATORS



OTHER COLLABORATORS

Universidad Complutense Madrid

Instituto de Investigación Contra la Leucemia Josep Carreras

Investigación Puerta de Hierro

CBM Severo Ochoa Centro de Biología Molecular CSIC UAM

leadartis molecular engineering for health

Cris contra el cáncer

Instituto de Salud Carlos III

Gobierno de España Ministerio de Ciencia e Innovación

deeptechMadrid fundación para el conocimiento madrid

healthstart madrid

STAb Therapeutics

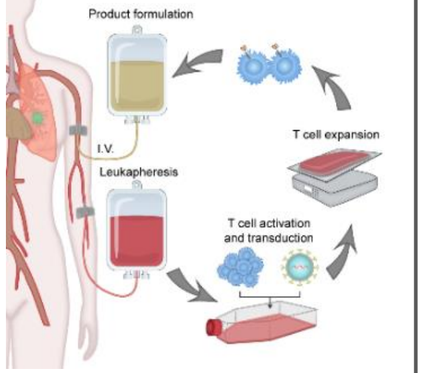
Clinical responses to immunotherapy remain a challenge in blood and solid tumors

T-cell redirecting (T-RED) immunotherapy available

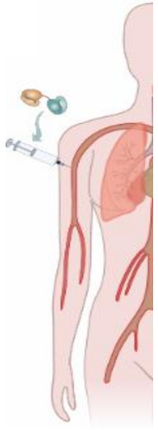
BLOOD TUMORS WITH AVAILABLE T-RED TREATMENTS

B-ALL, B-NHL, MM

CAR-T cells



TCEs



50% of patients **relapse** in B-cell malignancies

80% of patients **relapse** in MM

BLOOD TUMORS WITHOUT APPROVED T-RED TREATMENTS

No CAR-T cells & BsAbs approved

SOLID TUMORS

CAR-T cells unsuccessful

Only 1 TCE - approved for SCLC

Large clinical **unmet need in blood and solid tumors**

STAb Therapeutics

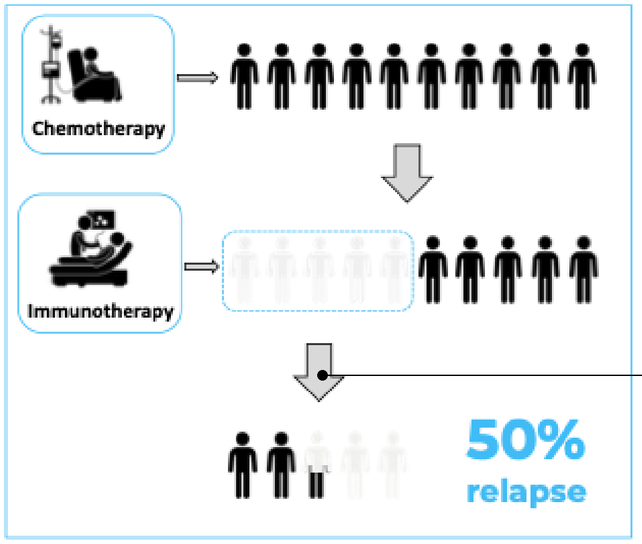
* TCEs, T-cell engagers

More than 500.000 deaths due to B cell malignancies

B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA (B-ALL)	B-CELL NON-HODGKIN LYMPHOMA (B-NHL)	MULTIPLE MYELOMA (MM)
700.000 cases/year globally	463.000 cases/year globally	187.000 cases/year globally

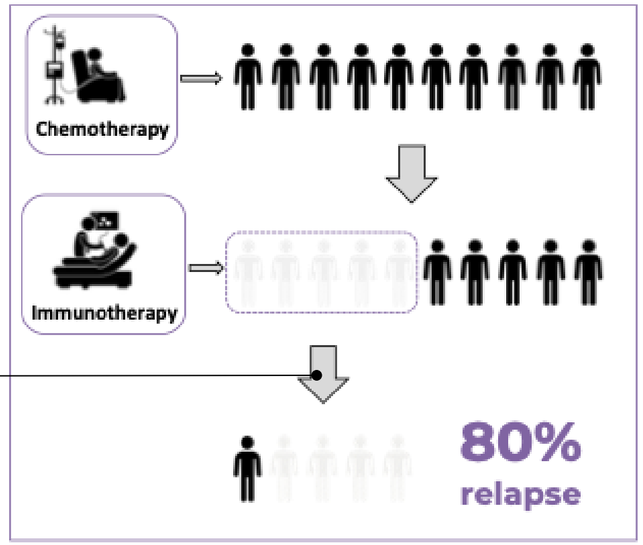
More than 400,000 people die every year

More than 121,000 people die every year



Yescarta (Axi-Cel)
Kymriah (Tisa-Cel)
Tecartus (Brexu-Cel)
Breyanzi (Liso-Cel)
Blincyto (Blinatumomab)
Lunsumio (Mosunetuzumab)
Epkinly (Epcoritamab)
Columvi (Glofitamab)

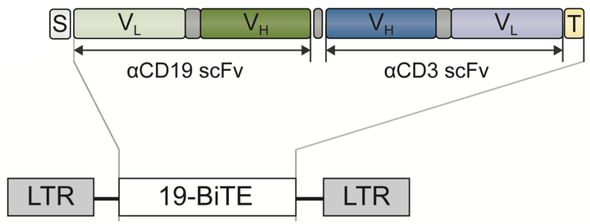
ABECMA (Ide-Cel)
Carvitky (Cilta-Cel)
Tecvayli (Teclistamab)
Elrexfio (Elranatamab)
Talvey (Talquetamab)



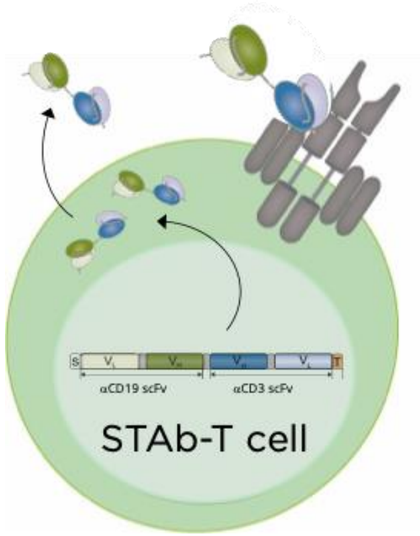
STAb Therapeutics

STAb-T19: a unique approach for T cell-redirecting immunotherapy in B-cell malignancies

STAb-T cells are **autologous T cell** engineered with a lentiviral vector encoding **a T cell engager (TCE)**



CD19 - TCE *in situ* secretion



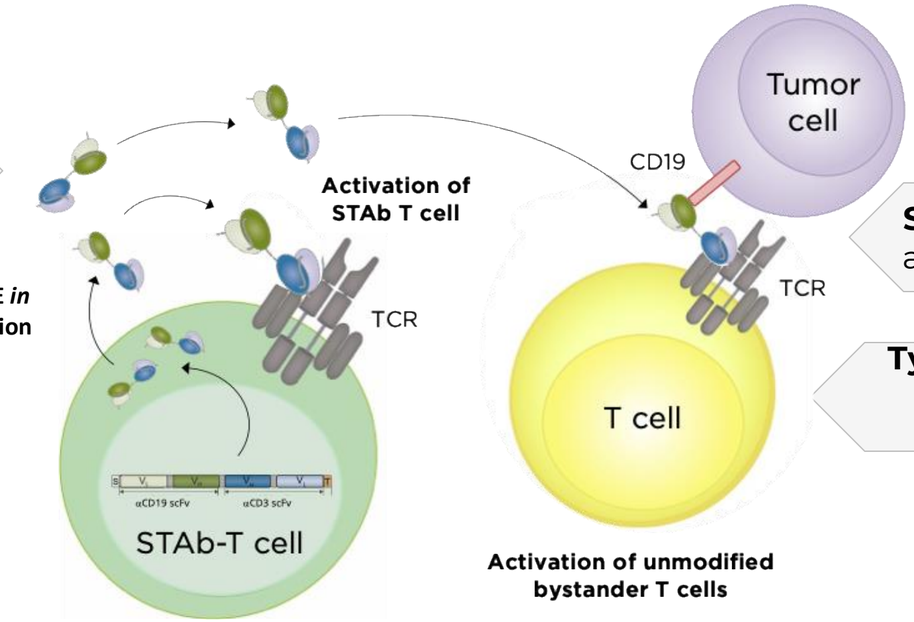
- **INDUCE PHYSIOLOGICAL T CELL ACTIVATION**
- **PROMOTE SUSTAINED RESPONSES**
- **HIGH POTENCY AT LOW DOSES**
- **POTENTIALLY PREVENT RELAPSES**

Exhausted STAb T cells **activate bystander T cells**

CD19 - TCE *in situ* secretion

Active trafficking to tumor

In vivo generation of **memory STAb-T cells**

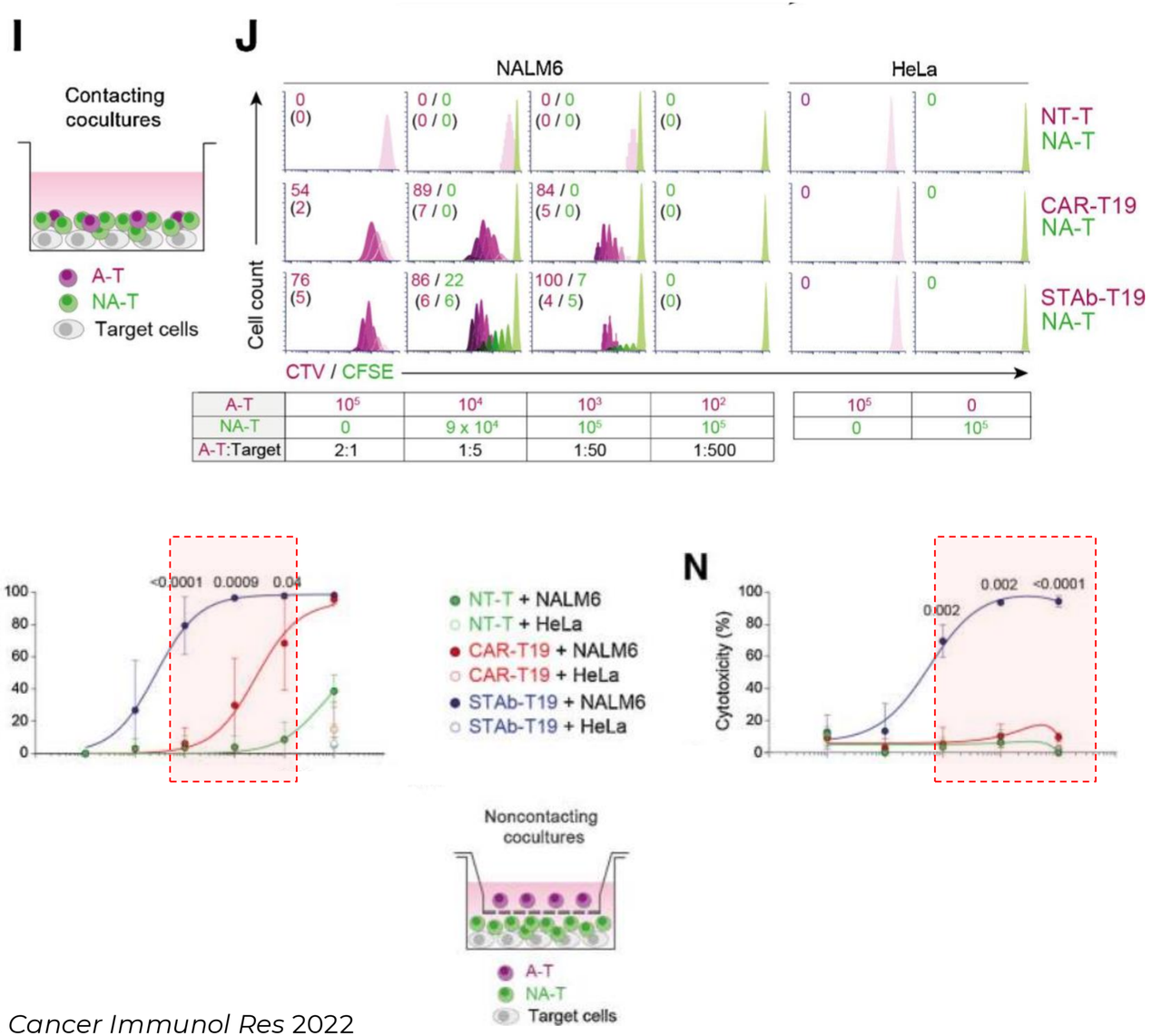


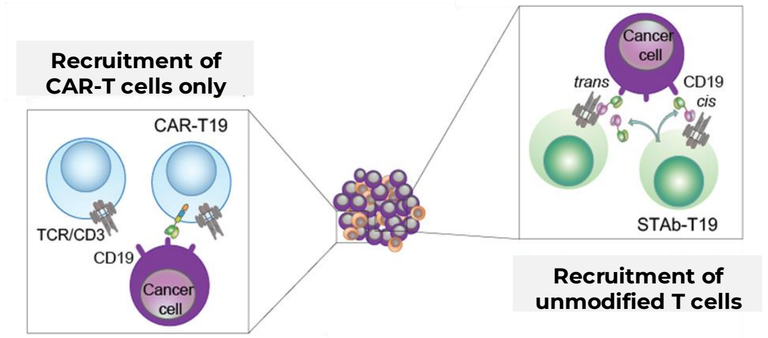
Serial triggering and **serial killing**

Typical synapse through TCR activation

Polyclonal activation of unmodified T cells

STAb-T19 cells recruit and activate unmodified bystander T cells

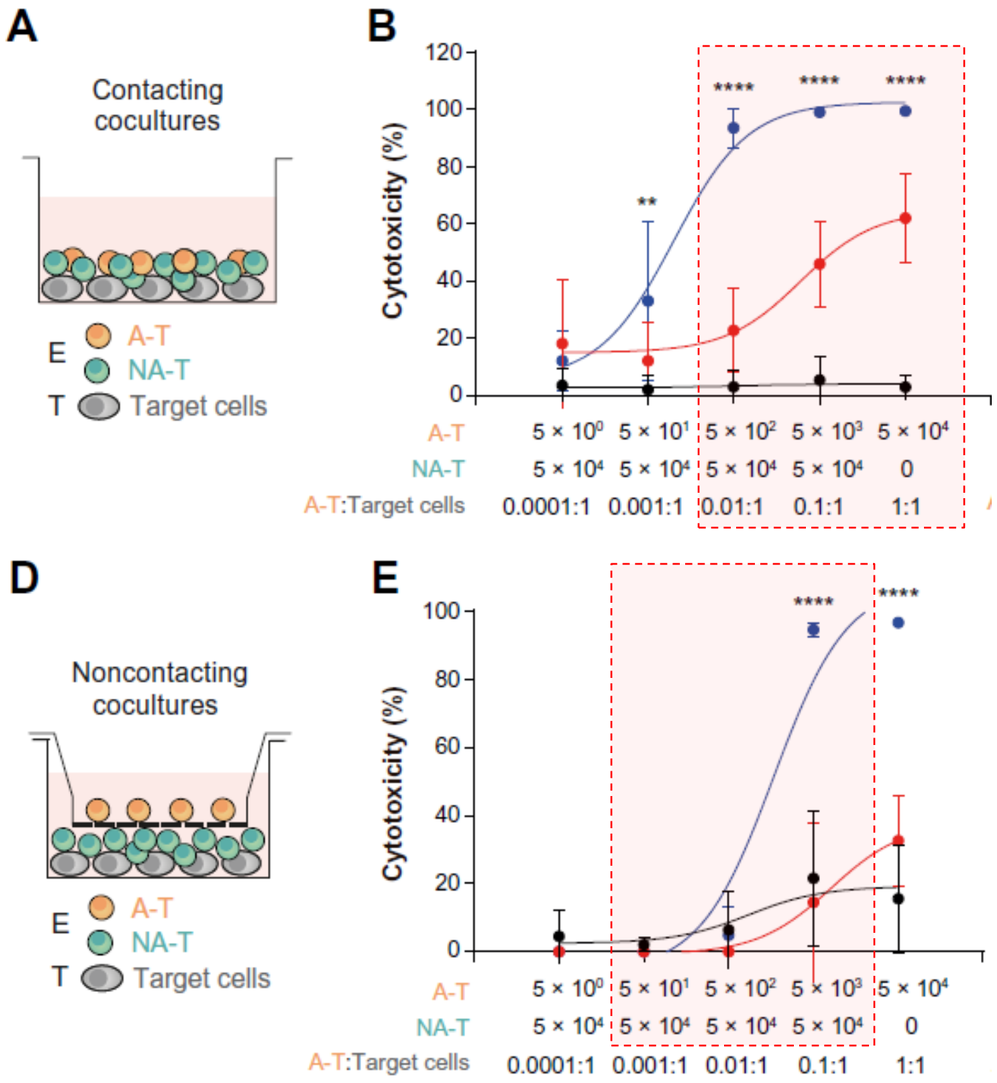


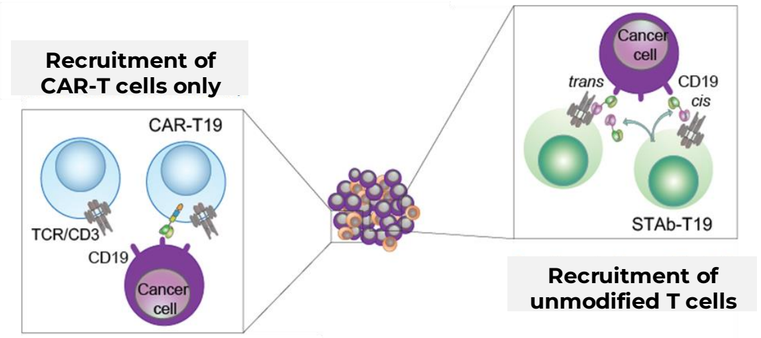


Blanco B. *Cancer Immunol Res* 2022

STAb Therapeutics

STAb-TBCMA cells recruit and activate unmodified bystander T cells



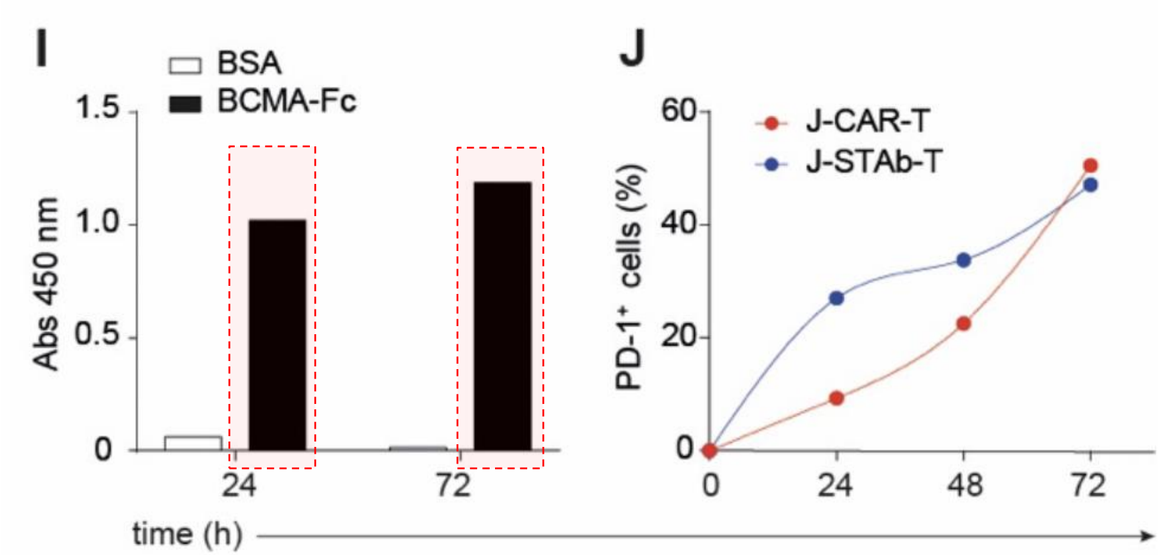


Diez-Alonso L. *Science Translational Medicine* 2024

STAb Therapeutics

Exhausted STAb-T cells continue secreting high levels of TCE

Functional BCMA-TCE secreted by exhausted Jurkat STAb-T BCMA cells



* BCMA-specific Jurkat STAb-T cells (J-STAb-T) and Jurkat CAR-T cells (J-CAR-T) were co-cultured for 24 and 72 hours with BCMA⁺ U266 cells at a E:T=1:1.

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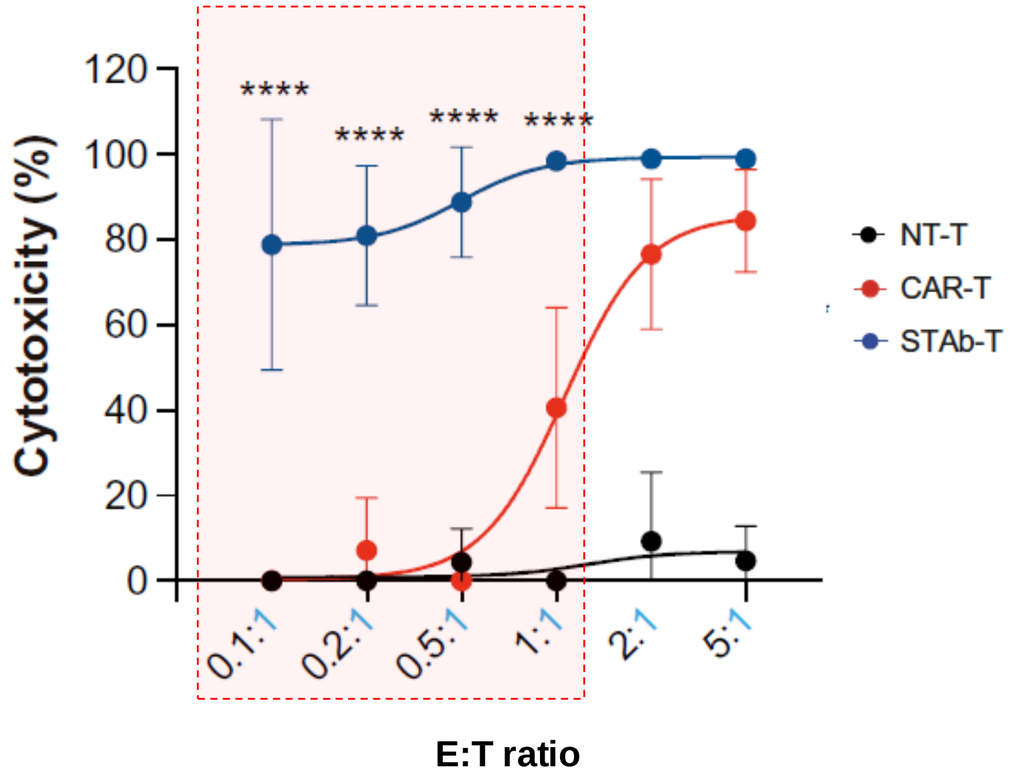
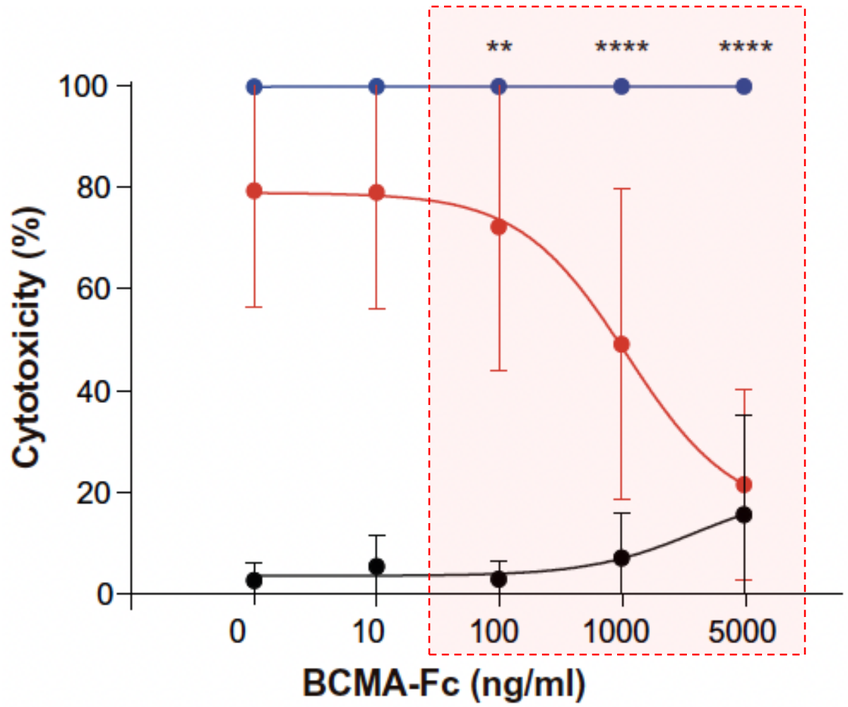
STAb Therapeutics

STAb-TBCMA cells show significant advantages over BCMA-specific CAR-T cells in MM

STAB-TBCMA cells induce specific cytotoxicity at extremely low effector-to-target ratios (E:T)



Soluble BCMA (sBCMA) has no impact on STAb-TBCMA mediated cytotoxicity

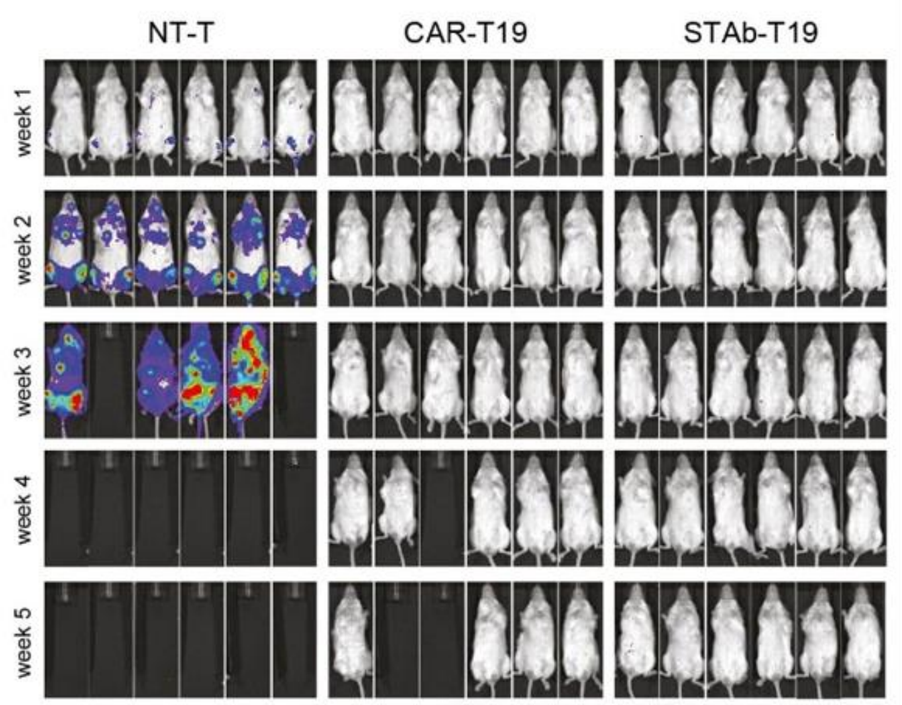


Diez-Alonso L. *Science Translational Medicine* 2024

STAb Therapeutics

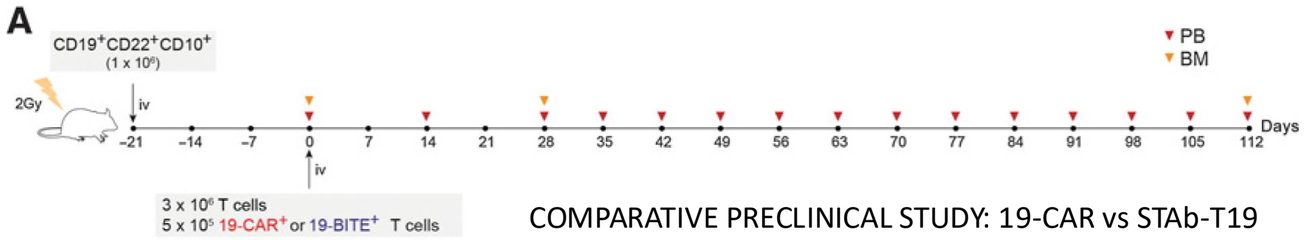
Long-term superior efficacy of STAb-T19 over CAR-T19 in an *in vivo* model of B-ALL

STAB-T19 therapy show similar short-term efficacy compared to CAR-T19

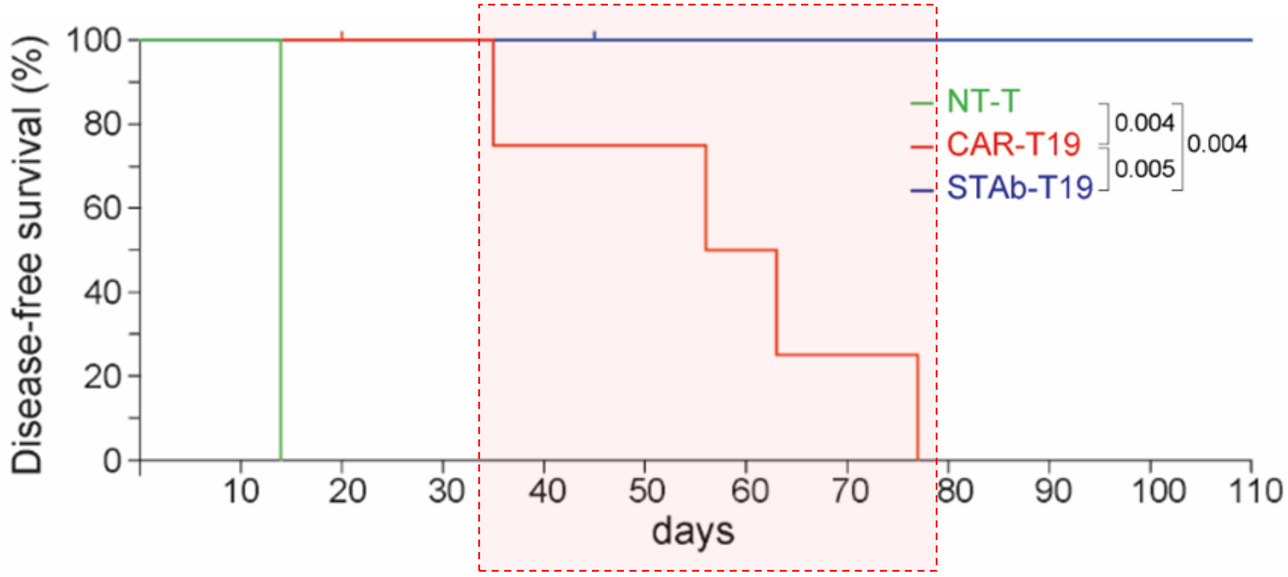


Blanco B. *Cancer Immunol Res* 2022

STAB-T19 therapy - but not CAR-T cells -prevent long-term leukemia relapse in a PDX model



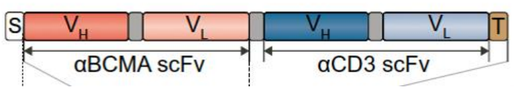
COMPARATIVE PRECLINICAL STUDY: 19-CAR vs STAb-T19

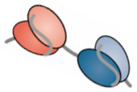


Milestone: Phase 1, first-in-human, study to evaluate safety of STAb-T19 therapy to start Q1 2025

STAb Therapeutics

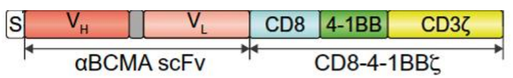
STAb-TBCMA cells are more effective than CAR-TBCMA cells in a model of multiple myeloma (MM)

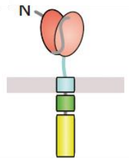




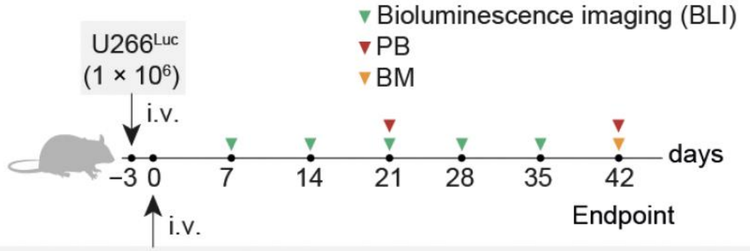
STAb-TBCMA (BCMAxCD3 BiTE)

COMPARATIVE PRECLINICAL STUDY

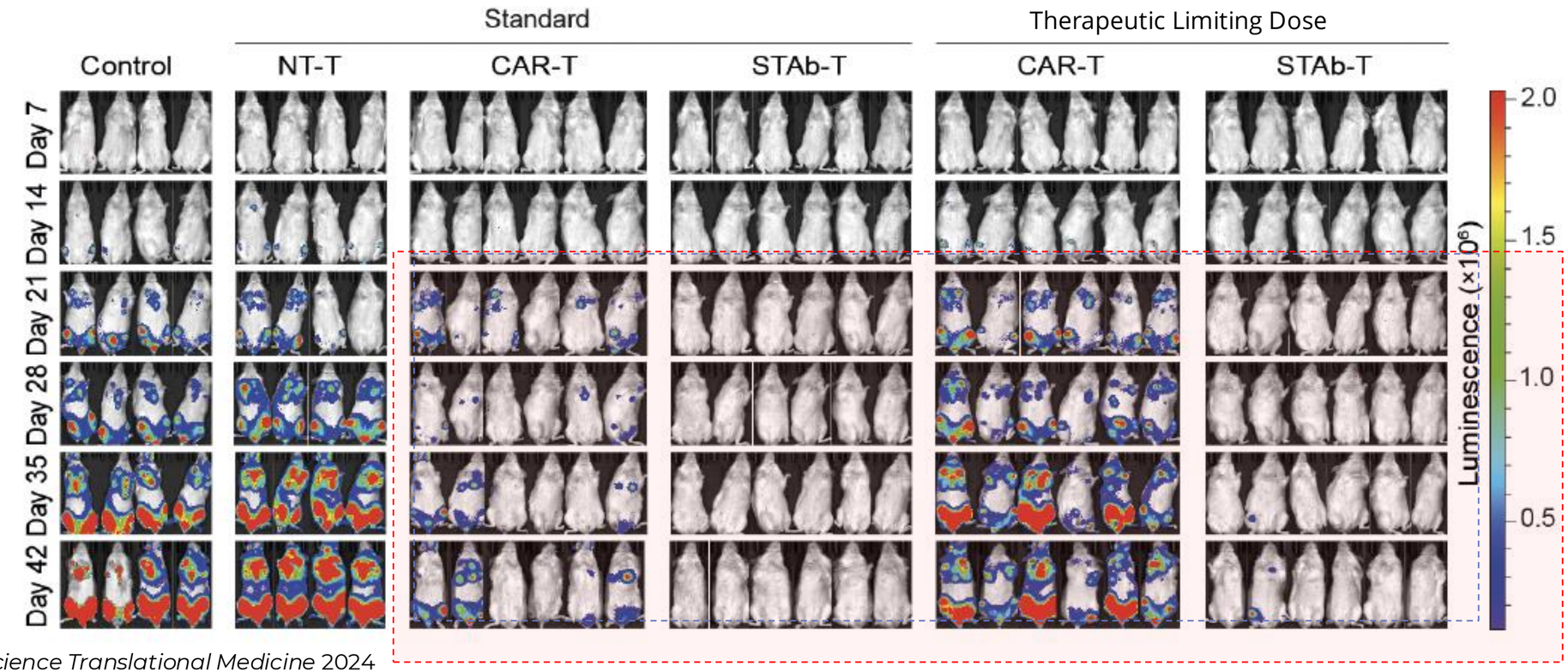




BCMA-CAR
(2nd generation CAR)



Standard: 5 × 10^6 T cell (1 × 10^6 BCMA-CAR⁺ or BCMA-TCE⁺ cells)
Therapeutic limiting dose (TLD): 3 × 10^6 T cells (6 × 10^5 BCMA-CAR⁺ or BCMA-TCE⁺ cells)

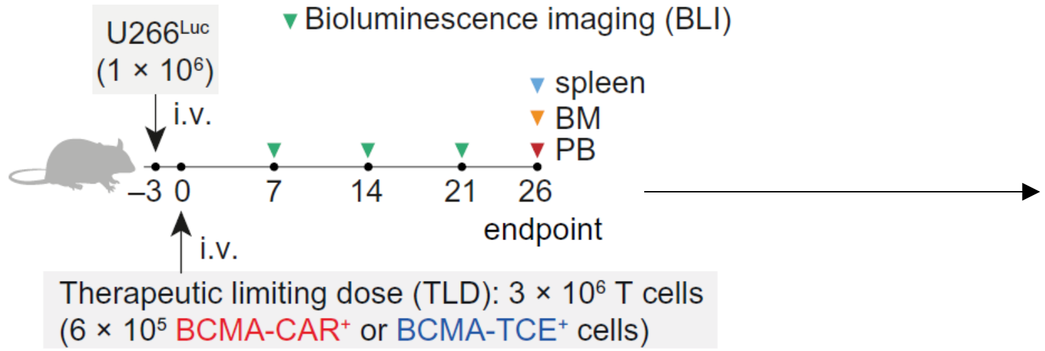


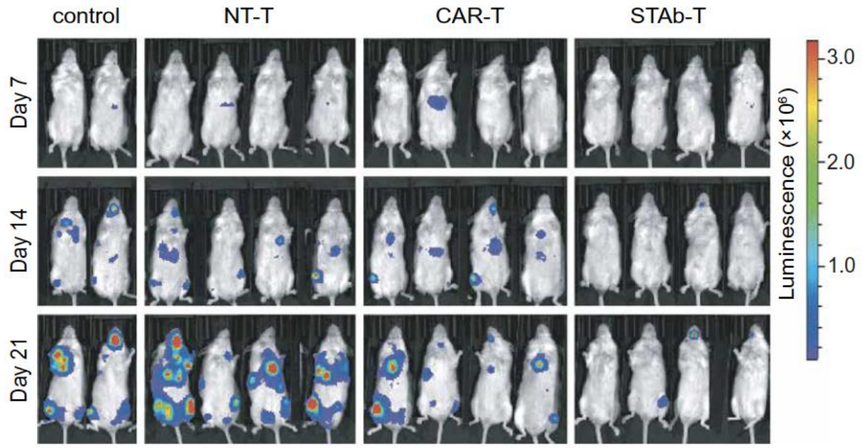
Diez-Alonso L. *Science Translational Medicine* 2024

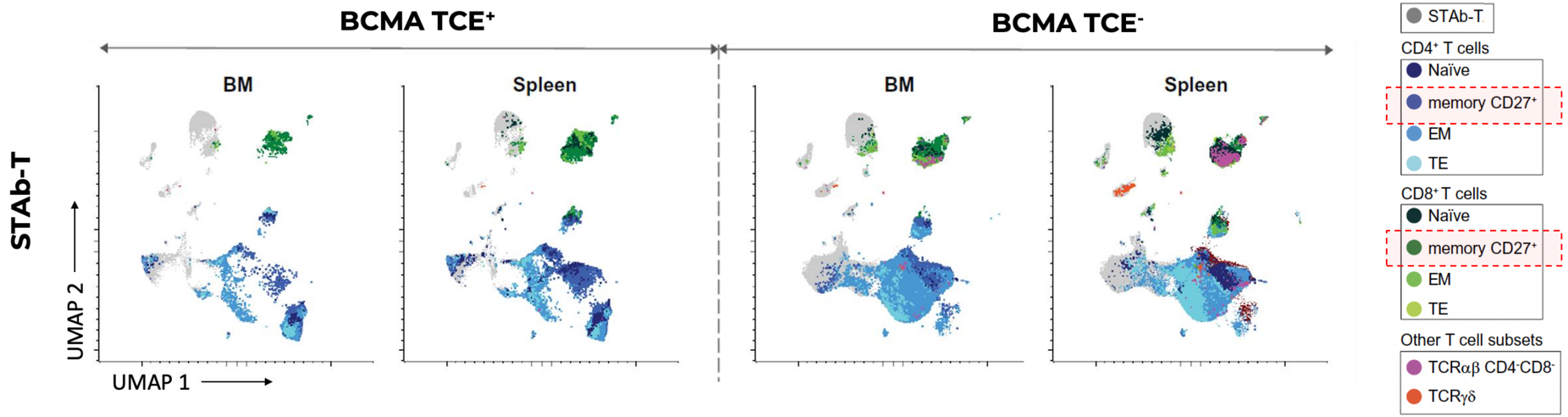
STAb Therapeutics

Generation of memory STAb-T cells *in vivo* in a model of MM

Xenograft MM mouse model transplanted with human T cells







*EM, effector memory; TE, terminal effector: BM, bone marrow

ROBUST EXPANSION AND PERSISTENCE OF LONG-LIVED **MEMORY STAb-TBCMA CELLS *IN VIVO***

Diez-Alonso L. *Science Translational Medicine* 2024

STAb Therapeutics

Advantages of STAb-T cells over other immunotherapies

	STAb-T	CAR-T	TCE/BiTE	dual CAR-T	*In vivo* CAR
SUSTAINED RESPONSES Sustained & robust T cell responses	✓	✓	✗	✓	-
PHYSIOLOGICAL T CELL INTERACTIONS STAb-T cells promote canonical immune synapses	✓	✗	✓	✗	✗
IMMUNE MEMORY *IN VIVO* STAb-TBCMA induces immune STAb T memory cells	✓	✓	✗	✓	✓
BYSTANDER REDIRECTION STAb-T cells recruit bystander T cells & induce a potent cytotoxic at low effector:tumor cell ratios	✓	✗	✓	✗	✗
REDUCED DOSE REQUIRED STAb-T cells could be an alternative for patients with limited number of effector T cells	✓	✗	-	-	-
RESISTANCE TO TUMOR ESCAPE STRATEGIES STAb-T cells prevent CD19 downmodulation and leukemia escape & resist inhibition by soluble BCMA	✓	✗	✓	✗	✗

STAb-T cell products in the pipeline

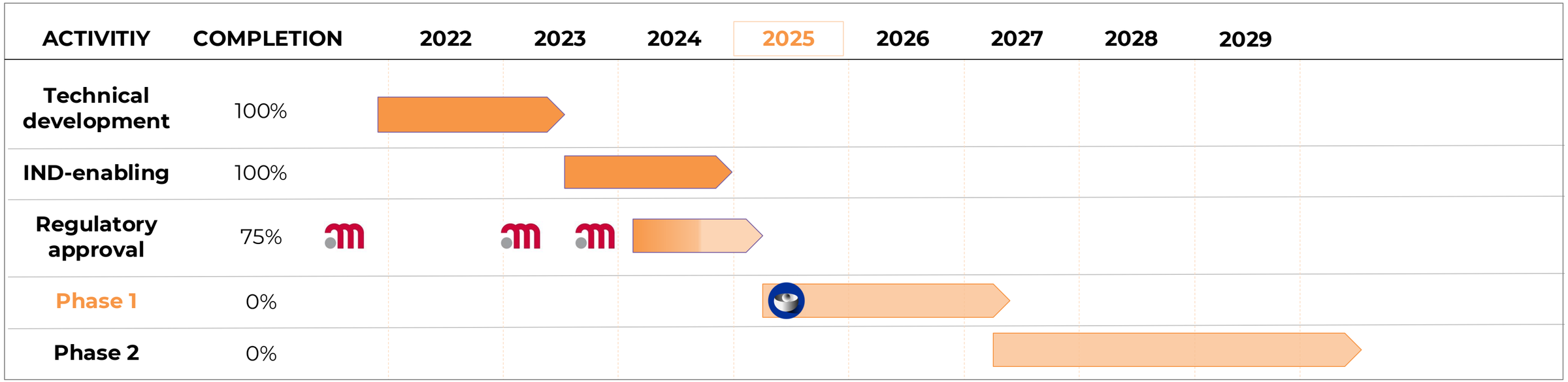
STAb-T Therapeutic Candidates in Hematological Cancers & Solid Tumors

PROGRAM	TARGET	INDICATION	DISCOVERY	PRECLINICAL	IND-ENABLING	CLINICAL	IP STATUS
STAb – T19 Autologous – stable expression	CD19	B-ALL, B-NHL				**1.2 M €** Instituto de Salud Carlos III	Exclusive license National phases (EP, US) Priority 17/02/2020
STAb – TBCMA Autologous – stable expression	BCMA	Multiple Myeloma				**1.2 M €** Instituto de Salud Carlos III	Exclusive license under negotiation Priority patent filed
STAb – TS03 Autologous – stable expression	EGFR	Lung cancer					
STAb – TS04 Autologous – transient expression	Undisclosed	Solid tumor					
STAb – TS05 Autologous – stable expression	Undisclosed	Solid tumor		**680K €** MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES AGENCIA ESTATAL DE INVESTIGACIÓN			

STAb Therapeutics

Clinical development of STAb-T19 in B-ALL/NHL

PHASE 1 STUDY ONGOING TO LAUNCH IN Q1 2025 AS A FIRST-IN-HUMAN USE OF STAb-T THERAPY



Spanish Agency of Medicines and Medical Devices (AEMPS)

EUROPEAN MEDICINES AGENCY

STAb Therapeutics

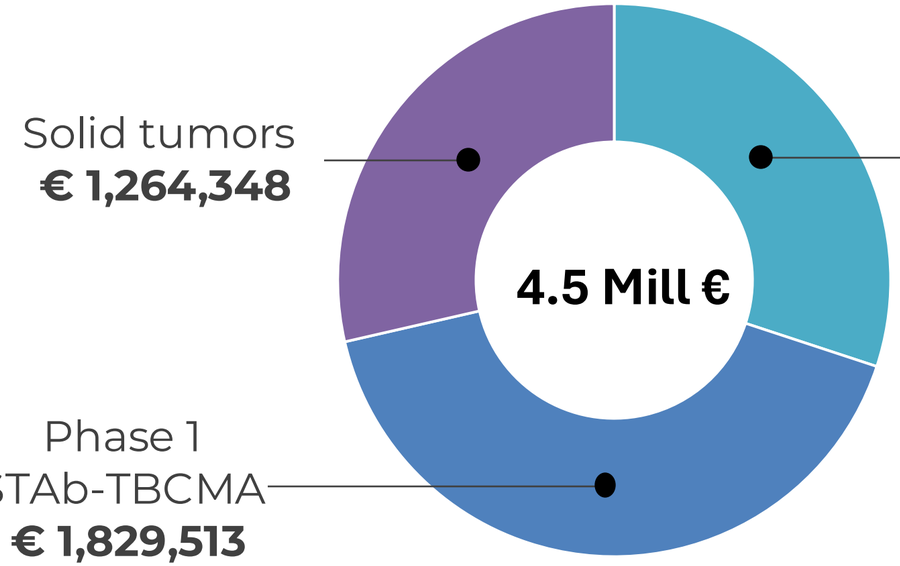
FPT – First patient treated

SEED capital raise 2024 – use of funds

SEED+ ROUND - € 4.5 Mill | Closing: **Q4 2024**

MINISTERIO DE CIENCIA, INNOVACIÓN Y UNIVERSIDADES
AGENCIA ESTATAL DE INVESTIGACIÓN

315K € grant for STAb-T cell in solid tumor



Instituto de Salud Carlos III

1.2 Mill € grant for phase 1 STAb-T19

Instituto de Salud Carlos III

1.2 Mill € grant for phase 1 STAb-T19

STAb Therapeutics

Partnering opportunities

INVESTMENT OPPORTUNITY IN ONGOING SEED ROUND

PARTNERSHIPS FOR STAb-T CELLS IN CLINICAL DEVELOPMENT

COLLABORATION FOR NEW ASSETS IN TUMOR INDICATIONS

STAb Therapeutics

STAb Therapeutics

Thank you!

Carolina Pola, PhD – CEO cpola@stabtherapeutics.com