Hemocentro RP
Centro Regional de Hemoterapia
HCFMRP - USP

Universidade de São Paulo

FAPESP France Week 2025

Building an Academic CAR-T Cell Platform in Brazil:

From a Pioneering Project to a Center for Advanced Therapies

Diego V. Clé, MD, MBA, PhD
Assistant Professor

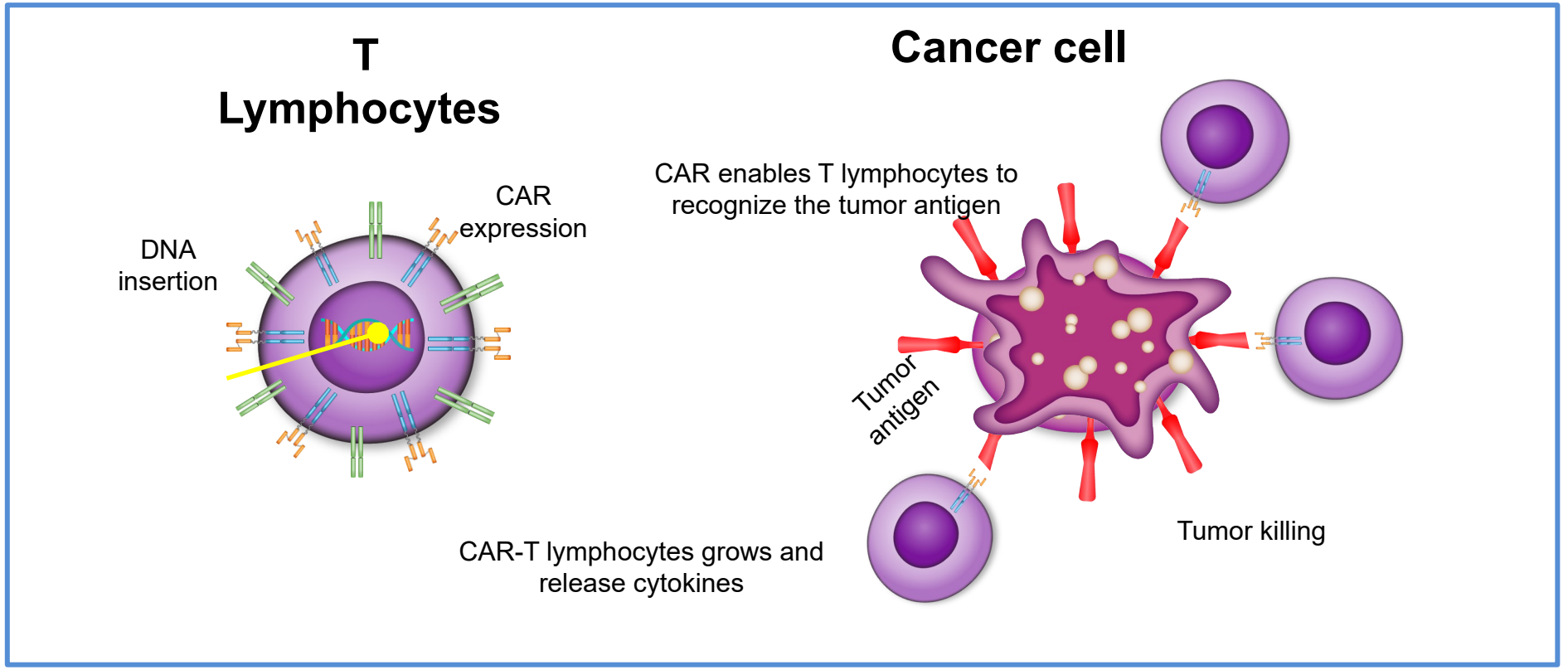
Ribeirão Preto Medical School, University of São Paulo, Brazil



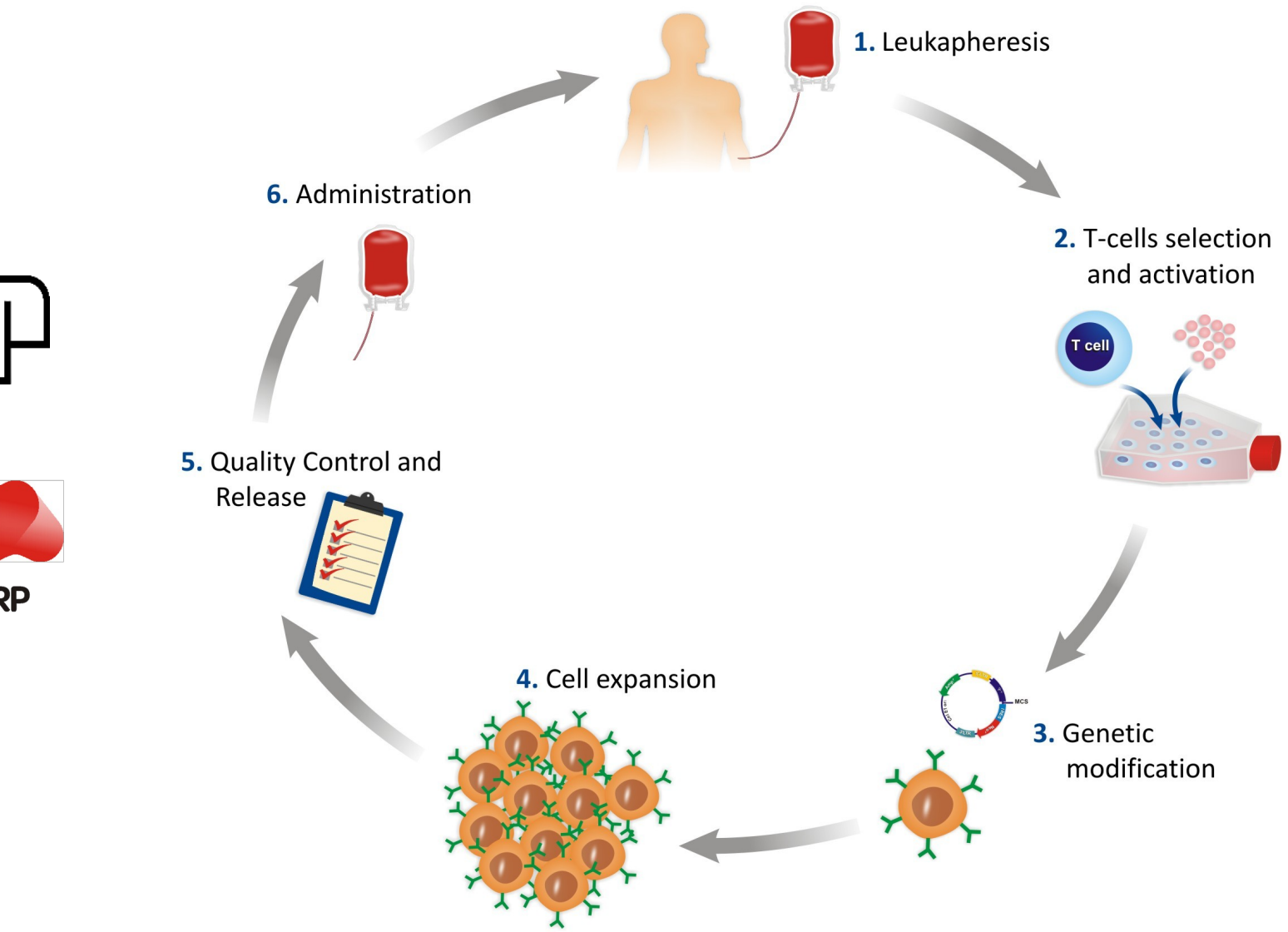
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USP

CAR-T cells: Mechanism of action



Production Flowchart



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Mizukami and Swiech, 2019. Platforms for Clinical-Grade CAR-T Cell Expansion. Chimeric Antigen Receptor T Cells pp 139-150, Methods in Molecular Biology.

Commercial anti-CD19 CAR-T available in Brazil

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KYMRIAH® (tisagenlecleucel) Suspension for IV infusion

2022

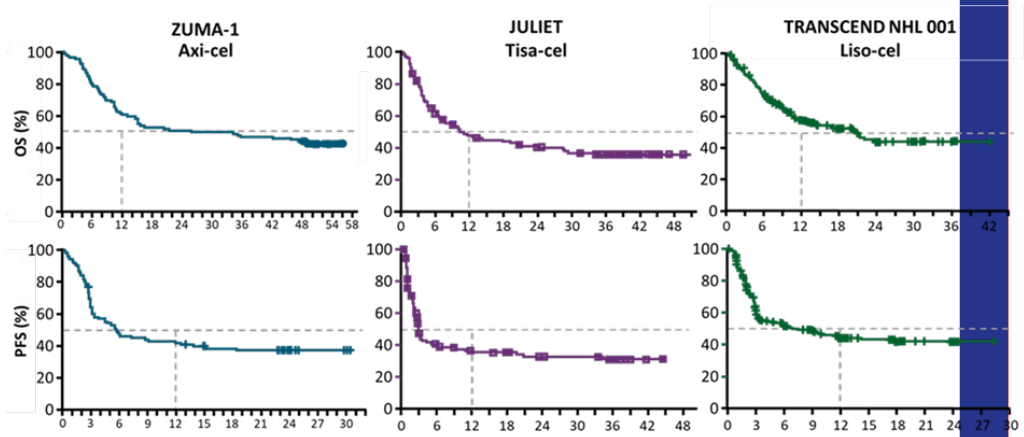
YESCARTA® (axicabtagene ciloleucel) Suspension for IV infusion

2022

TECARTUS® (brexucabtagene autoleucel) Suspension for IV infusion

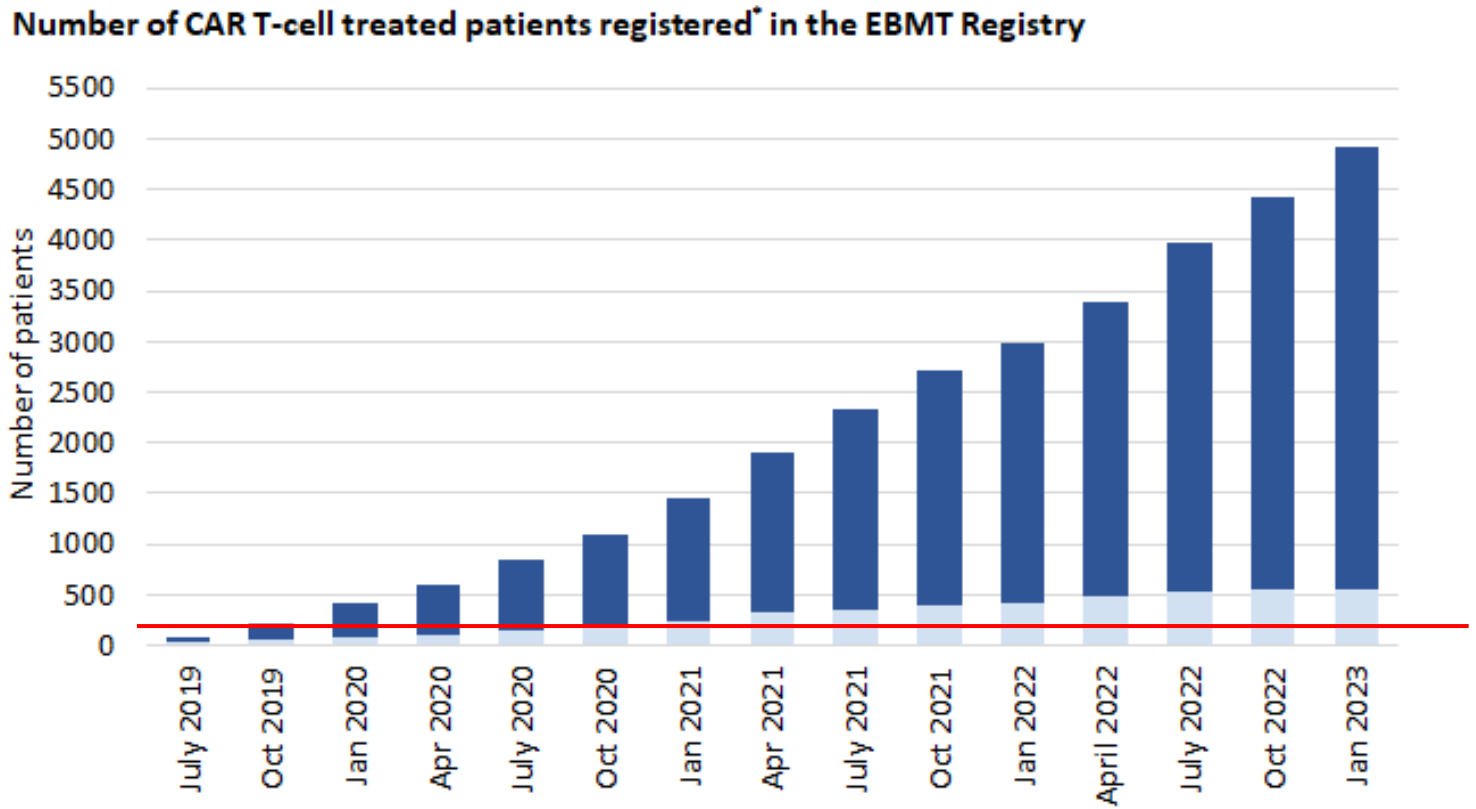
2023

- Kymriah, Yescarta and Tecartus approved in Brazil
- **Financial toxicity –US$ 400,000 each patient**
- Brazil: >70% public health system (SUS)



Locke. Lancet Oncol. 2019;20:31-42; Jacobson. ASH 2020. Abstr 1187; Schuster. NEJM. 2019;380:45-56; Jaeger. ASH 2020. Abstr 1194; Abramson. Lancet. 2020;396:839-852; Maude SL. N Engl J Med. 2018;378(5):439-48; Neelapu. Blood Adv. 2021;5:4149-4155.

CAR-T in clinical practice



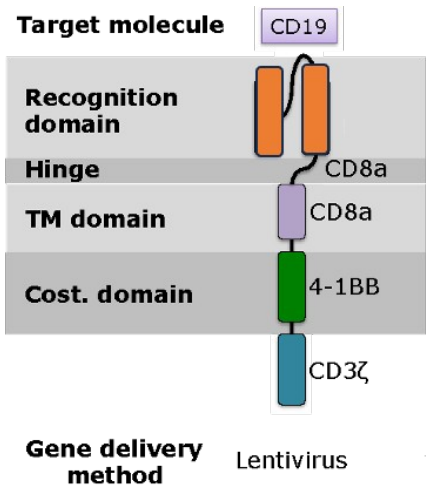
USA: > 30.000 patients

Brazil: Less than 100

Source: EBMT Registry, January 2023

**Patients identified and marked with a CAR T-cell treatment, having at least minimal data on the diagnosis and treatment.*

Academic CD19 targeted CAR-T cell



Early collaborations

PURDUE UNIVERSITY

PURDUE INSTITUTE FOR DRUG DISCOVERY

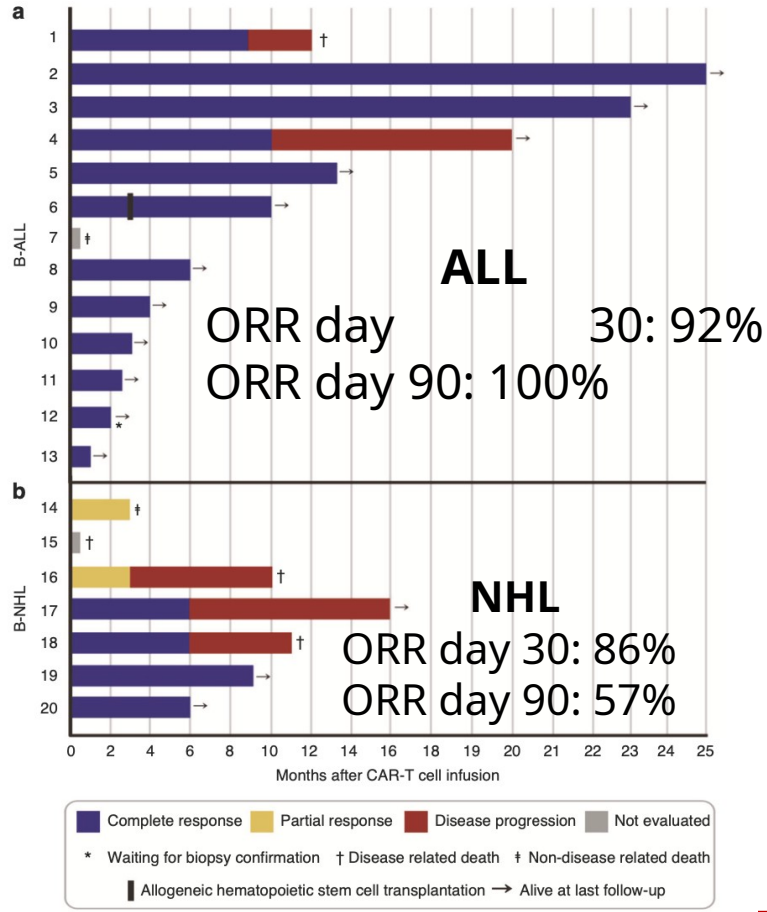
Jensen Lab
Advanced Lymphocyte Engineering

Academic CD19 targeted CAR-T cell – first results

Preclinical results with CAR-T cells - 2019

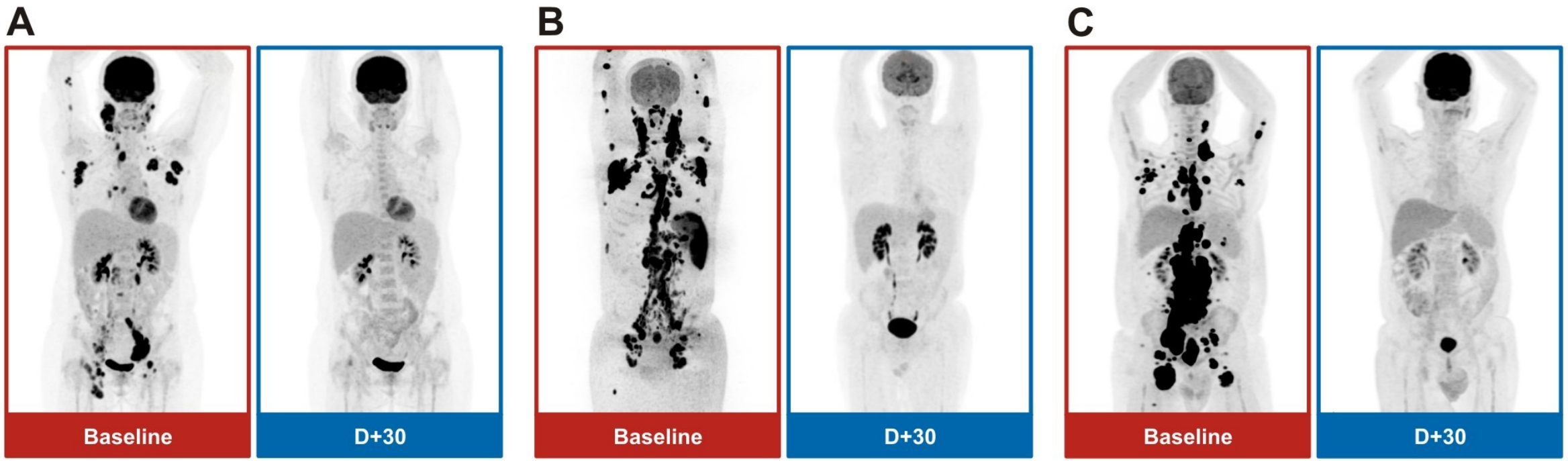
Clinical aplication-2024

Safety and efficacy of a new academic CD19-directed CAR-T cell for refractory/relapsed non-Hodgkin lymphoma and acute lymphoblastic leukemia in Brazil



1- Picanço-Castro *et al*, *HTCT* 2019. 2- Donadel C. *et al*. BMT 2024

Complete responses in NHL: 3 exemples



Donadel C. *et al*. BMT 2024

Patient 12 – Follicular Lymphoma (POD24)











D9
Tocilizumab

CAR-T infusion

D5
Myalgia
Headache

D7
Fever
(38,2°C)

D14
Hospital
discharge

Lymphodepletion

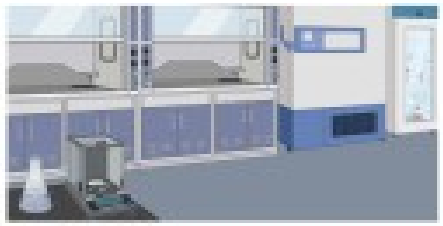
CRS grade 1

17/AUG/2022 22/AUG/2022 26/AUG/2022 28/AUG/2022 30/AUG/2022 05/SEP/2022

Translation of Academic Research to Clinical Product Development

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Closed system

Risk-based process development

Infrastructure

Dedicated space and equipment harmonized with GMP

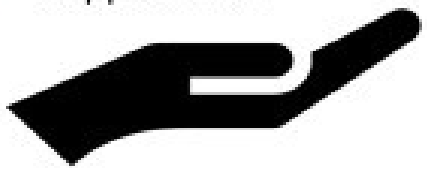
Regulatory and quality requirements

Experienced staff available to train and provide competence

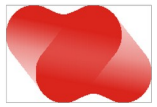
Qualified and trained professionals

Purchasing sector

Support with



GMP



Hemocentro RP



Hemocentro RP

FMRP-USP

FACULDADE DE MEDICINA DE RIBEIRÃO PRETO

USP

fundação butantan

INSTITUTO BUTANTAN
A serviço da vida

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NUTERA – Ribeirão Preto

Center for Advanced Therapies





To scale production: Partnership with Butantan Institute
NUTERA (US$ 50mi)

Construction of a new Cell Therapy Facility: NUTERA

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Partnership

USP

Hemocentro RP

INSTITUTO BUTANTAN
A serviço da vida

Financial Support

FAPESP
FUNDAÇÃO DE AMPARO À PESQUISA DO ESTADO DE SÃO PAULO

CNPq
Conselho Nacional de Desenvolvimento Científico e Tecnológico

HC FMRP-USP
RIBEIRÃO PRETO

FUNDAÇÃO PRÓ-SANGUE
HEMOCENTRO DE SÃO PAULO

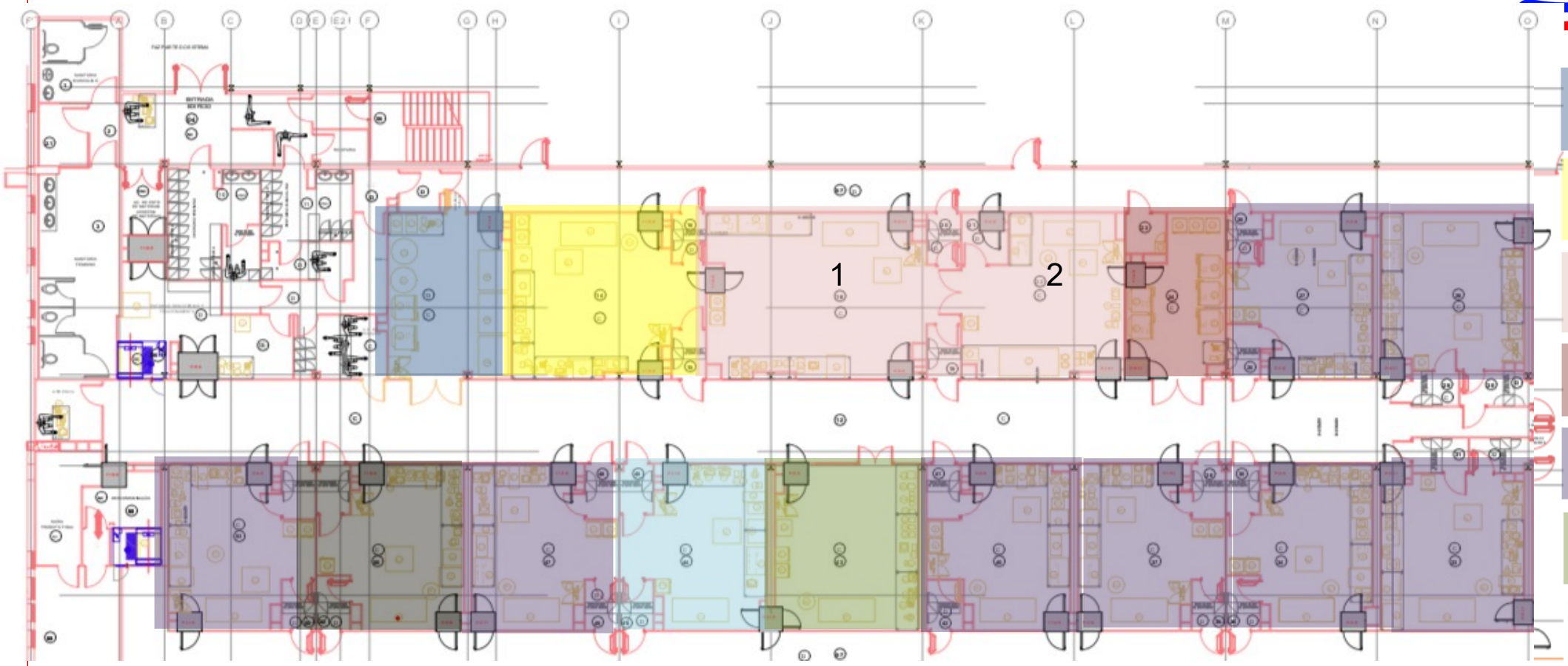
SÃO PAULO
GOVERNO DO ESTADO
SÃO PAULO SÃO TODOS

Finep
INOVAÇÃO E PESQUISA

MINISTÉRIO DA SAÚDE

NUTERA's mission is to establish local CAR-T cell manufacturing, providing patients within Brazil's public healthcare system with access to this innovative therapy.

NUTERA - BLUEPRINT



- Cryopreservation room
- DNA production room
- Lentivirus production room: 1-upstream e 2-downstream
- Stock support
- Clean rooms (CAR-T)
- Room for Preparation of Solutions
- Quality Control Laboratory (QC) LV
- Cell isolation

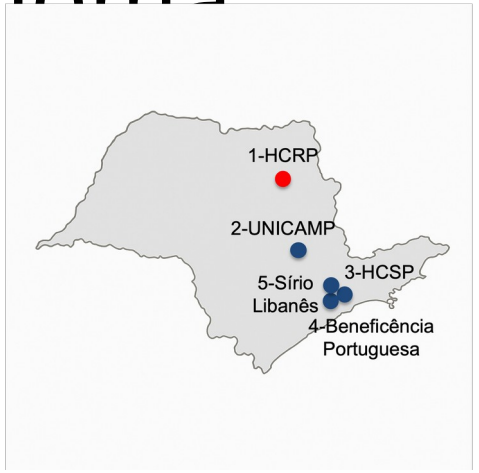
✓ 16 GMP clean rooms in 1.000 m^2: 8 rooms for CAR-T cell manufacturing, CQ laboratories, DNA production area, lentiviral vector production area.

Clinical Trial

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CARTHEDRALL– CAR-T THerapy anti-CD19 for R/R Acute Leukemia and Lymphoma

- Phase 1/2 clinical trial
- 81 patients
- Multicentric:
  - HCFMRP-USP – Ribeirão Preto, SP
  - UNICAMP – Campinas, SP
  - HCFM-USP – São Paulo, SP
  - Beneficência Portuguesa – São Paulo, SP
  - Hospital Sírio Libanês – São Paulo, SP
- Currently: Recruiting



Support:

MINISTÉRIO DA SAÚDE

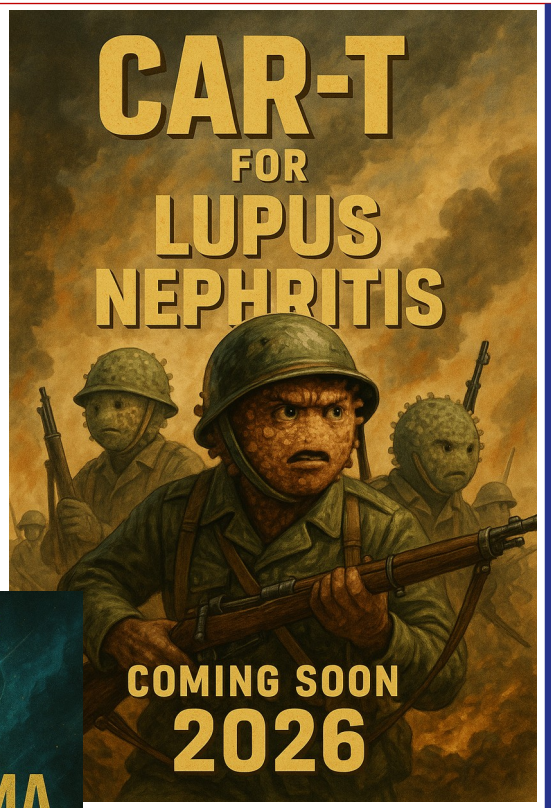
GOVERNO FEDERAL BRASIL UNIÃO E RECONSTRUÇÃO

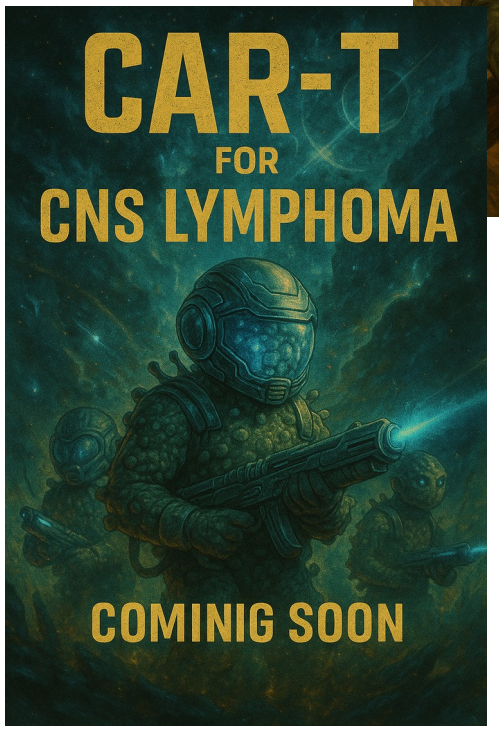
Funding from The Ministry of Health (US$ 18mi)

NUTERA



Innovations





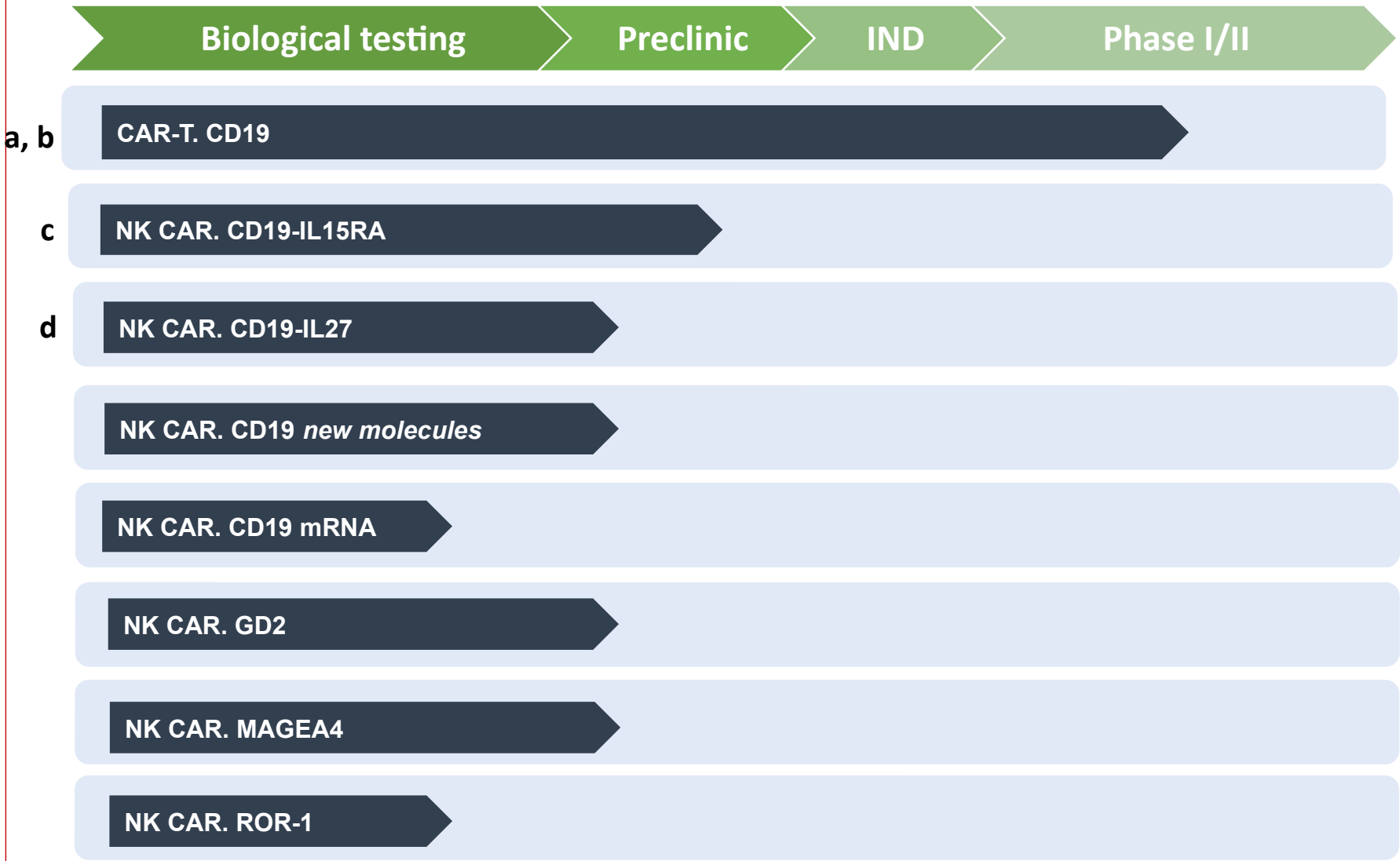
Production of viral vectors under GMP conditions

CAR-T cell production under GMP conditions

- Partnership with Institut Curie
- U r



Pipeline



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Virginia Picanço Castro



[a] Donadel CD et al., 2024. Bone Marrow Transplant.

[b] Picanço-Castro V et al., 2019. Hematol Transfus Cell Ther.

[c] Silvestre RN et al. 2023. Front Immunol.

OVERALL PIPELINE – GENE TRANSFER LABORATORY

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Performance and New targets	Design and cloning production of vectors	*In vitro* funcional assays	Proof-of-concept *in vivo*
CAR anti-GD2 (+GITRL) (Glioblastoma)			
TCR anti-NY-ESO-1 (Melanoma)			
CAR anti-MAGE-A4 (Multiple Myeloma)			
CAR anti-MUC1/HER2 (Breast Cancer)			
Non-activated CAR-T cells			
Metabolic reprograming			
Allo-CAR-T			
CAR-T γδ (CD19)			
U-CAR-T (CD19)			

CRISPR/Cas9



Lucas Botelho

Collaborations

FACULDADE DE CIÊNCIAS FARMACÊUTICAS DE RIBEIRÃO PRETO · USP · SCIENTIA LUX SALUTIS

MIE UNIVERSITY

WISCONSIN INSTITUTE FOR DISCOVERY

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Medical team
Gil de Santis
Camila Donadel
Leonardo Palma
Thiago Eleuterio
Gabriela Altizani
Rafael Pacca

Biotechnology Laboratory
Virginia Picanço
Dayane Schmidt
Sima Ebrahimabadi
Mariane Tirapelle
Matheus H. dos Santos
Felipe Biggi
Camilly G. Ferreira
Mara E. da Silva

Gene Transfer Laboratory
Lucas Botelho

Cell Therapy Laboratory
Maristela Delgado Orellana
Sâmia Rigotto Caruso
Taísa Risque Fernandes
Rosane Maria Falasco Bolzoni

Laboratory of Cell Culture (LCC)
Mário Abreu Neto
Rafaela Rossetti
Pericles N. da Costa
Heloisa Brand

Flow Cytometry Laboratory
Patricia Bonini
Camila Bonaldo
Rita de Cássia

Experimental Animal Laboratory
Profa. Lorena Pontes
Cleide Lucia Araujo

FiPro Office
Elaine Faria
Joao Pedro Pignata

TERAPIA CELULAR · HC FMRP-USP RIBEIRÃO PRETO · FUNDAÇÃO PRÓ-SANGUE HEMOCENTRO DE SÃO PAULO · Hemocentro RP Fundação Hemocentro de Ribeirão Preto · USP Universidade de São Paulo · Fundação Butantan · INSTITUTO BUTANTAN A serviço da vida · SÃO PAULO GOVERNO DO ESTADO SÃO PAULO SÃO TODOS

Thank you



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