PlasmidFactory®

PlasmidFactory GmbH

The CDMO and service provider for plasmid and Minicircle DNA

Webinar

From bench to bedside: Development of a virus-free clinical CAR-T manufacturing protocol

Fraunhofer IZI

PlasmidFactory 25 YEARS

Your trusted CDMO Partner

Why choose PlasmidFactory

- 25+ years of DNA manufacturing expertise
- Independent, flexible & trusted European CDMO
- Scalable production: Research → High Quality → GMP Grades
- Proprietary technologies: Minicircle, ITRPROTECT®, ITRRESCUE®, POLYARESCUE®, MIDGE®
- 3,500+ plasmid & Minicircle projects delivered
- 99.9% success rate

Company info

Comprehensive DNA Portfolio

PlasmidFactory®

Custom DNA

- Plasmid DNA
- Minicircle DNA
- MIDGE® vectors

Tailor-made DNA vectors produced from Research to GMP Grade.

In-Stock DNA

- Reporter & pEPito plasmids
- AAV plasmids and Minicircles
- Molecular size markers

Ready-to-use plasmids & Minicircles · reporters, AAV tools, markers

Services & Analyses

- Capillary gel electrophoresis (CGE)
- GMP-compliant DNA storage
- Linearized DNA & cloning services
- ITRPROTECT® / ITRRESCUE® / POLYARESCUE®

Proprietary technologies and QC services · ensuring stability, purity & compliance

Available Quality Grades

Scientific Quality (SQ) Grade

Advanced research standard.

- 4 parallel production lines
- Scalable process starting from 0.5 mg*
- 2 options available:
  - *Research Grade* for basic requirements
  - *CCC Grade* with ≥ 95% supercoiled DNA

Key features
- Bioreactor fermentation

High Quality (HQ) Grade

Highest non-GMP standard.

- 2 HQ facilities
- According to EMA guidelines
- Production scale 10 mg – 10 g**
- Also available as "HQ in GMP“ Grade

Key feature
- Complete traceability

GMP Grade

Full clinical & commercial compliance.

- Dedicated state-of-the art GMP facility
- GMP / FDA-compliant
- End-to-end single-use processes
- Late-stage clinical trials and commercial supply

Key feature
- Single use equipment

GMP Manufacturing You Can Trust

Designed for highest plasmid & Minicircle DNA quality requirements

State-of-the-art GMP facility

- Dedicated building for GMP Grade plasmid & Minicircle DNA
- 450 m^2 cleanrooms suites (grades C & D)
- Facility designed to prevent cross-contamination

Flexible manufacturing with highest safety standards

- End-to-end single-use USP- and DSP- process
- Ph. Eur. / USP grade WFI supply
- EU GMP (Annex 1 & 2) compliant
- Various fill & finish options
- QP batch release

Full GMP compliance

- Data integrity measures and systems in place
- Annex 11 / 21 CFR Part 11
- EU GMP-Part 2 and AMWHV

GMP info

Minicircle: Clinical Footprint

Snapshot of registered and planned clinical trials using Minicircle for cell engineering

Registered clinical trials

2020 — **CARAMBA-1 - SLAMF7 CAR-T (Multiple Myeloma)** — Recruitment ended

- Phase I/IIa (FiH) • EUCT 2024-512643-23-00 • NCT04499339
- Virus-free Sleeping Beauty gene transfer using Minicircle DNA + transposase mRNA
- Opened Jun 2020 • 33 participants • DE site (multi-country approvals reported in EU project updates)

2024 — **TranspoCART19 - CD19 CAR-T (r/r B-cell Lymphoma)** — Recruiting

- Phase I/IIa • EUCT 2024-514544-90-00 • NCT06378190
- Non-viral Sleeping Beauty transposon delivered as a Minicircle + SB100X mRNA
- Start Mar 2024 • 27 participants • 9 sites (Spain)

2025 — **LION-1 - ROR1 CAR-T (ROR1$^+$ tumors)** — Recruiting

- Phase I (FiH) • EUCT 2024-512019-36-00 • NCT pending (CTIS)
- Start Apr 2025 • 46 participants • 1 site (Germany)
- Includes hematologic + solid tumors (e.g., MCL, CLL, TNBC, OC, ACC)

Studies in preparation

Oncology (engineered cells)

- ROR2 CAR-T (Uniklinikum Würzburg)
- FLT3 CAR-T (Uniklinikum Würzburg)
- SLAM/F7 program (T-CurX)

Autoimmune / gene therapy

- Nimvec™ AM510 (Amarna; Type 1 Diabetes)

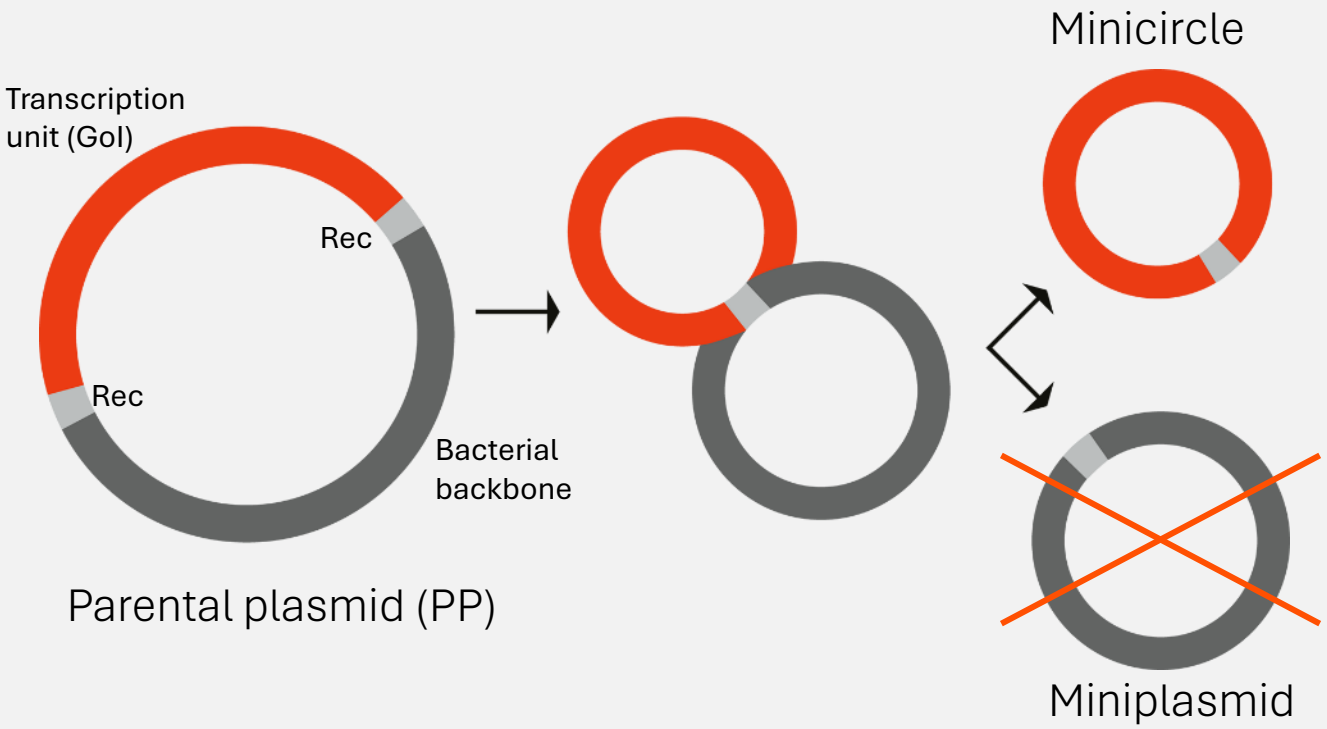
Undisclosed / confidential

- At least 4 additional clinical studies in preparation

Minicircle: Proprietary Production Method

Minimalistic DNA vector reduced to the gene of interest (GoI)

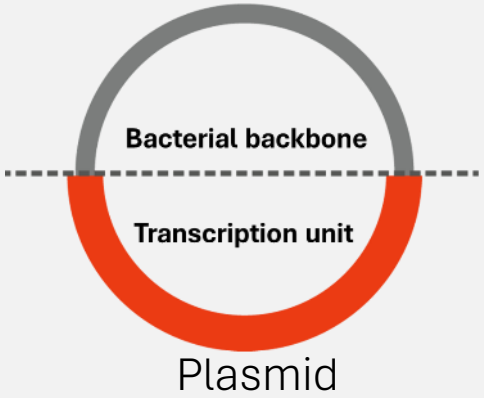
Minicircle production



Minicircle vs. plasmid features

- No bacterial backbone
- Small, supercoiled

- Bacterial sequences
- Larger size



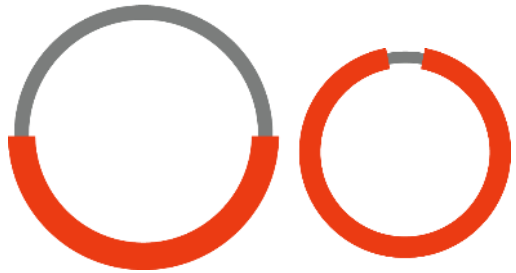
Minicircle: Small, monomeric, supercoiled

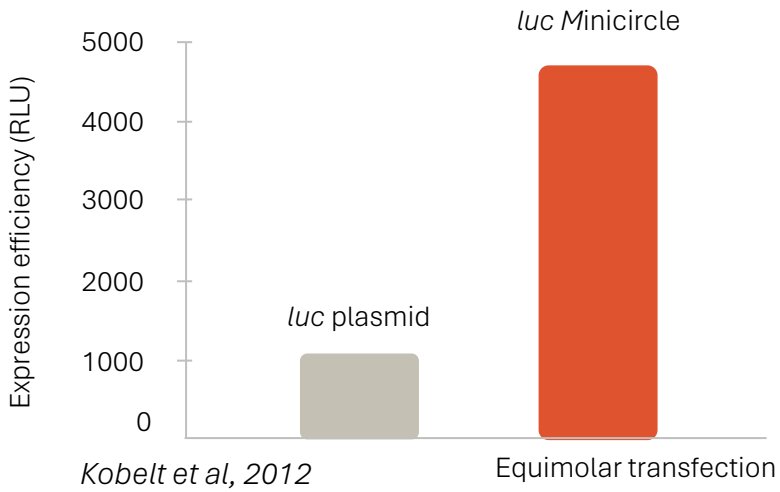
Minicircle: Advantages at a Glance

Bacterial backbone-free Minicircles

- No antibiotic resistance or other bacterial markers
- Less immunogenicity
- Reduced transgene silencing
- Lower DNA toxicity
- Higher transfection efficiency
- Stronger, more stable gene expression
- Improved yield – minimized costs
- Almost no cargo size restriction
- **Ideal for virus-free gene transfers**

Part of several clinical trials





Kobelt et al, 2012

Minicircle: Small, monomeric, supercoiled

Minicircle info

From bench to bedside: Development of a virus-free clinical CAR-T manufacturing protocol

PlasmidFactory

Fraunhofer IZI

PlasmidFactory

Dr. Katrin Mestermann

- PhD in Biology, University of Würzburg, 2019
- CAR T-cell research with Prof. Michael Hudecek
- Expert in lab-scale and GMP-grade immune cell manufacturing
- Joined Fraunhofer IZI Würzburg in 2024
- Co-leading GMP Development Unit since 2026
- Focus: CAR T, NK cells, macrophages, and ATMP translation

From bench to bedside:
Development of a virus-free clinical CAR T manufacturing protocol

Dr. rer. Nat. Katrin Mestermann

Webinar on non-viral manufacturing, 30th of June 2026

Agenda

1. Fraunhofer IZI – who are we – what do we do?
2. Deep-dive: virus-free CAR T engineering using transposase-mediated gene transfer
3. GMP compliant manufacturing
4. The fast lane to clinical translation

01

Fraunhofer IZI

Fraunhofer
IZI

Fraunhofer Institute for Cell Therapy and Immunology

Locations:	Leipzig (HQ), Potsdam, Halle (Saale), Rostock, Erfurt, Würzburg
Employees:	~ 600
Project revenue:	~ 40 - 50 Mio. € per year
Research scope:	Immuno-Oncology Infectious Disease Pathology
Business model:	~ 70 % contract research ~ 30 % basic funding provided by German federal and state governments

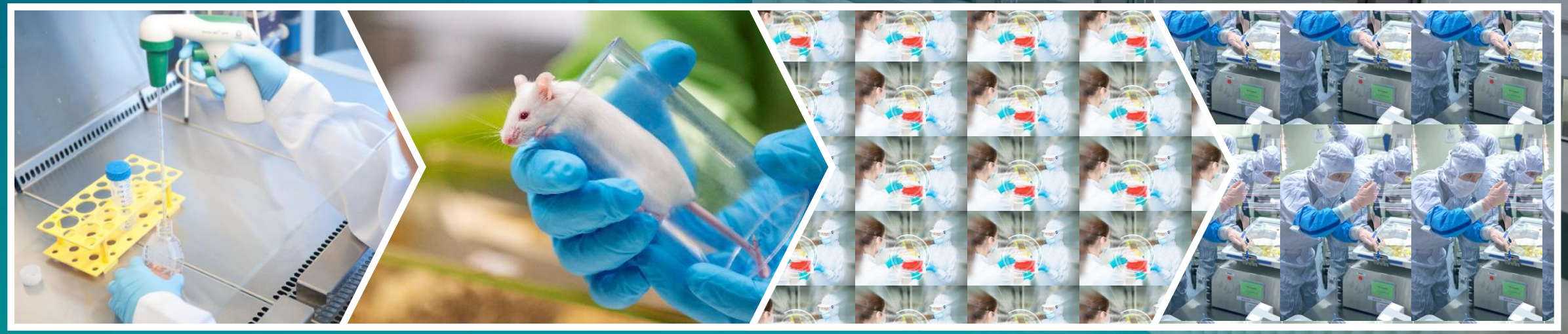
Cell & Gene Therapy

Early Development

GLP Safety & Efficacy

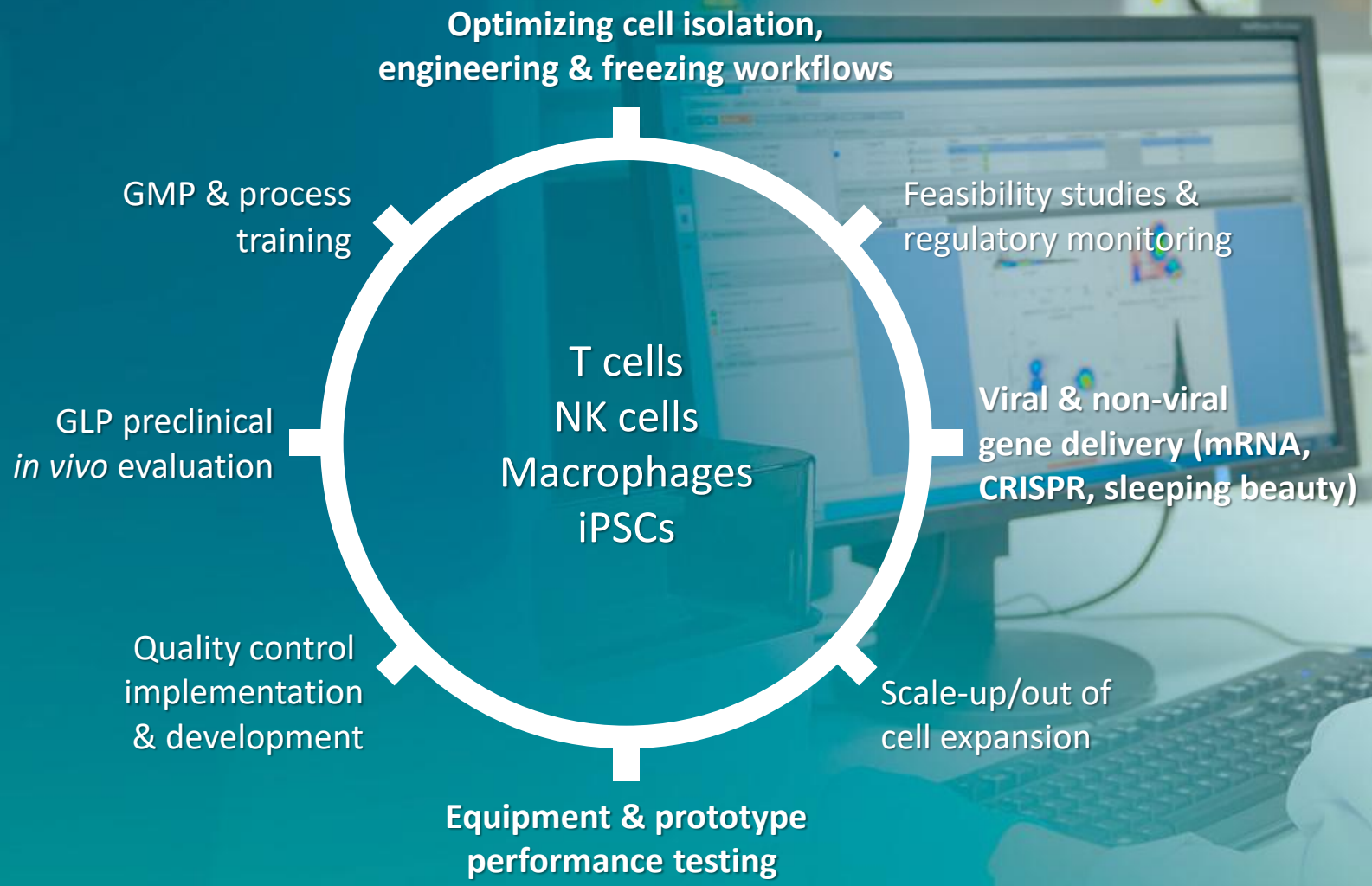
GMP Development

GMP Manufacturing



Fraunhofer IZI

Cell & Gene Therapy – Development Services



Fraunhofer IZI

Upscaling and automation

Mapping processes to automated devices

CliniMACS Prodigy®

Cocoon® Platform

Cytiva VIA Freeze™

Sefia Select™ System

Ambr® 15 Bioreactor

CTS Rotea

MaxCyte

Xuri™ Wave Bioreactor

Fraunhofer IZI

Fraunhofer IZI

Two state-of-the-art GMP manufacturing facilities for cell-based therapeutics

One of Europe’s largest manufacturers of cell and gene therapies

20 years of experience in the development and translation of cell and gene therapies

4,500 cell and gene therapy batches manufactured (including 700 CAR-T cell therapies)

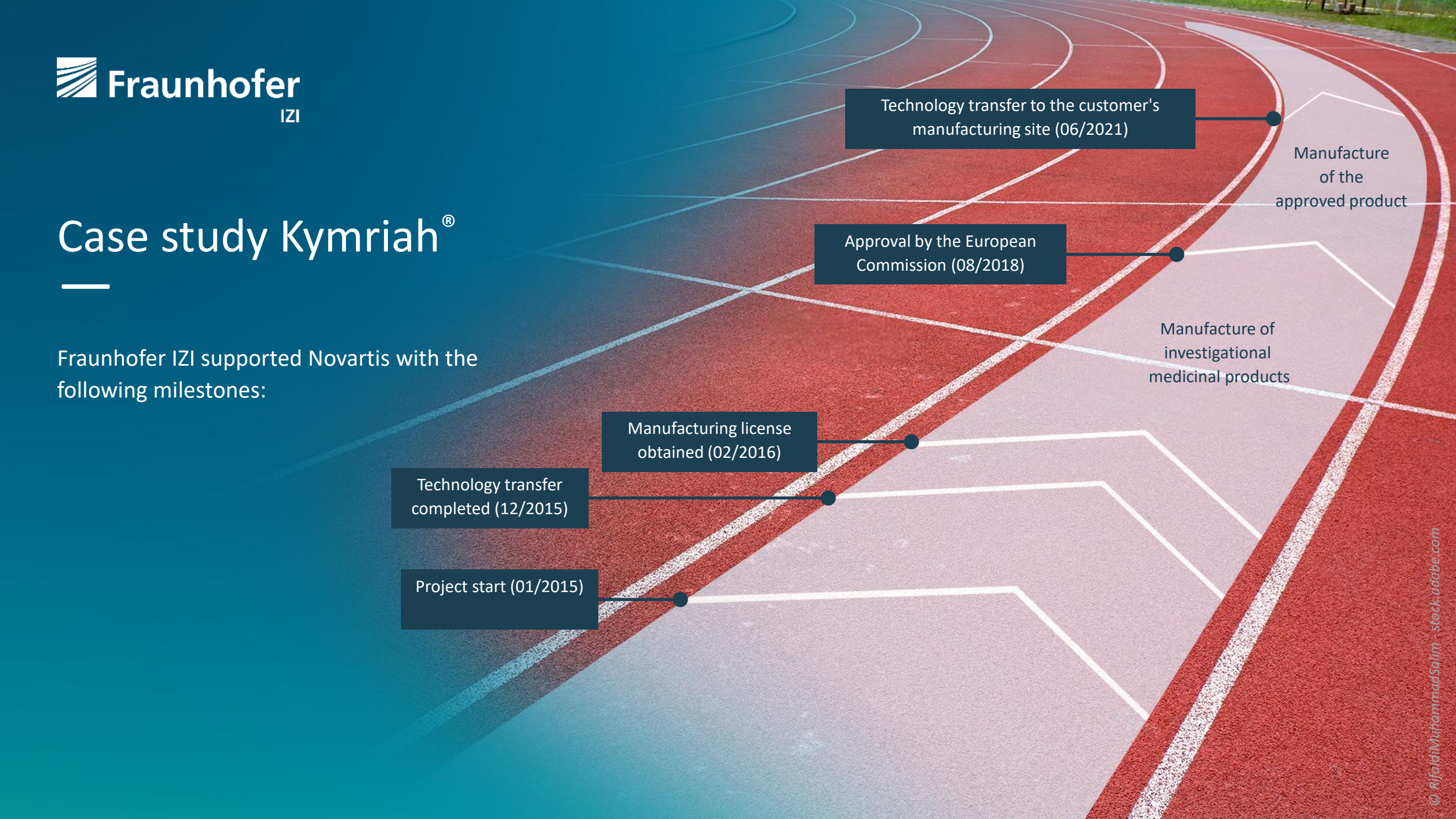
Successful large volume manufacturing projects with Novartis, BMS, and innovative start-ups

15 successfully completed regulatory inspections and numerous customer audits

Fraunhofer IZI

Case study Kymriah®

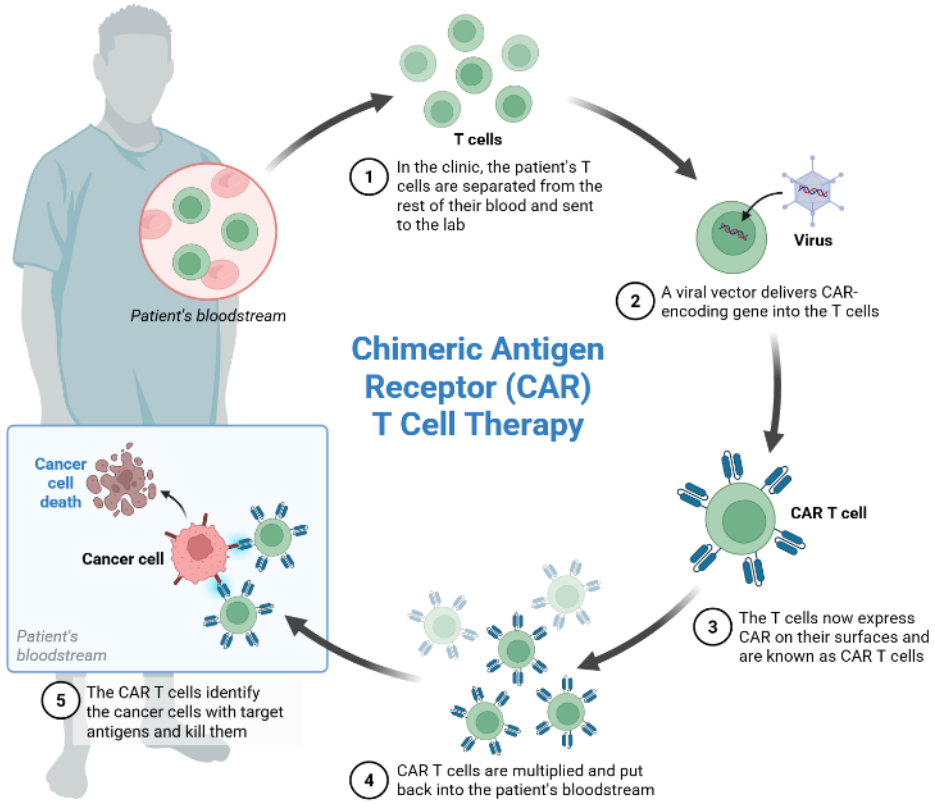
Fraunhofer IZI supported Novartis with the following milestones:



02

Deep-dive: virus-free CAR T engineering using transposase-mediated gene transfer

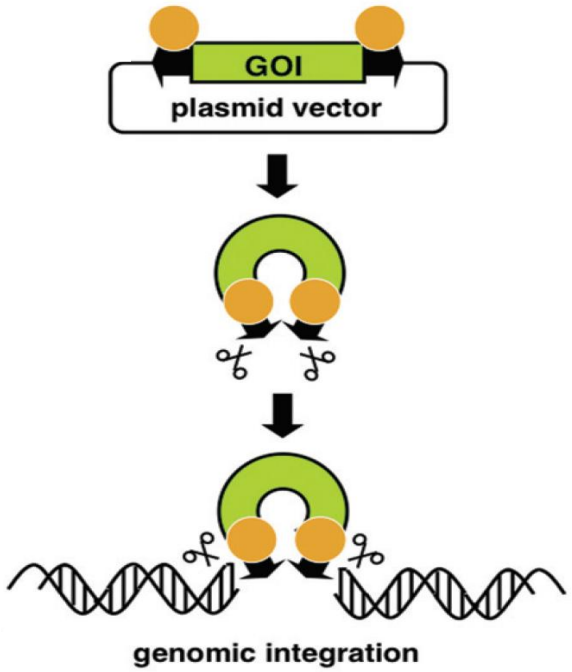
State-of-the-Art: viral manufacturing of CAR T and treatment schedule

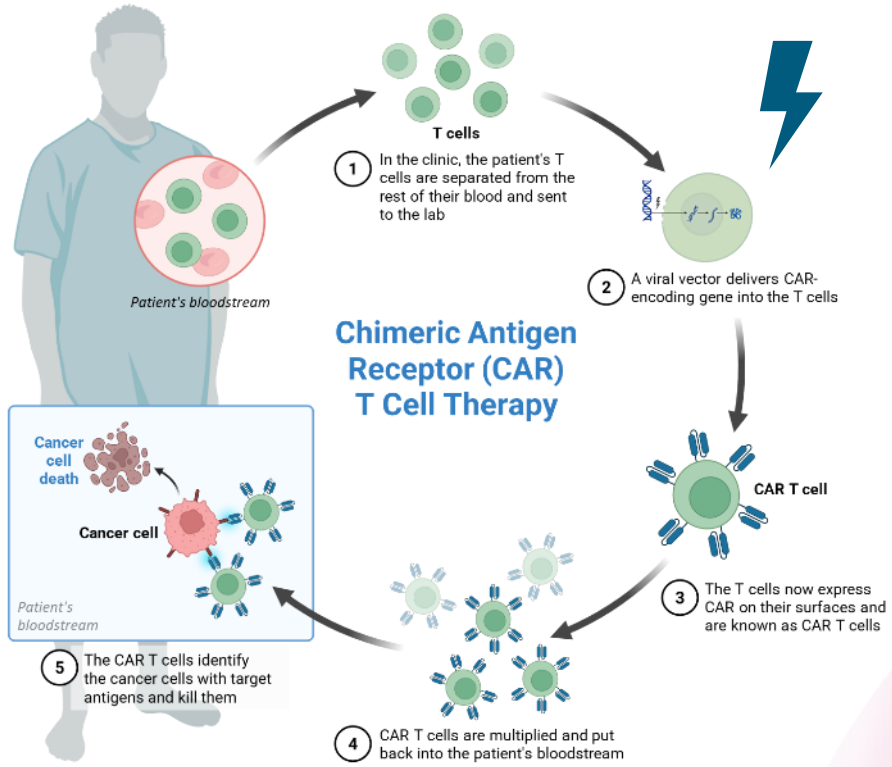


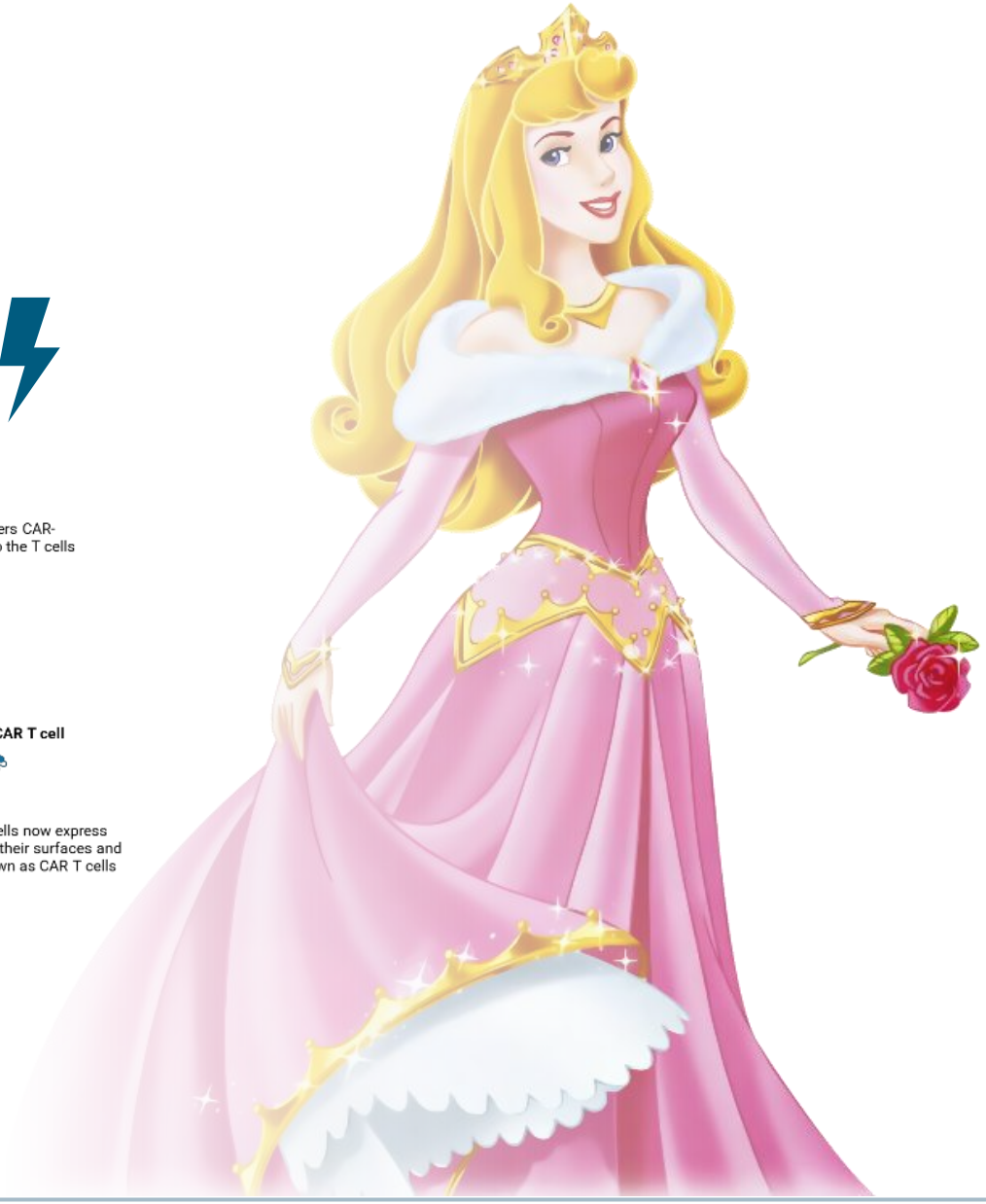
Product Name (Brand)	Target	Primary Indications
Tisagenlecleucel (Kymriah)	CD19	Relapsed/refractory (r/r) B-cell ALL (up to age 25), r/r Large B-cell Lymphoma (LBCL), and r/r Follicular Lymphoma
Axicabtagene ciloleucel (Yescarta)	CD19	r/r Large B-cell Lymphoma, r/r Primary Mediastinal Large B-Cell Lymphoma, and r/r Follicular Lymphoma
Brexucabtagene autoleucel (Tecartus)	CD19	r/r Mantle Cell Lymphoma and r/r B-cell Acute Lymphoblastic Leukemia (ALL)
Lisocabtagene maraleucel (Breyanzi)	CD19	r/r Large B-cell Lymphoma, Follicular Lymphoma, Mantle Cell Lymphoma, and Chronic Lymphocytic Leukemia (CLL)
Idecabtagene vicleucel (Abecma)	BCMA	r/r Multiple Myeloma (typically after ≥3 prior lines of therapy)
Ciltacabtagene autoleucel (Carvykti)	BCMA	r/r Multiple Myeloma (typically after ≥1 prior line of therapy)
Obecabtagene autoleucel (Aucatzyl)	CD19	Adult patients with r/r B-cell precursor ALL

Sleeping Beauty Transposase mediated gene transfer

Stable gene integration and CAR expression



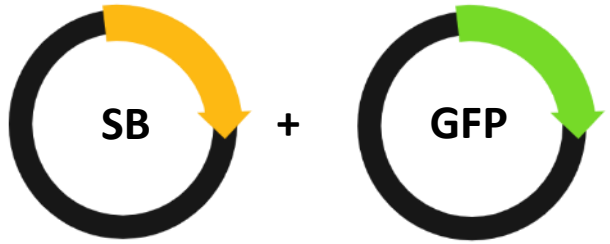


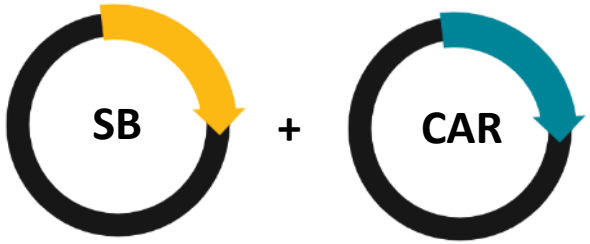


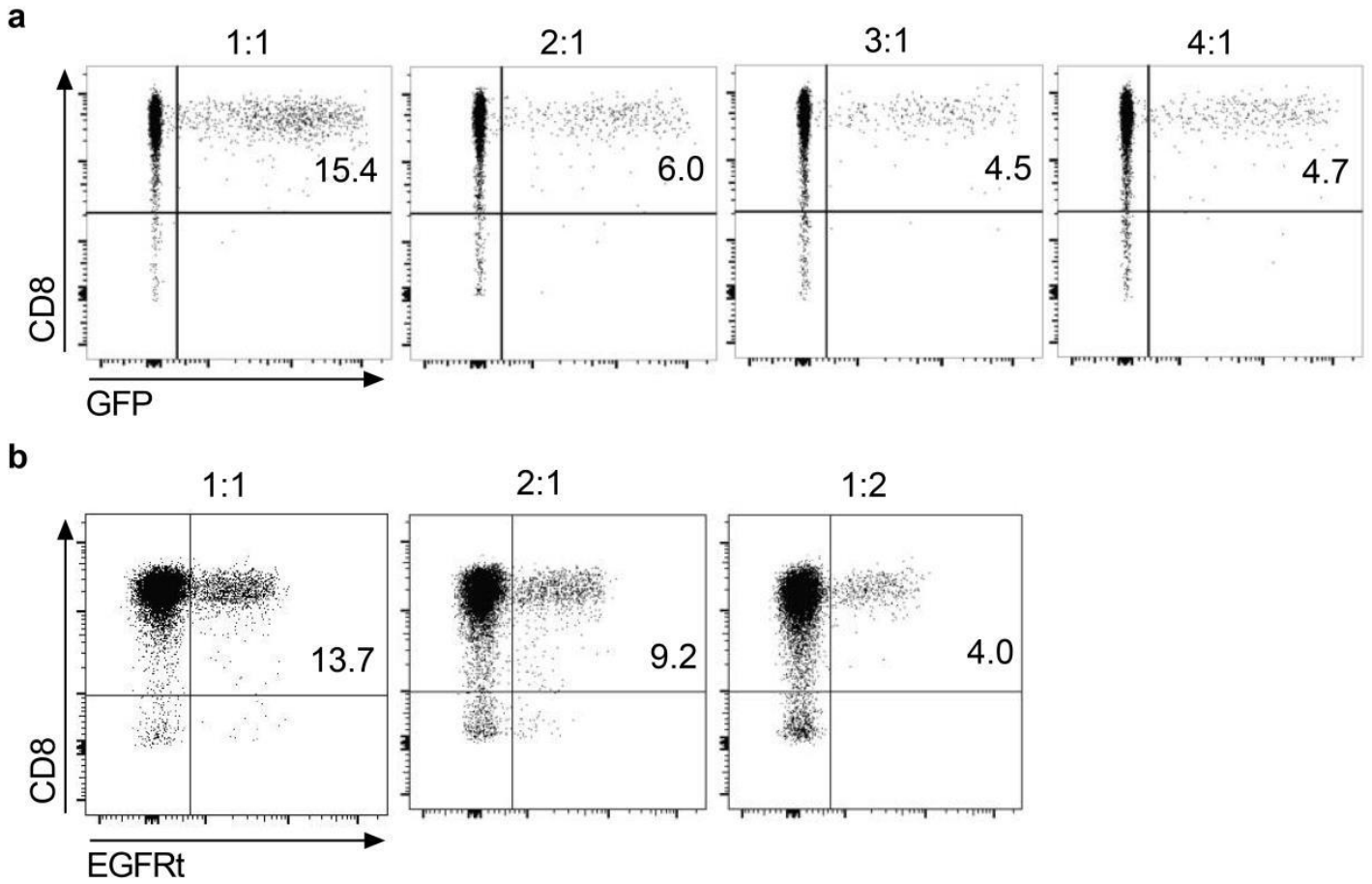
Voigt et al., *Nat Commun* 2016

SB mediated gene transfer – the beginning

Proof-of-concept with state-of-the-art plasmids





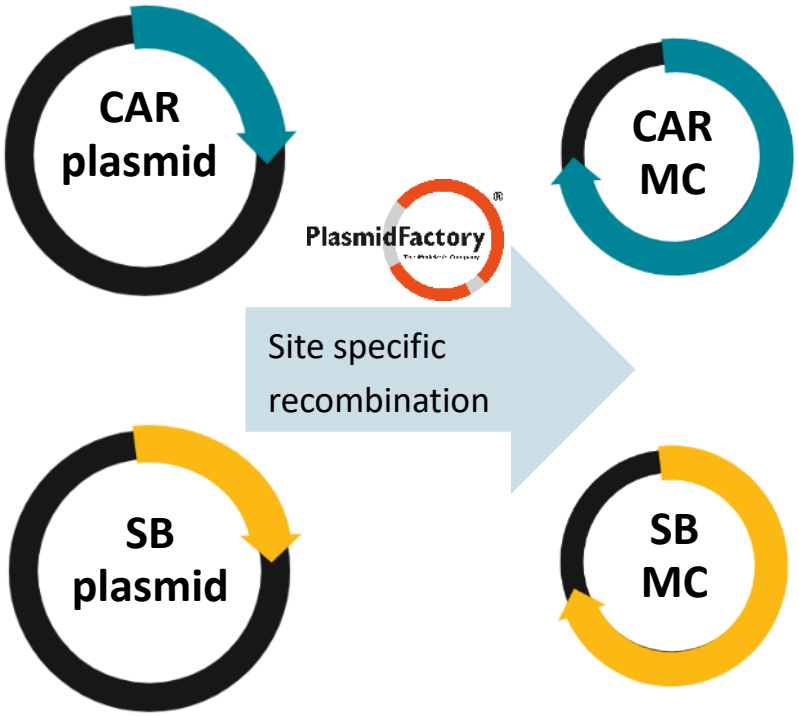


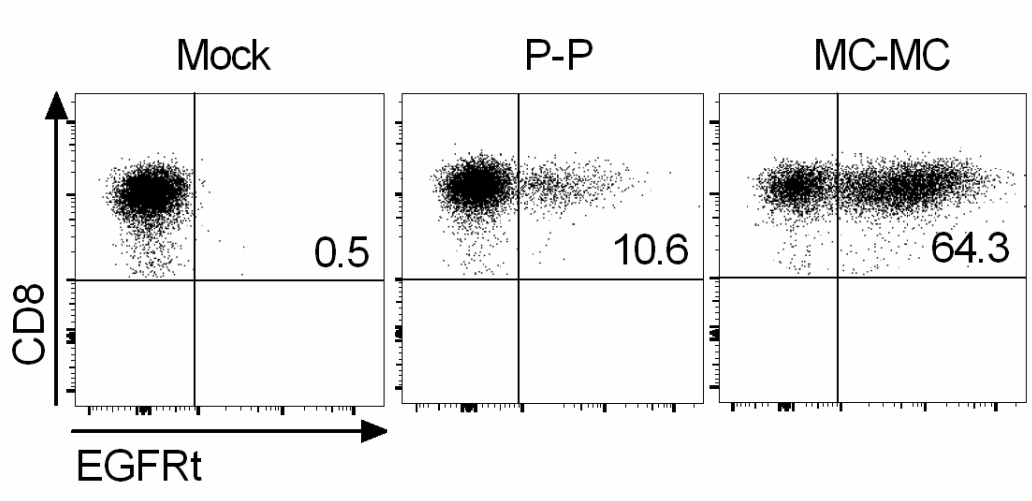
Adapted from Monjezi, R., et al. Leukemia 2017

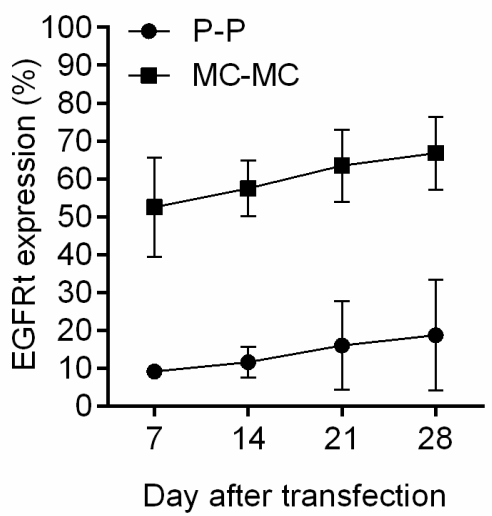
PlasmidFactory

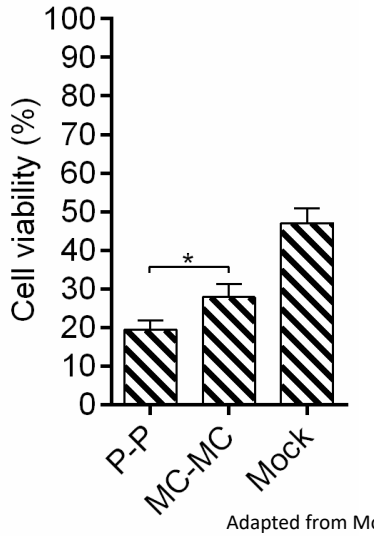
Fraunhofer IZI

Use of Minicircle plasmids increases gene transfer rate and viability









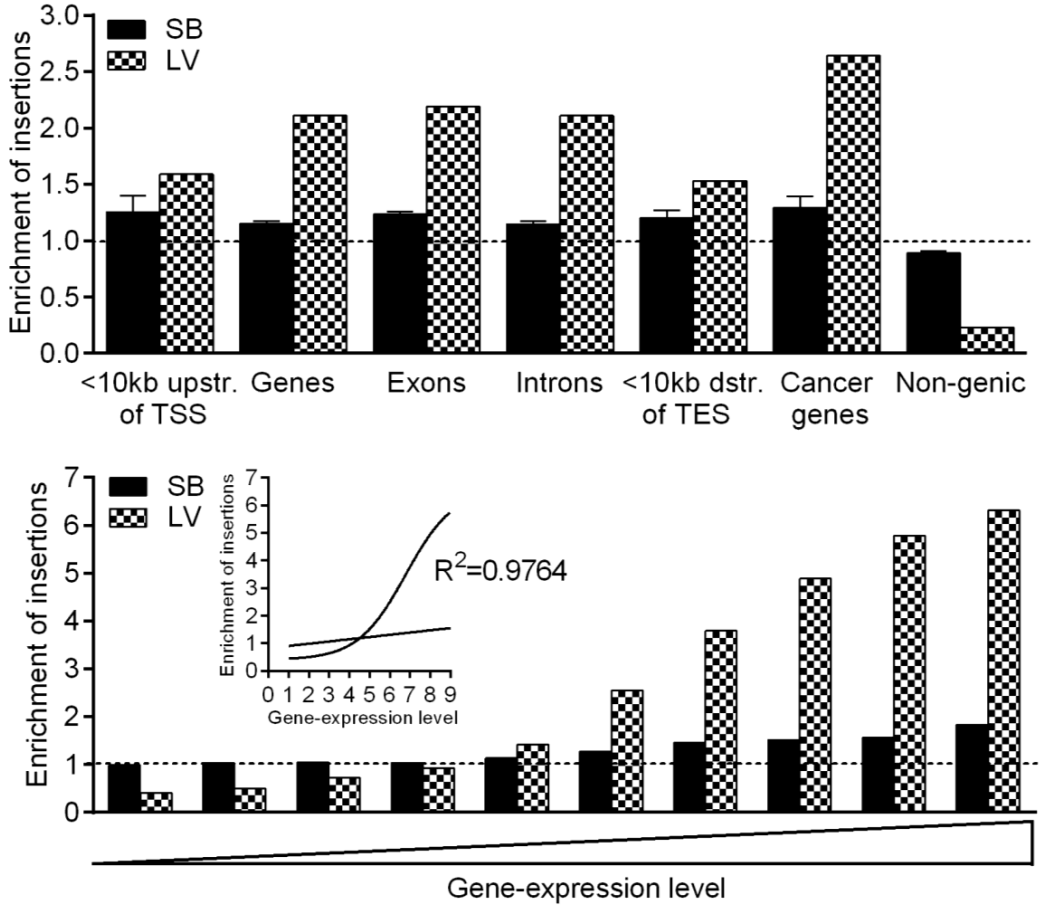
Adapted from Monjezi, R., et al. Leukemia 2017

PlasmidFactory

Fraunhofer IZI

Regulatory aspects – genomic safety

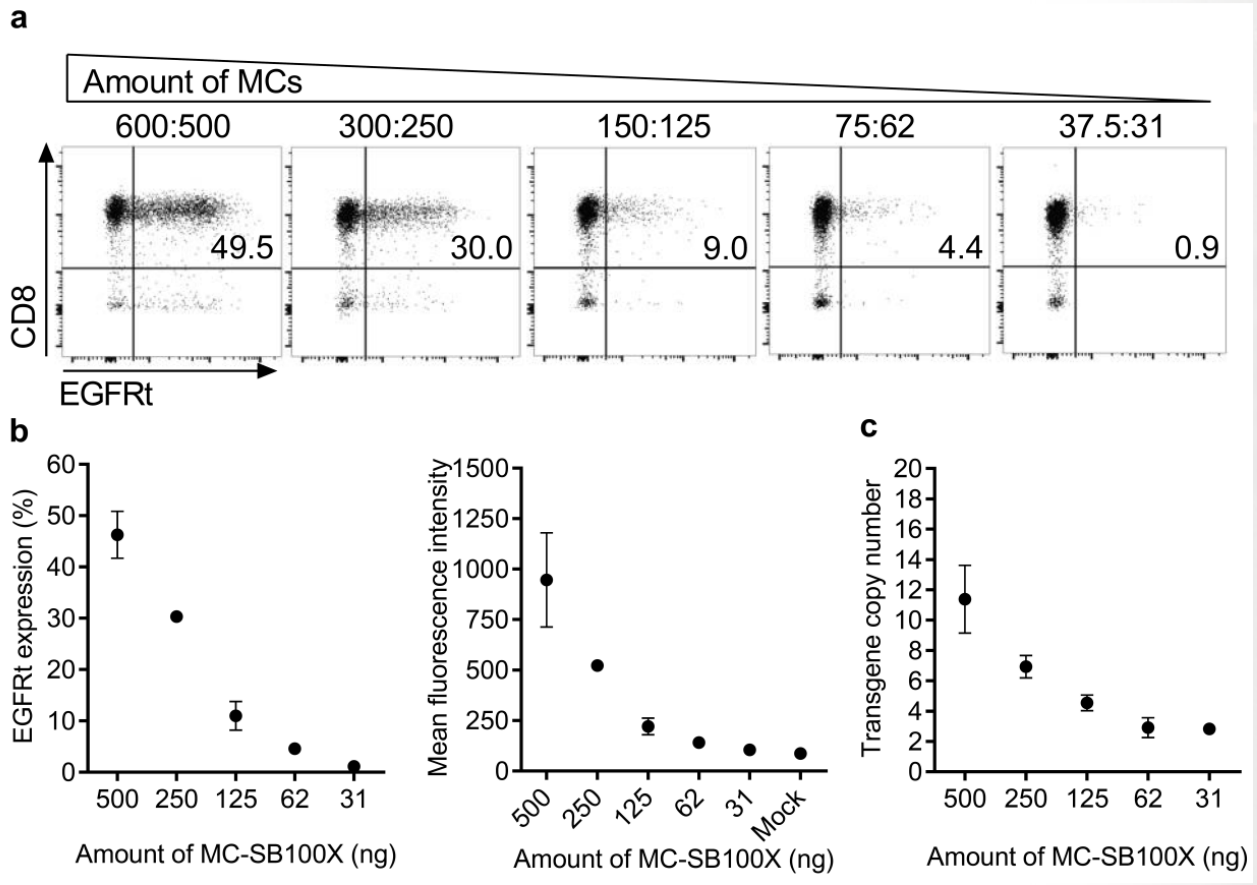
Insertion site analysis



Adapted from Monjezi, R., et al. Leukemia 2017

Regulatory aspects – genomic safety

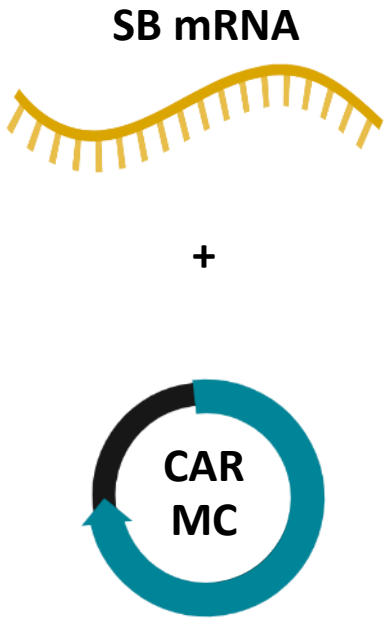
Transgene copy number

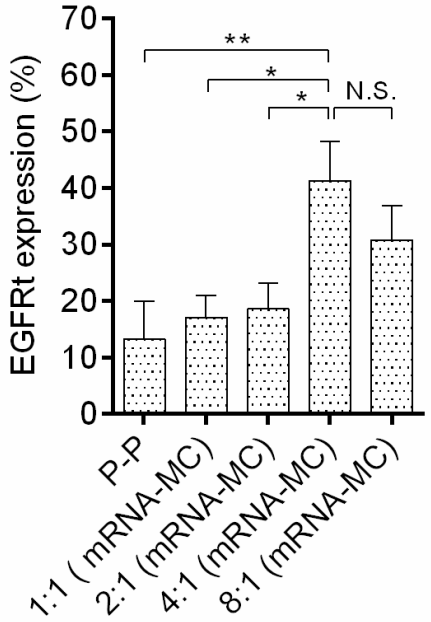


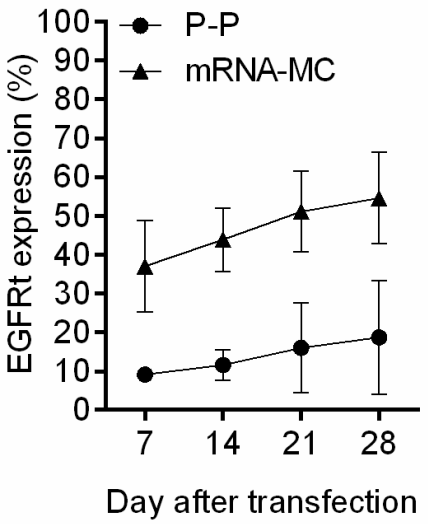
Adapted from Monjezi, R., et al. Leukemia 2017

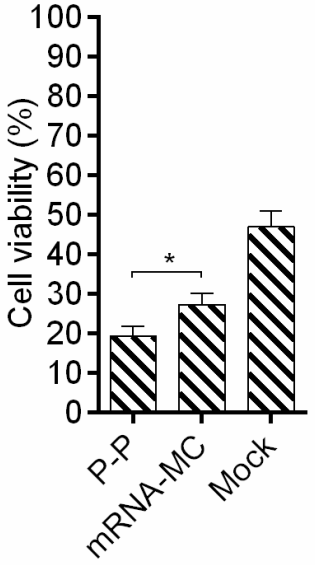
Fraunhofer IZI

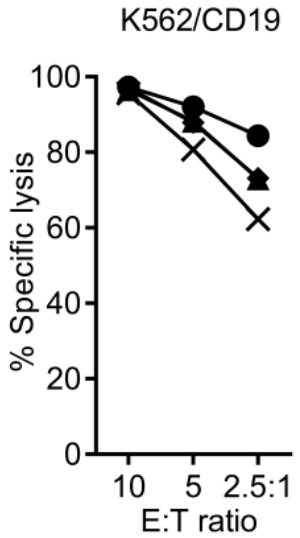
Regulatory aspects : avoid long term expression of SB in the cells











Adapted from Monjezi, R., et al. Leukemia 2017

PlasmidFactory

Fraunhofer IZI

03

GMP compliant manufacturing

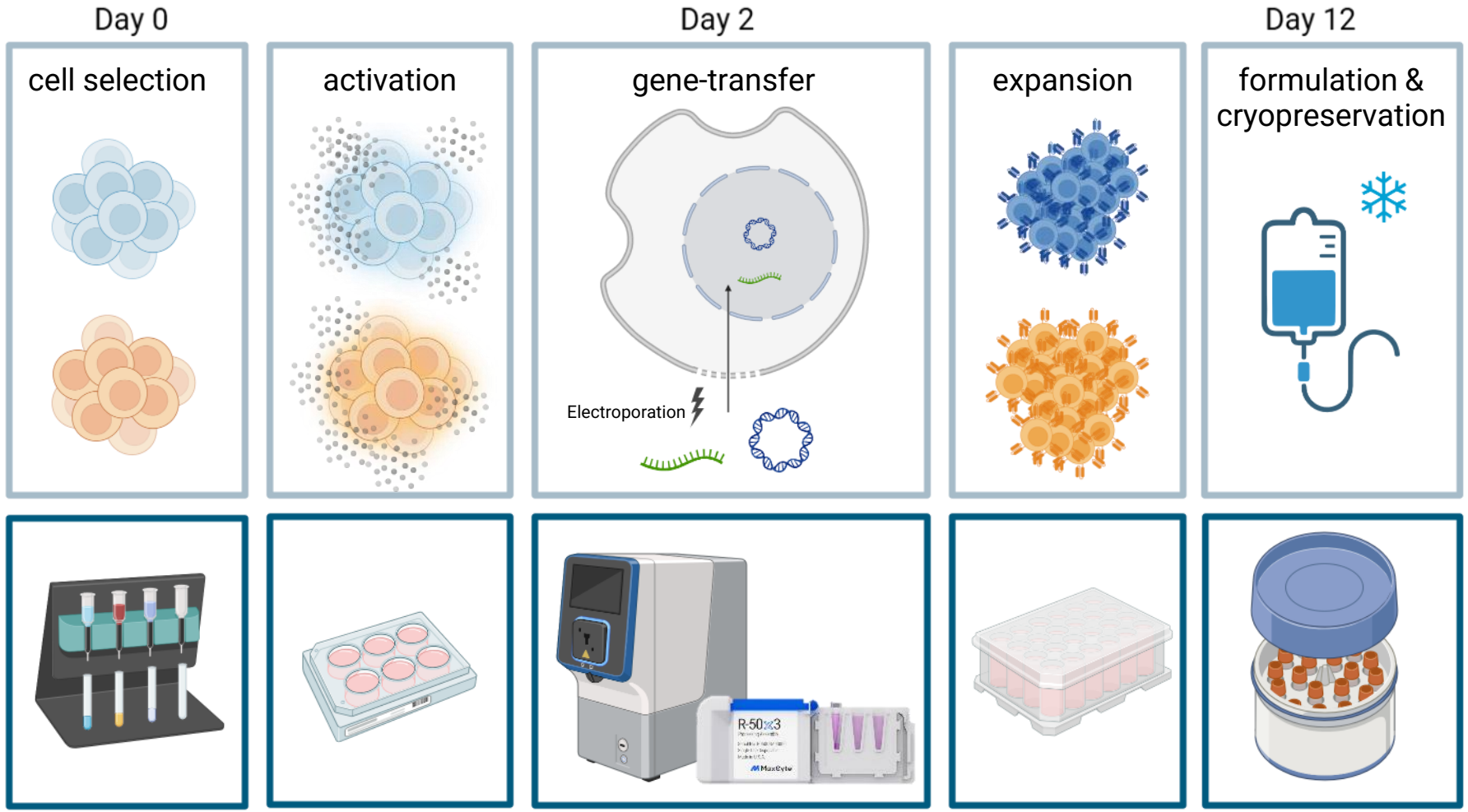
Fraunhofer IZI

Fraunhofer IZI

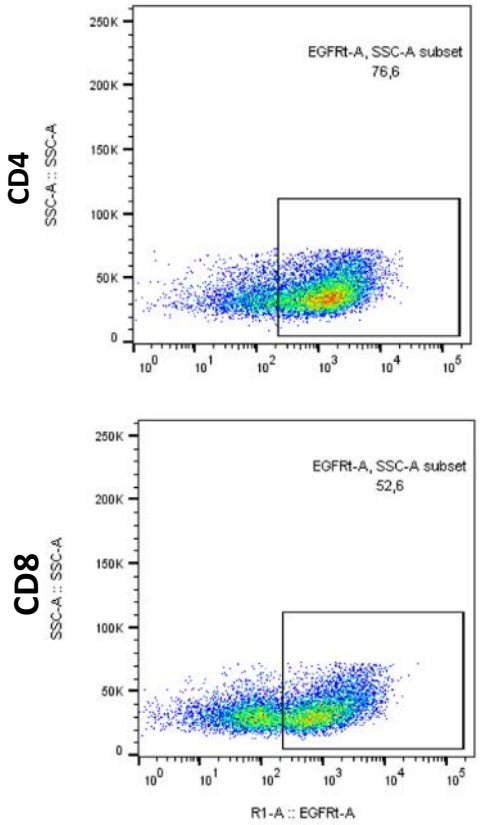
- 1st patient treated
- Clinical manufacturing
- Clinical trial application
- Preclinical data package
- Validation runs
- Process freeze
- upscaling
- Small scale protocol optimization

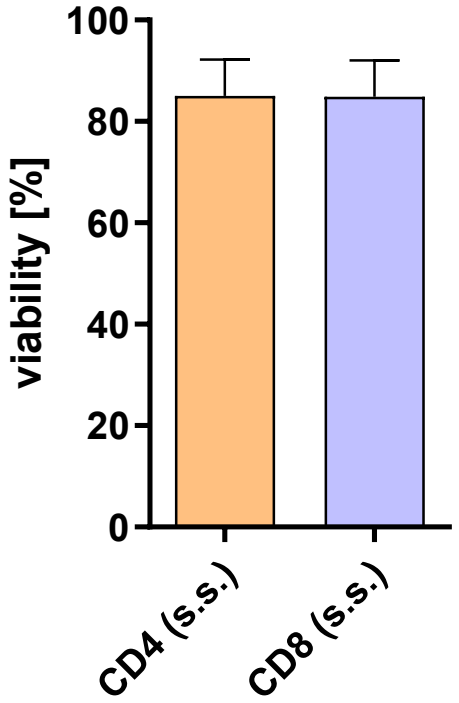
Manual, non-viral CAR T cell production

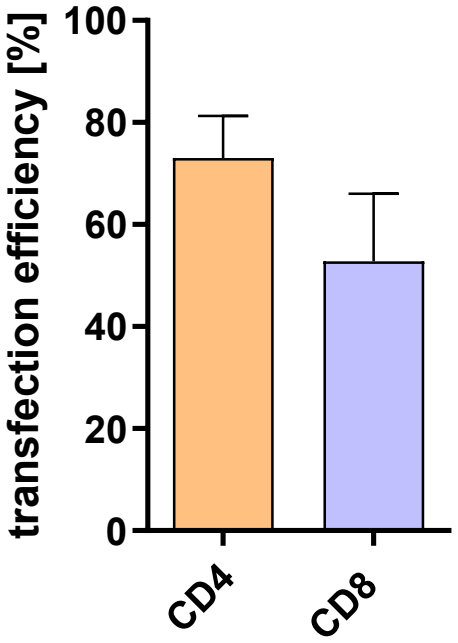
Defining a small-scale process



small scale protocol after process optimization

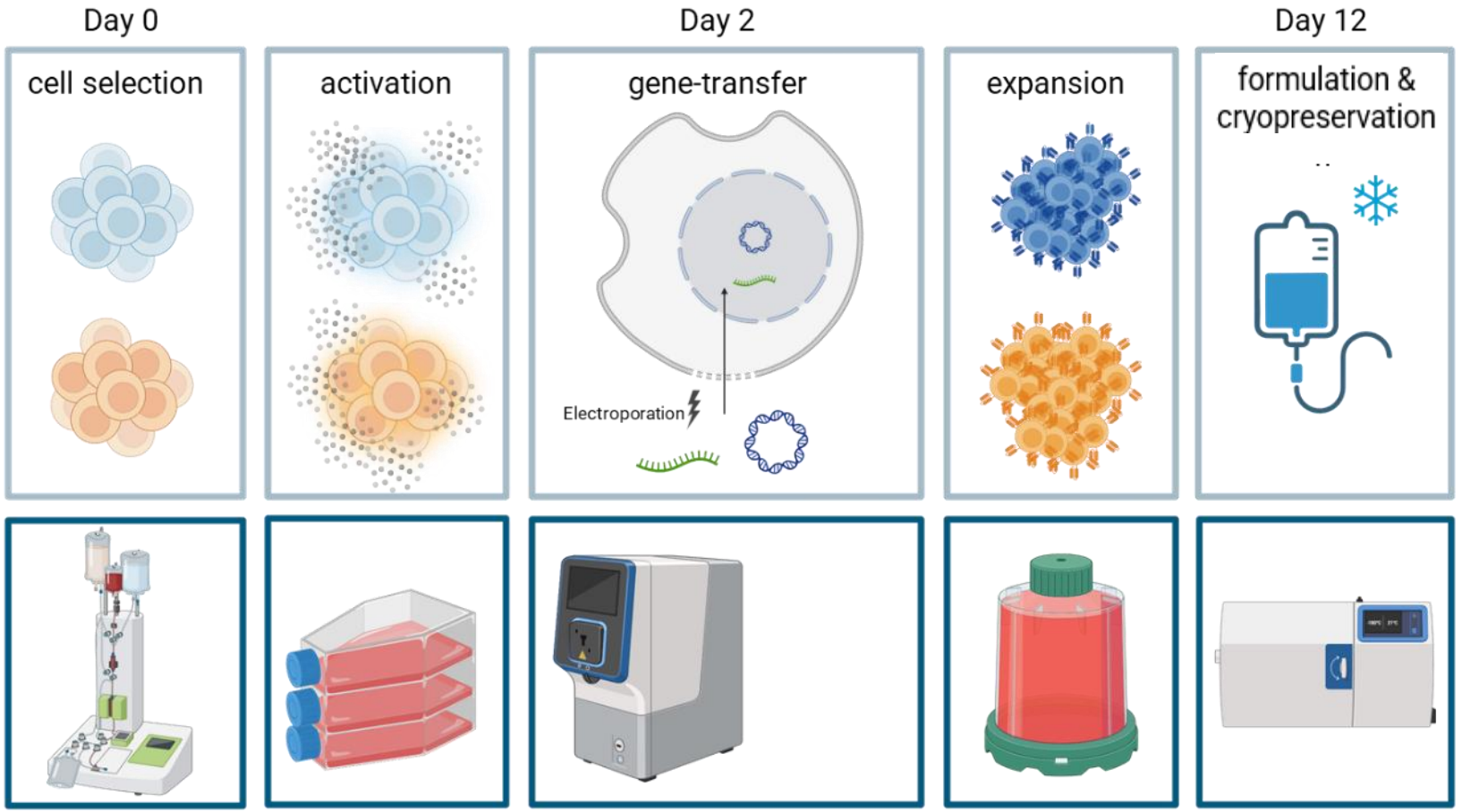




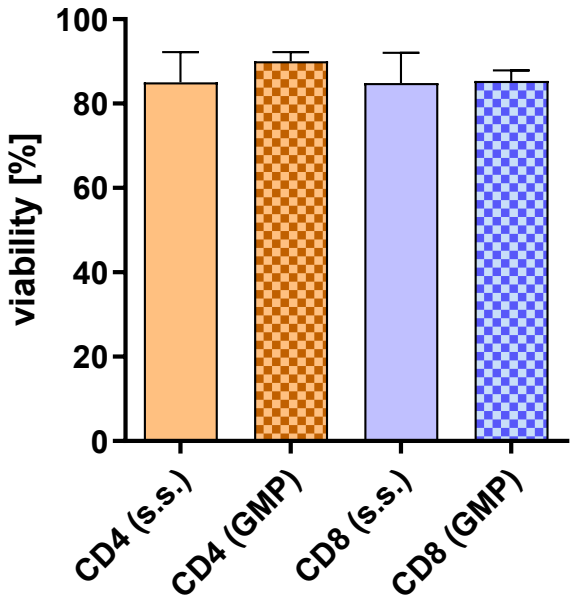


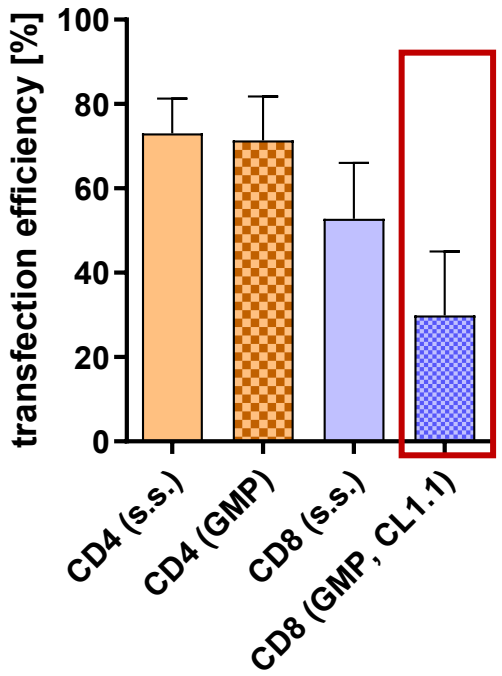
Mestermann et al, in preparation

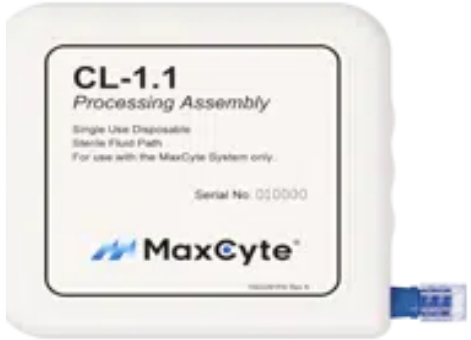
GMP compliant, large scale, non-viral CAR T cell production



Upscaling and Validation



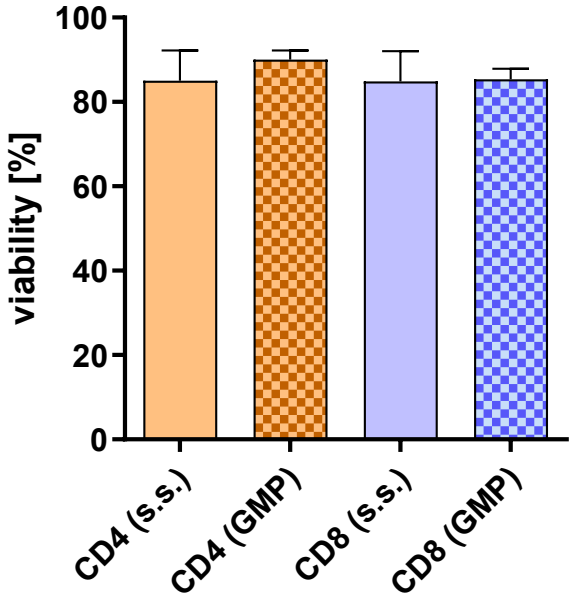


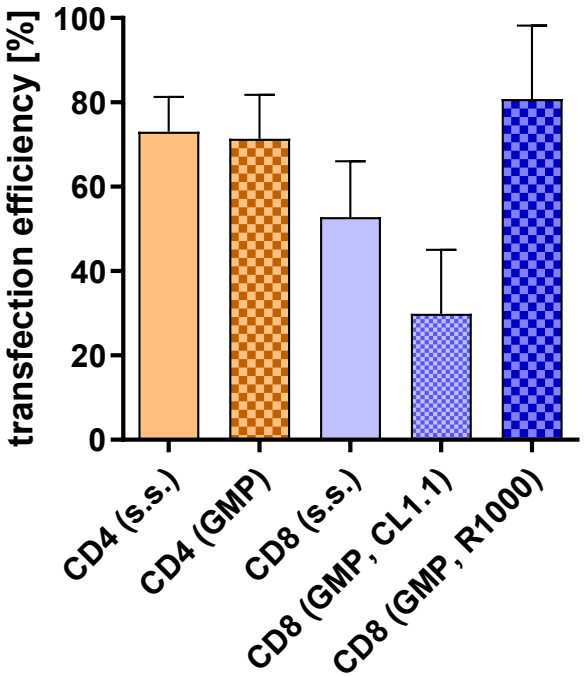


Mestermann et al, in preparation

Upscaling and validation

Process optimization improves manufacturing efficiency



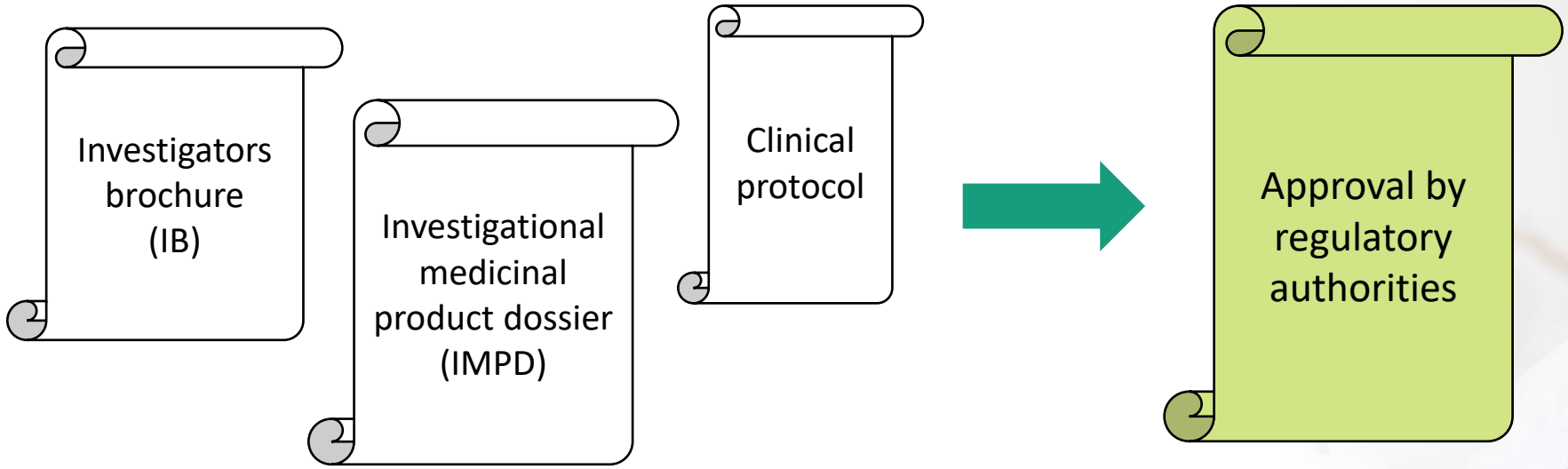


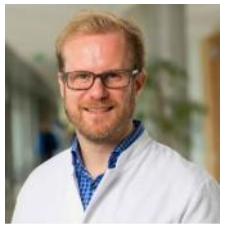
Specifications

- ☐ Identity
- ☐ Purity
- ☐ Viability
- ☐ Transfection efficiency
- ☐ Number/Dosage
- ☐ Sterility
- ☐ Vector copy number

Mestermann et al, in preparation

Clinical trial application





Michael Hudecek
Medizinische Klinik II /
Lehrstuhl für Zelluläre Immuntherapie
Universitätsklinikum Würzburg

LION-1

A Phase I clinical trial to assess safety and tolerability of autologous ROR1 CAR-T cells in ROR1+ tumors

Universitätsklinikum Würzburg

NCT NATIONALES CENTRUM FÜR TUMORERKRANKUNGEN

T-CURX

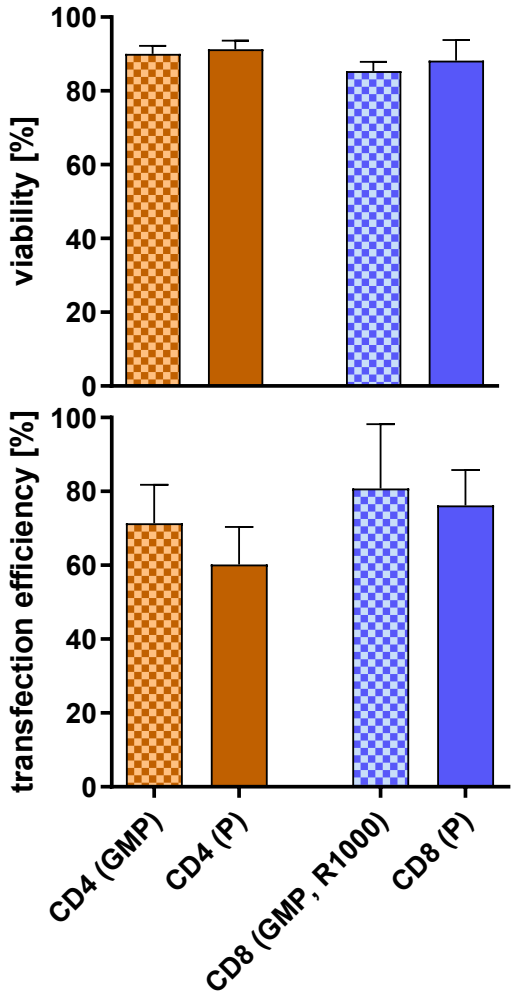
Bundesministerium für Bildung und Forschung

MPE Myeloma Patients Europe

Fraunhofer IZI

The process proves to be robust using patient material

n=3



Specifications

- ☑ Identity
- ☑ Purity
- ☑ Viability
- ☑ Transfection efficiency
- ☑ Number/Dosage
- ☑ Sterility
- ☑ Vector copy number

Fraunhofer IZI

04

the fast lane to clinical translation

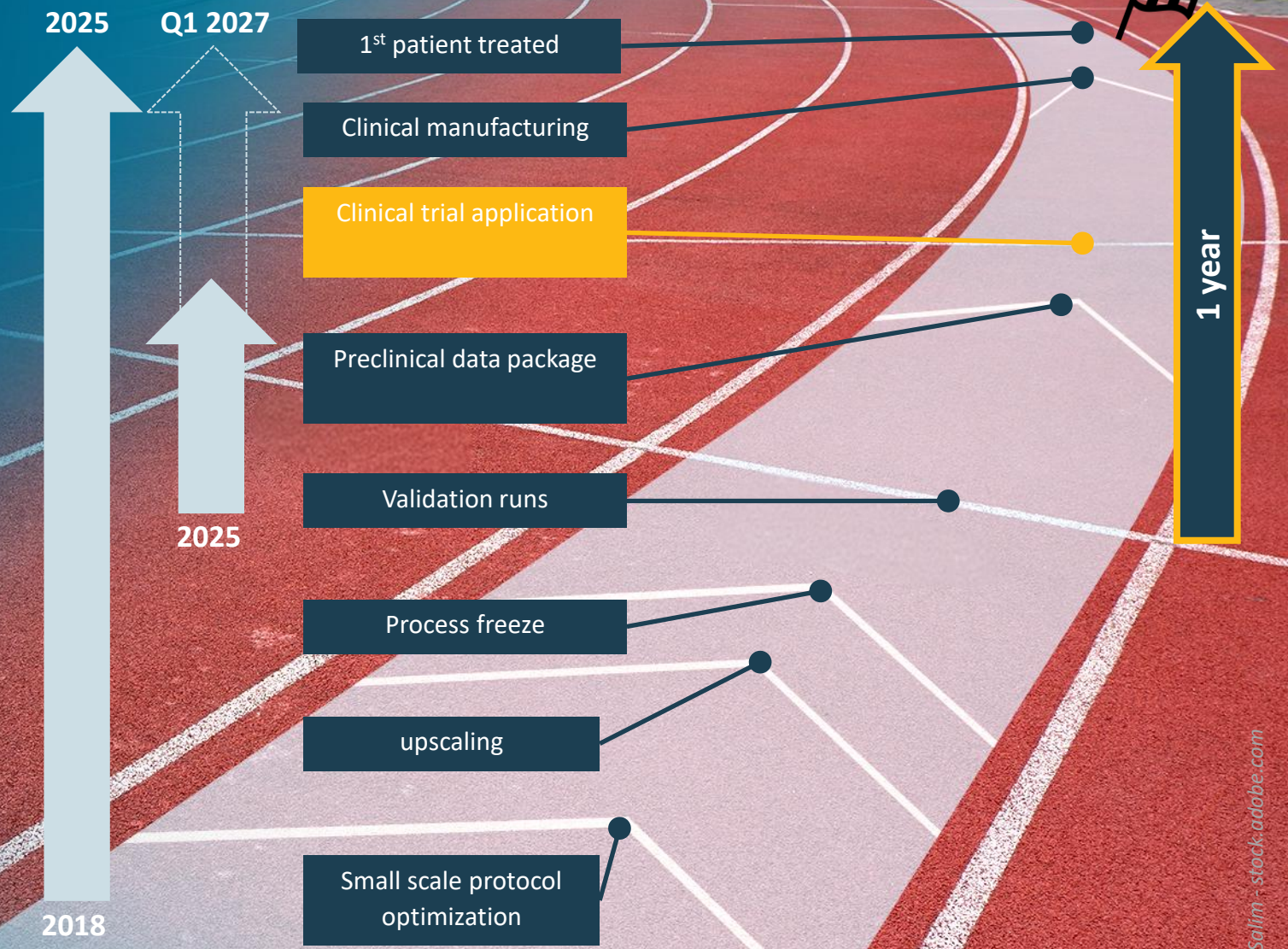
Fraunhofer IZI

Fraunhofer IZI

The road to clinical translation

Fraunhofer IZI supports academic trials with the following milestones by:

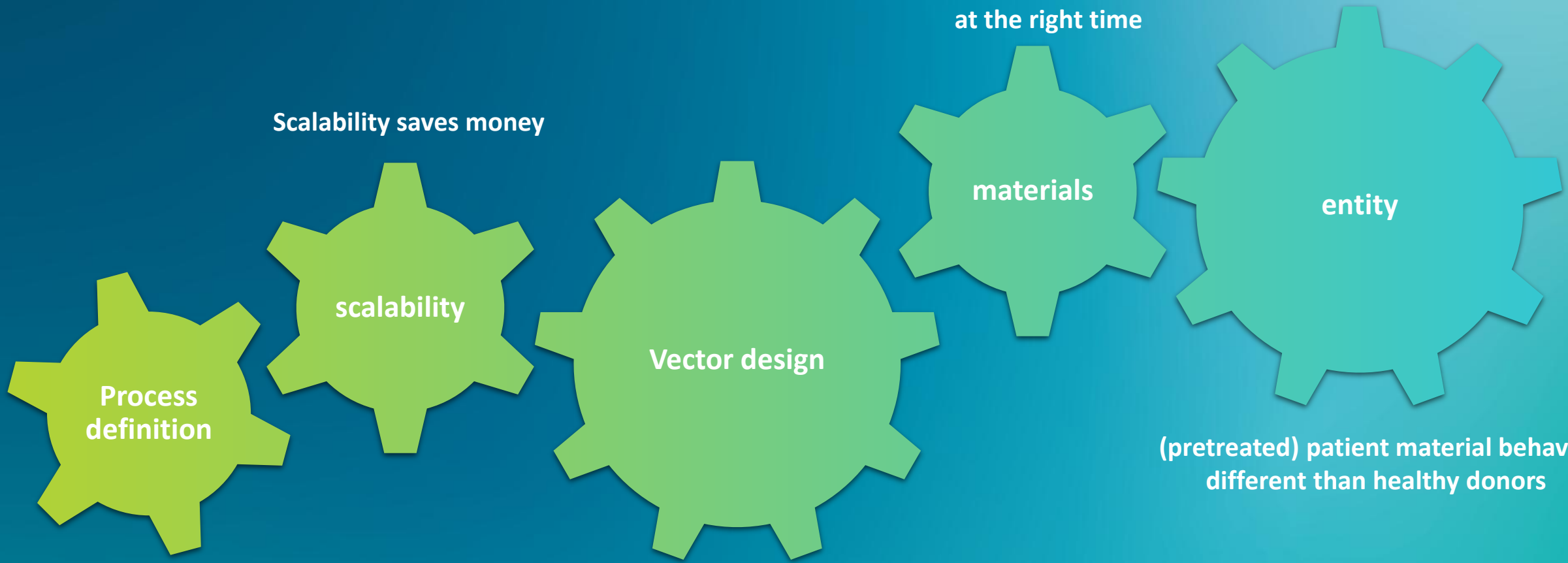
- Established, clinical manufacturing protocol
- Granted general manufacturing license
- Regulatory approval



Fraunhofer IZI

Choose the right quality at the right time

Scalability saves money



(pretreated) patient material behaves different than healthy donors

The process is part of the product
A good process takes time

The vector is also part of the product
Know your vector and keep it

Fraunhofer IZI

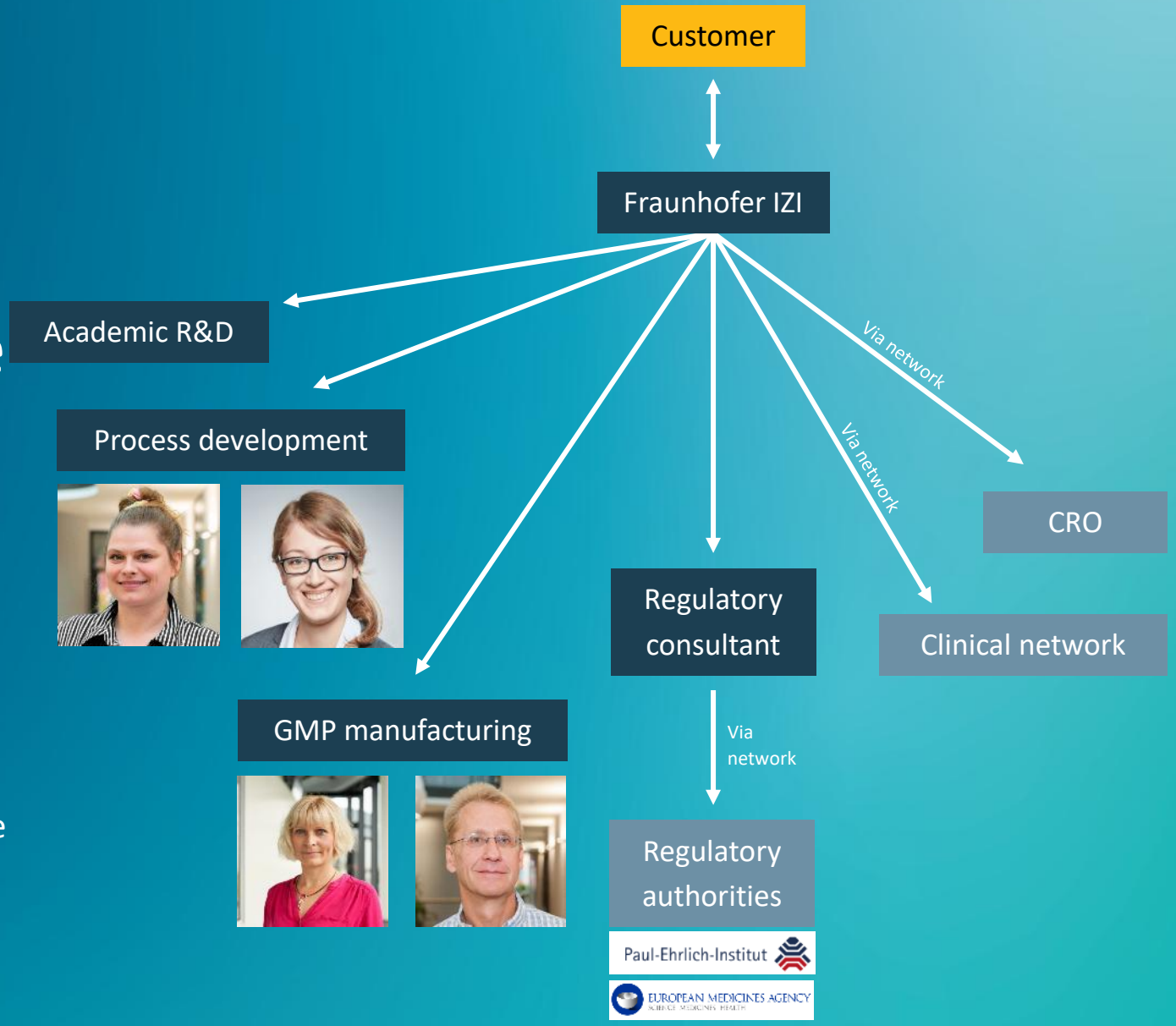
Fraunhofer IZI – One partner for the entire journey

Minimize costs, time, and errors by working with one integrated non-competing partner.

Trusted by regulators and academia

As a publicly funded non-profit research organization, we do not compete with your commercial interests.

We act as your European execution arm.



Contact me
Katrin Mestermann

Group Lead
»GMP development«

Scientific Lead
»Cellular Immunotherapy«

at Fraunhofer IZI,
branchside Würzburg

Katrin.Mestermann@izi.fraunhofer.de

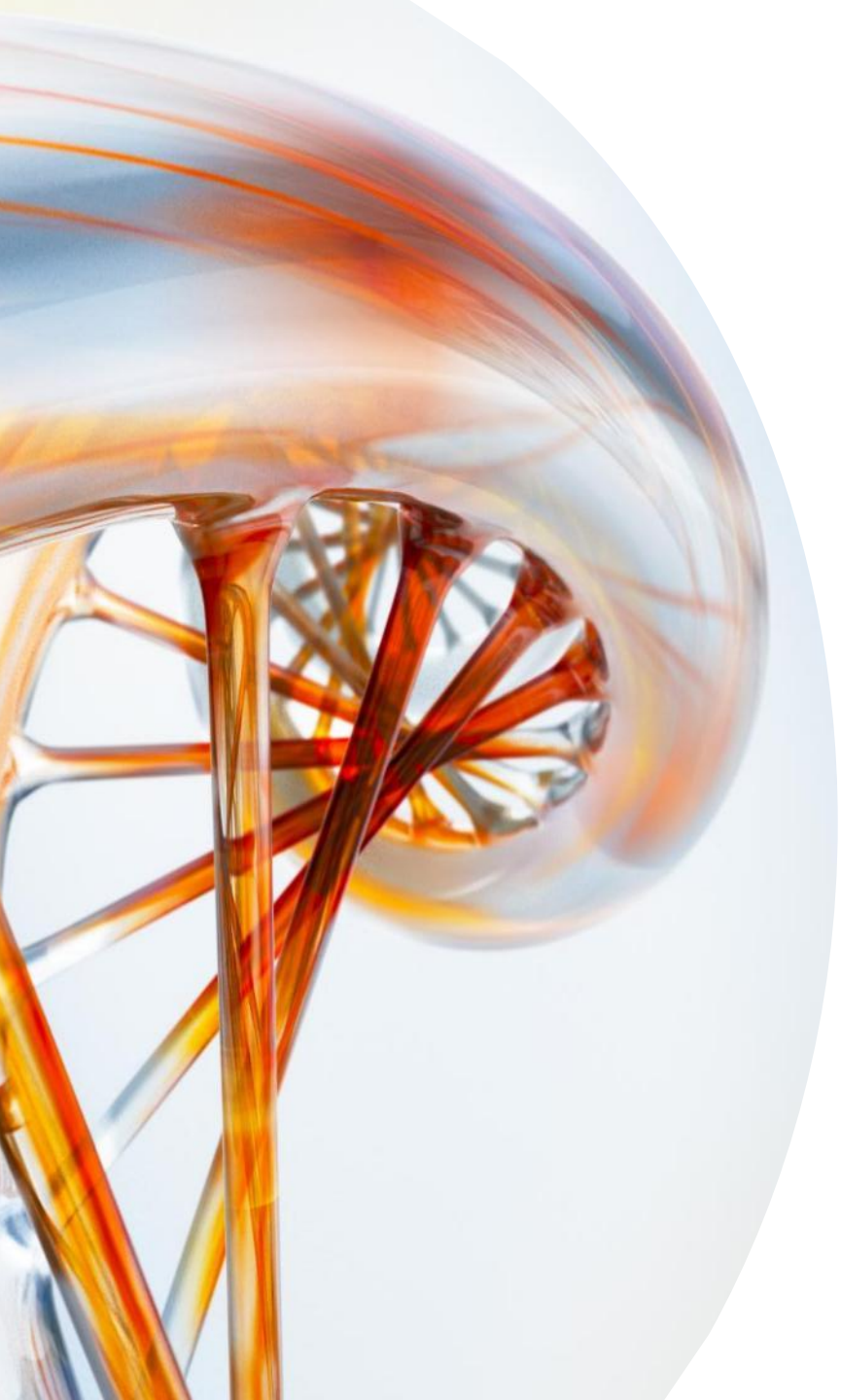
Fraunhofer IZI

LinkedIn

Disclosures

- In addition to the affiliation stated above, I am an employee of the University Hospital Würzburg, Germany.
- I hold a patent in relation to control of CAR T side effects (WO2019110815A1)
- Parts of this presentation were created in BioRender


LION
LEIPZIG
IMMUNE ONCOLOGY
CONFERENCE
2026
BE PART OF IT.
Meet clinicians, scientists, and industry professionals focused on immuno-oncology.
November 24–25, 2026
Leipzig, Germany
www.LION-conference.com
Abstract submission for poster-presentations is still open!
Organized by
Fraunhofer IZI
Universitätsklinikum Leipzig
Anstalt öffentlichen Rechts



PlasmidFactory®

PlasmidFactory GmbH

Meisenstraße 96 | 33607 Bielefeld | Germany

www.PlasmidFactory.com

LinkedIn

PlasmidFactory 25 YEARS