iPSC/MSC engineered cell therapy for inflammatory disease

KIJI Therapeutics

October 2023

A new paradigm – Professionalizing MSCs

Kiji Therapeutics

Challenge

Why we need a new paradigm for MSCs:

- MSCs have unfulfilled efficacy
- MSC manufacturing has limitations

Solution

Addressing unmet medical need in inflammatory diseases:

- Genetically engineer MSCs for potency
- Proprietary IL10/CXCR4 for GvHD; IBD; Skin
- iPSC technology for improved scale, manufacturing efficiency and consistency

A new era for the treatment of autoimmune diseases with iMSCs

Engineered iPSC/MSC derived cell therapies for inflammatory and other major diseases

Kiji Therapeutics

Game-changing

- Transformative off-the-shelf
- Engineered cell therapy
- iPSC based
- Broad platform

Advanced

- Validating trial partially financed by a grant (60%) to start in 2024.
- Extensive *in vitro* and *in vivo* multiple model PoC for Autoimmune Diseases (GvHD, IBD, Skin, other)
- iPSC and gene engineering tools

Ready to proceed

- Highly experienced team, advisors and corporate structure
- Collaborations with Ciemat & Clinica Universidad de Navarra
- CDMO Industrial collaboration for iPSC

GOBIERNO DE ESPAÑA MINISTERIO DE CIENCIA E INNOVACIÓN Ciemat Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas

Clínica Universidad de Navarra

We built Kiji Therapeutics to deliver engineered cell therapies for life threatening disease

Kiji Therapeutics Snapshot

Kiji Therapeutics

Mission	• Develop transformative off-the-shelf engineered iPSC derived cell therapies for life threatening diseases
Product	• KJ01: LentiVirus-transduced MSCs overexpressing IL10 & CXCR4 • On track to enter in the clinic in Q4 2024 for refractory aGvHD • FIH study to deliver first product and engineered MSC platform validation
Platform	• Genetically engineered cells for increased potency and efficacy • iPSC/iMSC for optimal and flexible manufacturing • Genetically-modified iMSCs for transformative therapeutic efficacy
Team	• Experienced Scientific Founders, Management and Scientific/Clinical Advisory Board
Financing	• Created in Feb 2023 in France and Spain with initial financial support from AdBio Partners • Raising €10M seed round to generate clinical PoC KJ01 and platform development

Experienced Management Team

Kiji Therapeutics

Miguel Forte, MD, PhD
CEO

Anthony Ting, PhD
CSO

Michel Andraud,
CFO

Stefanos Theoharis, PhD
CBO

Francesc Dosrius
Operations Manager

Maria Fernandez Garcia, PhD
Dir R&D / PM

Management team experienced in **C&GT product development**, corporate development and **international clinical trials**

- Operational readiness for R&D and GMP production through Service Agreement with Ciemat and Clínica Universidad de Navarra
- Clinical trial execution in collaboration with the Universidad de Navarra
- Industrial partnership for virus production

Expert Advisory Board

Kiji Therapeutics

Juan Bueren, PhD

(Chair)

Head of Division

Director of Biomedical Innovation Unit

President ESGCT

CIEMAT

Spain

C> MSC

Massimo Dominici, MD, PhD

Professor and Director of the Program of Cellular Therapy and Immuno-oncology

University Hospital of Modena and Reggio Emilia

Italy

C> MSC

Felipe Prosper, MD, PhD

Head of Cellular Therapy Unit
Co-director of Haematology and Haemotherapy Unit
Haematology and Oncology Specialist

Clínica Universidad de Navarra, Spain

GvHD

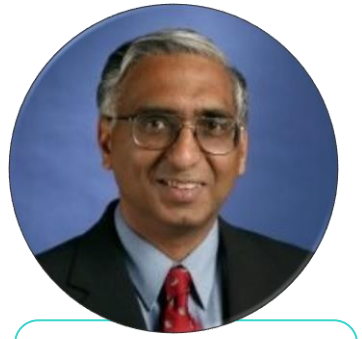
Jean-Frederic Colombel, MD

Professor of Medicine
Director of The Clinical Susan and Leonard Feinstein IBD;

Director of Center and The Research Leona M. and Harry B.Helmsley IBD

Icahn School of Medicine, Mount Sinai Hospital, US

IBD



Mahendra Rao, PhD

Pluristyx, US CSO,
Pancella Therapeutics former CEO,
Head of Stem Cell and Regen Med division at **LiFE Technologies**,
Chair **CBER (FDA)** advisory committee (CTGTAC),
founding Director of the **NIH Center of Regenerative Medicine**

iPSC; MSC

Richard Maziarz, MD

Professor of Medicine and former medical director of the adult stem cell transplant program

Oregon Health Sciences University

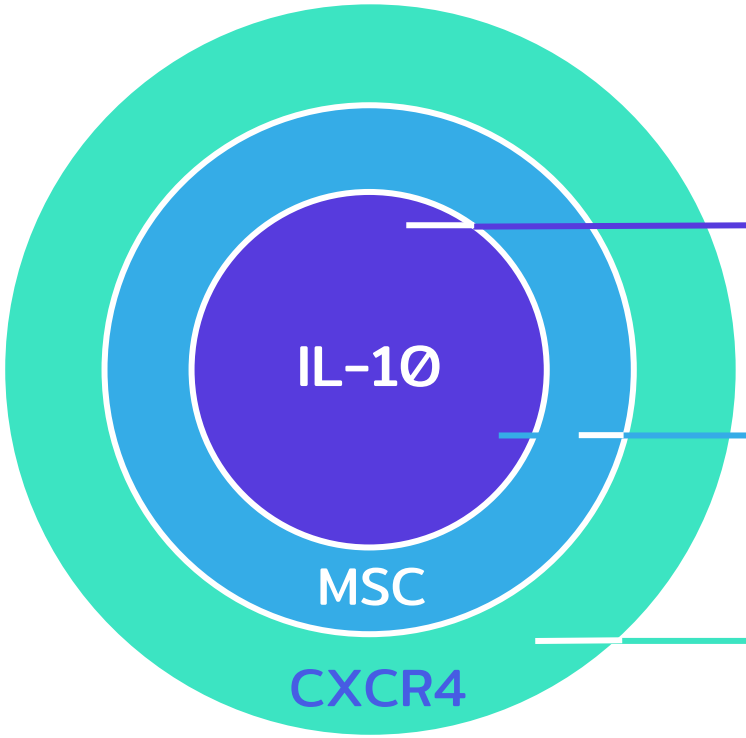
US

GvHD

International Scientific and Clinical Advisory Board with Opinion Leaders in Cell and Gene Therapy (C&GT), MSC product development, iPSC technology and clinical indications for GvHD and IBD

We built Kiji Therapeutics to deliver engineered iMSCs for inflammatory diseases

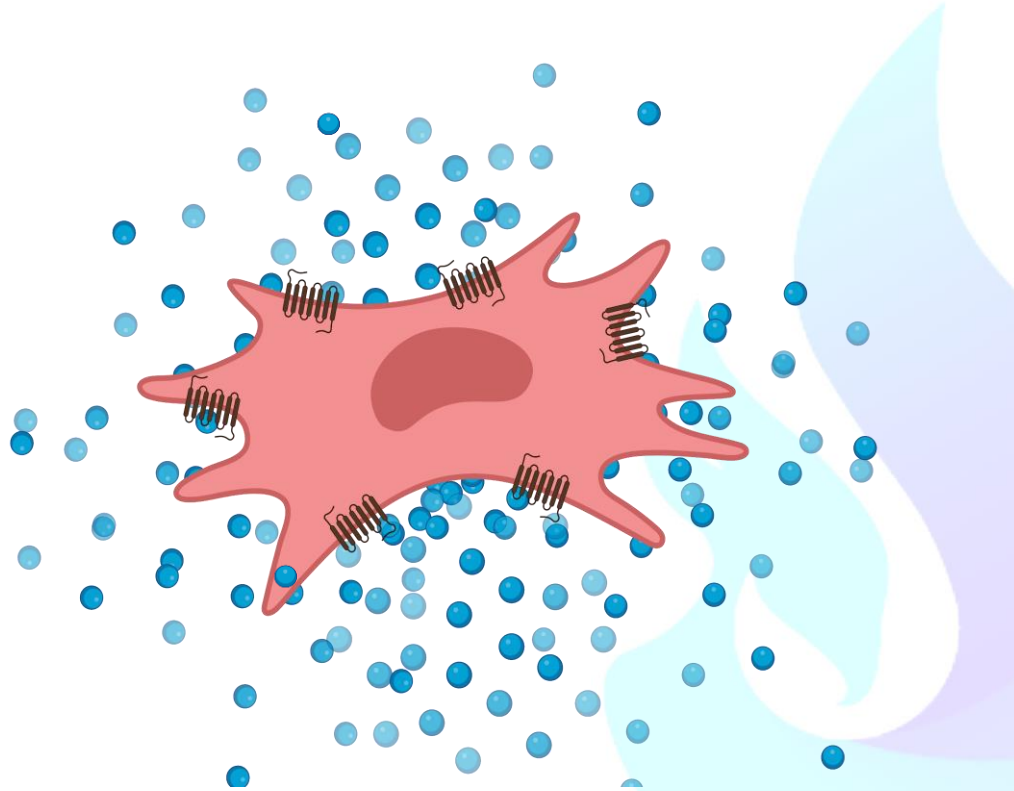
Kiji Therapeutics



- "Immune Master Switch"
- Promotes Th2 (regulatory)

- Potent immunomodulation
- Clinical PoC

- Critical chemokine receptor
- Targeting inflammation



Kiji Tx delivers targeted immunomodulatory IL10 through genetically engineered MSCs for optimized therapeutic effect

IL10

CXCR4

Kiji pipeline/platform

Kiji Therapeutics

	Technology (Allo; Off-the Shelf)	Indication	Stage		
			Discovery/ Pre-clinical	Pre-clinical/ IND enabling studies	Clinical
KJ01	Donor Ad-MSC (IL10/CXCR4)	SR-aGvHD	IND package available; Pre-GMP product		4Q24
KJ02	iPSC-derived iMSC (IL10/CXCR4)	IBD, Skin, Solid Organ Transplant, Lung	Discovery / R&D product		Expected 2026-27
KJ03	iPSC-derived iMSC New genes and gene editing	Inflammatory, Oncology and other diseases	Discovery		TBD

Continuous platform development maximizes the efficacy for multiple diseases

KJ01 pre-clinical immunomodulatory PoC summary

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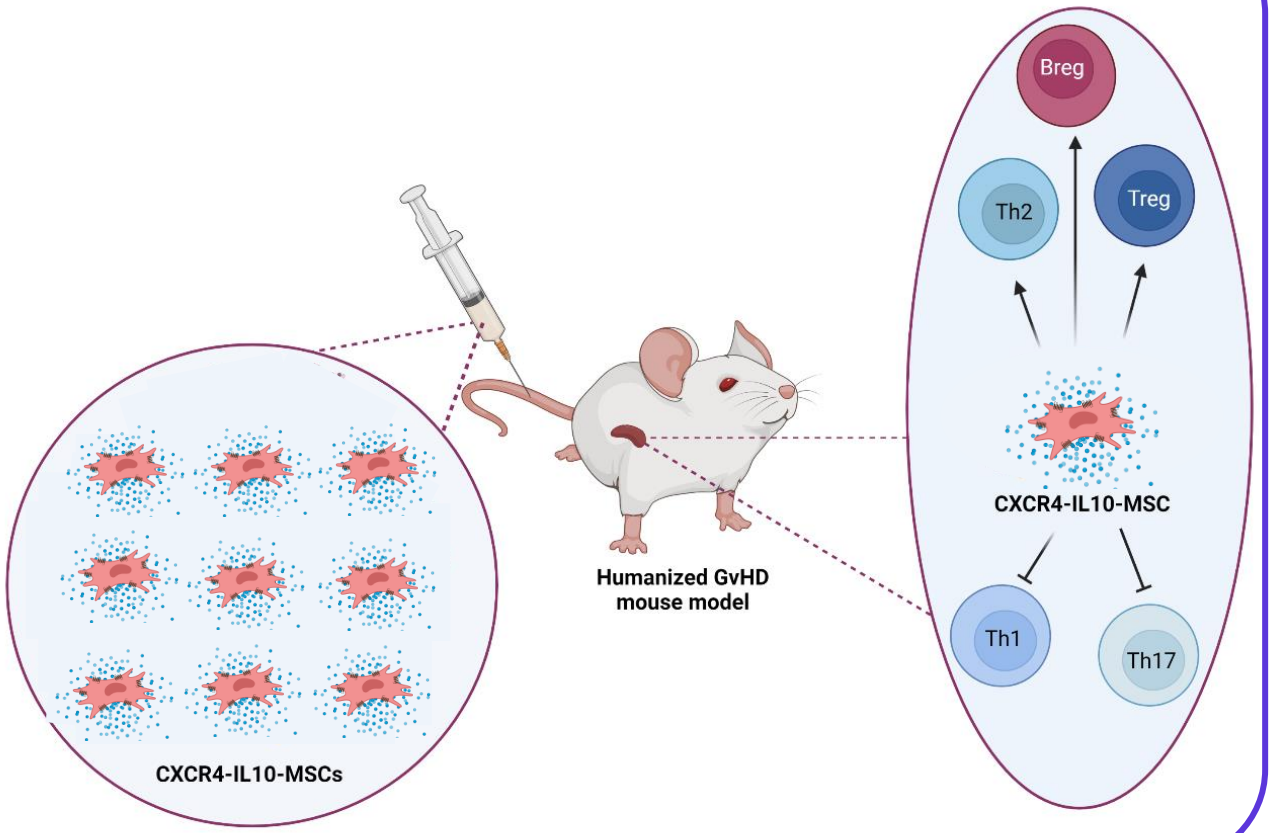
IMPROVED GvHD CLINICAL SCORE



Anti-inflammatory profile

- Modulatory factors (IL10, PGE2, TGFb, FoxP3)
- Regulatory T-cells (CD4+CD25+FoxP3+)
- Regulatory B-cells secreting IL10

Pro-inflammatory profile

- T-cell proliferation in blood and spleen
- Effector T-cell CD4+ & CD8+ subpopulations
- mRNA and secretion of proinflammatory cytokines (IL17, IL22)

Improved efficacy of mesenchymal stromal cells stably expressing CXCR4 and IL-10 in a xenogeneic graft versus host disease mouse model
Frontiers in Immunology (February 2023)

IL-10/CXCR4 expression improves MSC functionalities *in vitro*

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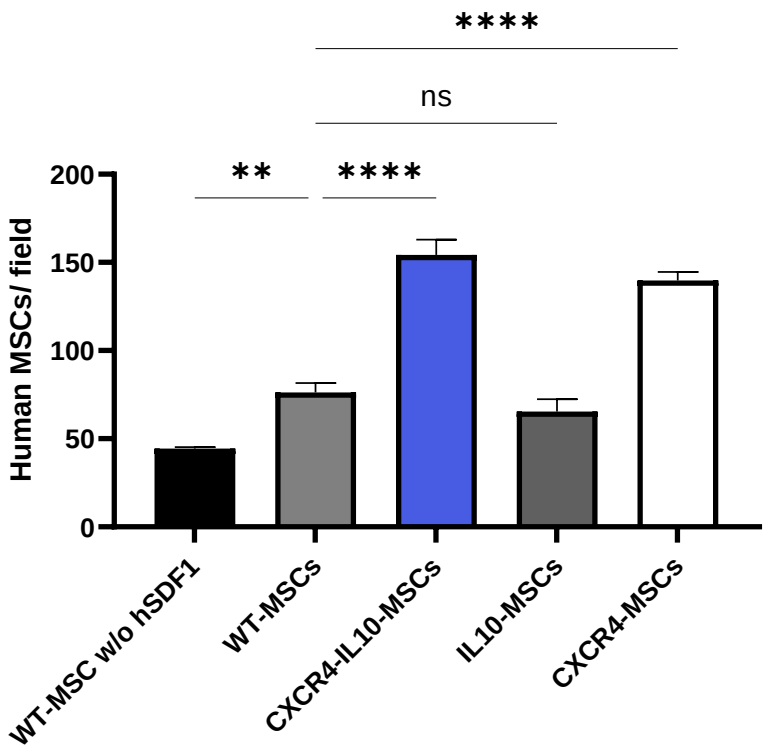
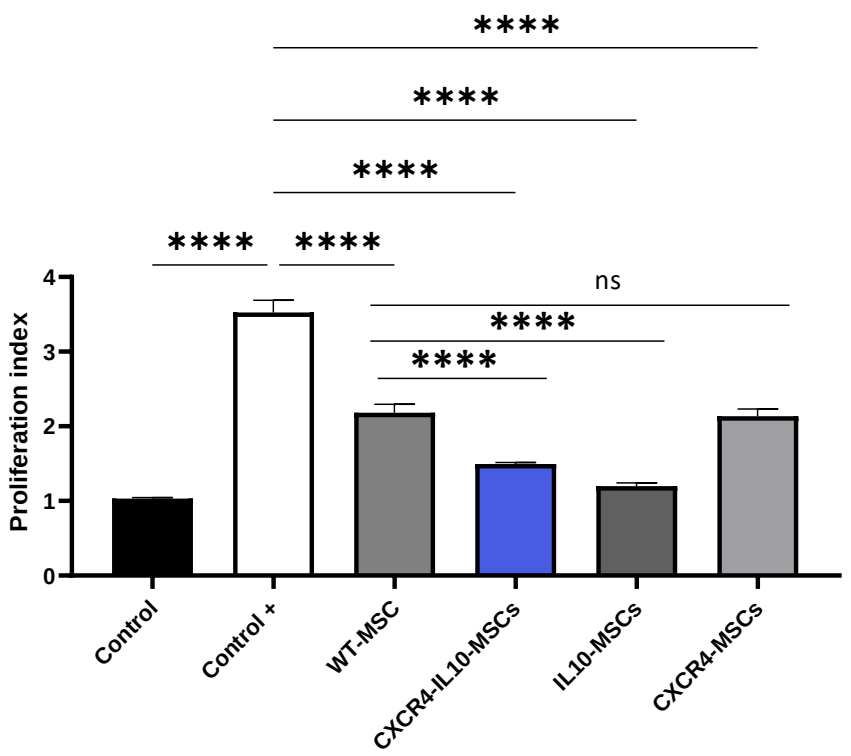
MIGRATION TRANSWELL ASSAY



IMMUNOSUPPRESSION ASSAY



Enhanced Migration:

CXCR4-MSCs and CXCR4-IL10-MSCs evidenced an enhanced migration capacity to human SDF1α, compared with WT-MSCs and with IL10-MSCs.

Better Immunosuppression:

αCD3/IL2 stimulated T-cell proliferation significantly reduced by all MSCs. Significantly higher inhibition achieved with CXCR4-IL10-MSCs and IL10-MSCs compared with wild type (WT).

n.s. no significant, **p < 0.01, ***p<0.001****p < 0.0001

IL-10/CXCR4 MSCs are more effective against GvHD

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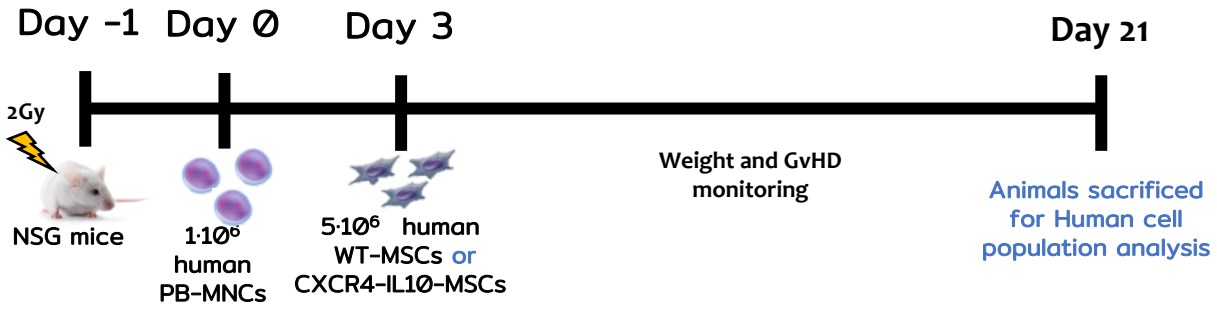
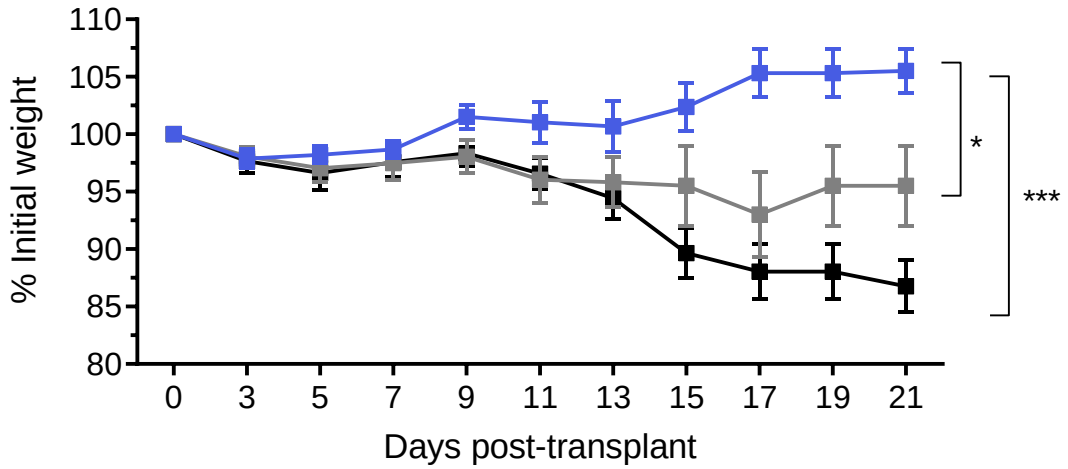
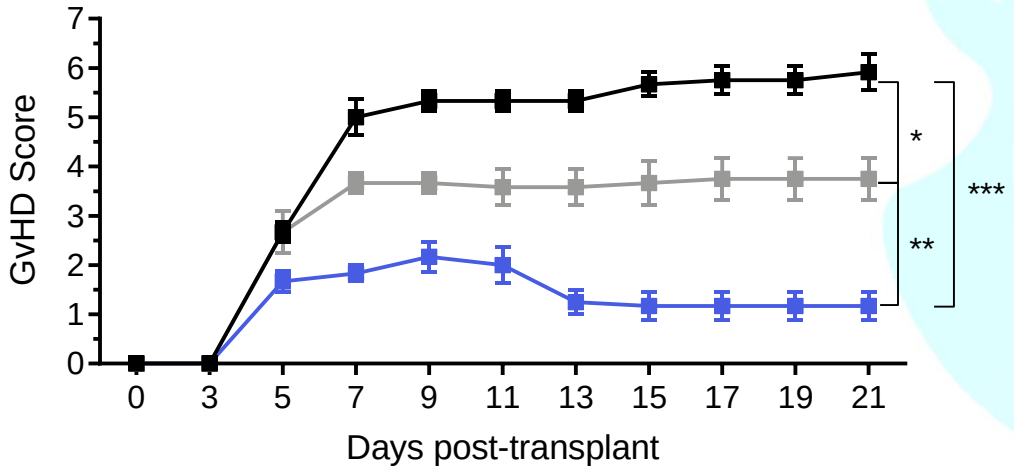
Humanized GvHD mouse model



Weight evolution



GvHD clinical score



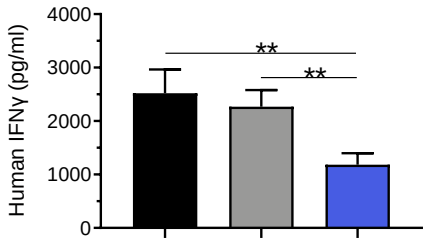
GvHD WT-MSCs CXCR4-IL10-MSCs

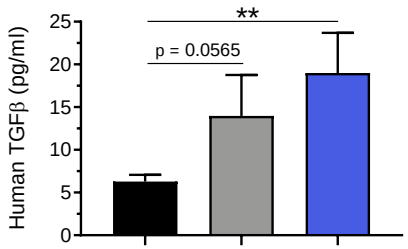
NO WEIGHT LOSS

LESS SEVERE SIGNS OF ILLNESS

*p < 0.05; **p < 0.01; ***p < 0.001

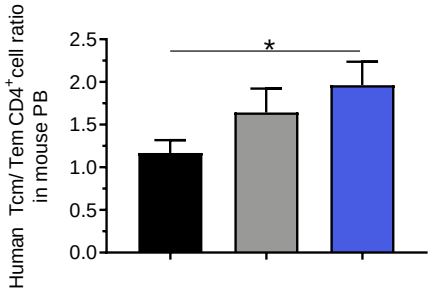
IL-10/CXCR4 MSC immunomodulatory MoA

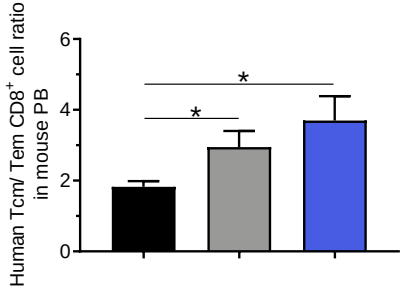




Serum anti-Inflammatory cytokine profile

- Reduced levels of pro-inflammatory cytokines:
  - IFNγ; IL17α; IL1β; IL8; IL12; TNF
- Increased levels of anti-inflammatory cytokines:
  - IL10; TGFβ; IL6

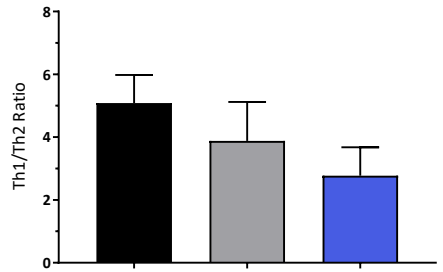


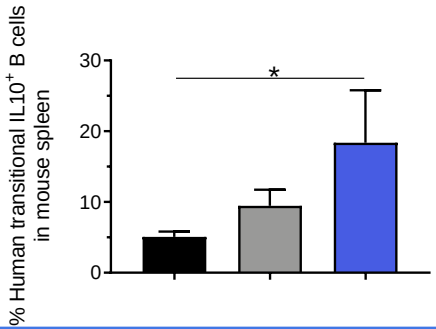


Blood anti-inflammatory lymphocyte profile

Human CD4 and CD8 Lymphocytes

- T central memory vs ⬆ T effector memory ⬇
- T effector vs ⬇ T naïve cells ⬆





Regulatory T and B profile in spleen

T Lymphocytes showing a lower TH1/Th2 ratio

- IL10 Treg and ⬆ IFN γ Inflammatory T cells ⬇

Spleen human Breg Lymphocytes

- IL10 transitional Breg and ⬆ memory Breg ⬆

GvHD WT-MSCs CXCR4-IL10-MSCs

Improved efficacy in IBD with IL10/CXCR4-MSCs

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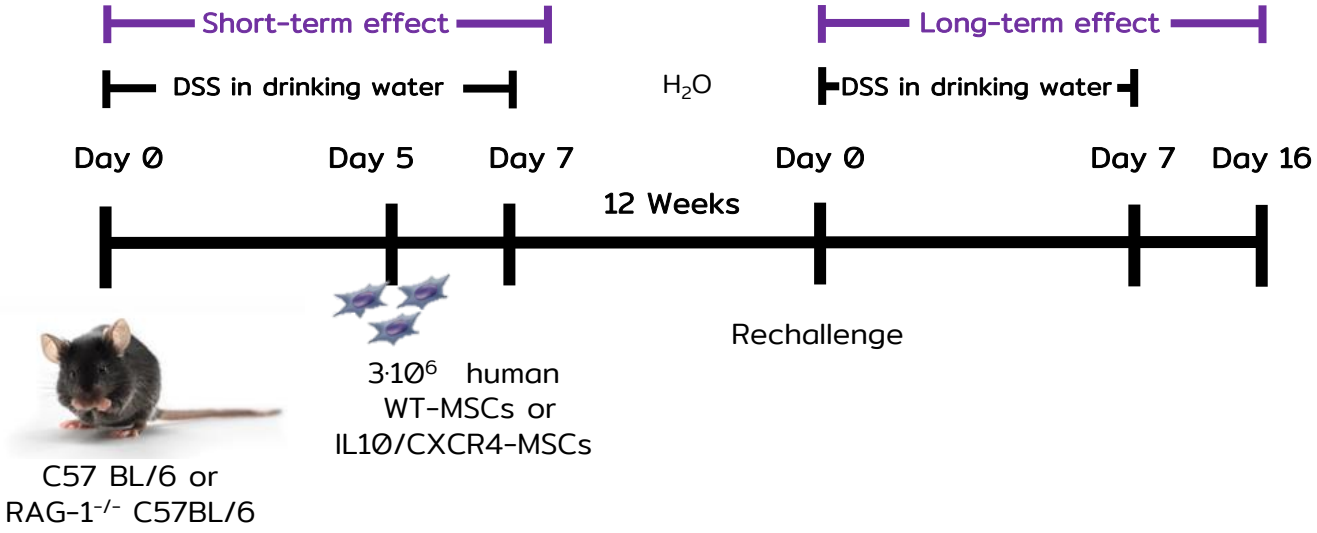
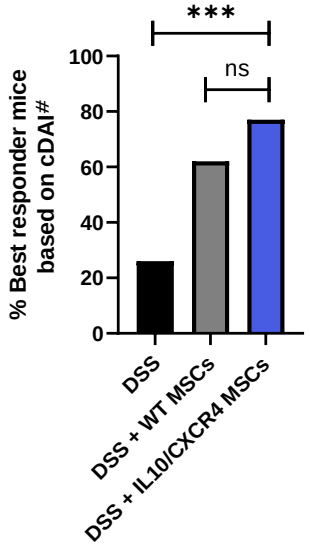
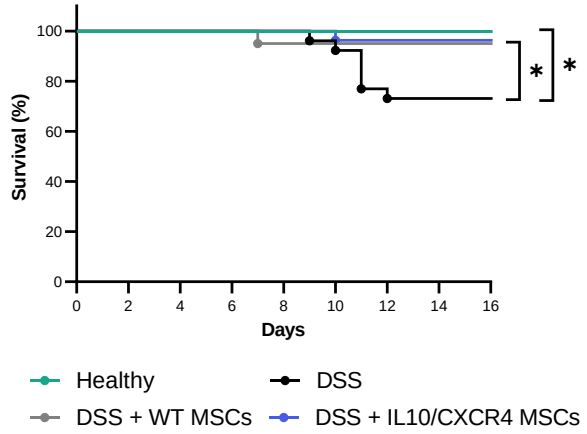
DSS-induced colitis mouse model

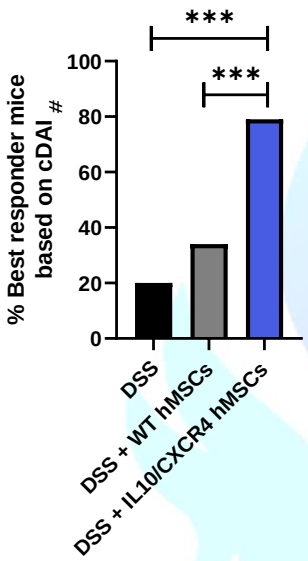


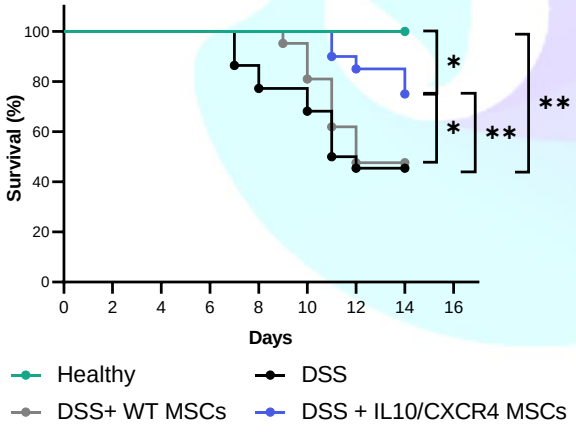
Short-term effect





Long-term effect





Improved efficacy with IL10-CXCR4
Long-term effect
Potential effect on innate immune system

Cumulative Disease Activity Index; Best reponders (mice at top 25th percentile of CDAI)

GvHD: Still a significant unmet medical need

Kiji Therapeutics

Common **complication of allogeneic hematopoietic stem cell transplant** (HSCT) with a significant morbidity and mortality (overall >10%). **Orphan Drug Indication**.

Non-existing treatment options for steroid resistant and ruxolitinib resistant or intolerant acute GvHD (***25% of total patients***).

Over 50% patients with no response and **mortality up to 68% vs 35%** in steroid responders

Poor second line options, with significant toxicities, failure rates and poor survival:

- JAK inhibitors: ruxolitinib (approved in US and Europe for 2nd line)
- Extracorporeal photophoresis (ECP)
- Anti-TNFα antibodies 1 (infliximab 2, etanercept 2); Anti-IL-2R antibodies (daclizumab, basiliximab, inolimomab)
- Mycophenolate mofetil 1 (immunodepressor); Antithymocyte globulin (ATG)

GvHD market in the 7 MM* was **$383M in 2018**, projected to be $819M in 2028 (CAGR of 7,9% 2018 to 2022)

3,400- 4,900 patients without standard treatment / year

Joint Working Group established by the British Committee for Standards in Hematology and the British Society for Bone Marrow Transplantation
American Society for Blood and Marrow Transplantation
F. Malard et al., Treatment and unmet needs in steroid-refractory acute graft-versus-host disease. Leukemia, 2020
Kelly, K and Rasko, JEJ, Mesenchymal Stromal Cells for the Treatment of Graft Versus Host Disease, Frontiers in Immunology (2021)
Westin, JR, *et al*, Steroid-Refractory Acute GVHD: Predictors and Outcomes, Advances in Hematology, (2011)
Allied Market Research

(*) 7MM: US, France, Germany, Italy, Spain, UK, and Japan

KJ01 Target Product Profile; Phase I/IIa

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KJ01 – TPP

- Allogeneic; Donor-derived
- Adipose-derived stromal cells (CXCR4/IL10)
- Cryopreserved Vials: 35 and 50 Million cells (3,5 and 50x10^7)
- Bed-side thaw and administration
- Target dose/regimen: Combination of 2 dose level formulations (1,8-2 Million KJ01/Kg)
- Regimen: 4 IV infusions, weekly

Study	**Phase I/IIa – FIH and PoC** **Collaboration with Ciemat/CUN; 5 sites in Spain**
Indication	Steroid resistant and failure or non-eligible for ruxolitinib aGvHD
Target patient	Age between 18 and 75 old with grade II-IV aGvHD Steroid-refractory and non-eligible or ruxolitinib refractory patients
Design	Open Label (OL); Dose ascending N=15 patients in 2 cohorts: low (n=3) and standard dose (n=12)
Main Objective	Feasibility and safety assessment (AEs and SAEs) at 28 days
Secondary Objectives	aGVHD stage/grade evolution **Response status** (CR; PR; OR) at 28, 100 days 12 months (**Target**: Superior to ±60% OR at 28 days) Time to 1st response and time to best response; OS at day 100 and 12 months; Biomarkers

Competition

Jakafi (Ruxolitinib – JAK 1-2 inhibitor)

- Approved US and EU (2022)
- Phase 2 OL: Reach 1: OR (CR+PR): 54,9%
- Phase III Controlled – Reach 2: OR (CR+PR): 62%
- AE: Cytopenia, infection

Remestemcel-L (unmodified MSCs)

- Several Studies – Adults: 35-65%
- Phase III – Pediatric (post-hoc): OR (CR+PR) 64%
- Well tolerated
- Mesoblast/FDA study in 3rd line aGvHD – September 2023

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Martin, PJ et all, Endpoints for Clinical Trials Testing Treatment of Acute Graftversus-host Disease: A Consensus Document; Biol Blood Marrow Transplant. 2009
MacMilla, ML, et all, The best endpoint for acute GVHD treatment trials, Blood 2010
Kebriaei, P et all, A Phase 3 Randomized Study of Remestemcel-L versus Placebo Added to Second-Line Therapy in Patients with Steroid-Refractory Acute Graft-versus-Host Disease; Biol Blood Marrow Transplant. 2020
Zeiser, R et all, Ruxolitinib for Glucocorticoid-Refractory Acute Graft-versus-Host Disease, NEJM 2020

Allogeneic, cryopreserved, off-the-shelf iPSC derived engineered cell product

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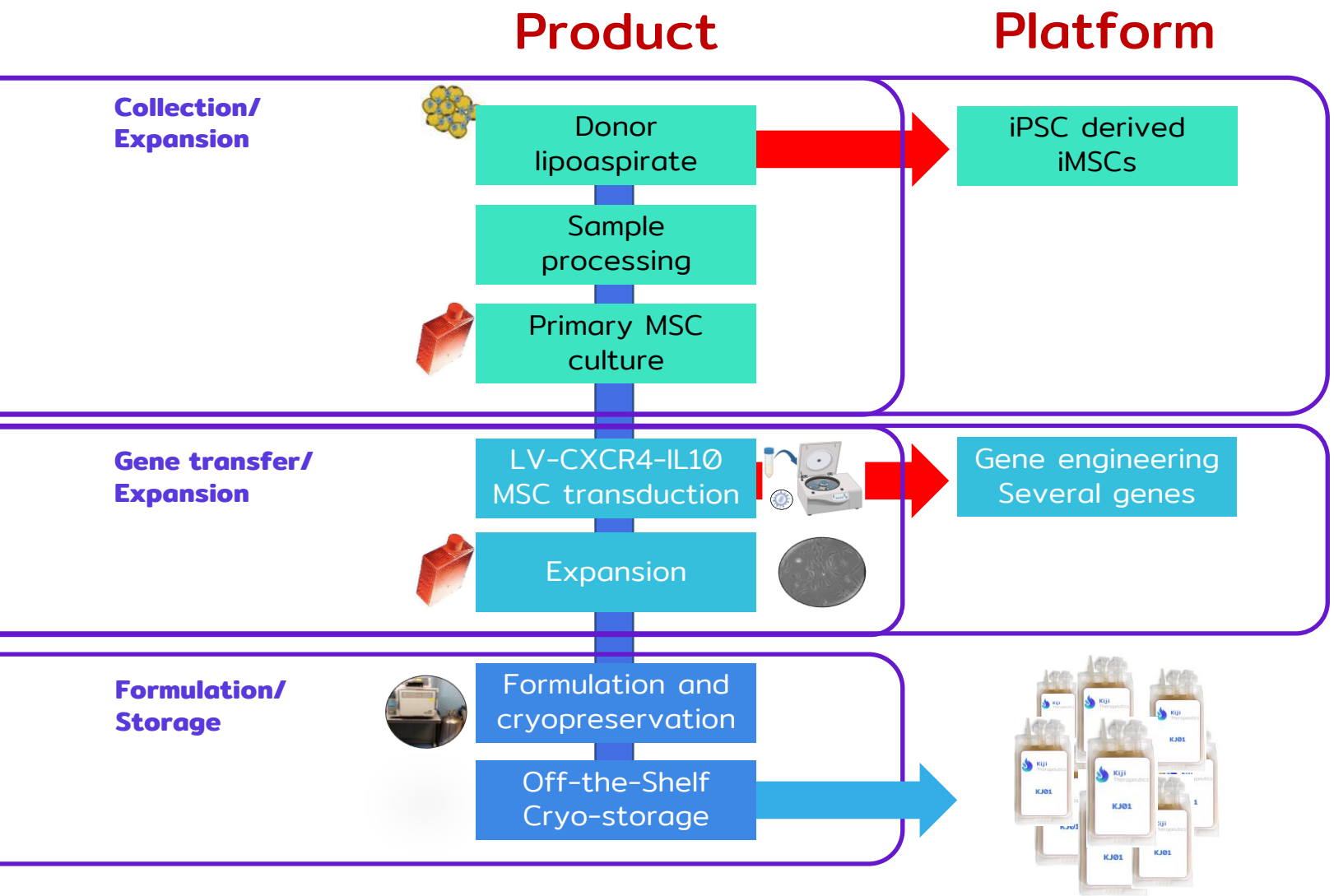

Platform manufacturing process

- **MSC source: Ad-MSC; iMSC**
- **Established characteristics**, **release criteria** and **potency assay**
- **Fluxibility, consistency and efficiency**
- **Low COGS**: a fully used donor collection delivers 1000's doses
- Formulated **ready for direct IV administration**

Release and in-process controls

- **GMP control**
- **VCN**
- **CXCR4 expression**
- **IL10 expression**
- **Potency assay**

Continuous platform development

Gene engineering for efficacy and iPSC for manufacturing

Kiji Therapeutics

Gene engineering platform validation
Now

+ iPSC technology

iMSC Product
Short term

+ Additional genes
+ Gene editing

Further gene engineering
Medium term

KJ01 Adipose-derived MSCs	iPSC-derived cells	iPSC-derived cells
IL10/CXCR4	IL10/CXCR4	New genes & other modifications
2D manufacturing process in place	3D scale-up; GMP iMSC	Large-scale 3D manufacturing
GMP Ad-MSC-IL10/CXCR4 R&D iMSC-IL10/CXCR4	iMSC IL10/CXCR4 transduction achieved	MSC gene editing initial results
aGvHD. Clinical trial funded to start recruitment H2 2024; Licensable	IBD, Skin, Solid Organ Transplant, Lung (animal model data)	Inflammatory disease, autoimmunity, regenerative medicine, cancer

exit prospects

Value proposition platform development will maintain Kiji Tx leading position in the field and increase exit prospects

Milestones and Inflection points

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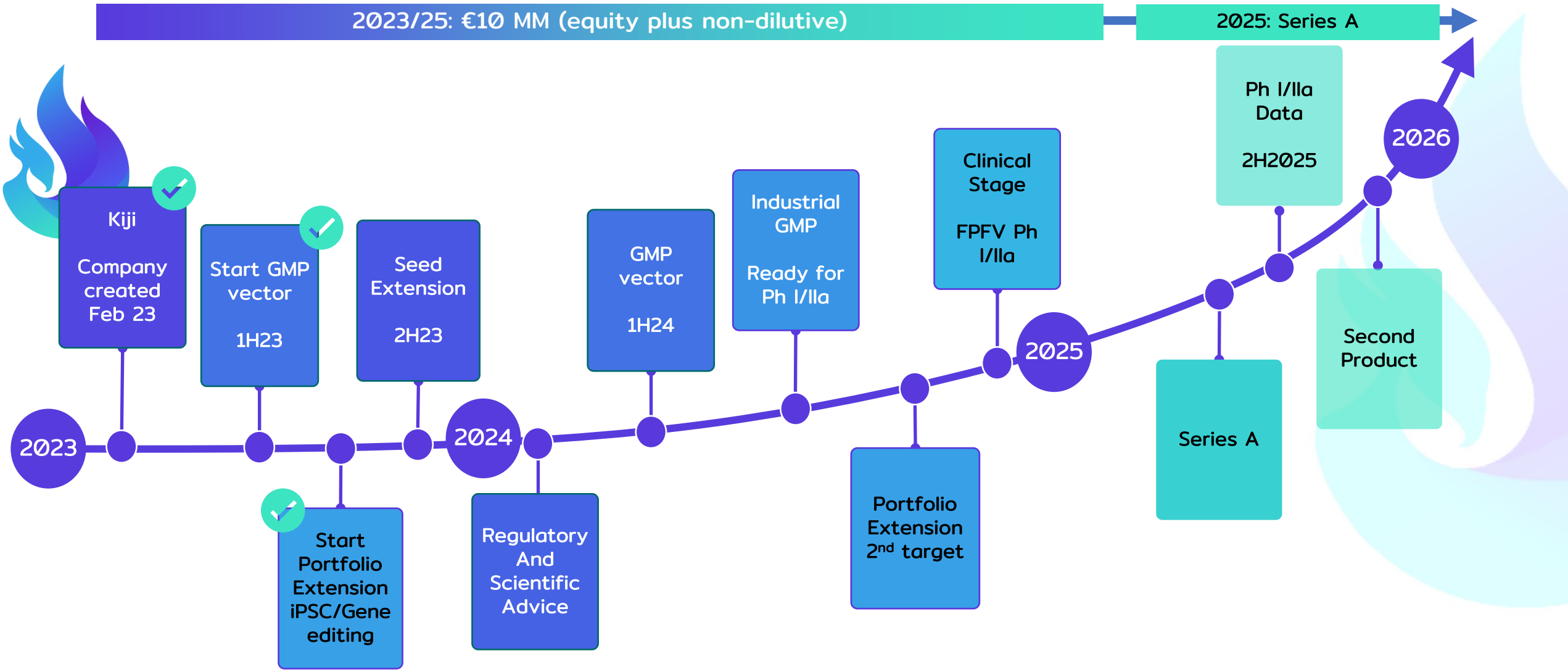

KJ01 activities and associated milestones

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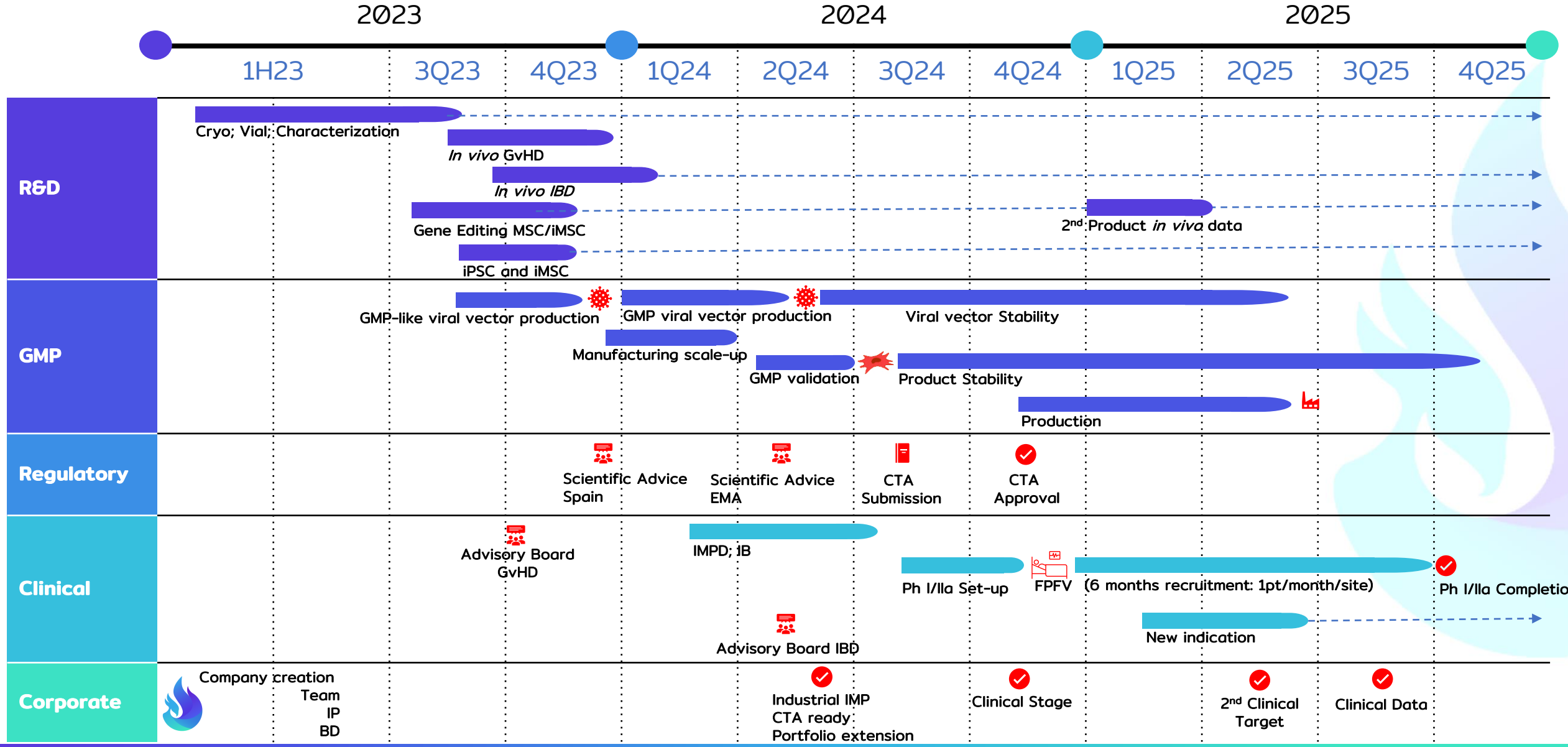


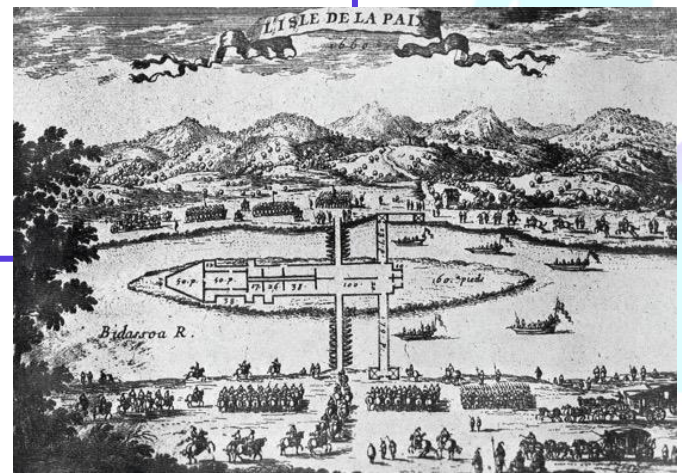
Take-away message:

Transformative gene engineered iMSC platform/portfolio

- ✓ Addressing unmet medical needs in autoimmune diseases

- ✓ Established rationale with PoC
- ✓ Industrial GMP product available in 1 year
- ✓ Nearly clinical stage ready with clinical data expected in 2 years
- ✓ Strong team and available operational capabilities

Kiji to be the leading company in gene engineered cell therapies with MSCs-iPSC



€10 MM to clinically validate gene engineering approach and develop iPSC/iMSC platform

iPSC/MSC engineered cell therapy for inflammatory disease

KIJI Therapeutics

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