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TWO DECADES OF

Curing the Incurable



Stem cell gene therapy for rare genetic diseases



**Stanford Center for
Definitive and Curative Medicine**
Cell and Gene therapy From bench to bedside



From Treatment To Cure Of Inflammatory and
Autoimmune Diseases

Tr1X Is Developing Tr1 Treg & CAR-Tr1 Treg Cell Therapies for Autoimmune and Inflammatory Diseases

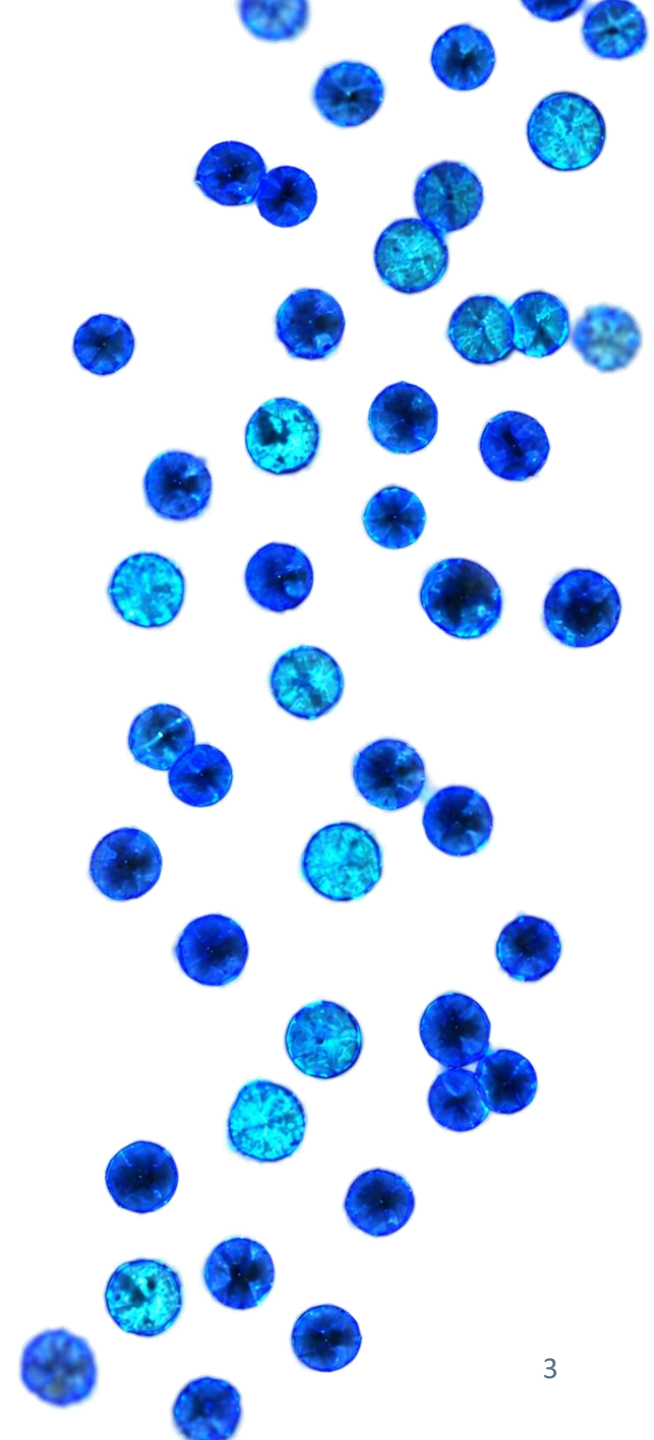
From Therapy to Cure:

Today's drugs, when they work, suppress the immune system and must be taken for life. No approved therapy restores immune self-tolerance.

Tr1X's goal is to restore health.

We infuse engineered regulatory T cells, made from healthy donors, that suppress the harmful cells and teach the patient's own immune system to stop attacking itself. About 50 patients have been treated so far. None has had a serious reaction to the product, and in some of the sickest patients, the disease has improved significantly.

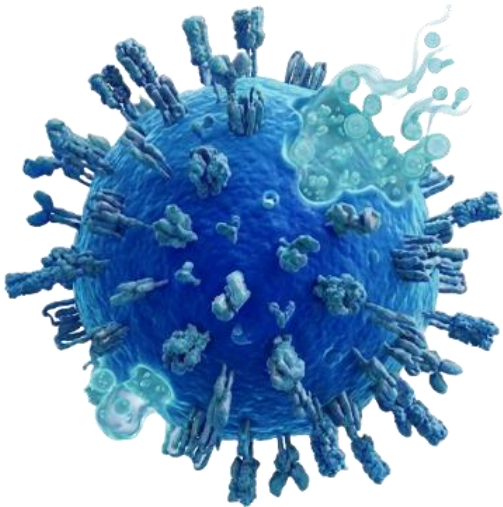
Patients treated across TRX103 and TRX319 trials, Tr1X data on file, Sep 2026. Cell image is an illustration, not patient data.



THE SCIENCE, IN PLAIN WORDS

Your immune system has its own regulatory cells. **In autoimmune diseases, diseases, they are not doing their job.**

Tr1X's cells



WHAT REGULATORY CELLS DO NATURALLY

They go where the trouble is	They travel on their own to inflamed tissue, whether that is the gut, the brain or a new transplant.
They calm the attack	Once there, they release a calming signal, IL-10, and switch off the cells doing the damage.
They recruit reinforcements	They teach the patient's own cells to do the same job, so the effect can outlast the original cells.

HOW TR1X TURNS THEM INTO MEDICINE

We make the regulatory cells ourselves	Patients make too few regulatory cells, or ones that do not work. We take T cells from healthy donors, add the IL-10 gene and turn them into regulatory cells that can be given as a medicine.
One donor can treat many	The same gene also hides the cells from the recipient's immune system. Billions of cells from one run, held ready on the shelf.

Tr1 biology: Groux, Nature 1997; Roncarolo, Immunity 2018; Gagliani, Nat Med 2013. Calming signal is IL-10. Impairment in autoimmunity: Astier, J Clin Invest 2006. Engineered Tr1: healthy-donor CD4 T cells transduced with a lentiviral vector carrying IL-10 and a CD271 vector carrying IL-10 and a CD271 marker; IL-10 also lowers HLA class II and costimulatory molecules, which limits recognition by the recipient, Uyeda et al., Front Immunol 2026; over 7 billion cells per manufacturing lot.

THE THREE DISEASES TR1X IS TREATING TODAY

Three diagnoses, one immune system that cannot stop itself

Disease	What goes wrong	Where medicine stops today
● After a stem cell transplant Graft-vs-Host Disease	A blood cancer patient is given a new immune system from a donor. It can turn on the person who received it: skin, gut, liver. The transplanted cells and the host immune system attack each other.	Broad immune suppression, for months It leaves patients defenseless against infection and gives the cancer room to come back.
● Crohn's disease Severe, treatment-refractory	The immune system attacks the lining of the gut and will not let go. Ulcers, narrowing, pain, and a life organized around the disease.	One drug class after another Each works for a while, then stops. When three or four advanced therapies have failed, what is left is surgery.
● Progressive multiple sclerosis Primary and secondary	Immune cells sit behind the blood-brain barrier and strip the insulation from nerves. Function is lost a little at a time, and does not come back.	Antibodies that cannot efficiently reach the brain They clear B cells from the blood, not from the brain. At best, decline is slowed.

Transplant: GvHD-free, relapse-free survival after HLA-mismatched HSCT with PTCy, ACCESS, Blood Adv 2026. Crohn's: endoscopic response on placebo after biologic failure, U-ENDURE, Clin Gastroenterol Hepatol 2024; surgery risk after four or more therapies, MarketScan n=15,547, Surg Endosc 2025. Progressive MS: compartmentalized B-cell inflammation behind an intact blood-brain barrier, Magliozzi, Brain 2007; Absinta, Nature 2021. Tr1 biology: Roncarolo, Immunity 2018.

WHO THIS IS FOR

The patients today's medicine has run out of answers for

1 in 2

cancer patients receiving a mismatched bone marrow transplant
develop Graft-vs-Host Disease or relapse within a year of a transplant meant to cure them.

80,000

people with Crohn's disease
in the US and Europe who have failed three or more advanced therapies. Surgery is usually what comes next.

65,000

people with progressive MS
still losing function on the best available therapy.

A typical leukemia patient in our transplant trial

63%

of mismatched-transplant patients are from racial or ethnic minority groups.

29%

chance of a fully matched donor for a Black American patient

100+

days before the donor immune system is rebuilt

20%

do not survive the first year, on the best care available

For these patients, a mismatched transplant is the only route to a cure. Making it safer is where we start.

Transplant: GvHD-free, relapse-free survival at one year 51% (7/8) and 55% (<7/8), one-year overall survival ~80%, and 63.5% of recipients ethnically diverse — ACCESS, Blood Adv 2026. Day-100 CD4 recovery tracks survival: Al Malki, Blood Adv 2021; Perales, Blood Adv 2025. Typical-patient panel uses published mismatched-donor data pending TRX103-01 medians (Tr1X data on file). Crohn's pool: Tr1X model on Lewis, Gastroenterology 2023 and Kapizioni, JCC 2024.

WHAT WE ARE BUILDING

Three medicines built on the same underlying biology. Two are already in patients.

Medicine	What it is, and who it is for	Where it stands
 TRX103 Healthy donor engineered regulatory cells	Given with a mismatched stem cell transplant to stop Graft-vs-Host Disease before it starts. Also, an outpatient treatment for severe refractory Crohn's disease. Two trials, one product.	 43 patients treated to date: stem cell transplant and Crohn's Orphan Drug in transplant, Fast Track in in Crohn's. Results this year and next.
 TRX319 Regulatory cells with a CAR	The same cells, equipped to remove the B cells that drive progressive multiple sclerosis, including inside the brain, while calming the inflammation around them.	 First patients dosed: progressive MS Fast Track in MS. Early signals late 2026.
 TRX501 Regulatory cells made inside the body	A simple injection that turns a patient's own T cells into targeted regulatory cells, with no cell manufacturing. First aimed at scarring diseases of the lung (3-5 years of life expectancy after diagnosis).	 Lab and animal studies: lung and liver fibrosis First human trial targeted 2028.

Stage as of Sep 2026. TRX103: TRX103-01 (HLA-mismatched HSCT, NCT06462365, Orphan Drug) and RESTORE (Crohn's, NCT06721962, Fast Track); also an investigator-led trial in uveitis at Stanford. TRX319: IMPACT (NCT07477639, Fast Track). TRX501: IND targeted 2028.

THE ROLE OF CIRM



Funded by CIRM at every step: \$20M across three awards

Tr1X's awards	What it funds	Where it stands
\$4M CLIN1-14840 Awarded March 2024	Late-stage preclinical and IND-enabling work on TRX103, the first allogeneic engineered Tr1 regulatory T cell: manufacturing, potency, toxicology and the regulatory package.	Complete. IND cleared FDA cleared the TRX103 IND in 2024 and the first patients were dosed the same year.
\$8M CLIN2-17080 Awarded April 2025	Phase 1/2a of TRX103 to prevent Graft-vs-Host Disease in patients receiving an HLA-mismatched stem cell transplant for blood cancer. NCT06462365; PI M.G. Roncarolo.	Enrollment completed Safety demonstrated; mode of action validated; immune defenses rebuilt faster; efficacy data emerging.
\$8M CLIN2-19848 Awarded June 2026	Phase 1/2a first-in-human dose escalation of TRX319, a CAR-Tr1 Treg, in progressive multiple sclerosis. IMPACT, NCT07477639. PI M. Londei, co-PI M.G. Roncarolo	First patients dosed Fast enrollment, Early signal of safety. FDA Fast Track. Dose escalation Phase 1 expected to be completed by July 2027 or sooner.

THE ROLE OF CIRM

CIRM's impact reaches far beyond the trials it funds

FUNDED BY CIRM

TRX103 – CLIN1

Scale-up and IND-enabling
 CLIN1-14840 · \$4M · 2024

TRX103 – CLIN2

Stem cell transplant trial
 CLIN2-17080 · \$8M · 2025

TRX319 – CLIN2

Progressive MS trial
 CLIN2-19848 · \$8M · 2026

WHAT THAT FUNDING BUILT

A shared platform

- Allogeneic Tr1 manufacturing process
- Potency and release assays
- Toxicology and regulatory package
- First-in-human safety and efficacy data

NOT FUNDED, BUT ACCELERATED

NO DIRECT CIRM FUNDING

TRX319

Scale-up and IND-enabling

Ran on the manufacturing process, assays and tox package built under CLIN1-14840.

NO DIRECT CIRM FUNDING

TRX103

Crohn's disease trial

Used the same product and the safety experience from the CIRM-funded transplant trial.

TRX319 scale-up and IND-enabling work and the TRX103 Crohn's disease trial (RESTORE, NCT06721962) are funded outside these awards; both drew on the process, assay, toxicology and clinical experience generated under them.

WHAT WE HAVE SEEN IN PATIENTS · SAFETY

About 50 patients treated across multiple trials. **No cytokine storm, no serious side effect caused by the cells. A safety profile suited for autoimmune indications.**

0 cases of cytokine storm The runaway immune reaction that has stalled CAR-T cell therapies in autoimmune disease.	0 serious side effects from the cells Doses have risen nine-fold in Crohn's with no safety ceiling reached.
0 traditional chemotherapy (flu/cy) needed needed CAR-T cell therapies need it to make room for the cells. Ours does not, so treatment can be an outpatient visit.	3 mild related events, quickly resolved Two infusion reactions and one episode of bone pain, in 24 transplant patients.

Why this matters

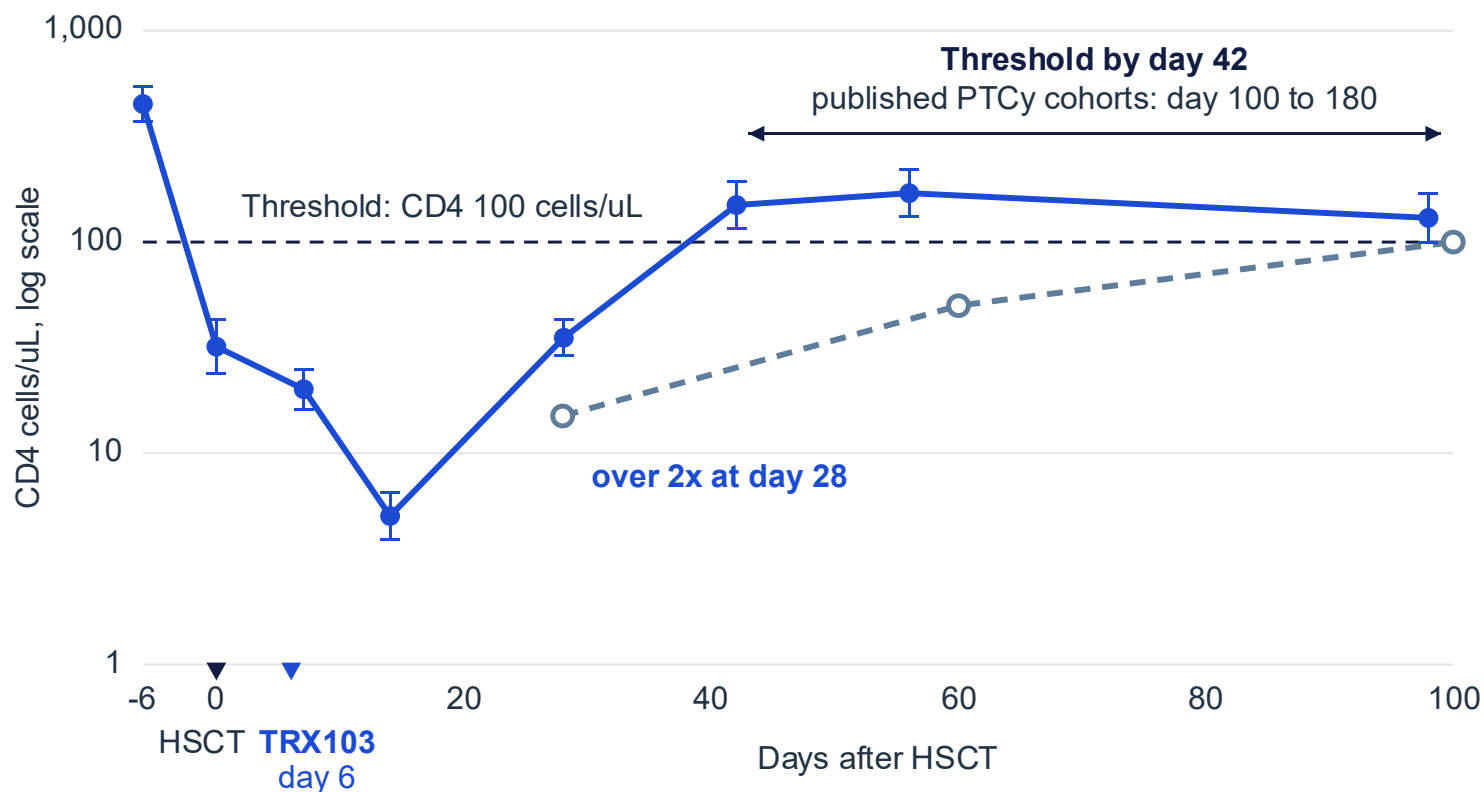
This year three patients died in trials of a CAR-T cell therapy for autoimmune diseases. Two companies paused their programs as a result.

Regulatory cells exist to calm the immune system down and restore balance. So far patients have tolerated them as that biology would suggest.

Tr1X data on file, Sep 2026: TRX103-01 (24 dosed), RESTORE and IMPACT. No cytokine release syndrome or ICANS of any grade, no HLH, no dose-limiting toxicity, no serious related adverse event. Crohn's doses 75M to 675M cells. No fludarabine/cyclophosphamide lymphodepletion in any Tr1X trial; RESTORE and IMPACT include optional low-dose cyclophosphamide or bendamustine arms. Field setbacks: Novartis rap-cel, three IEC-HS deaths; BMS zola-cel pause; BioPharma Dive and Fierce Biotech, 31 Aug 2026.

● TRX103 · HEMATOPOIETIC STEM CELL TRANSPLANT

After HSCT, patients given TRX103 **rebuilt their immune defenses faster.**



- **With TRX103**, 17 patients
- **Without**, 5 past patients

The weeks after a stem cell transplant are the most dangerous: almost no defense against infections until the new marrow rebuilds it. That gap is linked to relapse and death.

Getting T cells sooner is linked to better survival. Every patient's new marrow engrafted; severe Graft-vs-Host Disease stayed low.

NCT06462365; cutoff 6 Jul 2026. CD4 T cells per microliter, means at dose levels 3 and 4; threshold 100 cells/uL. Controls are historical (n=5), not randomized. Threshold by day 100 tracks with survival: Al Malki, Blood Adv 2021; Perales, Blood Adv 2025. Engraftment 20 of 20 at therapeutic dose levels; grade III-IV acute GvHD 15% at day 100 (n=20).

● **TRX103 · CROHN'S DISEASE**

At the highest TRX103 dose, **all six refractory Crohn's disease patients showed healing.**

Who was treated

4 advanced therapy classes failed (median) before TRX103; 5 individual agents

95% failed anti-TNF and anti-IL-23; most also anti-integrin or JAKi

Most had prior bowel resection; 13 years median disease duration

How TRX103 performed at week 12

8 of 12 evaluable patients at high doses improved on SES-CD

6 of 6 evaluable patients at high doses improved

-4.7 mean SES-CD point change at high doses

Why this is worth attention

4%

Of similar patients on placebo reached this bar over a full year in one large trial.

3x

More patients improved at the high dose than at the intermediate dose.

This data does not yet show whether the healing lasts. Fifteen more patients at this dose will report in 2027.

Phase 2b/pivotal planning follows.

NCT06721962. Tr1X data on file, Sep 2026. SES-CD change from screening to week 12, three-reader median. Lower doses: with or without cyclophosphamide, n=6 evaluable. Top dose: single or x3, n=6 evaluable. Responded: decrease of 50% or more (U-EXCEED definition). Top dose mean change -4.7 points (95% CI -9.5 to +0.2); 6 of 6 direction p=0.031, sign test; dose trend p=0.001. Open-label, no control arm; the safety cohort is excluded. Placebo: U-ENDURE maintenance, prior biologic failure, endoscopic response 4% at 52 weeks, Clin Gastroenterol Hepatol 2024; different trial, timepoint and population.

In progressive MS the damage comes from inside the brain, **out of reach of today's drugs**

The problem

Antibody drugs clear harmful B cells from the blood, but cannot get into the brain. Patients keep declining despite therapy, which at best slows progression.

What TRX319 does

A regulatory cell with a homing receptor for B cells. It enters tissue, removes them, and calms the inflammation around them.

Why not a cancer CAR-T

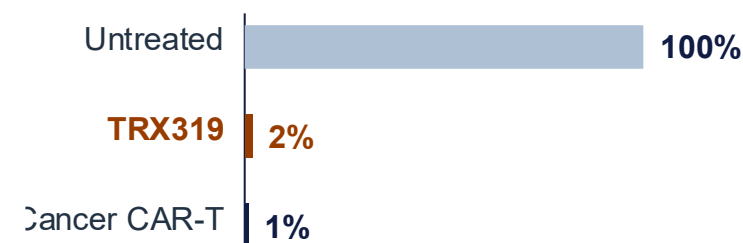
Those clear B cells too, but create inflammation and need and need chemotherapy first. In the lab, TRX319 removed 98% of B cells, the same as a CAR-T, with only a third of the inflammation.

Where we are

First patients dosed in 2026, off the shelf, no traditional chemotherapy (flu/cy) needed. Early signals by signals by year end.

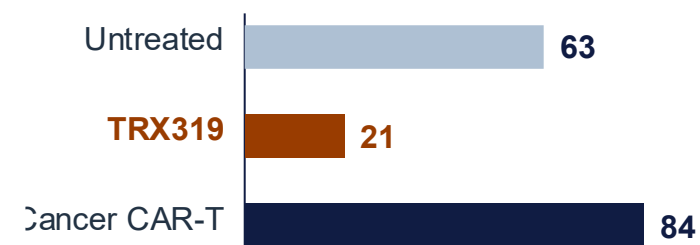
Clears B cells like a CAR-T

B cells from MS patients remaining (%)



Without the inflammation

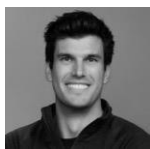
Inflammation signal from brain immune cells (pg/mL)



IMPACT trial, NCT07477639, FDA Fast Track; primary or secondary progressive MS progressing on current therapy; cohorts with and without bendamustine pre-conditioning. Lab data: Tr1X data on file; MS patient PBMC, B cells remaining vs B cells only; comparator CD3 CAR-T. Right, lower: IL-1 β from NLRP3-activated human microglia given conditioned media, baseline 63, TRX319 21, CD4 CAR-T 84 pg/mL, means, n=2 to 3. Progressive MS pool 65k US + EU, Tr1X model.

THE PEOPLE

A team experienced with taking new medicines from the lab to patients



David de Vries
Co-founder and CEO

Co-founded Arine, a healthcare AI company serving millions of patients. Harvard, Cambridge.



James Adams
Chief Technical Officer

Built cell therapy manufacturing at Sonoma and Fred Hutch; 20-plus trial applications.



M.G. Roncarolo, M.D.
Co-founder, President and R&D

Discovered Tr1 cells. Former Stanford professor; led the first successful ex vivo gene therapy.



Janine Powers, PhD
Head of Translational Medicine

Former VP, Translational Medicine at Nurix; 20 years reading what a drug does in patients.



Marco Londei, M.D.
Chief Medical Officer

Led immunology development at Novartis and BMS; over 70 early trials, six medicines to market.



V. Megrabova
VP, Regulatory Affairs

Led regulatory strategy for off-the-shelf cell therapies at Fate Therapeutics.



Backed by

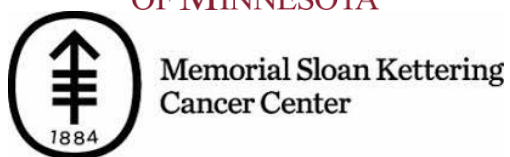


\$145M

raised: \$125M equity (Series A and B) plus \$20M in CIRM funding

CLIN2-17080
Stem cell transplant

**Collaborating
institutions:**



Acknowledgements



Patients, Families & Caregivers

CLIN2-19848
Multiple Sclerosis

**Collaborating
institutions:**

UC San Diego

UC Irvine



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Thank You