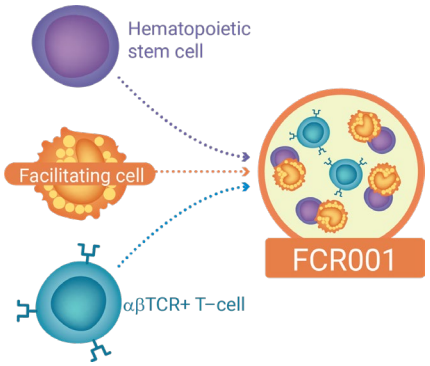
Talaris Therapeutics FCR001 Clinical Program Overview

What is FCR001?

FCR001 is a cryopreserved facilitated allogeneic stem cell therapy derived from mobilized peripheral blood of the kidney donor that is delivered as a single dose with a nonmyeloablative conditioning regimen. FCR001 contains the donor's CD34+ hematopoietic stem cells (HSCs), facilitating cells, and αßTCR+ T-cells.

The goal of FCR001 treatment is to induce immune tolerance by creating a "dual immune system" (part donor and part recipient) in the transplant recipient. These two immune systems coexist, recognizing both the recipient's own body as well as the donated organ as "self." This is also referred to as achieving chimerism in the recipient's immune system.

Achieving durable chimerism in a recipient's immune system potentially enables long-term immune tolerance in the absence of chronic immunosuppression.



The Potential of FCR001

Reprogram

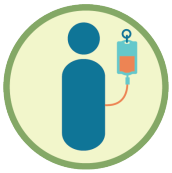
Solid organ transplantation

Reprogram the immune system to recognize the donated organ as "self," thereby avoiding organ rejection without the degree of toxicities, risks, comorbidities, and burden of compliance associated with chronic immunosuppression

Restore

Severe autoimmune disease

Restore self-tolerance by eradicating autoreactive cells and regenerating a new and healthy supply of immune cells, thereby halting the autoreactive cells' attack on one's own body



Replace

Severe nonmalignant blood, immune, and metabolic disorders

Replace the defective or deficient HSCs in a patient's bone marrow with normal-functioning HSCs from a healthy donor

Unmet Need

Unmet Need with Current Standard of Care

While solid organ transplantation can be a life-saving procedure, continued risk for graft rejection remains a primary obstacle.[1] Dependence on immunosuppression (IS) drugs has been important to prevent rejection. Current immunosuppressive regimens are not always sufficient to prevent organ rejection over time and may cause toxicity (e.g., kidney toxicity with calcineurin inhibitors) that may compromise the health of the transplanted organ.[1-3]

Chronic IS therapies are also the treatment for autoimmune diseases, where they control the autoimmune reaction that develops as a result of loss of self-tolerance; however, IS only minimizes the impact on affected organs and is not curative.

An unmet need remains for alternative therapies that minimize or eliminate the requirement for indefinite IS through the induction of immune tolerance.

Overview of Ongoing Clinical Trials

In an ongoing phase 2 study* in 37 LDKT recipients treated with FCR001:

70%
26 of 37 patients off all IS therapies**

- Across all HLA mismatches
- 82% success rate (14 of last 17) once key parameters were optimized

100%
Taken off IS, remain IS-free

- Median follow-up: >7 years
- Six patients followed >10 years
- Longest follow-up: >12 years

7/7
Tolerized patients with prior kidney auto-immune condition had no recurrence

- Recurrence ordinarily seen in 20%—60% of patients***

5.4%
Incidence of GvHD

- Despite high levels of HLA mismatch

*Data as of June 15, 2022. Includes 33 patients under Phase 2 protocol and 4 compassionate-use patients.
**One year after transplant. ***Kienzl-Wagner 2018, Lim 2019, Moroni 2019.
GvHD, graft-vs-host disease; HLA, human leukocyte antigen; IS, immunosuppression; LDKT, living-donor kidney transplant.

Talaris has three actively recruiting clinical trials of Facilitated Allo-HSCT Therapy. For more information, please visit https://talaristx.com/clinical-trials/overview/

	FREEDOM-1[5]	FREEDOM-2[6]	FREEDOM-3[7]
Study Design	NCT03995901: Phase 3, randomized, controlled, multicenter, safety and efficacy study of FCR001 cell-based therapy relative to a tacrolimus- and mycophenolate-based regimen in LDKT recipients and safety in FCR001 donors	NCT01649388: Phase 2, randomized, controlled, multicenter, safety and efficacy study of FCR001 cell-based therapy relative to a tacrolimus- and mycophenolate-based regimen in de novo LDKT recipients and safety in FCR001 donors	NCT05098145: Phase 2, single-arm, open-label, multicenter, proof-of-concept exploring the safety and clinical activity of FCR001 in patients with a rapidly progressive form of scleroderma
Participants	**Recipients:** Adults (≥18 years old) undergoing a first or second LDKT **Donors:** Age 18–60 years and willing to undergo mobilization, apheresis, and 12-month safety follow-up	**Recipients:** Adults (≥18 years old) who received a first kidney transplant from a living donor 3–12 months prior to study enrollment **Donors:** Age 18–60 years and willing to undergo mobilization, apheresis, and 12-month safety follow-up	**Recipients:** Adults (≥18 and <70 years old) with rapidly progressive diffuse cutaneous systemic sclerosis at risk of organ failure with modified Rodnan Skin score >15 and <40; <5 years from first non-Raynaud's phenomenon symptom; past or current IS **Donors:** Age 18–60 years and willing to undergo mobilization, apheresis, and 12-month safety follow-up
Status & Enrollment	Currently enrolling patients. For more information, visit https://freedom1study.com/	Currently enrolling patients. For more information, visit https://freedom-2study.com/	Currently enrolling patients. For more information, visit https://talaristx.com/our-programs/severe-autoimmune-disease/

References

1. Perkey and Maillard. *Annual Review of Pathology*. 2018;13:219-245.
2. Scherer et al. *Langenbeck's Archives of Surgery*. 2007;392(5):511-523.
3. Leventhal and Ildstad. *Human Immunology*. 2018;79(5):272-276.
4. Leventhal et al. 63rd American Society of Hematology Annual Meeting and Exposition December 11-14, 2021; Atlanta, GA.
5. Clinicaltrials.gov. https://clinicaltrials.gov/ct2/show/NCT01649388. Accessed December 8, 2021.
6. Clinicaltrials.gov. https://clinicaltrials.gov/ct2/show/NCT03995901. Accessed December 8, 2021.
7. Clinicaltrials.gov. https://clinicaltrials.gov/ct2/show/NCT05098145. Accessed December 8, 2021.

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