UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 30, 2022

TALARIS THERAPEUTICS, INC.
(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-40384**	**83-2377352**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

93 Worcester St. **Wellesley, Massachusetts**	**02481**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's Telephone Number, Including Area Code: 502 398-9250

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	**TALS**	**The NASDAQ Global Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01. Other Events.

On June 30, 2022, Talaris Therapeutics, Inc. ("Talaris," the "Company," "we," or "our") announced a clinical update on its ongoing Phase 3 FREEDOM-1 study in living donor kidney transplant ("LDKT") recipients.

To date, Talaris has enrolled 22 donor-recipient pairs in the Phase 3 FREEDOM-1 study of FCR001. Seven patients have been successfully dosed at five different trial sites. All three patients who were dosed more than 12 months prior to the data cutoff date have been successfully weaned off all chronic anti-rejection drugs without evidence of rejection and with stable kidney function. All of these patients, including the first patient who is now 24 months post-transplant, continue to remain off all anti-rejection drugs. Furthermore, all patients treated with FCR001 at least three months prior to the data cutoff date have achieved and maintained T-cell chimerism levels >50% at each of the 3-, 6- and 12-month timepoints post-transplant. The safety profile observed was generally consistent with that expected in patients receiving a kidney transplant and an allo-HSCT. Three cases of low-grade acute graft-versus-host disease ("aGvHD") were reported, all of which were treatment-responsive and have since resolved. One of these patients is more than 12 months post-transplant and has been successfully weaned off all anti-rejection drugs. As a result of an internal review triggered by the GvHD cases, Talaris has modified its mobilization protocol and added a second post-transplant dose of cyclophosphamide for GvHD prophylaxis. Trial enrollment continues.

Phase 3 FREEDOM-1 Highlights[1]

- **Enrollment, demographics and degree of HLA mismatching.** A total of 22 LDKT donor-recipient pairs have been enrolled to date in the FREEDOM-1 study at 10 different clinical sites. Of these, 13 were randomized to receive FCR001, 8 were randomized to the control arm and 1 failed final screening criteria. Currently, 7 of those randomized to FCR001 have received their kidney transplant and have been dosed with FCR001. The clinical trial continues to enroll donor/recipient pairs across all degrees of HLA mismatch. Figure 1 shows the distribution of all FCR001 recipients dosed to date, by the number of HLA mismatches between the donor and the recipient.
- **Efficacy data in FCR001-dosed patients.** As shown in Figure 2, a total of 7 patients have been dosed and all patients dosed at least three months prior to the cutoff date have achieved and maintained T-cell chimerism levels >50% at each of the 3-, 6- and 12-month timepoints post-transplant. All 3 of the patients dosed more than 12 months prior to the data cutoff date have been successfully weaned off all chronic anti-rejection drugs. The longest of these has been followed for 24 months post-transplant.

  In the context of transplantation, chimerism refers to a state wherein both the donor's and the recipient's hematopoietic stem cells ("HSCs") coexist in the recipient's bone marrow. Talaris believes chimerism to be an important potential study biomarker, predictive of inducing a state of allogeneic tolerance in the recipient, whereby the recipient tolerates the donated organ without the need for chronic anti-rejection drugs. Achieving high levels of durable donor T-cell chimerism in the LDKT recipient is one of the goals of the Company's Facilitated Allo-HSCT Therapy. In the Company's Phase 2 study, establishment and maintenance of >50% donor T-cell chimerism in an LDKT recipient at 3, 6 and 12 months after administration of FCR001 all correlated strongly with the patient's ability to durably discontinue chronic anti-rejection drugs approximately one year after transplant, without subsequent graft rejection.
- **Safety profile in FCR001-dosed patients.** Adverse events ("AEs") and serious adverse events ("SAEs") observed in FCR001-dosed patients are consistent with those generally expected in someone receiving both a kidney transplant and an allogeneic stem cell transplant involving non-myeloablative conditioning. Three cases of low-grade (grade II) aGvHD were reported, all of which responded to treatment and resolved. One of these patients is more than 12 months post-transplant and, notwithstanding their treatment-responsive aGvHD, has been weaned off all anti-rejection drugs. One of the three aGvHD patients was subsequently diagnosed with moderate chronic GvHD and is also responding to treatment. No trial stopping rules were triggered by the GvHD cases, and trial screening and enrollment continued. However, to investigate these aGvHD cases, Talaris conducted an internal review of all GvHD cases in Phase 2 and 3. Through this review, a correlation was identified between these cases and the use of plerixafor as a donor mobilizing agent, the use of which has been higher to date under the Phase 3 mobilization protocol compared with the Phase 2.

  Based on this analysis, the Company has modified the FREEDOM-1 trial protocol to eliminate plerixafor from the donor mobilization regimen in all but exceptional cases, and has also added a second dose of post-transplant cyclophosphamide ("PTCy") for the FCR001 recipient. The revised mobilization protocol better aligns with current customary donor mobilization practices and the additional dose of PTCy reflects the current standard of care for GvHD prophylaxis in HLA-mismatched allogeneic stem cell transplants. All findings and recommendations were reviewed and endorsed by a panel of external scientific advisors as well as the FREEDOM-1 data monitoring committee, which supported continuation of the trial with these modifications.

1. All data reported is as of the June 15, 2022 data cutoff date.

Figure 1:

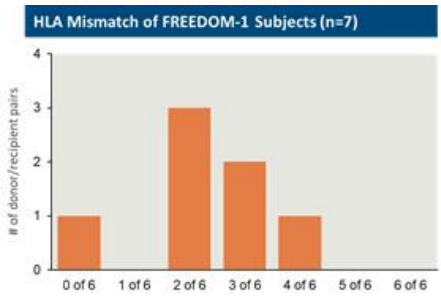
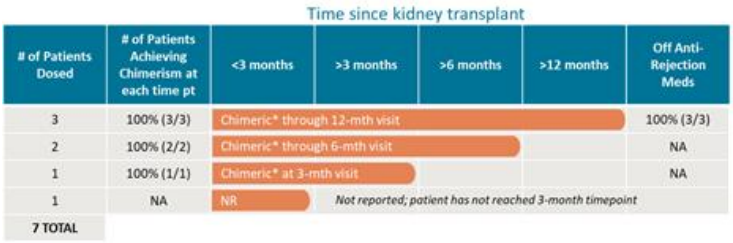


Figure 2:



A copy of the Company's presentation materials for the announcement is attached hereto as Exhibit 99.1 to this Current Report on Form 8-K and incorporated herein by reference.

Cautionary Note Regarding Forward-Looking Statements

This report contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, implied and express statements regarding Talaris' strategy, business plans and focus; the progress and timing of the preclinical and clinical development of Talaris' programs, including FCR001. The words "may," "might," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "expect," "estimate," "seek," "predict," "future," "project," "potential," "continue," "target" or the negative of these terms and similar words or expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, risks associated with: the impact of the ongoing COVID-19 pandemic on countries or regions in which the Company has operations or does business, as well as on the timing and anticipated timing and results of its clinical trials, strategy and future operations, including the expected timing and results from FREEDOM-1, the risk that the results of Talaris' prior clinical trials may not be predictive of or consistent with future and/or final results in connection with the Company's ongoing or future clinical trials; the therapeutic benefits expected from FCR001 and the Company's ability to successfully demonstrate its safety and efficacy. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2022, as well as any subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent Talaris' views only as of today and should not be relied upon as representing its views as of any subsequent date. Talaris explicitly disclaims any obligation to update any forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Talaris Therapeutics Presentation dated June 30, 2022.
104	Cover page interactive data file (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Talaris Therapeutics, Inc.

Date: June 30, 2022

By: /s/ Scott Requadt
Scott Requadt
President and Chief Executive Officer

Exhibit 99.1

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FREEDOM-1 CLINICAL UPDATE

June 30, 2022

Disclaimer

This Presentation contains forward-looking statements and information of Talaris Therapeutics, Inc. ("Talaris," "we," "our,") within the meaning of the Private Securities Litigation Reform Act of 1995. All statements other than statements of historical facts contained in this Presentation, including statements regarding our strategy, future financial condition, future operations, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "expect," "intend," "plan," "anticipate," "believe," "estimate," "target," "seek," "predict," "potential," "continue" or the negative of these terms or other comparable terminology. Although we believe that the expectations reflected in these forward- looking statements are reasonable, these statements relate to our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements in this presentation include, but are not limited to, statements about: the initiation, timing, progress, results and cost of manufacturing and conducting clinical trials of FCR001, as well as our research and development programs and our current and future preclinical and clinical studies, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available, and our current and future programs; our ability to identify research priorities and apply a risk-mitigated strategy to efficiently discover and develop additional product candidates; our ability to initiate, recruit and enroll patients in and conduct our clinical trials at the pace that we project; our ability to scale-up our manufacturing and processing approaches to appropriately address our anticipated commercial needs, if FCR001 is approved; obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations or warnings in the label of any of our product candidates, if approved; our ability to compete with companies currently marketing or engaged in the development of treatments that our product candidates are designed to target; our reliance on third parties to conduct our clinical trials and to manufacture drug substance for use in our clinical trials; the size and growth potential of the markets for any of our current product candidates or other product candidates we may identify and pursue, and our ability to serve those markets; our ability to identify and advance through clinical development any additional product candidates; the commercialization of our current product candidates and any other product candidates we may identify and pursue, if approved, including our ability to successfully build a specialty sales force and commercial infrastructure to market our current product candidates and any other product candidates we may identify and pursue; the scope of protections we are able to establish and maintain for intellectual property rights covering our product candidates and our Facilitated Allo-HSCT Therapy; our ability to retain and recruit key personnel; our expectations regarding government and third-party payor coverage and reimbursement; our estimates of our expenses, ongoing losses, capital requirements and our needs for or ability to obtain additional financing; our expected uses of the net proceeds to us from this offering; the potential benefits of strategic collaboration agreements, our ability to enter into strategic collaborations or arrangements, and our ability to attract collaborators with development, regulatory and commercialization expertise; our financial performance; developments and projections relating to our competitors or our industry; the effect of the on-going COVID-19 pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations, including but not limited to our preclinical studies and future clinical trials. We caution the Recipient not to place considerable reliance on the forward-looking statements contained in this presentation. The forward-looking statements in this presentation speak only as of the date of this document, and we undertake no obligation to update or revise any of these statements. Our business is subject to substantial risks and uncertainties, including those referenced above.

Any forward-looking statements are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, risks associated with the impact of the on-going COVID-19 pandemic where the Company has operations or does business, as well as on the timing and anticipated timing and results of its clinical trials; the risk that the strategy and future operations of the Company, including the expected timing, enrollment, and results from FREEDOM-1 will not meet expectations; the risk that early data from the FREEDOM-1 study may not be predictive of or consistent with future and/or final results; the risk that the results of Talaris' earlier clinical trials may not be predictive of results in any of the Company's ongoing or future clinical trials; and the risk that the Company may not be able to successfully demonstrate the safety and efficacy of its drug candidates, including FCR001. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2022, as well as any subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent Talaris' views only as of today and should not be relied upon as representing our views as of any subsequent date. Talaris explicitly disclaims any obligation to update any forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements. Certain information contained in this Presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and the Company's own internal estimates and research. While the Company believes these third-party sources to be reliable as of the date of this Presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, all of the market data included in this Presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.

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Talaris at a Glance

Novel, single-dose, investigational cell therapy with potential to transform standard of care in solid organ transplantation and multiple severe immune and non-malignant blood disorders

- **Lead product, FCR001, in open-label Phase 3 to induce durable immune tolerance in living donor kidney transplant (LDKT) recipients**
  - Compelling Phase 2 data
  - Highly predictive, near-term surrogate marker of long-term success identified in Phase 2
  - Phase 3 protocol substantially mirrors optimized Phase 2; Orphan drug and RMAT designation from FDA
    - Reported encouraging initial results on first patients in late 2021
- **FCR001 has pipeline-in-a-product potential across multiple therapeutic applications**
  - Large market opportunity
  - Two additional Phase 2 studies initiated Q4 2021
- **Robust, reproducible and fully in-house manufacturing**
- **Strong IP position and high barriers to entry**
- **Well-financed; ~$225M cash on hand as of March 31, 2022**

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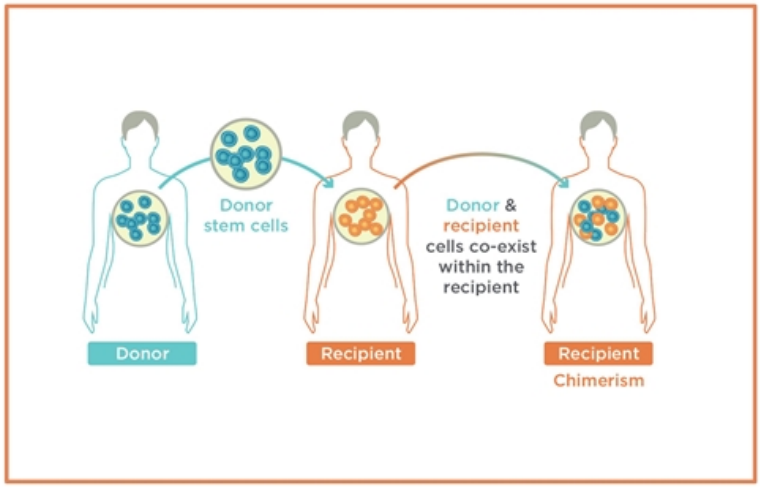
Allogeneic Tolerance and Chimerism

Nobel Prize 1960*

Goal: **facilitate allogeneic tolerance** by establishing **durable chimerism**

Allogeneic tolerance: An approach to enable donor HSCs to coexist with recipient HSCs in the recipient's bone marrow ("chimerism"), and mature into mutually-tolerated, functional immune cells and blood cells



*Nobel Prize in Physiology or Medicine 1960 was awarded jointly to Sir Frank Macfarlane Burnet and Peter Brian Medawar 'for discovery of acquired immunological tolerance.'

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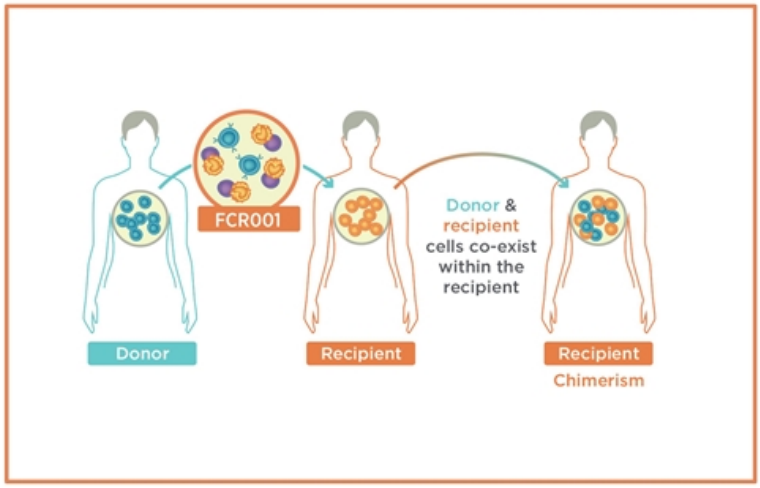

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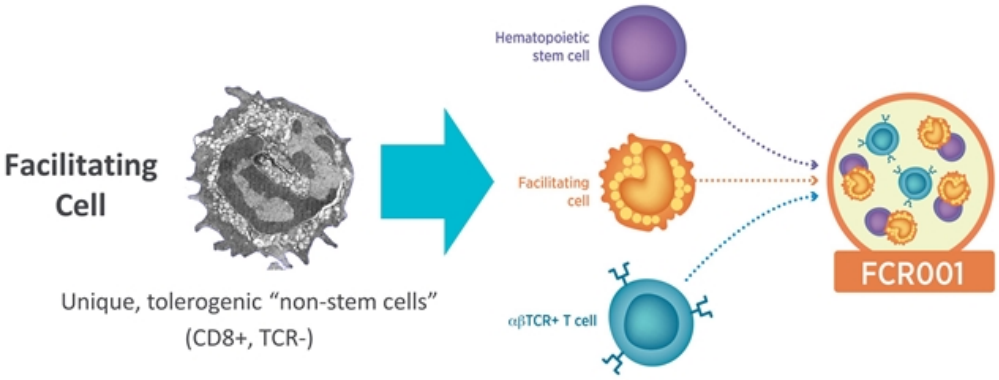
FCR001: A Modified, Allogeneic HSC-based Therapy

Proprietary composition of donor's CD34+ cells, Facilitating cells and αβ T-cells



Potential to:

- ✓ Promote stem cell engraftment in unmatched recipients
- ✓ Prevent GvHD in mouse models
- ✓ Induce antigen-specific T_{reg}
- ✓ Induce B_{reg}

- FCR001 is administered with **non-myeloablative conditioning**, at doses and using protocols optimized over two decades of study
- Broad, issued composition of matter patents

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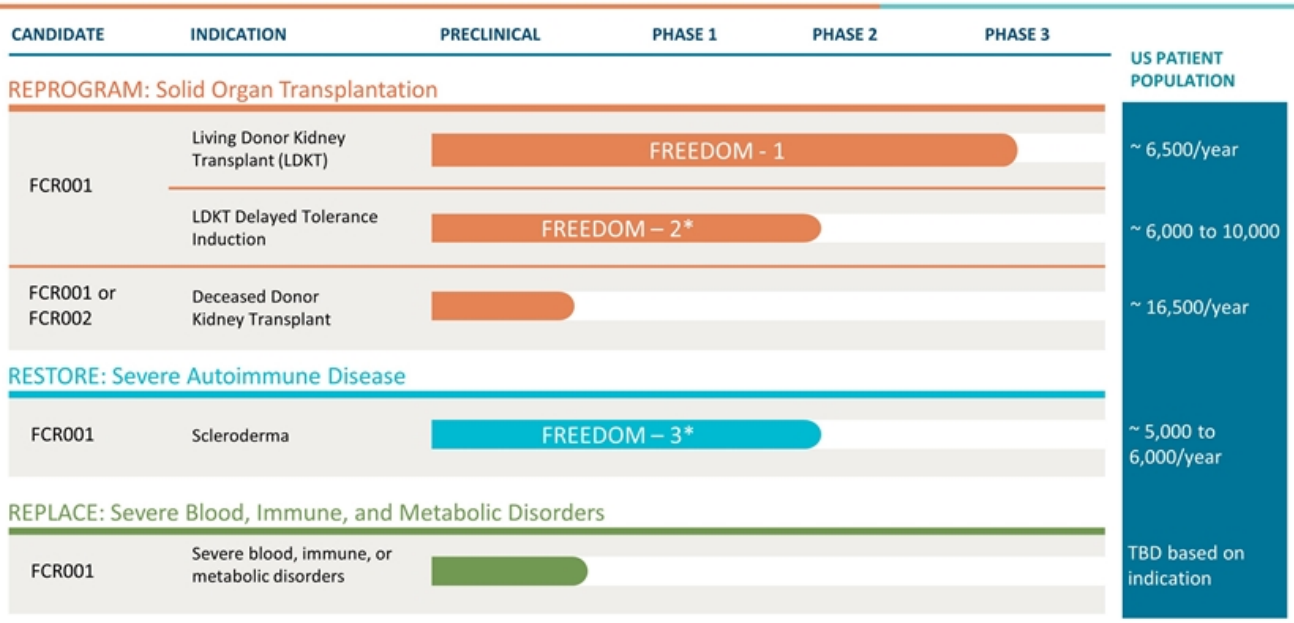
Our Pipeline



* Open IND permits us to move directly into Phase 2 based on existing FCR001 safety data

** Organ transplant population estimates based on UNOS/OPTN data; scleroderma estimates derived from epidemiology and third-party market research; LDKT Delayed Tolerance Induction patient numbers based on 1 year to 18 months delayed from incident LDKT; Scleroderma estimated point prevalence of diffuse cutaneous SSc patients with early, rapidly progressing disease and internal organ involvement

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Unmet Need in Organ Transplant:

"Ideally you want to avoid getting sick or being around sick people because your immune system is suppressed. Unfortunately, in the world we live in, you're going to get sick. The first couple of times I got sick, I was terrified."

- Male living donor kidney recipient in 40's

"While others might breeze out the door in the morning, I am already preoccupied with preventing rejection, infection, and cancer."

- FDA Voice of the Patient Panellist

Challenges of Chronic Immunosuppression

- **Immunosuppression is not disease-modifying; requires lifelong chronic immunosuppression**
- **Kidney toxicity**
  - ~35% of living donor transplants and ~50% of deceased donor transplants fail within 10 years[1]
- **Significantly increased risk of cancer[2]**
- **Hypertension, diabetes, high cholesterol, weight gain[3]**
  - Cardiovascular (CV) issues are leading cause of post-transplant mortality
- **Increased risk of serious infection[4]**
- **High cost, pill burden (>20 pills/day for life) and decreased QoL**
  - Cost ~$25K in first year and $5K-$10K annually for life of organ[1]
  - Poor compliance can lead to rejection or organ loss
  - Sleep disturbance, CNS issues, depression, and other AEs affecting QoL

Sources: patientslikeme; The Voice of the Patient FDA Meeting (Sep 2016): Patients who Have Received an Organ Transplant
1. USRDS 2020 Annual Data Report, Fig 6.16: https://adr.usrds.org/2020/end-stage-renal-disease/6-transplantation
2. Engels et al JAMA 2011; 306(17): 1891-1901
3. Nankivell BJ et al, Lancet 2011, 378:1428-37
4. Karuthu et al, Clin J Am Soc Nephrol. 2012 Dec;7(12):2058-70
QoL: Quality of life; CNS: Central Nervous System

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Highlights from our Phase 2 Study (+ long-term followup)*

37 adult living donor kidney transplant (LDKT) patients were dosed with our therapy at two leading US transplant sites between 2009 - 2016

70%

(26 OF 37) OFF ALL IMMUNOSUPPRESSION THERAPIES **

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

100%

TAKEN OFF IMMUNOSUPPRESSION REMAIN IS-FREE

- Median follow up: >6 yrs
- Six patients > 10 years
- Longest >12 yrs

7/7

TOLERIZED PATIENTS WITH PRIOR KIDNEY AUTO-IMMUNE CONDITION HAD NO RECURRENCE

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

** Data as of January 31, 2022. Includes 33 patients under Phase 2 protocol and 4 compassionate use patients*
*** One year after transplant*
**** Kienzl-Wagner 2018, Lim 2019, Moroni 2019*

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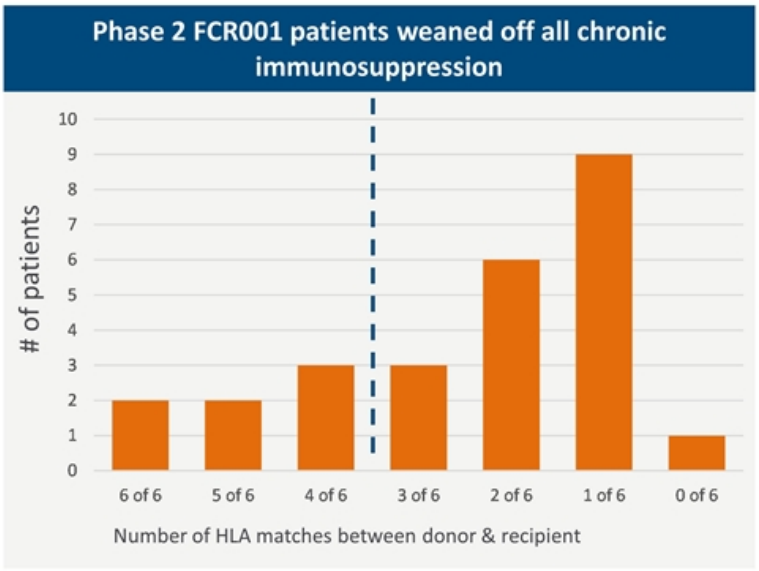
Strong Phase 2 Results Across All Degrees of HLA-Match



Data as of January 31, 2022

- 19/26 (73%) durably off all chronic immunosuppression had HLA match of 3 or less between LDKT donor & recipient
- Comparable kidney and patient survival for all FCR001 vs standard of care (SoC) LDKT patients
- FCR001 safety & tolerability data generally consistent with separate SoC kidney transplant + allogeneic HSCT with non-myeloablative conditioning
- No acute rejection or donor-specific antibodies in FCR001 patients off immunosuppression

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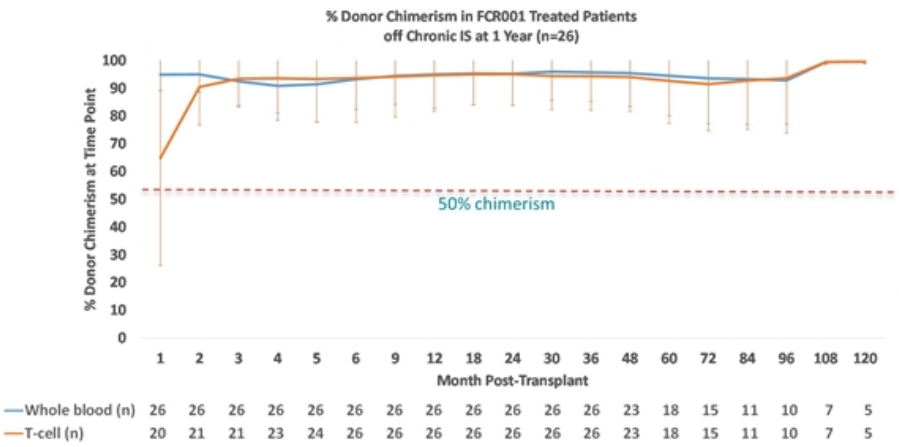
Phase 2 Three- and Six-Month Chimerism Results Were Highly Predictive of Durable Immune Tolerance



Values are mean +/- standard deviation. N indicates the number of FCR001 treated patients weaned off IS at approximately one year post-transplant for whom % whole blood and T-cell donor chimerism were measured at that time point

Data as of January 31, 2022

- **"Chimerism"**
  - % of recipient's T-cells that are donor-derived
  - Simple blood test, measured at multiple time points
- **26/29 patients** (90%) who achieved chimerism at **month 3** were able to be weaned off chronic immunosuppression (IS)
- **26/27 patients** (96%) who achieved chimerism at **month 6** were able to be weaned off chronic IS
- **Every patient** weaned off chronic IS by **month 12** has remained off chronic IS for full duration of follow up
  - Median follow up >6 years
  - Longest follow up >11 years

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FREEDOM-1 Phase 3 Registration Study

STUDY OVERVIEW	
Study Design	• **Open-label**, randomized, controlled, parallel group study of FCR001 in 120 first time, adult living donor kidney transplant (LDKT) recipients, randomized 2:1 between FCR001 : standard of care (SoC) • Five-year follow up for safety
Protocol; inclusion / exclusion criteria	• Near-identical to optimized Phase 2 protocol
Primary Endpoint	• Proportion of FCR001 recipients who are free from chronic immunosuppression, without biopsy proven acute rejection (BPAR), at Month 24 post-transplant
Key Secondary Endpoint	• In FCR001 recipients only, no meaningful decline in renal function from post-transplant baseline (Month 1) to Month 24
Additional Endpoints	• Chimerism, kidney function, safety
Sites / Territory	• Targeting ~20 sites in U.S. (17 active sites as of June 15, 2022)

- Neither primary nor key secondary endpoint involves statistical comparison to the SoC patients

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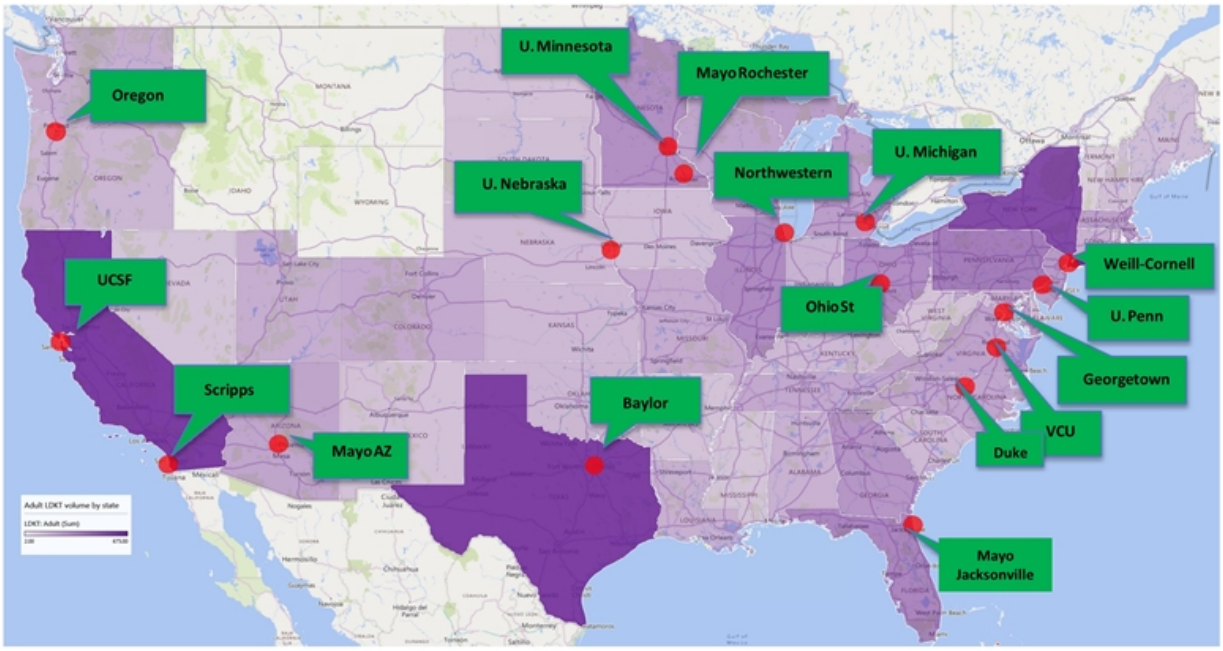
FREEDOM-1

We Now Have 17 Active FREEDOM-1 Sites



Data as of June 15, 2022

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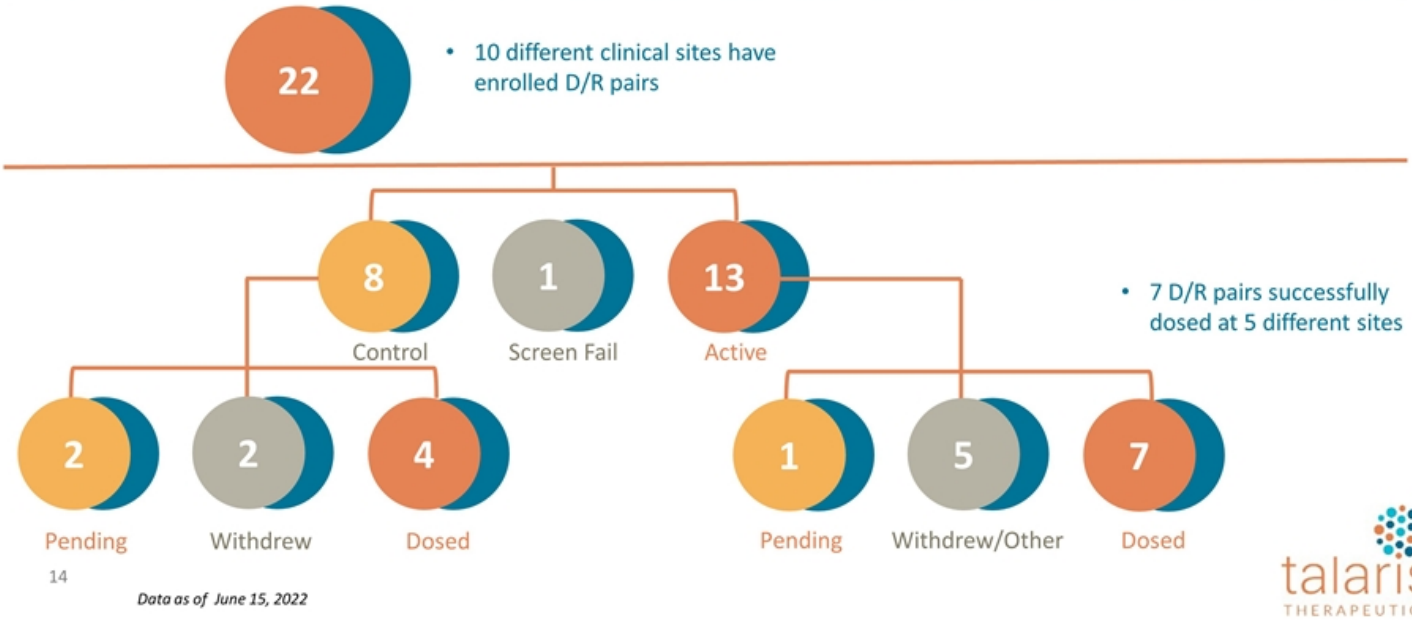
Phase 3 Update: Enrollment, Demographics

Enrollment & Demographics



- 10 different clinical sites have enrolled D/R pairs
- 7 D/R pairs successfully dosed at 5 different sites

Data as of June 15, 2022

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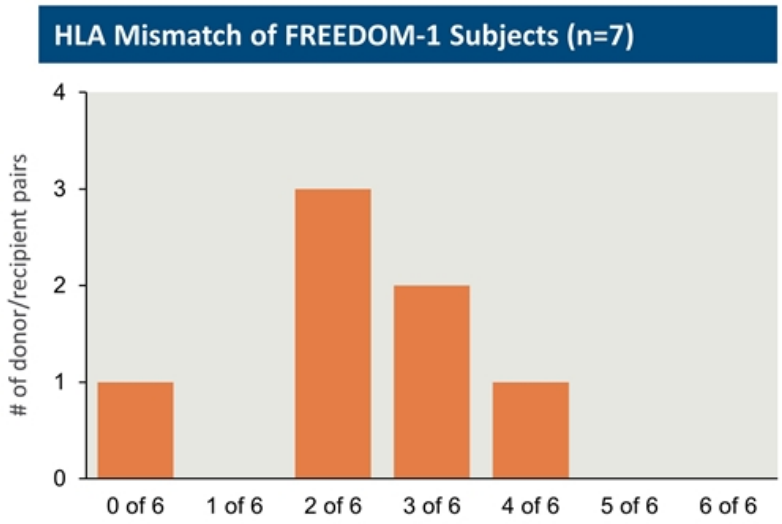
Study Continues to Enroll Across Degrees of HLA Mismatch



In addition to HLA mismatching data, high-resolution (HR) matching data (using a 12-point scale) is used in the BMT medical community. HR matching, however, is not available at all sites. Pairs for which HR matching data is available include 3/12, 6/12, 6/12 and 7/12 matches.

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Phase 3 Update: FCR Chimerism and Chronic IS Status

# of Patients Dosed	# of Patients Achieving Chimerism at each time pt	Time since kidney transplant: <3 months	>3 months	>6 months	>12 months	Off Anti-Rejection Meds
3	100% (3/3)	Chimeric* through 12-mth visit				100% (3/3)
2	100% (2/2)	Chimeric* through 6-mth visit				NA
1	100% (1/1)	Chimeric* at 3-mth visit				NA
1	NA	NR	*Not reported; patient has not reached 3-month timepoint*			
7 TOTAL						

- All FCR-001 patients have achieved and maintained chimerism*
- No instances of BPAR or DSA in any FCR-001 patients
- All have maintained stable kidney function
- Longest follow up: 24 months with no BPAR

* Chimeric: Achieved and maintained >50% T-cell chimerism at each designated study visit timepoint

Data through June 15, 2022

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Phase 3 Update: Safety Profile

- **Summary of safety profile in FCR001 patients**
  - AEs and SAEs observed are consistent with those generally expected with kidney and allogeneic stem cell transplantation involving non-myeloablative conditioning
  - No events occurred that caused data monitoring committee (DMC) to stop the study; no stopping rules triggered
- **Three cases of low-grade aGvHD; all cases were treatment responsive and resolved**
  - Cases were grade II, with symptoms limited to skin and/or GI
  - One of these three patients also diagnosed with moderate cGvHD and is responding to treatment
  - One of the patients with aGvHD who is more than 12 months post-transplant has been successfully weaned from tacrolimus and MMF
- **Trial enrollment continues without interruption**
  - Talaris proactively conducted a full review
  - Review findings and subsequent recommendations reviewed and endorsed by both external scientific advisory panel and DMC

** Data through June 15, 2022*

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Phase 3 Update: GvHD Review & Protocol Adjustment

- **Plerixafor introduced in mid-Phase 2 as option for donor mobilization**
  - Used in mobilization protocol to reduce potential need for second mobilizations
  - Used much more frequently in Phase 3 than Phase 2
- **Identified a correlation between aGvHD cases and increased use of plerixafor in Phase 3**
  - Evident in four of five aGvHD cases when analyzing across Phase 2 and Phase 3 cohorts
- **Plerixafor was associated with increased cell counts and decreased recoveries of FCs in our product**
- **Eliminated plerixafor from donor mobilization regimen* and added second post-transplant dose of cyclophosphamide (PTCy) for recipient GvHD prophylaxis**
  - Since completion of our Phase 2 trial in 2016, two doses of PTCy has emerged as the standard of care in allo-HSCT settings

**Plerixafor may be used in exceptional circumstances after consultation with patient and investigator*

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Phase 3 Update: Summary

- **Efficacy:**
  - All FCR patients have achieved and maintained > 50% T-cell chimerism at all measured timepoints
  - Observed durable chimerism (irrespective of HLA mismatch) and immunosuppression weaning and/or withdrawal at multiple clinical sites
  - Longest follow-up is 24 months with no biopsy-proven acute rejection (BPAR)
- **Safety:**
  - Three grade II, treatment-responsive and resolved aGvHD cases; one of these three patients also diagnosed with moderate chronic GvHD and is responding to treatment
  - Revised protocol better aligns with customary donor mobilization practices as well as emerging standard of care for GvHD prophylaxis in haplo-identical allo-HSCT
- **Enrollment:**
  - Sites continuing to enroll; donor apheresis and FCR001 dosing proceeding

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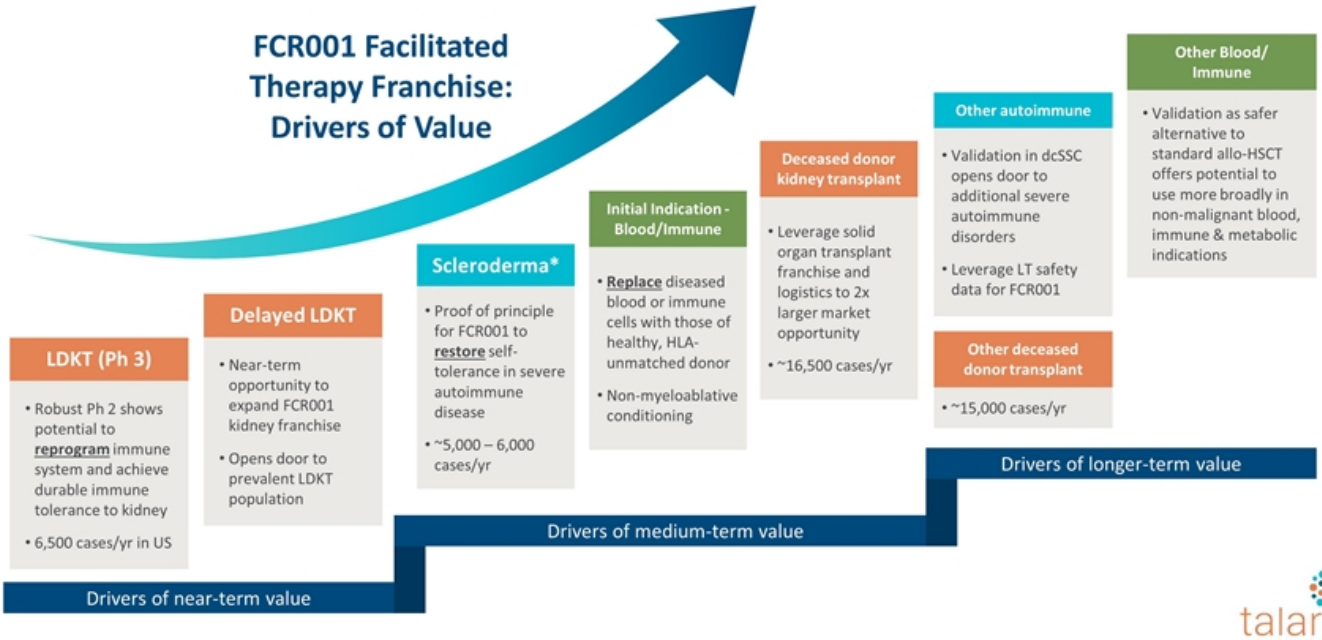
A Path to Significant Value Creation



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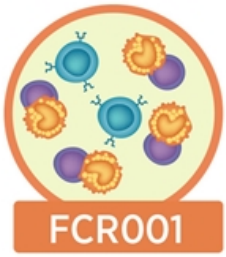
* Diffuse cutaneous systemic sclerosis (dcSSc) patients with early, rapidly progressive disease

Summary



Novel, single-dose, investigational cell therapy with potential to transform standard of care in solid organ transplantation and multiple severe immune and blood disorders

- Lead product, FCR001, in Phase 3 to induce durable immune tolerance in living donor kidney transplant (LDKT) recipients; initial clinical results continue to be encouraging
- FCR001 has pipeline-in-a-product potential across multiple therapeutic applications
- Robust, reproducible and fully in-house manufacturing
- Strong IP position and high barriers to entry
- ~$225M cash on hand as of March 31, 2022

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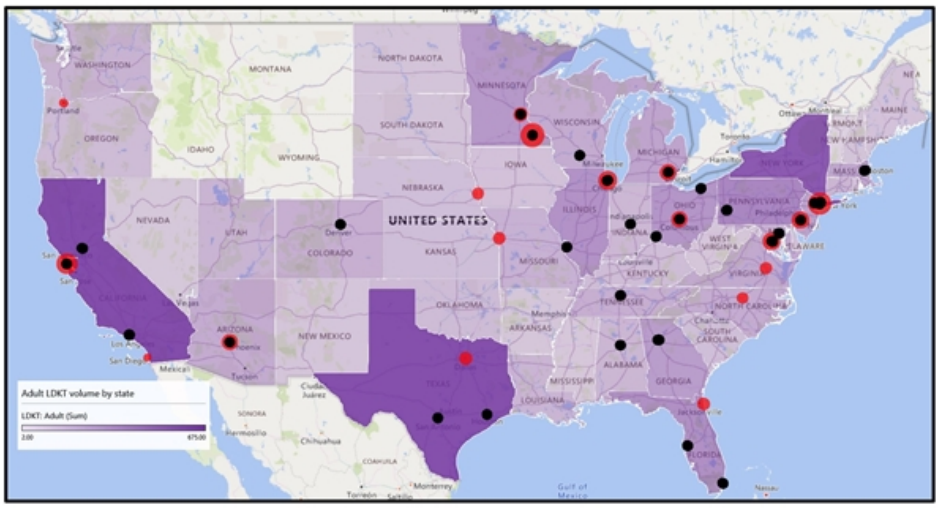
Backup Slides

Potential to Extend Across Solid Organ Transplant

Current & planned FREEDOM-1 centers perform ~25% of all US LDKT procedures



- Highest volume LDKT centers
- Current or proposed FREEDOM-1 sites (circle size proportional to LDKT volume)

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Durable Immune Tolerance: The "Holy Grail" of Transplant

TRANSPLANTATION

The Quest for Transplantation Tolerance: Have We Finally Sipped from the Cup?

James F. Markmann and Tatsuo Kawai*

New advances in achieving hematopoietic chimerism may facilitate immunological tolerance to kidney transplants.

www.ScienceTranslationalMedicine.org 7 March 2012 Vol 4 Issue 124 124fs5

If the Leventhal *et al.* results are sustained and expanded in number, they may potentially have an enormous, paradigm-shifting impact on solid-organ transplantion.

In 1953, Billingham *et al.* reported the Nobel Prize–winning finding that neonatal inoculation of mice with allogeneic lymphoid cells could induce long-lived donor hematopoietic chimerism and that the resulting intermingling of donor and host immune cells throughout the host yielded immunological tolerance to donor-strain grafts (*1*). This discovery brought with it the promise of organ transplantation without the morbidity of lifelong immunosuppression and set routine attainment of immunological tolerance as the field's seemingly unreachable Holy Grail. Now, Leventhal *et al.* (*2*) add to advances in the last few years that suggest that the 6-decade-long quest for tolerance for kidney transplant patients may finally be nearing its end.

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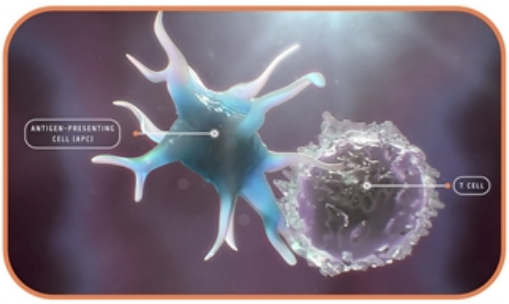
Facilitating Cell Mechanism of Action



Induces IL-10+ B_{reg} *in vitro*
Manuscript in Preparation
Nupur, *Exp Hematol* 2007, 5:1847-1857-1857

Gene arrays of mouse and human FC show strong B cell signature
Manuscript in Preparation
Nupur, *Exp Hematol* 2007, 5:1847-1857

Induces antigen-specific T_{reg} *in vivo*
Taylor KN. *J Immunol. 2007;* 179 (4): 2153-62
Huang Y. *Blood*. 2011; 117(8):2494-2505
Colson, *Blood* 2004, 104:3829-3835

Enhances homing and migration
Wen, *Stem Cells.* 2014; 32(1): 2732-43
Kaufman, *Blood* 1994, 84:2436-2446
Gandy, *Immunity* 1999, 11:579-590
Bridenbaugh, *Blood* 2008, 111:1735-1738

Prevents apoptosis of HSC and enhances clonogenicity of HSC
Rezzoug F. *J Immunol.* 2008; 180(1);49-57
Fugier-Vivier I. *J Exp Med.* 2005; 201(3) 373-383

Prevents GVHD in Mice
Manuscript in Preparation
Taylor KN. *J Immunol. 2007;* 179 (4): 2153-62
Colson, *Blood* 2004, 104:3829-3835

Black text= Ildstad laboratory publications
Red text = external publications

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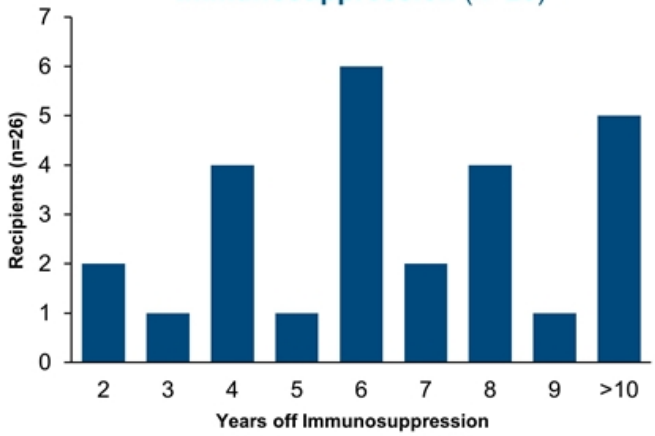
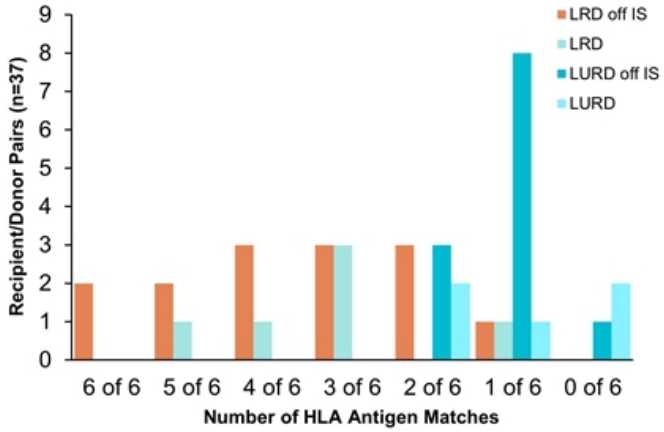
Follow-Up on Immunosuppression-Free Recipients

Years Since Discontinuation of Immunosuppression (n=26)[1,a]



HLA Antigen Match out of 6 (n=26)[2]



LRD, living related donor; LURD, living unrelated donor.

[a]The above data represent the time interval between the date each patient discontinued immunosuppression and that patient's last study follow-up visit that occurred prior to January 31, 2021.[2]

1. Leventhal J et al. *Am J Transplant*. 2021;21(suppl 3). Accessed February 9, 2022. https://atcmeetingabstracts.com/abstract/long-term-follow-up-of-a-phase-2-clinical-trial-to-induce-tolerance-in-living-donor-renal-transplant-recipients-3/ 2. Data on file.

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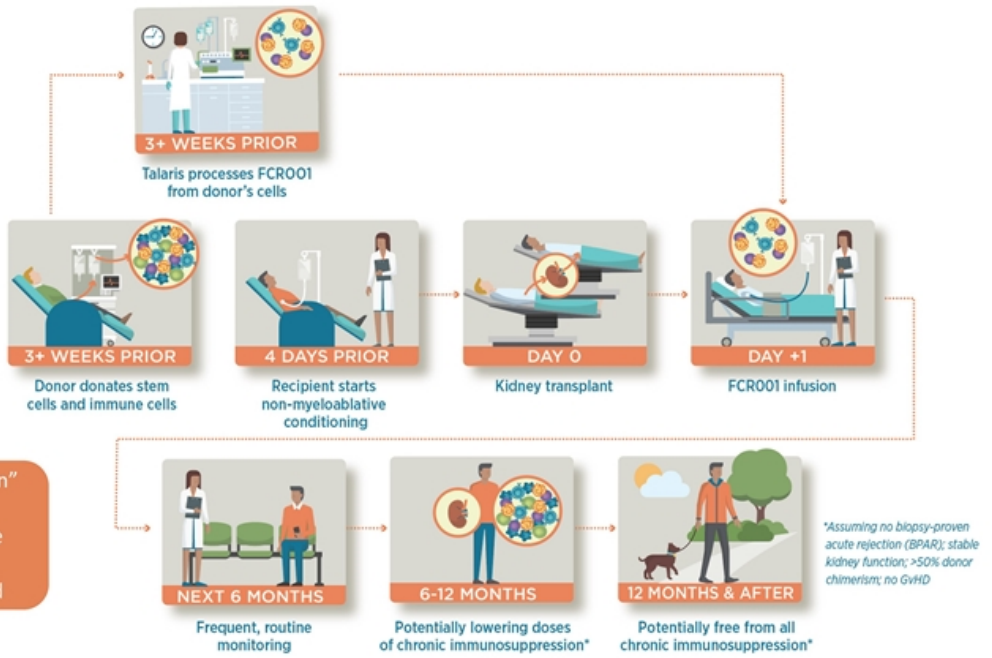
FCR001: The Donor-Recipient Journey



Our "vein to vein" process and protocols have been fully proceduralized

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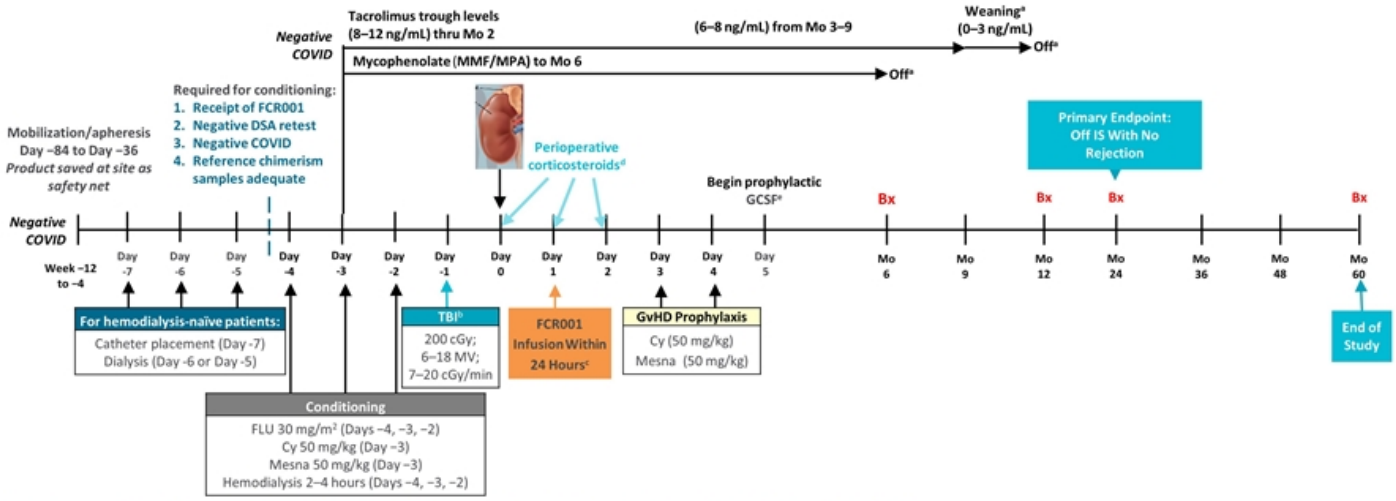
FREEDOM-1: FCR001 Protocol Overview



*Patients demonstrating stable donor chimerism (>50%), no history of rejection, no DSA, no GvHD, not using corticosteroids, and adequate kidney function.

[b]TBI dose of 200 cGy delivered as a single fraction at 10–18 MV at a rate of 15–20 cGy/min are the preferred energy and rate parameters and should be followed when possible.

[c]Administered using a central or dedicated peripheral line; infusion by gravity.

[d]Methylprednisolone 500 mg IV on Day 0 in OR; 250 mg Day 1 and 125 mg Day 2.

*Until absolute neutrophil count is >1000/mm³ for 3 consecutive days.

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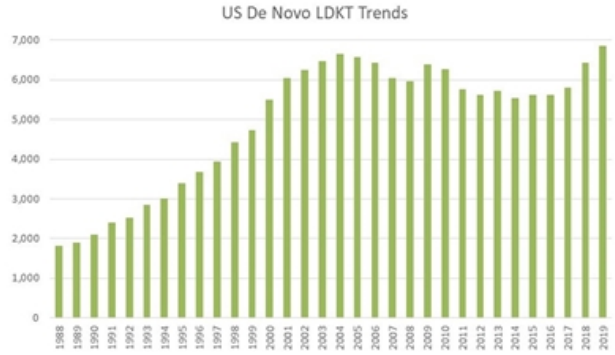
Overview of Living Donor Kidney Transplant (U.S.)

Incidence



- Since 2000, average 6,080 cases/year
- 2019 highest volume on record: 6,867
- ~30% of total kidney transplants annually

Sources: UNOS/OPTN 2019; USRDS 2020 Annual Data Report

Prognosis and Prevalence

Yr. Post LDKT	Graft Survival	Patient Survival
1 year	97%	99%
5 year	85%	94%
10 year	65%	79%

- Excellent short-term outcomes with LDKT
- Unmet need for improved long-term outcomes
- ~50K prevalent LDKT patients with functioning graft transplanted in past decade

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Value proposition for “One Transplant for Life”

Human Costs:
Lost Productivity
Impaired QoL

Clinical & Economic Costs:
IS Complications
IS Co-morbidities
Graft Loss
IS Costs

Value From Eliminating Chronic IS

- **Improve outcomes**
  - Fewer rejections, graft losses
  - No IS co-morbidities or complications
  - Enhance patient’s QoL and freedom
- **Reduce systematic costs**
  - IS and meds to manage co-morbidities
  - Avoid return to dialysis or 2nd transplant
  - Bolster recipients’ productivity

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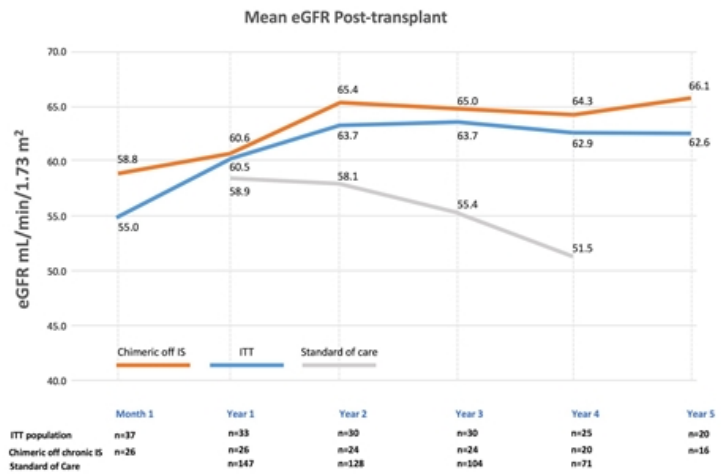
Evidence of Potential Longer-Term Clinical Benefit

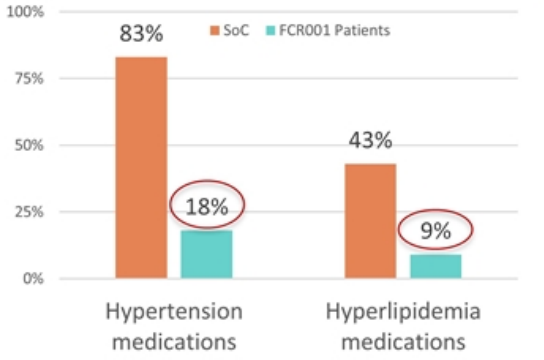
FCR001 improved Quality of Life[1], preserved kidney function and enabled lower reliance on cardiovascular medications[2][3]

Mean Estimated eGFR* Over Time Post- Transplant



	Month 1	Year 1	Year 2	Year 3	Year 4	Year 5
ITT population	n=37	n=33	n=30	n=30	n=25	n=20
Chimeric off chronic IS	n=26	n=26	n=24	n=24	n=20	n=16
Standard of Care		n=147	n=128	n=104	n=71	

Cardiovascular Medication Usage SoC vs Durably Chimeric FCR001 Patients



1. Results presented at ATC 2019 by Dr. D. Tollerud, based on cardiac and renal dysfunction measures under ESRD-SCL-TM and general health as measured by SF-36
2. Retrospective analysis by Dr. J Leventhal of transplanted SoC patients at same site between 2009-2012, who met Ph 2 eligibility criteria (n=132)
3. FCR001 patients off all chronic immunosuppression (n=26)

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