UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2021

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO**

Commission File Number 001-40384

TALARIS THERAPEUTICS, INC.

(Exact name of Registrant as specified in its Charter)

Delaware	**83-2377352**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
570 S. Preston St Louisville, KY	**40202**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (502) 398-9250

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, par value $0.0001 per share	TALS	The Nasdaq Global Market

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES ☐ NO ☒

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES ☐ NO ☒

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES ☒ NO ☐

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). YES ☒ NO ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		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. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO ☒

The aggregate market value of the voting and non-voting common stock held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on the Nasdaq Global Market on June 30, 2021, was $280,469,780. In determining the market value of non-affiliate common stock, shares of the Registrant's voting and non-voting common stock beneficially owned by officers, directors and affiliates have been excluded. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The number of shares of Registrant's Common Stock outstanding as of March 1, 2022 was 41,455,477.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's proxy statement for the 2022 annual meeting of stockholders to be filed pursuant to Regulation 14A within 120 days after the registrant's fiscal year ended December 31, 2021, are incorporated by reference in Part III of this Form 10-K.

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SUMMARY OF THE MATERIAL RISKS ASSOCIATED WITH OUR BUSINESS

Our business is subject to numerous risks and uncertainties, including those described in Part II, Item 1A. “Risk Factors” in this Annual Report on Form 10-K. The principal risks and uncertainties affecting our business include the following:

- Our business substantially depends upon the successful development and regulatory approval of FCR001, our lead product candidate. If we are unable to obtain regulatory approval for FCR001, our business may be materially harmed.
- We are a late-stage clinical biotechnology company and we have incurred net losses since our inception. We anticipate that we will continue to incur significant net losses for the foreseeable future, and may never achieve or maintain profitability.
- We have not yet completed any registrational trials and have no history of commercializing products, which may make it difficult to evaluate the success of our business to date and to assess our future viability.
- Our product candidates represent a novel therapeutic approach that could result in heightened regulatory scrutiny. The regulatory landscape that applies to our Facilitated Allo-HSCT Therapy is rigorous, complex, uncertain and subject to change.
- Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and the inability to successfully and timely conduct clinical trials and obtain regulatory approval for our product candidates would substantially harm our business.
- If we experience delays or difficulties in the enrollment of patients in clinical trials, development of our product candidate may be delayed or prevented, which would have a material adverse effect on our business.
- The results of preclinical studies or earlier clinical trials are not necessarily predictive of future results. Our existing product candidates in clinical trials, and any other product candidate we advance into clinical trials, may not have favorable efficacy or safety in later clinical trials or receive regulatory approval.
- Interim, “top line” or preliminary data from our clinical trials that we may announce or share with regulatory authorities from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.
- Our product candidates, or associated conditioning regimens or treatment protocols, may cause undesirable side effects such as infection or graft vs. host disease, or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label or result in significant negative consequences following any regulatory approval.
- We intend to develop FCR001, and potentially future product candidates, in other indications and in combination with other therapies, which exposes us to additional risks. Combination therapies and additional indications involve additional complexity and risk that could delay or cause our programs to stall or fail; development of such programs may be more costly, may take longer to achieve regulatory approval and may be associated with unanticipated adverse events.
- Even if our product candidates receive regulatory approval, we will still face extensive ongoing regulatory requirements and continued regulatory review, which may result in significant additional expense, and our products may still face future development and regulatory difficulties.
- We currently operate our own manufacturing facility and intend to scale-up our manufacturing and processing approaches to appropriately address our anticipated commercial needs for FCR001, which will require significant resources. We may fail to successfully operate our facility, which could adversely affect our clinical trials and the commercial viability of our product candidates.
- Our product candidates are uniquely manufactured for each patient and we may encounter difficulties in production, particularly with respect to scaling our manufacturing capabilities.
- If our manufacturing facility is damaged or destroyed or production at our manufacturing facility is otherwise interrupted, our business would be negatively affected.
- We are dependent on a limited number of suppliers and, in some cases sole suppliers, for some of our components and materials used in our product candidates.
- We rely on third parties to conduct our clinical trials and perform some of our research and preclinical studies. If these third parties do not satisfactorily carry out their contractual duties or fail to meet expected deadlines, our development programs may be delayed or subject to increased costs, each of which may have an adverse effect on our business and prospects.
- We depend substantially on intellectual property licensed from the ULRF, and termination of this license could result in the loss of significant rights, which would materially harm our business.

- We expect the product candidates we develop will be regulated as biological products, or biologics, and therefore they may be subject to competition sooner than anticipated.
- If we are unable to obtain and maintain sufficient intellectual property protection for our product candidates and manufacturing process, or if the scope of the intellectual property protection is not sufficiently broad, our ability to commercialize our product candidates successfully and to compete effectively may be adversely affected.
- Our business has been adversely affected by the ongoing COVID-19 pandemic, and could be further adversely affected by the effects this and other of public health epidemics in regions where we, or third parties on which we rely have significant research, development or production facilities, concentrations of clinical trial sites or other business operations.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). All statements other than statements of historical fact are "forward-looking statements " for purposes of this Annual Report on Form 10-K. In some cases, you can identify forward-looking statements by terminology such as "anticipate," "believe," "could," "estimate," "expects," "intend," "may," "plan," "potential," "predict," "project," "should," "will," "would" or the negative or plural of those terms, and similar expressions.

Forward-looking statements include, but are not limited to, statements about:

- the success, cost and timing of our product development activities and clinical trials, 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 research and development programs;
- the potential for COVID-19 or other pandemic, epidemic or outbreak of an infectious disease, to disrupt our business plans, product development activities, ongoing clinical trials, including the timing and enrollment of patients, the health of our employees and the strength of our supply chain;
- our expectations regarding the safety or efficacy profile of our product candidates
- our ability to advance any product candidate into or successfully complete any clinical trial;
- our ability to obtain regulatory approval for any of our candidates;
- our ability to successfully manufacture our product candidates for future clinical trials or for commercial use, if approved;
- the ability to license additional intellectual property relating to any future product candidates and to comply with our existing license agreement;
- our ability to commercialize our products in light of the intellectual property rights of others;
- the success of competing therapies that are or become available;
- our ability to obtain funding for our operations, including funding necessary to complete further development and commercialization of our product candidates;
- the commercialization of our product candidates, if approved;
- our plans to research, develop and commercialize our product candidates;
- our ability to attract collaborators with development, regulatory and commercialization expertise;
- future agreements with third parties in connection with the development or commercialization of our product candidates and any other approved product;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- the rate and degree of market acceptance of our product candidates;
- regulatory and political developments in the United States and foreign countries, including but not limited to the Russia-Ukraine conflict and associated sanctions;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- our ability to attract and retain key scientific or management personnel;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- the impact of laws and regulations; and
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates.

Factors that may cause actual results to differ materially from current expectations include, among other things, those set forth in Part I, Item 1A. "Risk Factors," below and for the reasons described elsewhere in this Annual Report on Form 10-K. Any forward-looking statement in this Annual Report on Form 10-K reflects our current view with respect to future events and is subject to these and other risks, uncertainties and assumptions. Given these uncertainties,

you should not rely on these forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, our information may be incomplete or limited and we cannot guarantee future results. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business and the markets for certain drugs and consumer products, including data regarding the estimated size of those markets, their projected growth rates and the incidence of certain medical conditions. Information that is based on estimates, forecasts, projections or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained these industry, business, market and other data from reports, research surveys, studies and similar data prepared by third parties, industry, medical and general publications, government data and similar sources and we have not independently verified the data from third party sources. In some cases, we do not expressly refer to the sources from which these data are derived.

PART I

Item 1. Business.

Overview

We are a late-clinical stage, cell therapy company developing an innovative method of allogeneic hematopoietic stem cell transplantation (**allo-HSCT**) that we believe has the potential to transform the standard of care in solid organ transplantation, certain severe autoimmune diseases and certain severe blood, immune and metabolic disorders. In the organ transplant setting, which is our initial focus, we believe our proprietary therapeutic approach, which we call **Facilitated Allo-HSCT Therapy**, could prevent organ rejection without the morbidity and mortality that has been associated with the use of lifelong anti-rejection medicines, also known as chronic immunosuppression. Beyond the organ transplant setting, our Facilitated Allo-HSCT Therapy also has the potential to treat a range of severe autoimmune diseases and severe blood, immune and metabolic disorders, in each case with potential for similar outcomes to what has previously been observed with HSCT, while mitigating the toxicities, morbidities and extended hospital stay associated with the conditioning regimen typically required by HSCT. We believe that our target indications, individually and collectively, represent a significant unmet need and commercial opportunity.

Our lead product candidate, **FCR001**, which is central to our Facilitated Allo-HSCT Therapy, is a novel allogeneic cell therapy comprised of stem and immune cells that are procured from a healthy donor, who is also the organ donor in the case of organ transplantation. FCR001 is rapidly processed in our GMP facility using our proprietary manufacturing methods. Then, at the time of transplant, FCR001 is administered to the recipient following nonmyeloablative conditioning, which is designed to be less toxic than myeloablative conditioning. A fully myeloablative conditioning regimen consists of a combination of agents and high doses of total body irradiation that destroy hematopoietic stem cells (**HSCs**) in the bone marrow and results in profound depletion of HSC-derived cells within one to three weeks following administration that is irreversible, and in most instances is fatal unless rescued by a stem cell transplant. The nonmyeloablative conditioning for FCR001 entails lower doses of chemotherapy and total body irradiation, causes less depletion of blood cells and does not require stem cell support for the recipient to resume the production of blood cells and platelets. We do not outsource any key aspect of our cell processing. We are developing FCR001 as a pipeline-in-a-product with the potential to address the therapeutic areas described above.

We are currently enrolling patients in FREEDOM-1, a randomized, controlled, open-label Phase 3 registration trial in the United States of FCR001 in 120 adult living donor kidney transplant (**LDKT**) recipients. The goal of this trial is to evaluate the potential of FCR001, when administered the day after the kidney transplant, to induce durable, drug-free immune tolerance in the recipient of the transplanted kidney. Inducing durable immune tolerance to a transplanted organ without the morbidities associated with lifelong immunosuppression is a goal that has been broadly referred to in the transplant field as the "*Holy Grail*" of solid organ transplant. The primary endpoint of FREEDOM-1 is the demonstration that the lower end of our confidence interval of FCR001 patients free from chronic immunosuppression and without biopsy-proven acute rejection (**BPAR**) at 24 months post-transplant. The secondary endpoint is to evaluate the change in renal function as measured by estimated glomerular filtration rate (**eGFR**), which estimates how much blood passes through the filters in the kidney that remove waste from the blood, from post-transplant baseline (month one) to month 24 in FCR001 recipients.

In November 2021, in connection with a medical meeting presentation, we provided an update on the first patients dosed in our FREEDOM-1 Phase 3 clinical trial. We announced that all patients treated with FCR001 at least three months prior had achieved T-cell chimerism levels greater than 50% at each of the 3-, 6-, and 12-month timepoints post-transplant, which has correlated strongly with the patient's ability to durably discontinue chronic immunosuppression ("**IS"**) without subsequent graft rejection. Further, we announced that the overall safety profile of Phase 3 patients dosed at the time with FCR001 was consistent with that observed in our Phase 2 study of FCR001.

We also have robust, long-term Phase 2 data supporting our lead indication in LDKT. The primary endpoint of our Phase 2 trial was to determine whether the administration of FCR001 can induce durable tolerance to the donated kidney and substantially reduce or eliminate the requirement for immunosuppression within 12 months following transplant. In our Phase 2 trial, 26 of 37 LDKT patients treated with FCR001 (70%) were able to completely discontinue their chronic immunosuppression approximately one year after receiving their transplant. After mid-course optimizations to the Phase 2 protocol, 14 of the last 17 patients (82%) in the trial were able to discontinue their chronic immunosuppression by approximately one year post-transplant. Every transplant recipient who was weaned off immunosuppression has remained off chronic immunosuppression, without any organ rejection, for the duration of their follow-up. As of March 1, 2022, we have followed these patients for a median of 6.6 years post-transplant, and the longest for 11.3 years post-transplant. These results were achieved despite significant degrees of immune system human leukocyte antigen (**HLA**) mismatch between the donors

and recipients, and the degree of immune mismatch between the donor and recipient did not appear to impact the safety or efficacy of our therapy candidate.

We have identified a near-term surrogate marker, chimerism, that we believe to be highly predictive of the ability of an organ transplant recipient to durably discontinue chronic immunosuppression at one year post-transplant without rejecting the transplanted organ. Chimerism refers to a state whereby the recipient's and donor's blood and immune cells co-exist in the recipient, creating a reciprocal state of immune tolerance called allogeneic tolerance. We use a simple blood test to measure and regularly monitor the degree of donor chimerism in the recipient, which has to date shown a close association in our research with long-term immune tolerance in patients who have received FCR001. In our Phase 2 trial of FCR001, we observed that 26 of 27 recipients (96%) who achieved donor chimerism at six months post-transplant were successfully weaned off chronic immunosuppression over approximately the next six months, including recipients who were highly HLA-unmatched and/or unrelated to their donors. In addition, donor chimerism at three months post-transplant, which we observed in 26 of 29 recipients (90%), was also highly predictive of successful weaning off chronic immunosuppression at approximately one year post-transplant.

We continue to monitor the patients in our Phase 2 trial for long term safety and durability of effect. Through March 1, 2022, we have accumulated approximately 280 patient-years of exposure to FCR001 in LDKT, and the safety profile in our patients is generally consistent with that expected if a patient were to separately receive both a standard kidney transplant and an allo-HSCT with nonmyeloablative conditioning. Specifically in our Phase 2 population, through March 1, 2022, there were four deaths and two cases of graft versus host disease (**GvHD**), which is a condition that occurs when donated stem cells attack the recipient. The most commonly reported serious adverse events were fever, deep vein thrombosis, including among several patients who had predisposing factors such as central venous catheter placements or Factor V deficiency, diarrhea, pneumonia and febrile neutropenia (or low white blood cell counts with a high fever). Preliminary data indicates that patients who were able to be weaned off immunosuppression with FCR001 had preserved kidney function and third-party data suggests a markedly lower reliance on cardiovascular medications at four years post-transplant compared to traditional transplants with chronic immunosuppression over a similar time frame. Based on the data generated from our Phase 2 trial, FDA has granted Regenerative Medicine Advanced Therapy (**RMAT**) and Orphan Drug Designation for FCR001 for LDKT.

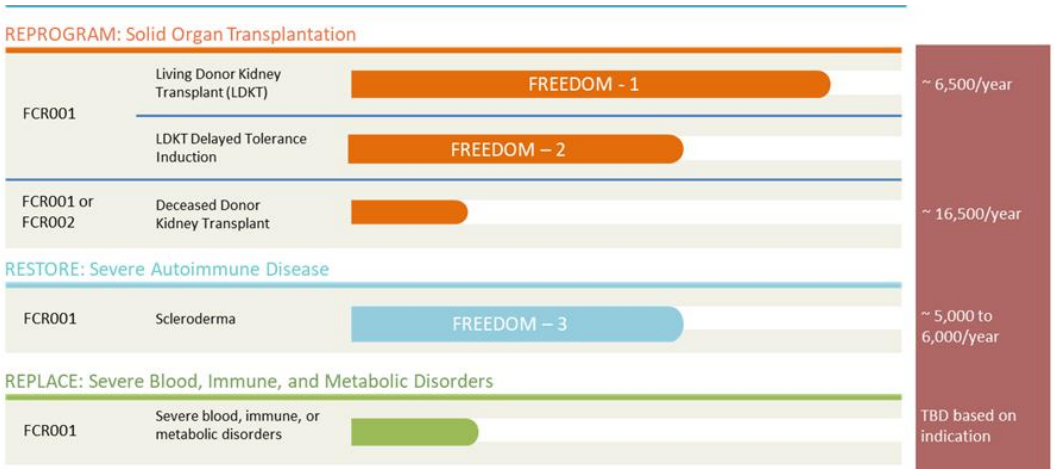
Under our open investigational new drug application (**IND**), the FDA has cleared us, based in part upon the data to date from our ongoing Phase 2 trial, to proceed with an updated protocol for our Phase 2 FREEDOM-2 trial, which we initiated in the fourth quarter of 2021. In FREEDOM-2, we will evaluate the potential of FCR001 to induce durable immune tolerance in patients who have previously received a kidney from a living donor, which is a process called delayed tolerance. In this trial, FCR001 will be administered between three and twelve months after the initial kidney transplant. Positive results in this trial would be the first step to potentially extending the use of FCR001 to a portion of the prevalent LDKT population and could also support extending our Facilitated Allo-HSCT Therapy to deceased donor transplant procedures. Every year in the United States, there are approximately four times as many deceased donor solid organ transplants as living donor transplants. We are conducting preclinical research to evaluate whether we can procure the same types of stem and immune cells from a recently deceased donor as from a living donor. If our preclinical studies are successful, we intend to assess the ability of FCR001, or a product candidate similar to FCR001 (**FCR002**), to induce durable allogeneic tolerance in a recipient of an organ from a deceased donor.

Additionally, the FDA has cleared our IND, based in part upon the data to date from our ongoing Phase 2 trial, to proceed with our Phase 2 FREEDOM-3 trial, which we initiated in the fourth quarter of 2021. In FREEDOM-3, we will evaluate the safety and efficacy of FCR001 in adults with a severe form of scleroderma, a debilitating autoimmune disease. In our Phase 2 LDKT trial, all seven LDKT patients who required a kidney transplant as a result of a kidney-related autoimmune disease, and who achieved durable chimerism and could be withdrawn from chronic immunosuppression at one year, have not experienced recurrence of their prior kidney-related autoimmune disease. We believe that this observation, as well as the current use of HSCT for severe scleroderma, supports the potential of our therapy in autoimmune diseases. We believe that positive data in the FREEDOM-3 trial in severe scleroderma patients could support the potential applicability of FCR001 to other severe, systemic autoimmune diseases.

There are also a number of severe non-malignant blood, immune and metabolic disorders for which allo-HSCT has already been observed to be potentially curative, but its use to date for these indications has been limited by two important considerations: (i) it necessitates matching the patient with a highly HLA-matched stem cell donor and (ii) it subjects the patient to the toxicities, morbidities and an extended hospital stay associated with fully myeloablative conditioning. The conditioning regimen is a key component of HSCT procedures that aims to provide sufficient suppression of the recipient's immune system to prevent rejection of the transplanted donor stem cells, and to provide sufficient space in the recipient's bone marrow to permit engraftment and maturation. Moreover, in certain disease states, the conditioning regimen also plays a role in eradicating

immune or blood cells that drive the underlying disease that prompts the need for an HSCT. A fully myeloablative conditioning regimen consists of a combination of agents (such as busulfan, cyclophosphamide, and high doses of total body irradiation) that destroy HSCs in the bone marrow and results in profound depletion of HSC-derived cells within one to three weeks following administration that is irreversible, and in most instances is fatal unless rescued by a stem cell transplant. Non-myeloablative conditioning regimens, which are designed to be less toxic than myeloablative regimens (due to lower doses of chemotherapy and total body irradiation), cause minimal depletion of blood cells and do not require stem cell transplant for the recipient to resume production of HSC-derived cells. Since our Phase 2 data suggest that our Facilitated Allo-HSCT Therapy can promote durable incorporation of the donated transplanted stem cells into the recipient where they will grow and reproduce, which is a process known as engraftment, and diverse immune reconstitution regardless of degree of HLA match and with a less toxic nonmyeloablative (as opposed to myeloablative) conditioning regimen, with a low incidence of GvHD, we intend to explore the potential of our Facilitated Allo-HSCT Therapy in one or more such disorders.

The pipeline-in-a-product potential of FCR001, and our Facilitated Allo-HSCT Therapy more broadly, is summarized in the graphic below:



We own unencumbered, worldwide rights to all of our product candidates and technologies.

Our manufacturing strategy is designed to meet the high quality and demand needs of clinical supply and commercial launch of any approved product. We manufacture FCR001 in less than a day at our GMP cell processing facility, employing robust, reproducible, proprietary methods which remain substantially unchanged as we have progressed FCR001 from Phase 2 to Phase 3. We do not outsource any key aspect of our cell processing. Unlike gene therapies or chimeric antigen receptor T-cell (**CAR-T**) therapies, our manufacturing process does not employ viral vectors, nor do we perform any transductions or *ex vivo* cell expansions.

Our Strategy

Our goal is to transform the standard of care in solid organ transplantation, severe autoimmune disease, and certain severe blood, immune and metabolic disorders, all with a single therapeutic approach. We plan to do this through our proprietary investigational therapy, FCR001, the cornerstone of our novel Facilitated Allo-HSCT Therapy. Our strategy is comprised of the following key elements:

- **Establish Talaris as a leader in developing, manufacturing, and ultimately commercializing cell therapies to address multiple areas of high unmet need.** Our Facilitated Allo-HSCT Therapy combines nonmyeloablative conditioning and optimized stem cell transplant protocols with our investigational therapy, FCR001. FCR001 consists of a unique and proprietary composition of donor stem and immune cells, which are processed via our proprietary manufacturing methods. We believe that FCR001 and our proprietary therapeutic approach have the potential to transform the standard of care for a range of severe blood, immune and metabolic disorders.
- **Advance FCR001 through clinical development, registration, and commercialization in LDKT.** Our lead product candidate, FCR001, is a single-dose, investigational cell therapy that is currently in an ongoing Phase 3 registration trial known as FREEDOM-1, for LDKT. The goal of this trial, in which FCR001 is administered the

day after the kidney transplant, is to assess the potential of our therapy to induce durable, drug-free immune tolerance in the transplant recipient to their donated kidney. In the fourth quarter of 2021, we initiated FREEDOM-2, a Phase 2 trial to evaluate the potential for FCR001 to induce durable immune tolerance to a donated kidney in patients who have previously received a kidney from a living donor, which we refer to as "delayed tolerance."

- **Extend FCR001 clinical development to severe autoimmune diseases.** We intend to investigate the potential of FCR001 to treat certain severe, systemic autoimmune diseases in which HSCT has already been observed to be potentially curative, albeit with significant risks. In the fourth quarter of 2021, we initiated FREEDOM-3, a Phase 2 trial that will evaluate the safety and efficacy of FCR001 in patients with a severe form of scleroderma. Scleroderma is a complex and heterogeneous systemic autoimmune disease affecting multiple tissues and organs. We believe that positive proof of concept data from FREEDOM-3 could support the potential of our Facilitated Allo-HSCT Therapy to be disease-modifying or even curative in scleroderma as well as certain other severe, systemic autoimmune diseases.
- **Further extend FCR001 clinical development to certain severe blood, immune or metabolic disorders.** We believe that our Facilitated Allo-HSCT Therapy has the potential to benefit patients in other severe settings where allo-HSCT has previously been associated with clinical benefit and/or curative potential, but where the use of allo-HSCT has been limited due to the challenge of identifying highly HLA-matched donors and the significant toxicities, co-morbidities, and lengthy hospitalization associated with myeloablative conditioning.
- **Explore the potential to extend our therapeutic approach to deceased donor organ transplantation.** Annually in the United States, there are more than four times as many deceased donor transplants as living donor transplants. We are conducting preclinical research to explore whether we can successfully procure and process cells from deceased donors to produce FCR001 or a product candidate similar to FCR001, which we would refer to as **FCR002**. If successful, this could extend the potential of our Facilitated Allo-HSCT Therapy to benefit recipients of organs from deceased donors, significantly expanding our commercial opportunity in kidney transplant and other solid organ transplant patients.
- **Further scale our in-house manufacturing and analytical capabilities and supply chain logistics.** We have developed a robust and reproducible proprietary manufacturing process and streamlined logistics to produce FCR001 in-house at our centrally located and dedicated cell processing facility. We also have a research facility focused on process and analytical development of our product. Our current facilities are sufficient for all of our currently contemplated clinical supply needs and we believe that, if FCR001 is approved, we are well positioned to serve our initial commercial markets with our existing and planned infrastructure. We intend to further scale our manufacturing and processing approaches to appropriately address our anticipated commercial needs, which will require significant resources.
- **Commercialize FCR001 independently in North America, if approved, and explore other markets through strategic collaborations.** We have global development and commercialization rights to FCR001 in all indications and geographies. Given the high concentration of Clinical Centers of Excellence performing allo-HSCT and solid organ transplant in North America, we plan to advance our Facilitated Allo-HSCT Therapy independently through clinical development and commercialization in these geographies in our three main areas of therapeutic interest. We intend to explore expanding into other high-value markets, notably EU and Asia, either alone or in collaboration with global or regional partners. We may also explore collaborations with partners in areas outside of our core areas of therapeutic interest.

Overview of Immune Intolerant Indications and Current Treatment Approaches

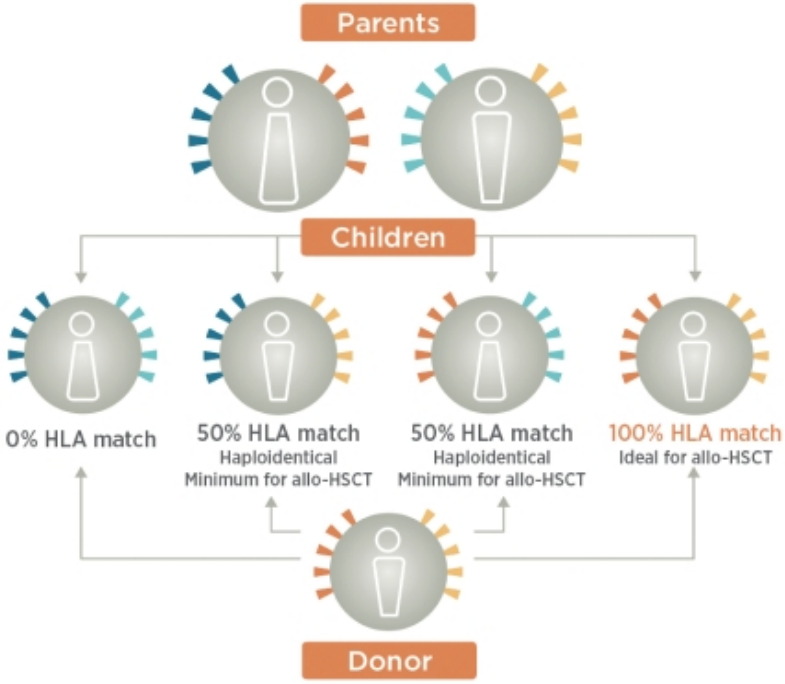
Immune Tolerance and HLA Inheritance

The human immune system is composed of cells that mature from hematopoietic stem cells (**HSCs**). HSCs are immature cells found primarily in the bone marrow that can develop into all types of blood and immune cells that protect individuals against infection, tumors, and other pathogens. In healthy individuals, the immune system distinguishes "self" antigens from "non-self" foreign antigens (e.g., transplanted organs, infectious agents or cancerous cells) and selectively mounts a protective attack against "non-self" foreign antigens while avoiding an attack on "self" antigens. The immune system's natural process for not mounting an immune response to antigens it deems as "self" is referred to as **immune tolerance**. An autoimmune disease occurs when the immune system mistakenly recognizes some aspect of "self" as "non-self" and attacks those cells or tissues.

The immune system distinguishes “self” versus “non-self” predominantly via the major histocompatibility complex (**MHC**). The MHC is a group of proteins expressed on the surface of most cells that function to present “self” or “non-self” antigens to lymphocytes, which mediate the immune response against antigens that are recognized as “non-self.” In humans, the MHC is composed of highly genetically diverse MHC proteins called human leukocyte antigens (**HLAs)**. As depicted in the figure below, human cells express combinations of multiple HLA proteins that collectively define an individual’s unique “tissue type” or a distinct molecular “self” signature.

The genes that encode HLAs are inherited in sets called haplotypes. An individual inherits one haplotype from each parent; as a result, their tissue type is 50% matched, or haploidentical to each parent’s tissue type. As shown in the figure below, if two children inherit the same HLA haplotypes from their parents, they are fully HLA matched. Siblings have a one in four chance of having a complete HLA match in their tissue types. Even if 100% HLA-matched, siblings are not genetically identical unless they are identical twins.

Illustration of HLA Matching



Although the immune system plays a vital role in eliminating pathogens and damaged cells, it poses significant challenges in two distinct areas where immune-mediated attack of antigens deemed non-self is detrimental: (1) allogeneic transplantation of solid organs, such as kidneys, or of HSCs; and (2) autoimmune diseases.

Allogeneic Transplantation of Solid Organs

In solid organ transplantation, practitioners generally seek a tissue-typing match of six HLA proteins between donors and recipients to lower the risk of the immune system recognizing the donated organ as “non-self”, which can trigger immune-mediated rejection of the donated organ by the recipient’s immune system, a process called allograft rejection. The greater the HLA match, the lower the risk of rejection because the recipient’s immune system is more likely to recognize the foreign cells as similar to “self.” However, with the exception of identical twin donor/recipient pairs, even recipients with a 6 out of 6 HLA match must take lifelong immunosuppression drugs to prevent life-threatening organ rejection. Organ rejection can occur immediately (hyperacute), within months (acute) or gradually over years (chronic) following transplant.

Normally, an organ transplant recipient’s immune system sees the donated organ as foreign and will attack it, which is a process called rejection. To prevent this process, anti-rejection medicines are used to suppress the transplant recipient’s immune system, and are accordingly termed immunosuppressants. Solid organ transplant recipients require a regimen of chronic

immunosuppression that entails daily treatment with these medications for as long as the recipient's graft continues to function, which can span several decades. A standard immunosuppression regimen typically includes one or more high dose immunosuppressant drugs administered in the hospital at the time of transplant, called induction therapy, followed by lifelong, daily maintenance treatment, typically with tacrolimus (Prograf®, Envarsus XR®, generics), mycophenolate mofetil (**MMF**: CellCept®, Myfortic®, generics), and frequently also includes a corticosteroid (usually prednisone). Other maintenance therapies used in lieu of tacrolimus include everolimus, sirolimus, and belatacept. Although immunosuppressants can be effective at preventing organ rejection, they have many drawbacks, including but not limited to the following:

- **Immunosuppressant medications do not induce tolerance to transplanted organs and require chronic dosing.** These medicines broadly impair the recipient's immune system to reduce the risk of rejecting the organ, but do not train the recipient's immune system to recognize the "non-self" antigens on the organ as "self." Thus, recipients must take immunosuppressants for as long as their donated organ is functioning.
- **Chronic immunosuppressant treatment can damage kidneys, ultimately leading to loss of the transplanted organ.** Ironically, long-term treatment with immunosuppressant medications such as tacrolimus can be toxic to, and can cause premature loss of, kidneys. Kidneys are the most commonly transplanted organs for which transplant recipients take immunosuppressants to prevent rejection. The half-life of a transplanted kidney is between 15.5 and 20.9 years, with one-third of LDKTs and approximately half of deceased donor kidney transplants failing within 10 years. Individuals whose transplants fail typically require hemodialysis, at an average Medicare fee-for-service cost in the United States of approximately $90,000 per year. Hemodialysis imposes a substantial negative impact on the patient's QoL and is associated with significant morbidity and mortality. If a patient whose transplant has failed is fortunate enough to locate another organ donor, they must undergo a repeat transplant. All of these factors lead to significant burdens individually on patients and systemically to our healthcare system. Total hospital charges for a solid organ transplant in the United States average $442,500. This figure does not include any costs outside of the 30-day window following the transplant.
- **Chronic immunosuppressant treatment is associated with an increased risk of cancer.** Several studies have demonstrated that the degree and duration of immunosuppression influence the risk for post-transplant malignancies. Most notably, in a study of over 175,000 solid organ transplant recipients from 1987 to 2008, more than 30 types of cancer were identified in over 10,650 cases, which correlated with a twofold increased incidence relative to the general population. Cancers with a fivefold or greater increase compared with the general population included Kaposi's sarcoma, skin cancers, non-Hodgkin's lymphoma, and cancers of the liver, anus, vulva and lip. Cancer accounts for nearly 25% of overall mortality in kidney transplant patients.
- **Chronic immunosuppressant treatment is associated with significant co-morbidities that prompt need for many other medications.** Patients on chronic immunosuppression medication typically need to take numerous medicines—often 20 or more pills per day—to manage the numerous negative side effects and significant co-morbidities that chronic immunosuppressant medicines cause, notably:
  - **Cardiovascular complications.** Cardiovascular death is the leading cause of mortality in kidney transplant recipients. Chronic use of immunosuppressant medications can lead to hypertension, hyperlipidemia, and hypertriglyceridemia, all of which are risk factors for cardiovascular morbidity and mortality and accordingly prompt the need for medical management along with lifestyle modifications.
  - **Infection**. Viral, bacterial, and fungal infections collectively are among the leading causes of post-transplant mortality after cardiovascular death. Transplants recipients on chronic immunosuppression must often take numerous prophylactic anti-infectives and adapt their lifestyles to avoid exposure to infection.
  - **Metabolic abnormalities.** Approximately 12% of kidney transplant recipients develop post-transplant diabetes mellitus (**PTDM**) within the first five years post-transplant. Both corticosteroids and tacrolimus contribute to this complication, which requires medication to manage glycemic control. PTDM is associated with an increased risk of cardiovascular events, failure of the transplanted organ, and death.
  - **Neurologic disorders.** Patients treated with tacrolimus over extended periods can experience a range of troubling neurologic adverse events including impaired cognition, tremors, neuropathies, depression, and sleep disorders.
- **The burden and cost of immunosuppressants can lead to non-compliance, which can adversely affect outcomes.** Reimbursement of immunosuppressant drugs, labs and associated medications for comorbidities varies greatly from patient to patient. The high cost (averaging nearly $25,000 in the first year and ranging from approximately $5,000 to $10,000 annually lifelong for tacrolimus and MMF alone) and decreased QoL associated

with chronic immunosuppression and other medications to manage its complications often leads transplant recipients to stop taking them, or to take them inconsistently, thus increasing their risk of organ rejection.

In light of the above, we believe that reprogramming a transplant recipient's immune system, with a one-time therapy, to durably tolerate the donated organ regardless of HLA match could potentially have significant benefits for patients and substantial cost savings for the healthcare system more broadly.

Allo-HSCT

Allo-HSCT has been used to replace diseased immune, blood or stem cells in patients with severe immune, blood or metabolic disorders. In allo-HSCT, an HLA-matched, healthy donor's HSCs are first procured, then the patient's own HSCs (and their associated immune and blood systems) are eliminated by high dose chemotherapy and radiation in a process known as myeloablative conditioning. The donor's HSCs are then transplanted to the patient. If the donor's HSCs engraft in the recipient's bone marrow, and are not rejected in the months following, then they will differentiate into donor-derived immune and blood cells.

In allo-HSCT, less-than-perfect HLA matching can increase the potential for GvHD. GvHD occurs when immune cells that are produced by donor-derived stem cells that have engrafted in the recipient attack the recipient's body as "non-self." GvHD, which can be acute (within the first 100 days following transplant) or chronic (beyond 100 days), can cause potentially life-threatening damage to the liver, skin, mucosal tissues, and gastrointestinal tract. Current medical practice for HLA matching in allo-HSCT is more stringent than for solid organ transplantation. Specifically, in solid organ transplant, HLA matching is based on a panel of six HLA proteins, whereas in HSC transplant, HLA matching is based on a more stringent panel of ten HLA proteins. Thus, in allo-HSCT, a ten out of ten match of HLA proteins is strongly preferred, with a minimum requirement for at least a haploidentical match of five out of ten. If individuals in need of allo-HSCT cannot find a suitable donor match, they cannot benefit from the curative potential of this procedure because the risk of GvHD is unacceptably high. As a result, although allo-HSCT also has the potential to restore self-tolerance in patients with autoimmune disease, it is seldom used for autoimmune disease because of the challenge of finding a highly HLA-matched donor and associated concerns over the risk of GvHD.

Although there is no currently approved, standard regimen to prevent GvHD, patients may receive peri-procedural treatment with cyclophosphamide, corticosteroids and other therapies. GvHD can develop in up to 50% of individuals receiving allo-HSCT, depending on the conditioning regimen, underlying disease, and degree of HLA mismatch between donor and recipient. Treatment of acute or chronic GvHD, which can range in severity from Grade 1 (mild) to Grade 4 (severe), depends on the extent of tissue and organ involvement, with corticosteroids generally serving as the typical first-line treatment. Nearly half of patients with acute GvHD are refractory to first-line steroid treatment and may receive treatment with second line therapies such as ruxolitinib. However, ruxolitinib can have limited efficacy, and its side effects include anemia, thrombocytopenia, neutropenia, infections, and edema. Thus, there is a significant need for an approach to allo-HSCT that could enable reciprocal tolerance between the donor's and recipient's tissues and immune cells, irrespective of the degree of HLA match, thereby lowering the risk of GvHD in the allo-HSCT recipient.

Autoimmune Diseases

In healthy individuals, the immune system produces cells that are potentially capable of attacking "self", but such cells are either eliminated or silenced by regulatory mechanisms within the body. However, if these mechanisms fail, or if an infection introduces a foreign antigen that mimics a self-antigen, the immune system can mount an attack on an individual's own cells, tissues, or organs, either locally or systemically. This phenomenon is termed autoimmune disease, and reflects the absence of immune tolerance to some aspect of self. There are more than 80 recognized types of autoimmune diseases.

The discovery and understanding of several key molecular pathways and mediators of pathological inflammation have led to the approval of several immunomodulatory therapies (e.g., anti-cytokines, co-stimulatory blockers and interferons) that improve symptoms and delay progression of debilitating autoimmune diseases such as rheumatoid arthritis and multiple sclerosis. However, these therapies require chronic, repeated administration to maintain significant benefit, and can be associated with side effects and toxicities similar to other immunosuppressive therapies. No therapies approved to date have been shown to be curative of autoimmune disease or to effectively restore durable immune tolerance to self-antigens.

HSCT is not an approved treatment for autoimmune disorders, but it has been observed to have curative potential for certain severe autoimmune diseases—notably scleroderma, multiple sclerosis and Crohn's disease—in clinical trials conducted by third parties, albeit with the significant limitations described above. To date, autologous HSCT has been preferred to

allo-HSCT in these trials because the latter carries a significant risk of GvHD, as well as a greater risk that the donated stem cells will fail to engraft in the recipient.

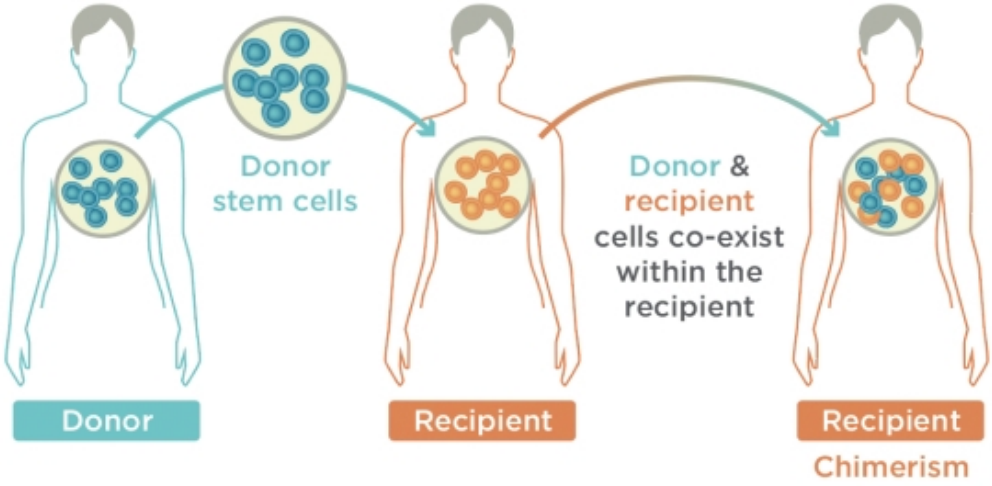
In **autologous HSCT**, a patient's HSCs are first procured and then the patient's entire immune system, including the autoreactive cells, is eliminated by myeloablative conditioning. The previously procured stem cells are then transplanted back into the patient, where they engraft and then differentiate into mature immune cells. The underlying principle is that these newly created immune cells have the potential to reset the patient's immune system, and enable disease remission.

Autologous HSCT has two major limitations. First, the acute toxicity of myeloablative conditioning, notably to the heart, lungs, and kidneys, necessitates a long and costly hospitalization—on average 20 days with billed charges of over $250,000—and restricts its use solely to the patients who can tolerate its intensity. Moreover, there are important long-term complications of myeloablative conditioning, including significantly increased risk of infections and hematological malignancies. Second, since these patients likely have a genetic predisposition towards autoimmune diseases, there is a higher risk of recurrence, which should be lower if stem cells were transplanted from a healthy allogeneic donor. Our Facilitated Allo-HSCT Therapy has the potential to mitigate both of these key limitations. As a result, we believe there is an opportunity with our Facilitated Allo-HSCT Therapy to improve and safely expand the practice of HSCT to a greater number of patients and induce durable remissions in severe autoimmune diseases.

Chimerism and Inducible Allogeneic Tolerance

As depicted in the figure below, **chimerism** refers to a state in which both the donor's HSCs and the recipient's HSCs co-exist in the recipient's bone marrow. These co-existing HSCs in turn produce blood and immune cells of both donor and recipient origin. We believe chimerism is the most robust means of inducing durable allogeneic tolerance.

The Concept of Chimerism



Allogeneic tolerance refers to a chimeric state in which the recipient's preexisting immune system and the donor's transplanted immune system (which co-exist in the recipient following our Facilitated Allo-HSCT Therapy) mutually recognize the other's cells and tissues as "self", thereby evading immune-mediated rejection and GvHD. We believe allogeneic tolerance can be achieved by transplanting a healthy donor's HSCs so that they coexist with the recipient's HSCs in the recipient's bone marrow, thereby creating a "dual hematopoietic system" (part-donor and part-recipient) in the recipient. The dual hematopoietic system in turn produces cells that constitute coexisting immune- and blood systems. If the donor's T-cells constitute more than 50% of the detectable T-cells in the recipient's blood for six months or longer after the transplant, our Phase 2 data have shown that this is highly predictive of the recipient having achieved durable chimerism, and thus durable allogeneic tolerance.

We believe inducible allogeneic tolerance has therapeutic potential in three broad categories of clinical applications: (1) solid organ transplantation; (2) severe autoimmune disease; and (3) severe blood, immune and metabolic disorders that have been shown to be potentially curable via allo-HSCT.

Our Therapeutic Approach: Facilitated Allo-HSCT to Induce Allogeneic Tolerance

The goal of our proprietary, investigational Facilitated Allo-HSCT Therapy is to induce allogeneic tolerance for the treatment of multiple therapeutic conditions with significant unmet need. While the principle of inducing allogeneic tolerance has been understood for decades, its clinical application in humans via allo-HSCT has proven elusive due to two key challenges: (1) minimizing the risks of graft rejection and/or GvHD, irrespective of the degree of matching of the donor's and recipient's HLA antigens and (2) identifying a better-tolerated, nonmyeloablative conditioning regimen (as opposed to a fully myeloablative conditioning regimen) that nonetheless enables durable engraftment of donor cells into the recipient. We believe that our Facilitated Allo-HSCT Therapy has the potential to address these two challenges and could represent a major advance in unlocking potential clinical applications for induced tolerance in the following ways:

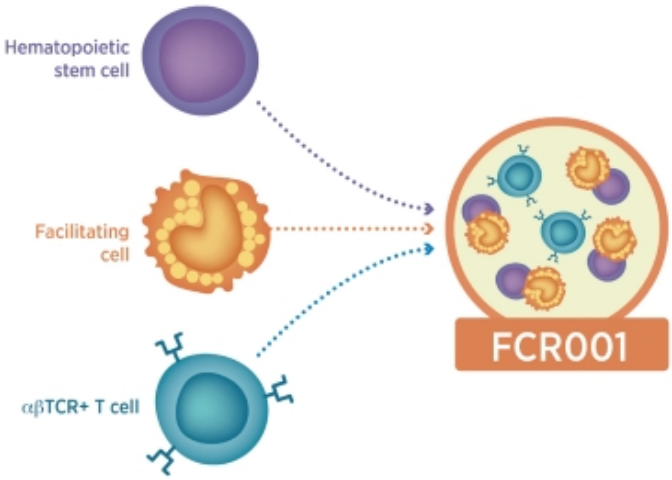
- **Reprogram—Solid Organ Transplantation—**By reprogramming the immune system to tolerate the donated organ without the need for chronic immunosuppression, we believe that our Facilitated Allo-HSCT Therapy has the potential to prevent immune-mediated organ rejection and thereby reduce or eliminate the co-morbidities, toxicities, costs and suboptimal patient survival rates and QoL associated with lifelong immunosuppression.
- **Restore—Severe Autoimmune Disease—**By restoring tolerance to self-antigens in patients with severe autoimmune diseases, we believe that our Facilitated Allo-HSCT Therapy has the potential to induce durable remission without the need for chronic immunosuppression.
- **Replace—Severe Blood, Immune and Metabolic Disorders—**By replacing defective or deficient HSCs, we believe that our Facilitated Allo-HSCT Therapy has the potential to correct a range of severe blood, immune and metabolic disorders that have been shown to be potentially curable with allo-HSCT, but with a less toxic conditioning regimen, reduced or no need for HLA-matching, and reduced risk of GvHD compared to standard allo-HSCT.

Our lead product candidate, FCR001, which is central to our Facilitated Allo-HSCT Therapy, is a proprietary, one-time, investigational cell therapy derived from donor-mobilized peripheral blood cells, which are processed to contain an optimized number of the donor's HSCs, FCs, and αßTCR+ T-cells. As depicted in the figure below, these three distinct cell types and the combination of these cell populations are critical for the safety and efficacy of FCR001. Specifically:

- ***HSCs*** are progenitor cells that are used to rebuild the hematopoietic and immune system of the recipient. As a result of their engraftment, the recipient's new immune system will reflect the donor's genotype and, thus, can potentially recognize the donor cells and tissues as "self" without the need for chronic immunosuppression.
- ***Facilitating Cells* (FCs)** are defined by the cell surface expression of the CD8 protein and by the lack of a functional T-cell receptor (**TCR**) ($CD8^+/TCR^-$). FCs are a mixed cell population that we believe to be responsible for fast and efficient engraftment of donor HSCs to promote chimerism. In addition, in preclinical studies, FCs have been observed to be associated with a reduced risk of GvHD relative to standard allo-HSCT. Consistent with these data, we have observed a very low incidence of GvHD in our Phase 2 trial of FCR001, despite a high degree of HLA mismatch between most donors and recipients.
- ***αßTCR+ T-cells*** are known to support donor HSC engraftment in recipients who receive allo-HSCT from an HLA-mismatched donor with nonmyeloablative conditioning, but they are also known to increase the risk of

acute GvHD in the recipient. FCR001 incorporates an optimized number of αβTCR+ T-cells that are intended to promote engraftment of the donor's HSCs in the recipient while minimizing the risk of acute GvHD.

Active Cell Type Composition of FCR001



The FCR001 manufacturing process is designed to limit the number of αβTCR+ T-cells to a desired number in the cell therapy product candidate while optimizing the yield of HSCs and FCs obtained after apheresis of the donor. See "*Preclinical Studies: Facilitating Cell Mechanism of Action*," below, for a summary of some of the key preclinical data supporting the mechanism of action of FCR001.

Our Pipeline

Based on the clinical evidence we have observed in our Phase 2 trial, we believe FCR001, and our Facilitated Allo-HSCT Therapy more broadly, can potentially be applied to numerous therapeutic areas. We are advancing a pipeline of three clinical and two preclinical programs across three therapeutic categories: (1) solid organ transplantation, (2) severe autoimmune disease, and (3) severe blood, immune and metabolic disorders that have been observed to be potentially curable via allo-HSCT. These initial areas of focus extend beyond kidney transplantation and include severe autoimmune disease in our planned trial targeting scleroderma and further research in blood, immune and metabolic disorders. We retain global development and commercial rights for FCR001 in all indications.

Our lead indication for FCR001 is living donor kidney transplant (**LDKT**). We are currently evaluating FCR001 in FREEDOM-1, a randomized, controlled, open-label, multi-center Phase 3 trial in the United States. This registration trial is designed to assess the safety and efficacy of FCR001 in first-time LDKT recipients, where FCR001 is administered the day after the kidney transplant. The goal of the FREEDOM-1 trial is to assess the potential of FCR001 to induce durable immune tolerance to the transplanted kidney without the need for chronic immunosuppression to prevent graft rejection. Based on the data generated from our Phase 2 trial, FCR001 has been granted Regenerative Medicine Advanced Therapy (**RMAT**) and Orphan Drug designations by the U.S. Food and Drug Administration (**FDA**) in this indication.

In the fourth quarter of 2021, we initiated FREEDOM-2, a Phase 2 trial to evaluate the potential for FCR001 to induce durable immune tolerance in patients who have previously received a kidney from a living donor, which is a process called delayed tolerance. In this trial, FCR001 will be administered between three and twelve months after the initial kidney transplant. Demonstrating that FCR001 can induce durable tolerance to a transplanted kidney, even if FCR001 is administered up to one year after the original LDKT, could enable broader clinical application of our Facilitated Allo-HSCT Therapy both to a portion of the prevalent LDKT population as well as potentially to the deceased donor solid organ transplant setting. We are also currently conducting preclinical research to explore whether we can manufacture FCR001 (or FCR002, if deemed a separate product candidate) from bone marrow procured from deceased organ donors. If these preclinical studies are successful, we plan to initiate IND-enabling studies of FCR001 or FCR002 in deceased donor kidney transplants.

Also in the fourth quarter of 2021, we initiated our first clinical trial in autoimmune diseases, FREEDOM-3, a Phase 2 trial exploring the safety and clinical activity of FCR001 in patients with a severe form of scleroderma. We believe that positive

proof of concept data in this trial could support the potential applicability of FCR001 to other severe, systemic autoimmune diseases.

Our Programs

Reprogram: Solid Organ Transplantation

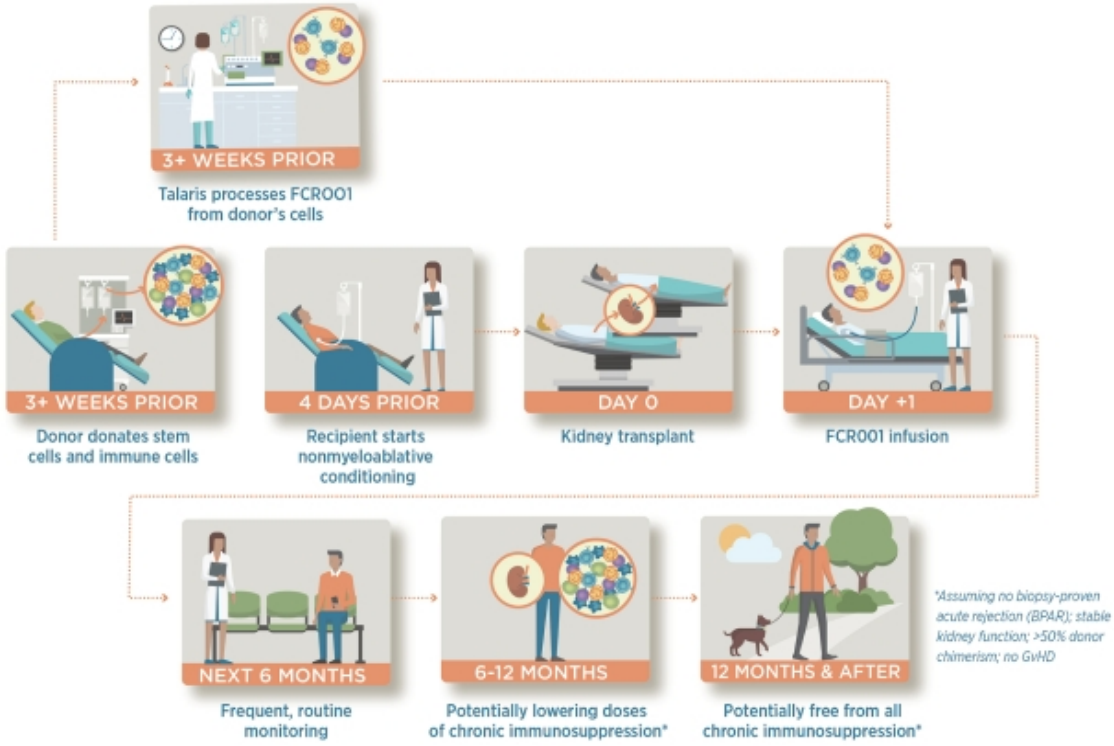
We believe that our Facilitated Allo-HSCT Therapy has the potential to reprogram the immune system of recipients of solid organ transplants to recognize the donated organ as "self," thereby avoiding organ rejection without the degree of toxicities, risks, co-morbidities, and burden of compliance associated with chronic immunosuppression. In the United States, there were 39,719 transplants of solid organs performed in 2019, up from 36,350 in 2018. These life-saving procedures entail procuring organs from either living donors (in the case of kidney and partial liver) or deceased donors (in the case of kidney, liver, heart, lung, pancreas and intestine) and surgically implanting them into appropriately matched recipients with end-stage organ failure. In 2019 (the most recent year before the COVID-19 pandemic temporarily reduced the number of transplants, such as LDKT, which are considered elective procedures), there were 7,397 transplants performed from living donors, of which 6,687 were kidney and 524 were partial liver. In addition, there were 32,322 transplants from deceased donors in 2019, as follows: 16,534 kidney, 8,372 liver, 3,552 heart, 2,714 lung, and 1,150 other organs, including heart/lung, kidney/pancreas, pancreas, and intestine.

Demand for solid organ transplants significantly exceeds the supply. As of March 1, 2022, there were more than 100,000 people in the United States on the waiting list for a transplant, of whom more than 90,000 were awaiting a kidney—with a median wait of 4.1 years. We believe that inducing durable tolerance to a transplanted organ without the need for chronic immunosuppression has the potential to prolong the viability of kidney transplants and ultimately other solid organ transplants, thereby reducing the need for the approximately 10% of organ transplants annually that are repeat transplants. Reducing the number of repeat transplants following failure of their initial transplant should, in turn, enable more patients on the waiting list to receive an initial transplant, and save significant associated healthcare costs.

Our Initial Focus: First-Time Living Donor Kidney Transplant

Long-term outcomes in LDKT are suboptimal due to the complications associated with taking lifelong chronic immunosuppression medications. We believe FCR001 has the potential to induce durable allogeneic tolerance in LDKT recipients to their transplanted organ, thereby permitting the LDKT recipient to discontinue all chronic immunosuppression within approximately twelve months of their transplant, without rejecting the transplanted organ. FCR001 is a single-dose, personalized investigational therapy that is made from stem and immune cells procured from the kidney donor, that are processed at our GMP facility to specifications that are optimized for the transplant recipient. FCR001 is infused into the transplant recipient within a day of the LDKT. The patient journey and our therapeutic approach in our Phase 2 and Phase 3 LDKT trials, including our vein-to-vein process from donor to recipient, is illustrated in the figure below.

The Patient Journey and Our Therapeutic Approach in Our Current LDKT Clinical Trials



Our approach begins with the procurement of a donor's stem and immune cells through a standard mobilization and apheresis procedure. At least three weeks prior to the scheduled LDKT, the kidney donor receives medication over a five-day period to mobilize their stem cells and immune cells and allow these cells to circulate out of the bone marrow and into the bloodstream. The mobilized cells that comprise FCR001 are then collected from the donor using our specified apheresis protocol.

The donated cells are shipped to our GMP cell processing facility in Louisville, Kentucky (which is also the location of UPS' WorldPort hub), where our proprietary process removes a calculated amount of the donor's αβTCR+ T-cells and relatively enriches the product for the donor's HSCs and FCs. The minimum doses of donor-derived HSCs and FCs in our FCR001 investigational therapy are customized for each patient, as is the target dose range of αβTCR+ T-cells. The final product is cryopreserved, and after clearing quality control specifications and processing, shipped to the transplant center, where it is stored until the transplant date.

Separately, commencing four days prior to the transplant, the recipient will receive nonmyeloablative conditioning to facilitate engraftment of the HSCs contained in FCR001. Our nonmyeloablative conditioning regimen consists of low total doses of fludarabine and cyclophosphamide and a one-time, low dose of total body irradiation (**TBI**), resulting in a less toxic regimen than fully myeloablative conditioning. Our nonmyeloablative conditioning regimen enables the patient to be managed primarily in an outpatient setting, with a relatively short hospital stay, whereas fully myeloablative conditioning typically requires inpatient management for 20 to 30 days. As the nonmyeloablative conditioning regimen employed as part of our Facilitated Allo-HSCT Therapy is mainly immunosuppressive and much less toxic to the recipient's stem cells than myeloablative conditioning, the patient's immune system is generally expected to recover on its own even if the donated HSCs do not engraft.

Three days prior to the LDKT, the recipient will begin a standard chronic immunosuppressive therapy of tacrolimus and MMF, to help prevent both graft rejection and GvHD after transplantation. On Day 1 post-LDKT, the recipient will receive a single intravenous infusion of FCR001 at their bedside. On Day 3 post-transplant, the recipient will receive a single dose of cyclophosphamide and Mesna to suppress the immune system and reduce undesired side effects of certain chemotherapy drugs.

Over the course of the next six months, the transplant recipient will remain on standard immunosuppressive therapy (i.e. tacrolimus and MMF) and will return to the clinic for routine monitoring. At approximately month six post-transplant, if the recipient demonstrates durable donor chimerism (defined as at least 50% donor T-cell chimerism), there is no evidence of rejection or GvHD, and kidney function remains stable, then MMF can be discontinued. Thereafter, tacrolimus can be tapered starting at month nine, and if the recipient continues to fulfill the preceding conditions, tacrolimus can be discontinued at approximately month 12 post-transplant.

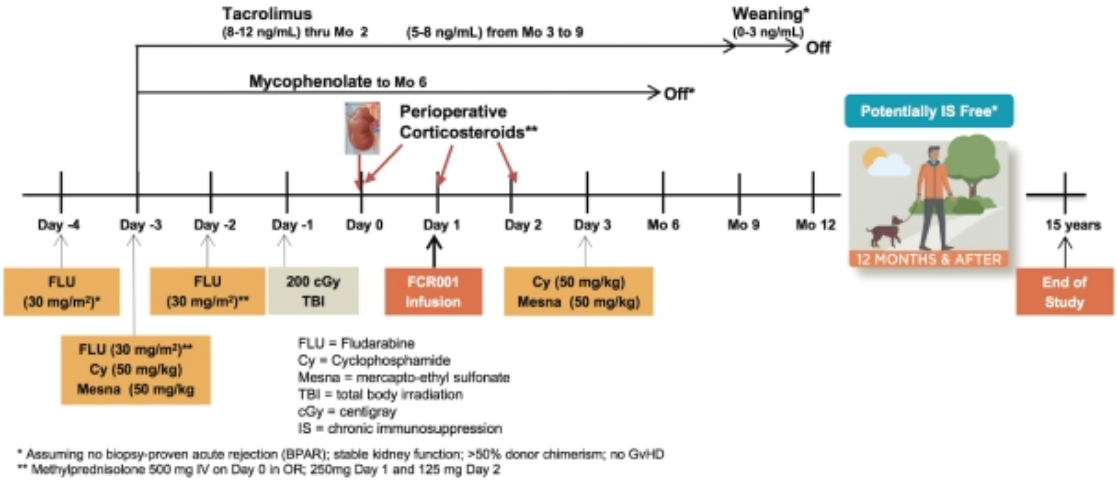
Overview of Our Phase 2 Trial

We conducted an our open-label, single-arm Phase 2 trial to investigate whether administration of FCR001 along with nonmyeloablative conditioning can induce durable immune tolerance to a donated kidney in adult LDKT recipients. Although this trial is no longer actively enrolling patients, this trial will continue to monitor the FCR001-dosed patients for up to 15 years from the time of their transplant and thereby provide long-term follow-up safety and durability data.

Thirty-seven patients were dosed between 2009 and 2016 at Northwestern Medical Center (n=36) and Duke University Hospital (n=1). The first four patients dosed at Northwestern Medical Center were treated under a compassionate use exemption, but we consider these patients to be part of our Phase 2 trial because they were treated with the same FCR001 product and under substantially the same protocol as the subsequent 33 patients. Eligible donor and recipient pairs were adults between the ages of 18 to 65 who met trial eligibility criteria. All levels of immune HLA mismatching between donor and recipients were allowed.

The primary endpoint of the trial was to determine whether the administration of FCR001 can induce durable tolerance to the donated kidney and substantially reduce or eliminate the requirement for immunosuppression within 12 months following transplant.

Phase 2 LDKT study design

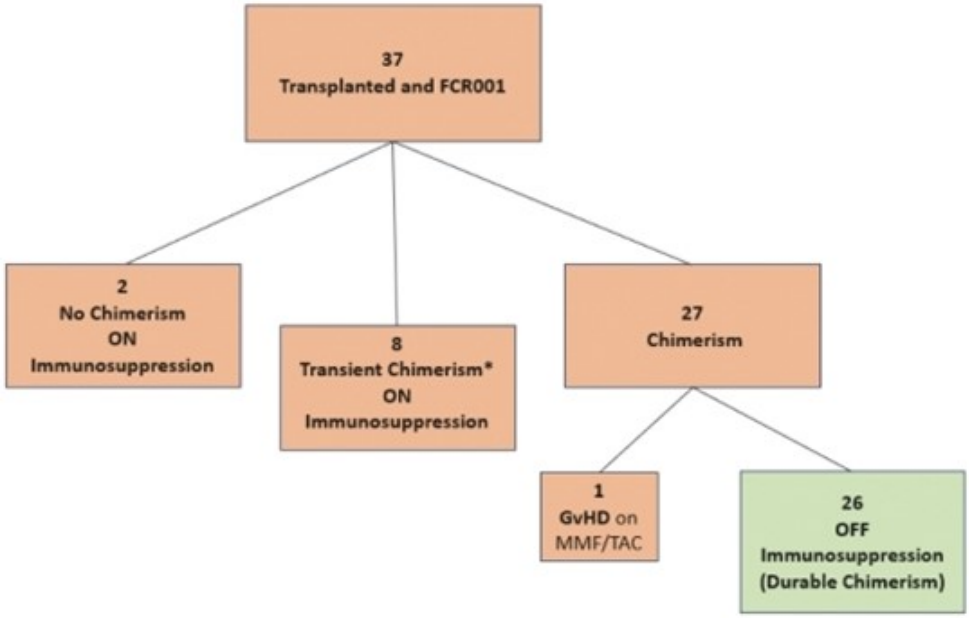


As of March 1, 2022, the median follow-up of the 37 patients who received LDKT and FCR001 was 6.6 years, with the longest follow-up being 11.3 years. Moreover, as of such time, 33 recipients have at least 36 months of follow-up, and 30 patients have had at least 60 months of follow-up. As of March 1, 2022, we have accumulated a total of approximately 280 patient-years of exposure to FCR001 in LDKT.

Our Phase 2 Results—Clinical Activity

As depicted in the flowchart below, 37 patients received LDKT as well as our investigational therapy, FCR001, plus nonmyeloablative conditioning. As of March 1, 2022, the results were as follows:

Phase 2 Clinical Trial Results as of March 1, 2022



* Chimerism lost between months 2 and 5 post-transplant.

In our Phase 2 trial, nearly every patient (26 of 27) who demonstrated chimerism at six months post-transplant was able to be completely weaned off all chronic immunosuppression by approximately twelve months post-transplant, and every patient (n = 26) who was weaned off all chronic immunosuppression at twelve months post-transplant has subsequently been able to stay off chronic immunosuppression, without organ rejection during their follow-up. As detailed below, two patients that remained off chronic immunosuppression died at years 3.5 and 4 post-transplant due to pneumococcal sepsis and lung cancer, respectively. We have followed these 26 patients for a median of 6.6 years, and the longest for 11.3 years since their transplant.

Induction of Durable Chimerism and Withdrawal of Immunosuppression

Of the 37 patients who received FCR001, 26 (70%) achieved durable donor chimerism (defined for purposes of the Phase 2 trial as whole blood or T-cell donor chimerism greater than 40% at six months post-transplant) and were successfully weaned from their chronic immunosuppression without developing acute rejection or donor specific antibodies. After mid-course optimizations to the Phase 2 protocol were implemented in late 2013, 14 of the last 17 patients (82%) in the trial achieved durable chimerism and could be withdrawn from chronic immunosuppression at approximately one year post-transplant.

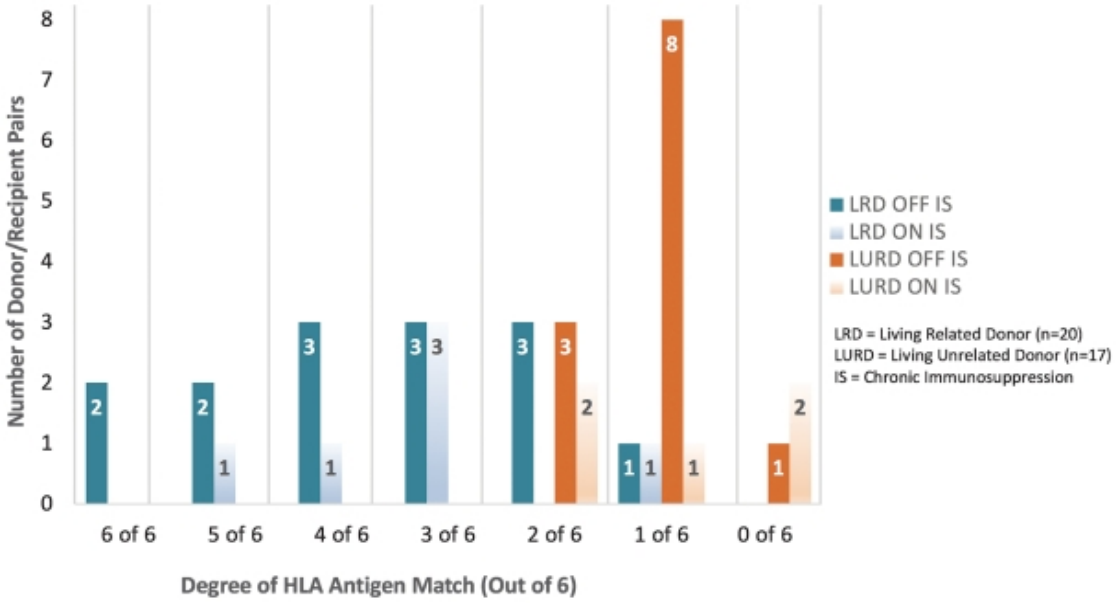
During approximately the first half of the Phase 2 trial, we identified certain factors that may have contributed to the failure of the donor's HSCs to durably engraft in some of our FCR001 recipients. These factors include suboptimal HSC/FC cell counts, failure to administer a post-transplant dose of cyclophosphamide per protocol, the presence of infection at the time of the transplant, a lack of adherence to best clinical practices for management of allo-HSCT patients, and a Panel Reactive Antibody (**PRA**) greater than 20%. A high PRA indicates that a patient has a disproportionate response to HLA antigens, and a PRA of greater than 20% (which is observed in approximately 10% of LDKT recipients) is a known risk factor for organ rejection in solid organ transplant. Based on these observations, we incorporated certain dosing and protocol refinements into our Phase 2 trial through late 2013. From that timepoint onward (denoted by the (2) in the figure above), 14 of the last 17 patients (82%) dosed in our trial achieved durable donor chimerism and were able to be weaned off their chronic immunosuppression without rejecting the transplanted organ. Based on two observed cases of GvHD in 2014 and 2015, each of which involved a female donor to unrelated male recipient (a known risk factor for GvHD in allo-HSCT), in October 2015 we further refined our Phase 2 protocol to exclude female donors to unrelated male recipients (denoted by the (3) in the figure

above). Once this protocol change was implemented, we did not observe any further cases of GvHD in the last seven patients in our Phase 2 trial who received FCR001.

Withdrawal of Chronic Immunosuppression Irrespective of HLA Mismatch

In our Phase 2 trial, the ability to discontinue chronic immunosuppression was observed across all levels of donor and recipient HLA matching, with 19 out of 26 recipients (73%) who were able to durably discontinue their chronic immunosuppression having an HLA match of three or less to their donor. We did not observe any correlation between the degree of HLA mismatch and any of durable chimerism, safety, or GvHD. We believe that the induction of durable allogeneic tolerance (as demonstrated by successful discontinuation of chronic immunosuppression) in a number of patients with poor HLA matching demonstrates FCR001's potential to overcome a major obstacle in solid organ transplantation and allo-HSCT. The figure below summarizes the distribution of all 37 FCR001-dosed patients in terms of the degree of HLA matching in each of living related donors and living unrelated donors. Results were comparable across all degrees of HLA matching, and whether the donor was related or unrelated. Of patients who received very low-matched (zero to two HLA match) kidneys from unrelated donors, 12 of 17 were durably weaned off their chronic immunosuppression.

HLA Matching and Relatedness—Patient Status



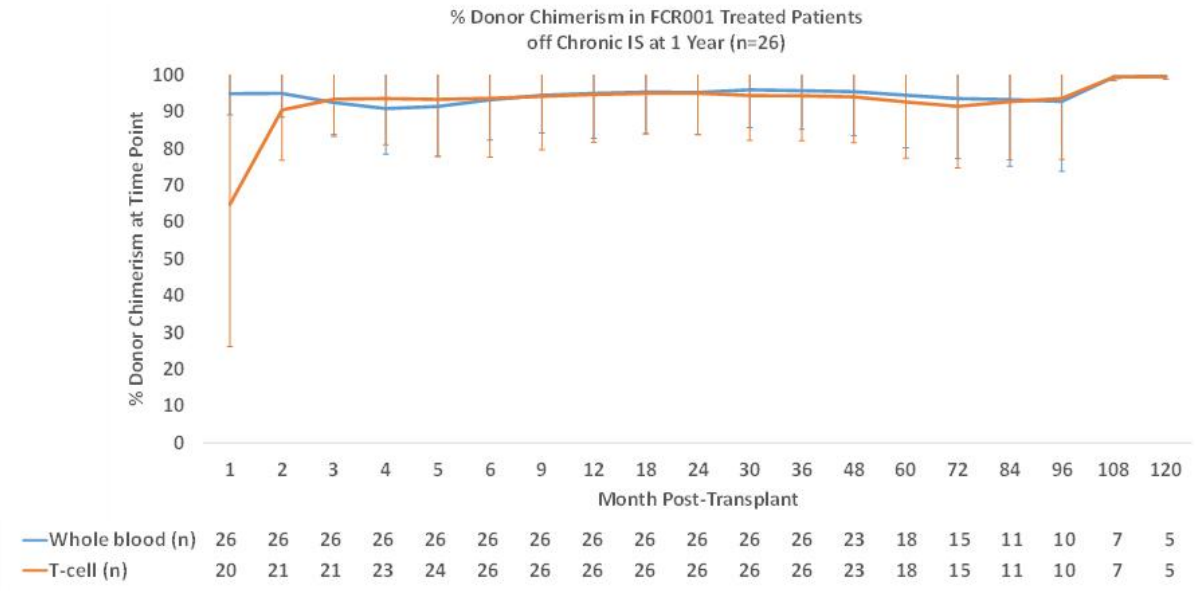
Chimerism as Predictor of Ability to Withdraw Chronic Immunosuppression at One Year Post-Transplant

Hematopoietic chimerism has recently emerged as a promising, near-term, surrogate marker for predicting allogeneic tolerance induction. In our Phase 2 trial, we observed that high levels (>50%) of donor chimerism at three and six months post-transplant correlated strongly with the ability to discontinue chronic immunosuppression approximately one year after transplant, without subsequent graft rejection. Durable whole-blood and T-cell donor chimerism was observed in 27 patients, of whom 26 were successfully weaned from chronic immunosuppression at approximately one year, with one durably chimeric subject dying due to complications from GvHD shortly before the one-year time point.

All 26 patients in our Phase 2 trial who could be withdrawn from chronic immunosuppression at approximately one year post-transplant attained high and durable levels of whole blood chimerism and/or T-cell chimerism. Of these 26 patients, 22 developed very high level (>90%) donor whole blood chimerism beginning the first month post-transplant, and 24 out of 26 patients had >90% chimerism at one year post transplant. As of March 1, 2022, all 26 patients had retained durable chimerism for the duration of their follow-up.

As depicted in the graph below, the mean percentage whole blood and T-cell donor chimerism levels for FCR001-treated patients weaned off their chronic immunosuppression at approximately one year post-transplant reached approximately 95% as early as one month post-transplant and remained at this level for as long as ten years.

Percentage of Donor Chimerism in FCR001-Treated Patients Who Are Off Chronic Immunosuppression



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

We believe that these collective observations support our belief that the establishment of high levels of donor chimerism is an early and consistent predictor of the ability to durably withdraw an LDKT recipient from chronic immunosuppression without rejecting the transplanted organ.

Of the ten FCR001-dosed transplant recipients in our Phase 2 trial who did not achieve durable chimerism, eight were transiently chimeric and two never engrafted. Transiently chimeric patients typically lost donor chimerism within the first two to five months post-transplant.

While none of the 26 patients in our Phase 2 trial who developed durable chimerism experienced biopsy-proven acute rejection (**BPAR**), seven of the ten patients who did not achieve durable chimerism did develop BPAR. BPAR was successfully treated in five of these seven patients, but severe infections in two patients required them to be removed from all immunosuppression, which resulted in graft loss. This is consistent with how severe infections would be treated in a standard of care solid organ transplant setting. At the time of their BPAR episodes, all but one patient was being maintained on lower-than-normal levels of immunosuppression, which would have significantly increased the risk of BPAR. In four of these seven patients, immunosuppression therapy was lowered to monotherapy (tacrolimus in three cases and sirolimus in one case), at the investigator's discretion, and/or lowered to a dose level below what would be permitted in our Phase 3 trial. Our Phase 3 protocol requires that standard of care immunosuppression therapy be maintained for all patients who do not maintain durable donor chimerism at and beyond month six post-transplant unless lowering of immunosuppression is otherwise determined to be medically necessary (e.g. due to a serious infection).

Overall Five-Year Kidney Graft Survival

As of March 1, 2022, five-year survival of the donated kidney was 34 out of 37 patients (92%) in our Phase 2 trial, compared to five-year kidney graft survival of 86% in patients tracked by the United Network for Organ Sharing (**UNOS**). The three cases of kidney graft loss in our Phase 2 trial occurred in patients who did not establish durable chimerism and were unable to discontinue chronic immunosuppression. As noted earlier, we revised our Phase 2 protocol (and maintained these

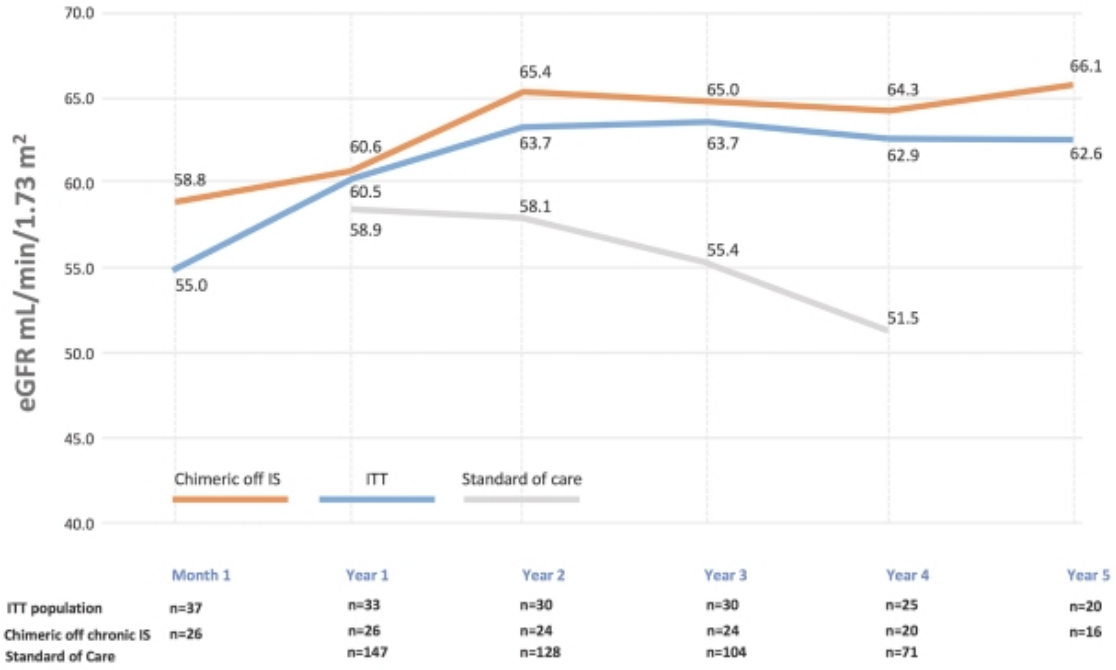
revisions in our Phase 3 protocol) to address certain factors that we believe may have played a role in these three graft losses, including incorporating into our Phase 2 protocol best clinical practices for management of allo-HSCT patients to minimize infections and excluding patients with a history of infection.

Observation of Renal Function

As shown in the graph below, average renal function in our Phase 2 patients, as measured by estimated glomerular filtration rate (**eGFR**) by Modification of Diet in Renal Disease, was observed to be preserved over time, both for the durably chimeric patients off chronic immunosuppression after approximately one year as well as for all FCR001 patients on an intent-to-treat basis (**ITT**). No abnormal histologic findings or instances of BPAR were observed on any protocol biopsies in durably chimeric patients off chronic immunosuppression.

Separately and apart from our Phase 2 trial protocol, the lead investigator at Northwestern Medical Center for our Phase 2 trial evaluated both longer-term kidney function and cardiovascular medication usage, as described further below, at up to five years post-transplant in FCR001-treated patients. These patients were compared to a cohort of standard of care LDKT patients who the investigator determined would have met all of our Phase 2 trial enrollment criteria and were transplanted at Northwestern between 2009 and 2012 (the first three years of our Phase 2 trial). In a retrospective analysis through year four post-transplant of these standard of care LDKT patients, mean eGFR of this cohort was observed to decline over time as depicted by the gray line in the graphic below.

Mean eGFR* Over Time Post-Transplant



**MDRD-4 (Modification of Diet in Renal Disease) equation*

Average renal function calculation excludes graft losses occurring prior to any given time point. Over time, sample size decreased due to 3 deaths, 3 graft losses, patients not yet out to the time point, or eGFR values missing. Note that ITT analysis excludes the five patients who were enrolled in the Phase 2 trial but did not actually receive FCR001.

Due to the retrospective nature of the analysis, which is not included in our database, data from the standard of care cohort (depicted by the gray line) does not include baseline eGFR data or year 5 data.

Cardiovascular Medication Usage

The evaluation of cardiovascular medication usage conducted by the lead investigator at Northwestern Medical Center for our Phase 2 trial as described above resulted in the findings summarized as follows. As shown in the table below, at four

years post-transplant, cardiovascular medication usage of FCR001 patients who were durably chimeric and off chronic immunosuppression compared favorably with that of the retrospectively gathered standard of care cohort of 132 transplant recipients who received their LDKT at the same site and during the same timeframe as the first half of our Phase 2 trial.

Comparison of Cardiovascular Medication Usage in Durably Chimeric FCR001 Patients vs. Historical Standard of Care Cohort, at Four Years Post-Transplant

	Durably chimeric FCR001 patients off immunosuppression (n=26)	Standard of care patients (n=132)
Anti-hypertension medications	18%	83%
Anti-hyperlipidemia medications	9%	43%

Baseline data not available

Evidence of Immunocompetence in FCR001-Treated Patients

One measure of successful immune system reconstitution is having a highly diverse repertoire of T cell receptor (**TCR**) clones, meaning a wide range of TCR clones, each capable of recognizing and targeting different foreign antigens. To examine TCR clone diversity in our LDKT patients, we randomly selected nine patients from our Phase 2 trial, of which five had achieved full chimerism and four did not, and analyzed blood samples 24 months after LDKT. We observed that, even though the clone diversity in TCR repertoire was somewhat reduced in all nine post-transplant recipients, the repertoire in these patients was diverse enough to suggest recovery of immune competence. As shown in the figure below, at least 97% and 95% of the total and top 1000 TCR clones, respectively, observed in a representative sample of these post-transplant recipients were not present in either donor or recipient pre-transplant. This suggests that a significant number of unique TCR clones (that were not previously present in either the donor or the recipient) were generated post-transplant, which is evidence of a competent immune system. Within the pool of shared sequences observed in the remaining 3% of clones, full chimerism correlated with a shift towards homology with the donor, meaning that the TCR clones were primarily derived from the donor HSCs, rather than from residual recipient HSCs, while loss of chimerism correlated more closely with the TCR clonal diversity in the recipient following autologous recovery of T-cells.

In another study, reported in Science Translational Medicine (2012), Dr. Ildstad and certain collaborators analyzed lineage reconstitution in the first eight recipients of FCR001 in our Phase 2 trial. In that study, Dr. Ildstad and certain collaborators observed evidence of reconstitution of immune and blood cell components (e.g. T-cells, B-cells, natural killer (**NK**) cells, monocytes, granulocytes) in those FCR001 recipients. In addition, in a separate analysis reported in Transplantation (2015), Dr. Ildstad and certain collaborators analyzed blood reconstitution in the first 20 recipients of FCR001 in our Phase 2 trial (with follow up on the durably chimeric patients between eight and 48 months post-discontinuation of chronic immunosuppression). In five of the 12 patients who achieved durable chimerism, donor-derived red blood cell production was observed. We believe that these observations support the potential of our Facilitated Allo-HSCT Therapy to address certain severe blood, immune or metabolic disorders that have previously been successfully treated with standard allo-HSCT.

Our Phase 2 Results—Safety

Through March 1, 2022, we have accumulated a total of approximately 280 patient-years of exposure to FCR001 in LDKT, and the safety profile observed in our patients was generally consistent with that expected if a patient were to separately receive both a standard kidney transplant and an allo-HSCT with nonmyeloablative conditioning. Moreover, as noted above, preliminary data indicates that patients who were able to be weaned off immunosuppression with FCR001 had preserved kidney function and third-party data suggests a markedly lower reliance on cardiovascular medications at four years post-transplant compared to traditional transplants with chronic immunosuppression over a similar time frame. Most adverse events occurred during the first 12 months post-transplant when the patients were on conventional immunosuppression, and no events of infusion toxicity following FCR001 administration were observed. We summarize the safety findings in greater detail below.

The most commonly reported adverse events were diarrhea, BK viruria/viremia, fever, cough, and nausea. The most commonly reported serious adverse events were fever, deep vein thrombosis, including among several patients who had predisposing factors such as central venous catheter placements or Factor V deficiency, diarrhea, pneumonia and febrile neutropenia. The most commonly reported infections were BK viruria/viremia, nasopharyngitis, cellulitis, upper respiratory tract infection, and urinary tract infection. BK urine/blood were monitored frequently per protocol and no cases of BK

nephropathy were observed. Cytomegalovirus (**CMV**) viremia was also observed at a rate consistent with what would be expected in a kidney transplant and allogeneic stem cell transplant population. There was not an increase in CMV incidence in donor/recipient pairs at higher risk of CMV incidence or activation. There were two cases of tissue invasive CMV disease (colitis), both of which occurred in the two FCR001 patients that experienced GvHD.

Five-year patient survival in our Phase 2 trial is comparable to that of LDKT patients as reported in the UNOS database, being approximately 89% and 92%, respectively. Out of the 37 patients in our Phase 2 trial who received FCR001, there were four patient deaths. The first death, of a patient who had durable chimerism through month 11 post-transplant, occurred eleven months post-transplant and was attributed to complications arising from progressive, treatment-resistant, Grade III GvHD with recurrent CMV colitis. There was a meaningful delay between onset of symptoms and when this patient presented to the transplant center for evaluation and treatment. The second death, of a durably chimeric patient approximately four years after transplant and approximately three years after the patient had discontinued chronic immunosuppression, was attributed to non-small cell carcinoma of the lung. This patient, whose death was deemed not study related by the DSMB, had a more than 40-year history of heavy smoking and refused treatment for his cancer. The third death, of a durably chimeric patient approximately 3.5 years post-transplant and approximately 2.5 years after the patient had discontinued chronic immunosuppression, was attributed to pneumococcus sepsis and human metapneumovirus infection. This patient was non-compliant with the trial's revaccination protocol (which is standard of care following allo-HSCT) and fell ill while traveling abroad. The fourth death, of a patient who did not achieve durable chimerism, occurred 4.5 years post-transplant and was attributed to respiratory failure secondary to septic shock and aspiration pneumonia. The DSMB deemed this death not study related.

There were two cases of GvHD, both in the setting of a female donor to an unrelated male recipient. This donor/recipient combination is known to have a higher risk of GvHD in allo-HSCT. The first case of GvHD occurred at 135 days post-transplantation and was fatal, as described above. The HLA match between this recipient and his donor was two out of six. The second case (Grade II acute GvHD) occurred at approximately two months post-transplant, almost immediately after the patient's immunosuppression medication was changed from tacrolimus to sirolimus due to tacrolimus-induced toxicity. The patient's acute GvHD resolved following treatment with corticosteroids. This patient was weaned off chronic immunosuppression and subsequently developed Grade I-II ocular/musculoskeletal chronic GvHD, which is currently well-managed. The HLA match between this recipient and his donor was one out of six. There were no other reports of acute or chronic GvHD. While other female-donor-to-unrelated-male-recipient pairs in our Phase 2 trial did not experience GvHD, we nonetheless excluded female donor to unrelated male recipients from the last seven patients in our Phase 2 trial, and no further instances of GvHD were observed. We are continuing to exclude these donor-recipient pairs from our FREEDOM-1 Phase 3 protocol.

Six patients in our Phase 2 trial were diagnosed with skin cancers (squamous cell and basal cell), all of which were successfully treated. Skin cancers account for 40% to 50% of malignancies in solid organ transplant, and solid organ transplant recipients are 65- to 250-fold more likely to develop squamous cell cancers and ten- to 16-fold more likely to develop basal cell skin cancers compared to the general population. One patient who was not durably chimeric and remained on chronic immunosuppression developed acute lymphocytic leukemia approximately seven years post-transplant and is in remission following chemotherapy. Approximately six years after transplant, this patient had received rituximab to treat an episode of acute, antibody-mediated rejection approximately nine months before this diagnosis. One patient was diagnosed approximately seventeen months post-transplant with papillary thyroid carcinoma, which was successfully surgically removed, and, as described above, one patient, a lifelong smoker, was diagnosed 4.5 years post-transplant with non-small cell carcinoma of the lung, which was ultimately fatal.

Adverse events reported by stem cell donors consisted of headache, fatigue, skeletal muscular pain, and nausea, and occurred around the timing of their granulocyte colony-stimulating factor administration for stem cell mobilization and apheresis. These adverse events were generally mild, fairly transient, and responded to nonsteroidal anti-inflammatory drugs or similar pain medications. There were no serious adverse events reported by any stem cell donors.

Our Phase 2 Results—Quality of Life (QoL)

Several clinical and real-world studies highlight that treatment with chronic immunosuppression significantly impairs patient-reported QoL in solid organ transplant recipients. To study the potential influence of withdrawal from chronic immunosuppression on transplant recipients' patient-reported QoL, 13 FCR001-treated patients from our Phase 2 LDKT trial who were successfully withdrawn from chronic immunosuppression at approximately one year post-transplant were compared with 12 patients who would have met inclusion criteria for the FCR001 tolerance protocol but were transplanted under standard of care therapy. Patients were administered three validated QoL self-administered questionnaires: the End Stage Renal Disease Symptom Checklist—Transplantation Module (**ESRD-TM**); the Short Form 36 (**SF-36**) questionnaire, the most frequently

used patient reported outcomes instrument in clinical trials today; and the EuroQol 5 Dimension (**EQ-5D-5L**) questionnaire. Investigators and statisticians were blinded to the treatment group. The patient demographics were similar between the two groups. FCR001-treated patients and the standard of care patients were surveyed an average of 50 and 75 months after their organ transplant, respectively.

In general, FCR001 treated patients reported better QoL than standard of care treated patients in all dimensions. In the ESRD-TM, standard of care patients reported statistically significantly greater cardiac and renal dysfunction and significantly greater levels of side effects from corticosteroids than FCR001 patients. The General Health Component of the SF-36 showed a statistically significant decrease in self-reported health among the standard of care patients compared to the FCR001 patients. In the EQ-5D-5L, standard of care patients reported a statistically significantly higher rate of pain and discomfort problems than FCR001 patients. A number of other categories in each of the three questionnaires showed positive trends in favor of FCR001 patients, but the findings were not statistically significant due to the small sample size. In addition to the dimensions of the SF-36 and ESRD-TM where FCR001 treated patients had a statistically significant benefit versus standard of care, patients treated with FCR001 had numerically favorable ratings on all other dimensions that did not reach statistical significance. Moreover, on the EQ-5D5L, in addition to the statistically significant benefit on pain/discomfort ratings, FCR001 treated patients had numerically favorable ratings versus standard of care on the dimensions of usual activity, anxiety/depression, and mobility. Both FCR001 and standard of care treated patients rated no problems on the dimension of self-care.

In summary, the three quality of life instruments used in this trial were in agreement that standard of care patients reported diminished mental health in the form of greater psychological stress, decreased overall mental health, and greater anxiety/depression scores compared to the FCR001-treated patients who had been able to discontinue their chronic immunosuppression. The three instruments also provided similar results in the areas of reported pain and discomfort as well as cognitive impairment, which again were notably higher in the standard of care patients compared to the FCR001-treated patients. Collectively, these preliminary results suggest that when our investigational FCR001 therapy enabled the discontinuation of all chronic immunosuppression medications, this outcome may be associated with significantly improved QoL in those FCR001-treated patients as compared to the QoL of standard of care patients who remained on chronic immunosuppression. Our FREEDOM-1 trial will further evaluate the potential QoL impact of FCR001 versus standard of care using the ESRD-TM and SF-36 questionnaires.

Our Phase 3 FREEDOM-1 Trial

Based on promising data from our Phase 2 LDKT trial, we have initiated FREEDOM-1, a 5-year multicenter, open-label, randomized, controlled, Phase 3 trial assessing the safety and efficacy of FCR001 in first-time, adult LDKT. We expect the trial to take place across 15 to 18 sites in the United States, of which 17 were activated as of March 1, 2022. A total of 120 LDKT recipients will be randomized 2-to-1 into the following two arms: (1) *the interventional arm*, where 80 patients will receive LDKT and FCR001 accompanied by nonmyeloablative conditioning, and will receive standard of care chronic immunosuppression that can potentially be eliminated by 12 months post-transplant, and (2) *the control arm*, where 40 patients will receive a LDKT plus standard of care chronic immunosuppression. The primary objective is to evaluate the proportion of FCR001 recipients who are free from chronic immunosuppression, without BPAR, at 24 months post-transplant. The secondary objective is to evaluate the change in mean renal function (eGFR by Modification of Diet in Renal Disease) from month one post-transplant to month 24 in FCR001 recipients. Because LDKT recipients on standard of care treatments do not discontinue immunosuppression without rejecting the transplanted organ, neither the primary endpoint nor the secondary endpoint of FREEDOM-1 involves a statistical comparison between the interventional arm and the control arm. Instead, the primary endpoint of FREEDOM-1 is the demonstration that the lower end of our confidence interval of FCR001 patients free from chronic immunosuppression and without BPAR at two years post-transplant is above 30%. The secondary endpoint of FREEDOM-1 is the demonstration that the lower end of our confidence interval for the mean renal function (as measured by eGFR) of the FCR001 patients is above a five-point decline in eGFR.

Our Phase 3 protocol incorporates several learnings from our Phase 2 trial in order to optimize the likelihood of achieving donor stem cell engraftment and durable chimerism and minimize the risks of graft rejection or GvHD. As depicted in the figure above entitled "*Phase 2 LDKT Trial: Summary of Patient Dispositions and Duration of Follow-Up,*" and the accompanying discussion, during our Phase 2 trial, we identified a number of factors that we believe negatively affected outcomes, and we adjusted our minimum cell doses and trial protocols accordingly. For example, we observed that highly sensitized patients were more likely to reject their stem cell graft. As a result, we are excluding certain types of highly sensitized patients from our Phase 3 protocol. Characteristics of highly sensitized patients include, but are not limited to, patients with a PRA greater than 20% and patients who have had recent blood product transfusions. We are also excluding

female-donor-to-unrelated-male-recipient pairings, as this pairing is known to increase the risk of GvHD in allo-HSCT, as well as transplant recipients who have had significant recent infections.

Further, we require adherence to our full nonmyeloablative conditioning regimen (including administration of the post-transplant dose of cyclophosphamide), and we require that our centers adhere to best clinical practices for allo-HSCT, including enhanced surveillance for, and proactive management of, GvHD; infectious disease prophylaxis and treatment with drugs that are not myelosuppressive; standard revaccination protocols; and avoiding medications that may induce cytopenia. We will also require all FCR001-dosed patients who are not durably chimeric and weaned off their chronic immunosuppression to be maintained at all times on standard of care maintenance immunosuppression unless it is medically necessary to reduce immunosuppression, such as in cases of severe infection.

Our Preliminary Interim Phase 3 FREEDOM-1 Trial Results

In November 2021, in connection with long-term Phase 2 follow-up data presented at the 2021 American Society of Nephrology meeting, we also announced preliminary data from the first patients dosed in our FREEDOM-1 Phase 3 clinical trial. At the data cutoff date, all patients treated at least three months prior to the cutoff date with our Facilitated Allo-HSCT Therapy, FCR001, achieved T-cell chimerism levels greater than 50% at each of the 3-, 6-, and 12-month timepoints post-transplant. In our Phase 2 study, establishment and maintenance of greater than 50% donor peripheral 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 IS approximately one year after transplant, without subsequent graft rejection. We believe this preliminary data supports continuation of the Phase 3 clinical trial and further development of FCR001 for additional therapeutic indications.

As shown in the figure below, a total of five patients had been dosed through the data cutoff date, two of whom were more than 12 months post-transplant. Both demonstrated >50% T-cell chimerism at each of the 3-, 6- and 12-month timepoints and had been discontinued from chronic IS. One patient was more than six months post-transplant and had demonstrated >50% T-cell chimerism at the 3- and 6-month timepoints. The remaining two patients had not yet met the 3-month timepoint at the data cut-off date. Additionally, the overall safety profile of Phase 3 patients dosed at the time with FCR001 was consistent with that observed in our Phase 2 study of FCR001. We plan to continue to provide periodic clinical updates as patient data continues to mature.

Time Since Kidney Transplant					
# of pts	<3mo	>3mo	>6mo	>12mo	>12/off IS
2	Chimeric* at 3, 6 and 12 mo timepoints & removed from IS				
1	Chimeric* at 3 and 6 mo timepoints				
2	NM	*Not measured; patient has not reached 3mo timepoint*			
5	*Total FCR001 Phase 3 patients dosed to date*				

Delayed Tolerance in LDKT: FREEDOM-2

In our FREEDOM-2 trial, we are assessing whether FCR001 can induce durable immune tolerance to the transplanted organ when it is administered, together with nonmyeloablative conditioning to LDKT recipients up to one year following their kidney transplant. The design of the FREEDOM-2 trial is virtually identical to the FREEDOM-1 trial, except that FCR001 will be administered three- to twelve months post-LDKT in FREEDOM-2, whereas it will be administered the day after the LDKT in FREEDOM-1. In both cases, nonmyeloablative conditioning will be administered commencing five days prior to the administration of FCR001. Positive results in FREEDOM-2 could potentially enable us to also address some portion of the prevalent LDKT population, rather than the incident LDKT population that is addressed by FREEDOM-1.

FREEDOM-2 is a five-year, multi-center, single-arm, open-label trial to assess the safety, preliminary efficacy, and overall benefit of FCR001 cell therapy in previously transplanted recipients of a kidney from a living donor. We filed an original IND and protocol for this trial in 2011, in which two patients were dosed on an exploratory basis. We have recently revitalized and amended this protocol to incorporate numerous learnings from our Phase 2 LDKT trial, including increasing

our minimal cell doses, exclusion of highly sensitized patients, and adherence to best allo-HSCT practices and use of appropriate prophylactic medications for HSCT. Similar to FREEDOM-1, the primary objective of FREEDOM-2 is to evaluate the proportion of FCR001 recipients who are free from chronic immunosuppression, without BPAR, at 24 months post-FCR001 infusion. The secondary objective is to evaluate the change in renal function from baseline (day one, prior to FCR001 infusion) to month 24 in FCR001 recipients. We reinitiated the FREEDOM-2 trial in the fourth quarter of 2021.

As noted above, in 2012, we enrolled two patients in an earlier version of our delayed tolerance protocol. Both patients continue to have stable renal function and are being managed as standard of care kidney transplant patients, even though neither achieved durable chimerism. As noted above, we have revitalized and amended this protocol to incorporate numerous learnings from our Phase 2 LDKT trial. Because neither of these patients was treated in accordance with the current protocol, nor received our optimized cell doses, these patients will not count towards the formal analysis of our FREEDOM-2 trial.

Although FREEDOM-2 initially contemplates administering FCR001 no more than one year after LDKT, we have the flexibility to amend the trial protocol to extend the period of time between LDKT and FCR001 administration if we see positive initial results from our FREEDOM-2 trial.

We believe that positive proof of concept in FREEDOM-2 could open to the door to broader clinical application of our Facilitated Allo-HSCT Therapy to deceased donor kidney and other solid organ transplantation settings. In the deceased donor setting, there is an inherent delay between the time that a deceased donor's solid organ is transplanted to a recipient, and when a product made from cells procured from the deceased donor could be processed and then subsequently administered to the transplant recipient. Demonstration in FREEDOM-2 of the feasibility of delayed tolerance induction would lend support to the potential of our Facilitated Allo-HSCT Therapy to induce durable immune tolerance in a recipient of a deceased donor's organ up to twelve months after their original organ transplant.

Deceased Donor Program

We believe that it may be possible to induce allogeneic tolerance in a recipient using HSCs procured and processed from a deceased donor. We are conducting preclinical research to explore whether we can successfully procure and process cells from deceased donors to produce either FCR001 or a similar product to FCR001, which we would designate FCR002.

Deceased donor kidney transplants represent a substantial portion of the kidney transplant recipient population, accounting for more than 70% of annual kidney transplants in the United States. If our Facilitated Allo-HSCT Therapy is shown to be capable of inducing durable immune tolerance in the deceased donor kidney transplant setting, then we also believe our therapeutic approach could be applied to the transplant of other solid organs from deceased donors. Collectively, the incident deceased solid organ transplant population is more than four times greater than the living donor transplant population.

Restore: Severe Autoimmune Disease

We believe that our Facilitated Allo-HSCT Therapy has the potential to restore self-tolerance in patients suffering from severe autoimmune diseases by eradicating diseased autoreactive cells and regenerating a new and healthy repertoire of immune cells, thereby halting the autoreactive cells' attack on one's own body.

We believe that our Phase 2 LDKT trial has already provided some proof of concept that our Facilitated Allo-HSCT Therapy could be used to treat severe autoimmune disease. Typically, 20% to 60% of kidney transplant patients whose end-stage renal disease is caused by a kidney-related autoimmune disease experience post-transplant recurrence of their kidney-related autoimmune disorder. Ten patients in our Phase 2 trial of FCR001 had an underlying, kidney-related autoimmune disease that led to their need for a LDKT. As shown in the table below, seven of these ten patients achieved durable donor chimerism and were able to be weaned off all chronic immunosuppression approximately one year post-transplant. As of March 1, 2022, none of these seven successfully tolerized patients has experienced recurrence of their prior kidney-related autoimmune disorder, with follow-up from four to ten years post-transplant. By contrast, recurrence of the prior kidney-related autoimmune disease was reported in two of the three other patients who experienced either transient or no chimerism.

Durable Chimerism vis-à-vis Disease Recurrence in our Phase 2 Trial

	Durable Chimerism		Disease Recurrence	
Condition	**Durable Chimerism**	**Disease Recurrence**	**Transient or no Chimerism**	**Disease Recurrence**
IGA Nephropathy	4	0	2	1
Focal Segmental Glomerulosclerosis	2	0	0	0
Membranous Glomerulonephritis	1	0	1	1
Total	7	0	3	2

We believe that this preliminary finding highlights the importance of achieving durable chimerism in order to induce durable allogeneic tolerance, as well as the potential of FCR001 to induce durable allogeneic tolerance in patients with an autoimmune disease.

Over the past 25 years, data from randomized trials and real-world experience gathered from more than 3,300 patients by the European Society for Blood and Marrow Transplantation Autoimmune Disease Working Party has shown that individuals suffering from a range of severe, refractory forms of rheumatologic, neurologic, and hematological autoimmune diseases appear to have benefitted from HSCT, primarily autologous HSCT. We believe that those data, together with our preliminary findings showing the potential of FCR001 to induce allogeneic tolerance in patients with a prior kidney-related autoimmune disease, support development of FCR001 for severe autoimmune disease. We initially have prioritized development of FCR001 in a severe form of scleroderma, also known as systemic sclerosis (**SSc**), given the high unmet need in this indication and third party data supporting the potential benefit of HSCT for SSc.

Background of Scleroderma or SSc

SSc is a rare, clinically heterogenous, progressive, multisystem, chronic autoimmune disorder that primarily affects the connective tissues. It has a prevalence of approximately 70,000 to 80,000 individuals in the United States, about 80% of whom are women aged 30 to 50. SSc is characterized by progressive fibrosis of the skin and visceral organs, vasculopathy, and the presence of autoantibodies against various cellular antigens. The etiology of this disorder is largely unknown, but research suggests it is due to both genetic and environmental factors that lead to dysregulation of the innate and adaptive immune systems, dysfunctional inflammatory responses, and connective tissue repair injury in susceptible individuals.

We estimate that approximately 40% of systemic sclerosis patients are diagnosed with the most severe form of SSc, diffuse cutaneous SSc (**dcSSc**). dcSSc has a poor prognosis, with a disease-related mortality of 5% to 10% per year. dcSSc may progress rapidly, affecting areas throughout the body. Progression from Raynaud's phenomenon—a condition that causes decreased blood flow to the fingers and toes—to skin thickening typically occurs within one year and can cause profound impairments to quality of life and morbidities, including disfigurement, difficulty opening the mouth, loss of facial expression, and joint contractures. Internal organ vasculopathy and fibrosis typically begin within five years of diagnosis. Commonly affected organs can include the gastrointestinal tract, heart, lungs and kidneys. Interstitial lung disease and pulmonary hypertension together account for nearly 50% of SSc deaths, followed by renal and cardiac complications.

The mortality rate in dcSSc is highest during the first five years of disease onset, when disease progression is most rapid. Patients with rapidly progressing dcSSc have an especially poor prognosis, with survival rates at five and ten years as low as 60% and 30%, respectively. There are no disease modifying therapies for dcSSc. Nintedanib and tocilizumab are the only FDA-approved therapies indicated for SSc but are only labeled to address interstitial lung disease in these patients. Other treatment options are only focused on symptom management and their costs can be substantial, especially in patients with advanced disease. A study published prior to the introduction of nintedanib—which costs nearly $140,000 annually—estimated that five-year direct healthcare costs in the United States for SSc patients with interstitial lung disease or pulmonary hypertension exceed $190,000 and $250,000, respectively.

Recently, however, HSCT has emerged as a promising and potentially disease-modifying treatment for patients with dcSSc at risk for organ failure.

HSCT as Potential Treatment for dcSSc

SSc is thought to be mediated by autoreactive T-cells and B-cells targeting self-antigens, eventually leading to organ damage. HSCT aims to reconstitute the hematopoietic system using either the patient's own (autologous) or healthy donor (allogeneic) stem cells to re-establish a naïve, self-tolerant immune system to both allo-antigens and auto-antigens. The

combination of lymphotoxic chemotherapy (e.g., cyclophosphamide and anti-thymocyte globulin) with or without TBI leads to a profound and long-lasting lymphopenia with persistently reduced levels of pathogenic autoantibodies. Aside from this nonspecific immunosuppression, there is growing evidence that HSCT can restore tolerance by establishing a diversified T-cell receptor repertoire and by increasing numbers of regulatory T-cells.

Autologous HSCT is increasingly being explored as a treatment option for patients with dcSSc and internal organ involvement. Cumulative data from three randomized, controlled trials conducted by third parties have observed the benefit of autologous HSCT therapy in dcSSc as assessed by multiple important outcome measures including clinical improvement, overall and event-free survival, and disease relapse. Further, based on these findings, the European League Against Rheumatism and the American Society for Blood and Marrow Transplantation both now recommend HSCT for patients with rapidly progressive dcSSc at risk for organ failure. Data to date indicate that autologous HSCT may require a myeloablative regimen to be most effective. Higher rates of relapse have been observed when less intensive conditioning regimens have been used. Nevertheless, disease recurrence still was observed in autologous HSCT patients, presumably in part because the patient's own diseased stem cells are being reinfused in the patient.

Allogeneic HSCT offers a promising alternative therapy to autologous HSCT for patients diagnosed with dcSSc. The advantage of allo-HSCT is its ability to replace the immune system with cells from healthy donors that lack the genetic predisposition for a return to autoimmunity, and with the potential of inducing tolerance to both auto-antigens and allo-antigens. Despite these benefits, allo-HSCT is not commonly used to treat dcSSc patients due to concerns over a potentially higher risk of transplant-related mortality (**TRM**) and GvHD, which affects between 20% to 70% of recipients. The risk of TRM and GvHD depends on the type of transplant, the degree of donor-recipient HLA compatibility, and the prophylaxis regimen.

Compared to autologous HSCT, standard allo-HSCT has the potential to offer patients with dcSSc additional benefit of lower rates of disease recurrence or potentially a cure. However, with current approaches, this procedure is accompanied by the significant risk of acute and chronic GvHD and a higher TRM. We believe that our Facilitated Allo-HSCT Therapy, which combines administration of FCR001 with a nonmyeloablative conditioning regimen, could offer a less toxic alternative to autologous HSCT (which generally requires a fully myeloablative conditioning regimen), and has the potential to enable broader use of allo-HSCT with a lower risk of severe GvHD for patients with dcSSc and potentially other severe autoimmune diseases.

Our Phase 2 Trial in dcSSc: FREEDOM-3

FREEDOM-3 is a two-year treatment and three-year follow-up, multi-center, single-arm, open-label proof-of-concept Phase 2 trial assessing the safety and efficacy of FCR001 in adults with dcSSc at risk for organ failure. The design of the FREEDOM-3 trial is substantially similar to that of the FREEDOM-2 trial, except without the kidney transplant. We plan to enroll up to 18 adults diagnosed with dcSSc within five years of first non-Raynaud's symptom, who have not adequately responded to at least one immunosuppressive agent and have significant cutaneous and pulmonary and/or renal involvement. In order to minimize any safety risks of allo-HSCT in this new disease indication, investigators are seeking HLA-matched recipient-donor pairs for the first subjects in the trial. The primary endpoint in this trial will be safety assessed by AE/SAEs, GvHD, AEs of special interest, neutrophil and platelet recovery time, safety lab assessments, autologous rescue infusion use and donor-specific antibodies. Secondary and exploratory endpoints will include T-cell chimerism over time, overall event-free survival and various efficacy markers (e.g., CRISS, a relatively new composite response index for dcSSc which has recently been validated in later stage clinical studies; DMARD use; and skin manifestation changes by Modified Rodnan skin score). We initiated this trial in the fourth quarter of 2021.

Replace: Potential of FCR001 to Treat Certain Other Severe Blood and Immune Disorders

Use of Allo-HSCT to Treat Certain Severe Blood, Immune and Metabolic Disorders

Standard allo-HSCT entails transplanting HSCs collected from a healthy donor into these patients, to potentially cure the patient's defective cells by replacing them with healthy, donor-derived cells. As depicted in the figures below, HSCs differentiate broadly into common blood (myeloid) and immune (lymphoid) progenitor cells. These cells in turn further differentiate into cells that, if defective, can correspond to various categories of hematological or immune disorders.

The therapeutic principle of allo-HSCT for the range of severe non-malignant disorders noted above is to replace the defective or deficient HSCs in a patient's bone marrow with normal-functioning HSCs from a healthy donor. Thereafter, the

donor HSCs would produce functional blood and immune cells that could potentially ameliorate or even functionally cure these disorders.

Many patients who might benefit from allo-HSCT do not receive it because they are unable to find a suitable HLA-matched donor. Approximately 30% of allo-HSCT candidates overall have suitable related donor matches. The risk of GvHD is positively correlated with the degree of HLA mismatch, and this risk is even greater if the donor is unrelated to the recipient. In 2017, less than half of allo-HSCTs for non-malignant indications were from HLA-matched sibling donors. According to the National Marrow Donor Program, which has over 25 million donors registered worldwide, there is a wide racial and ethnic disparity in the likelihood of finding a suitable match. As such, there is a significant unmet need for an approach to allo-HSCT that could enable better clinical outcomes regardless of the degree of HLA mismatch between donor and recipient, as mitigating the HLA-mismatch barrier could dramatically expand the pool of potential donors for allo-HSCT.

A second major limitation of allo-HSCT for non-malignant indications is that it usually entails fully myeloablative conditioning due to concerns that nonmyeloablative conditioning will not promote robust levels and durability of donor chimerism to effectively replace most of the defective HSCs in the recipient's bone marrow. The intensity and toxicity of myeloablative conditioning regimens is greater than for nonmyeloablative regimens and necessitates a long and costly hospitalization while the recipient's immune and blood systems reconstitute. According to the AHRQ HCUPNet, the average length of hospital stay for patients undergoing allo-HSCT in 2017 was 32 days, with an average charge per hospitalization of $572,945. Moreover, the risk of serious long-term sequelae, such as blood cancers, is significantly elevated by fully myeloablative conditioning. An analysis of more than 28,000 patients showed that one factor affecting the incidence of secondary cancers was the dose of TBI. Patients who received a single dose of greater than 1000 cGy (which is a dose consistent with fully myeloablative conditioning) were more likely to develop secondary cancers compared to those given a single dose of less than 1000 cGy, and this risk increased over time after transplant, reaching up to 7% at 15 years. Assuming a dose-response relationship, the risk of developing secondary cancers would be significantly reduced for patients that receive a significantly lower dose of TBI (e.g., 200 cGy), which is the dose that is currently used in our nonmyeloablative conditioning regimen.

Thus, we believe there is a significant unmet need for a nonmyeloablative approach to allo-HSCT for severe blood, immune and metabolic disorders that could enable high levels of durable donor chimerism with less short- and long-term toxicity and correspondingly shorter hospital stays and lower costs.

FCR001 for Certain Severe Disorders

We believe that FCR001, or our Facilitated Allo-HSCT Therapy more broadly, has the potential to address key limitations to current allo-HSCT, which has limited the use of allo-HSCT in severe blood, immune and metabolic disorders despite its potentially curative impact on such disorders.

In our Phase 2 trial of LDKT recipients, FCR001 treatment induced, in a significant portion of our patients, high levels (>95%) of durable (median of six years, longest up to 11 years) donor whole blood chimerism and T-cell donor chimerism despite a nonmyeloablative conditioning regimen. As noted above in "Evidence of Immunocompetence in FCR-Treated Patients," we have observed evidence of reconstitution of immune and blood cell components (e.g. T-cells, B-cells, natural killer cells, monocytes, granulocytes, and red blood cells) in FCR001 recipients. We have also observed a low incidence of acute GvHD (grade II-IV of 5%; grade III-IV of 3%) and of chronic GvHD (3%) in our Phase 2 trial, despite the fact that many of our donor-recipient pairs were significantly HLA-mismatched and unrelated. By contrast, in a trial conducted by a third party at Johns Hopkins, HLA-related patients with hematologic malignancies who were transplanted with unmodified HSCs and with a nonmyeloablative conditioning regimen that was similar to ours, but somewhat more intensive, had a relatively high incidence of acute GvHD (grade II-IV of 34%; grade III-IV of 6%) and of chronic GvHD (25%). Patients on the Johns Hopkins protocol were treated with two post-transplant cyclophosphamide doses, while those treated in our Phase 2 trial with our nonmyeloablative regimen for FCR001 received only one post-transplant cyclophosphamide dose. These data are derived from two different clinical trials with differences in trial design and patient populations. No head-to-head clinical trials have been conducted.

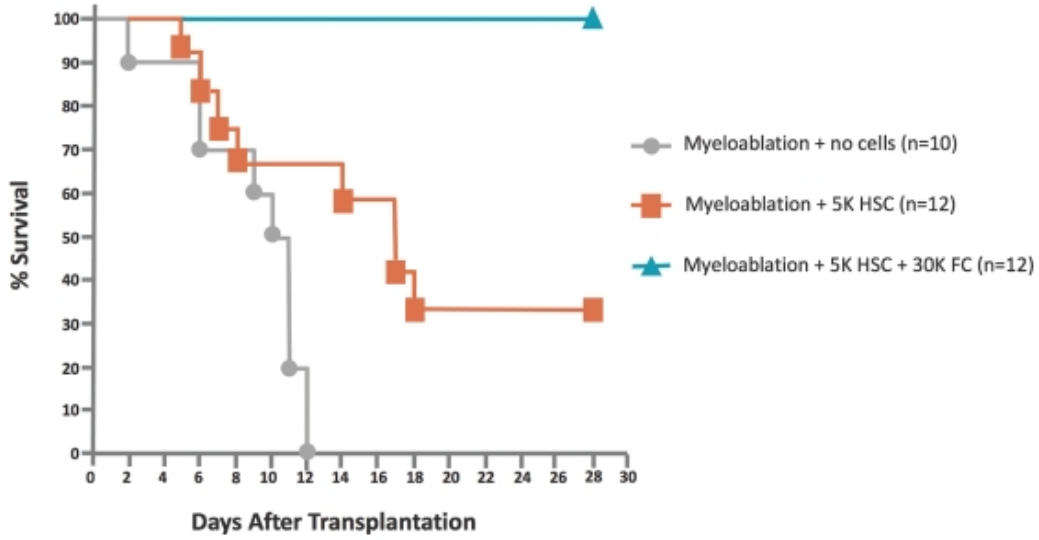
We have done a number of preliminary evaluations of potential indications in this therapeutic area, and continue to confer with hematologists, immunologists and stem cell transplant experts. We are evaluating both adult and pediatric indication opportunities where the FCR001 approach has the best potential for clinical differentiation.

Preclinical Studies: Facilitating Cell Mechanism of Action

Preclinical research conducted by third parties has observed that high doses of purified HSCs can reconstitute lethally conditioned, allogeneic recipients, but that significantly lower numbers of HSCs are needed when whole marrow is transplanted. A university team led by our founder and Chief Scientific Officer, Dr. Suzanne T. Ildstad, originally discovered that FCs may serve to facilitate engraftment of HSCs in allogeneic settings. Subsequently, FCs have been observed by other investigators to be associated with enhanced allogeneic HSC engraftments in both mouse and humanized mouse models. In addition, FCs have been observed to be associated with reduced rates of GvHD. Consistent with preclinical data generated in mouse models, enhanced engraftment of donor HSCs was observed in our Phase 2 trial of FCR001.

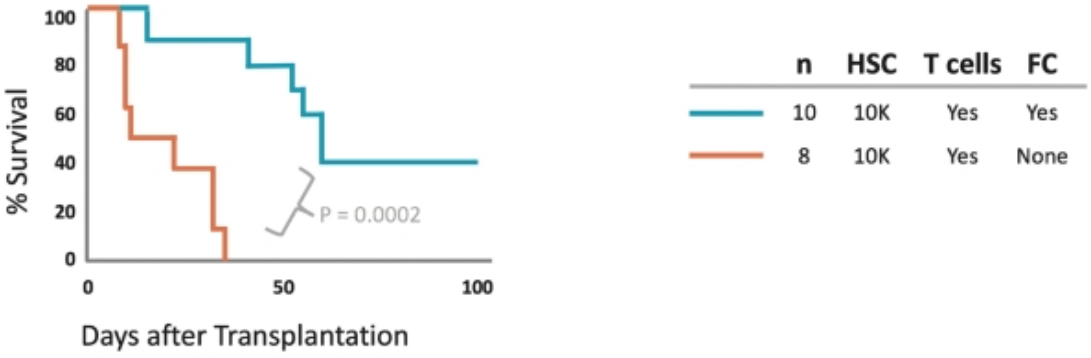
Our preclinical studies of FCR001 have observed the potential of FCs to augment engraftment of HSCs. Together with our former collaborator, Novartis, we evaluated the impact of FCs on HSC engraftment in lethally irradiated mice. We observed that, in lethally irradiated mice, transfer of 5,000 HSCs alone resulted in death due to engraftment failure; however, the transfer of 5,000 HSCs together with 30,000 FCs resulted in HSC engraftment and survival of all mice, as shown in the figure below. We believe that these data support the hypothesis that enriching the FC subpopulation in human HSC transplants may improve the outcome of allo-HSCT in the clinic.

Mouse FCs and Engraftment in allo-HSCT



Although a limited number of donor T-cells are known to improve HSC engraftment, these same donor T-cells can also elicit GvHD. As shown in the figure below, we have observed that co-transfer of FCs with HSCs and T-cells in an *in vivo* allogeneic mouse model was associated with delays and reductions in the development of GvHD. Recipient mice were conditioned with lethal doses of TBI. Both experimental groups were transplanted with HSCs and T-cells, and one of the groups also received FCs. We observed that all mice in the group that only received HSCs and T-cells died due to GvHD within 42 days, as shown in the orange line of the graphic. When FCs were also transferred, we observed delayed development of GvHD and survival of 40% of these animals, as represented by the blue line of the graphic. We believe that these data support the hypothesis that FCs provide a protective effect against the development of allogeneic GvHD.

Evidence that Mouse FCs Protect Against Death from GvHD



Competition

The biotechnology and pharmaceutical industries are characterized by the rapid evolution of technologies and understanding of disease etiology, intense competition and a strong emphasis on intellectual property. We believe that our approach, strategy, scientific capabilities, know-how and experience provide us with competitive advantages. However, we expect substantial competition from multiple sources, including major pharmaceutical, specialty pharmaceutical, and existing or emerging biotechnology companies, academic research institutions and governmental agencies and public and private research institutions worldwide. Many of our competitors, either alone or through collaborations, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient enrollment in clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. As a result, our competitors may discover, develop, license or commercialize products before or more successfully than we do.

Living Donor Kidney Transplant (LDKT) and Solid Organ Transplant

There are currently no FDA- or EMA-approved cell therapies for inducing durable immune tolerance to a transplanted solid organ. Medeor Therapeutics, Inc. is conducting a Phase 3 clinical trial for MDR-101, an allogeneic cell therapy, to induce immune tolerance to a donated kidney only in 6 out of 6 HLA-matched LDKT donor-recipient pairs. In 2018, Medeor announced its intent to initiate additional clinical trials to explore tolerance induction in LDKT, for which enrollment has not yet commenced. ITB-MED AB is conducting an early-stage safety study of siplizumab, a humanized anti-CD2 monoclonal antibody in LDKT recipients. In addition, there are other T-cell-based approaches in early development stages that seek to induce immune tolerance in the transplantation of solid organs such as research from Quell Therapeutics Ltd.

Furthermore, we also face competition more broadly across the solid organ transplantation market from cost-effective and reimbursable anti-rejection and immunosuppressive treatments. The most common medications used to prevent organ rejection are tacrolimus, mycophenolate mofetil and corticosteroids. In many cases, these drugs are administered in combination to enhance efficacy. FCR001 or other allo-HSCT candidates, if any are approved, may not be cost competitive with these existing drugs and other therapies. Some anti-rejection and immunosuppressive medicines are branded and subject to patent protection, while others are available on a generic basis. Insurers and other third-party payors may also encourage the use of generic products or specific branded anti-rejection and immunosuppressive products. As a result, obtaining market acceptance of, and gaining significant share of the market for, any of our therapies that we successfully introduce to the market may pose challenges. In addition, many companies, such as Novartis AG, are developing new therapeutics, and we cannot predict how the standard of care will evolve as our product candidates progress through clinical development.

Scleroderma and Severe Autoimmune Diseases

There are currently no FDA- or EMA-approved cell therapies for treating scleroderma. Current treatment options are focused on addressing organ or tissue-specific manifestations. Methotrexate is often prescribed for skin or musculoskeletal complications, proton pump inhibitors or H2 blockers for gastrointestinal reflux, and endothelin receptor antagonists, epoprostenol analogues or PDE-5 inhibitors for pulmonary artery hypertension. Boehringer Ingelheim's nindetanib and Roche's tocilizumab are the only FDA-approved therapies indicated for the treatment of SSc-associated interstitial lung disease. In addition, other companies, such as Acceleron Pharma, Inc., are exploring therapeutics for SSc, and others, such as Corbus Pharmaceuticals, Inc., Horizon Therapeutics, Plc., and Kadmon Holdings, Inc., are exploring therapeutics for dcSSc; however, these agents are not intended to be curative. Although not formally approved by FDA for this indication, autologous HSCT is occasionally used as a therapy for severe scleroderma and is reimbursed by some payors in the United States and Europe. In the future, we may pursue the development of FCR001 or another cell therapy as a treatment for other severe autoimmune diseases, and as a result, we may also face competition more broadly from other companies with approved products or product candidates in development.

Our Licenses and Collaborations

License Agreement with University of Louisville Research Foundation, Inc.

In October 2018, we entered into an amended and restated exclusive license agreement (ULRF License Agreement) with University of Louisville Research Foundation, Inc. (ULRF) as an agent of the University of Louisville, relating to certain licensed patent rights and know-how related to human facilitating cells for our Facilitated Allo-HSCT Therapy. Pursuant to the ULRF License Agreement, ULRF granted us an exclusive, worldwide license under such patents and a nonexclusive royalty-bearing, worldwide license for such know-how to research, develop, commercialize and manufacture FCR001 and products containing FCR001 in all fields, without limitation. ULRF also granted us the right to grant sublicenses in accordance with the ULRF License Agreement.

ULRF retained (i) the rights to publish the licensed technology, subject to our prior written approval and in accordance with the reciprocal nondisclosure agreement governing confidential information relating to the ULRF License Agreement, and (ii) the rights to practice the licensed patents and use the licensed technology, in each case solely for not-for-profit educational and non-commercial research purposes. The ULRF License Agreement is also subject to pre-existing rights of the U.S. government.

Pursuant to the terms of the ULRF License Agreement, we shall use commercially reasonable efforts to develop the products with the goal of achieving regulatory approval thereof and, following such approval, to commercialize such product in any country or countries for which such regulatory approval has been obtained.

As partial consideration for the license and rights, we have paid and will continue to pay ULRF a non-refundable, non-creditable annual license maintenance fee starting on the third anniversary date of the agreement through the seventeenth anniversary date. In addition, we are obligated to pay ULRF non-refundable, non-creditable research and development, regulatory and sales milestone payments upon the occurrence of certain milestone events in an aggregate amount of approximately $1.625 million for development, regulatory and sales milestones. Each milestone is payable only once. One milestone has been achieved to date under the ULRF License Agreement. As of December 31, 2021, we have paid ULRF $125,000 in milestone payments and $100,000 in annual maintenance fees, for a total of $225,000.

As partial consideration for the license and rights, we also granted to ULRF 65,186 shares of contingent equity consideration. On or prior to an initial public offering or deemed liquidation event, we will either issue shares of common stock equal to such consideration or make an equivalent cash payment of such share amount multiplied by the price per share of common stock at the time of the initial public offering or deemed liquidation event, in full satisfaction of the contingent equity consideration owed to ULRF pursuant to the ULRF License Agreement. If we grant stock to ULRF pursuant to the ULRF License Agreement, then ULRF has agreed to enter into a lockup agreement for such duration and in the form requested by the underwriters of the initial public offering in the same manner as our directors, executive officers and certain stockholders. Dr. Ildstad is entitled to a portion of this compensation pursuant to investor rights under the University of Louisville's Intellectual Property Policy.

Furthermore, on a licensed product-by-licensed product, indication-by-indication and country-by-country basis, we are required to pay future tiered royalties ranging from 1.5% to 4% on annual aggregate net sales of all products during the term of the ULRF License Agreement, subject to certain reductions in connection with obtaining a license for any patents owned or

controlled by a third party in order to commercialize the licensed product; provided, however, that the royalties due to ULRF shall not be reduced by more than fifty percent (50%). In the event that we sublicense the licensed patent rights, ULRF is also entitled to receive a tiered percentage of the non-royalty sublicensing revenue we receive. The Company's obligation to pay royalties continues until the expiration or abandonment of the last valid claim of any of the licensed patents under the ULRF License Agreement.

ULRF may terminate the ULRF License Agreement upon our material breach or bankruptcy. We may also terminate ULRF License Agreement upon prior written notice. Unless earlier terminated, the ULRF License Agreement will continue until the expiration or abandonment of the last valid claim of any of the licensed patents under the ULRF License Agreement.

Intellectual Property

The intellectual property that is available to us is critical to our business and we strive to protect it, including by obtaining, maintaining, defending, and enforcing patent protection in the United States and internationally for our proprietary technology, improvements, platforms, products and components thereof, novel biological discoveries, new therapeutic approaches and potential indications, and other inventions that are important to our business. For our product candidates, generally we initially pursue patent protection covering compositions of matter, methods of production, and methods of use. Throughout the development of our product, we will seek to identify additional means of obtaining patent protection that would potentially enhance commercial success, including through methods of clinical production and quality control.

As of December 31, 2021, our patent portfolio includes four patent families, which are exclusively in-licensed from ULRF in our field. These families include issued patents and pending applications related generally to our facilitating cell product, methods of making our facilitating cell product, methods of using our facilitating cell product therapeutically, and methods of evaluating the viability or potency of our facilitating cell product. Specifically, we have exclusively in-licensed a patent portfolio that currently includes at least three issued U.S. patents, 31 patents issued in foreign jurisdictions, and 10 patent applications pending worldwide. The issued patents from three of the four families in our portfolio are expected to expire around 2029, and any patents that issue from the fourth family in our portfolio are expected to expire around 2038, absent any applicable patent term adjustments or extensions.

The first family includes issued patents in Australia, Canada, and Europe; there are no pending applications in this family. All of the issued claims in this family are directed to compositions that include at least 30% facilitating cells, methods of making such compositions, and/or methods of using such compositions. The European patent is validated in five European countries including France, Germany, Italy, Spain, and United Kingdom. This family of patents is in-licensed under an exclusive license agreement with ULRF, and is expected to expire in 2029, absent any applicable patent term adjustments or extensions.

The second family includes one issued U.S. patent, with claims directed to methods of increasing the number of facilitating cells by exposing them to the DOCK-2 protein. This patent is in-licensed under the same exclusive license agreement with ULRF, and is expected to expire in 2032, absent any applicable patent term adjustments or extensions.

The third family includes two issued U.S. patents and one pending U.S. application, at least one issued patent in each of Australia, China, Europe, India, and Japan, and a pending application in Canada. The claims in this family are directed to compositions that include at facilitating cells, methods of making such compositions, and/or methods of using such compositions absent a requirement for any particular amount of facilitating cells. The European patent is validated in 17 European countries, including Austria, Belgium, Denmark, France, Germany, Greece, Hungary, Ireland, Italy, Netherlands, Norway, Poland, Spain, Sweden, Switzerland, Turkey, and the United Kingdom, and also is validated in Hong Kong. This family of patents is in-licensed under the same exclusive license agreement with ULRF. The U.S. members of this family claim the benefit of priority to members of the first family (i.e., as a Continuation-in-Part), and are expected to expire in 2029, while the non-U.S. members of this family are expected to expire in 2031, absent any applicable patent term adjustments or extensions.

The fourth family includes pending applications in the U.S., Australia, Canada, China, Europe, India, Japan and Russia. These pending applications generally have claims directed to determining the potency of a composition that includes facilitating cells. This family of patents is co-owned by us and ULRF; this family of patents also falls within the same exclusive license agreement with ULRF. Patents that issue in this family are expected to expire in 2038, absent any applicable patent term adjustments or extensions.

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the U.S., the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the U.S., the term of a patent may be lengthened by patent term adjustment (PTA), which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office (USPTO) in examining and granting a patent or the term of a patent may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a patent that covers a drug or biological product may also be eligible for patent term extension (PTE) after FDA approval for a portion of the term effectively lost as a result of the FDA regulatory review period, subject to certain limitations and provided statutory and regulatory requirements are met. PTE can be for no more than five years, typically only one patent per approved product can be extended, the extension cannot extend the total patent term beyond 14 years from approval, and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. In addition, the length of the adjustment or extension granted could be less than that requested, and we may not receive the full PTA or PTE available if we fail to exercise due diligence during the testing phase or regulatory review process, fails to apply within applicable deadlines, fails to apply prior to expiration of relevant patents, or otherwise fails to satisfy applicable requirements.

As with many biotechnology and pharmaceutical companies, our ability to maintain and solidify our proprietary and intellectual property position for our products will depend on our success in obtaining effective patent claims and enforcing those patent claims. However, our owned and in-licensed pending patent applications, and any patent applications that may be filed in the future or licensed from third parties, may not result in issuance. The breadth of claims that may be allowed or enforced in our patents also cannot be predicted. Any of our issued patents or patents obtained in the future may be challenged, invalidated, infringed or circumvented. In addition, because of the extensive time required for clinical development and regulatory review of a therapeutic product that may be developed, it is possible that, before any of our products can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby limiting the protection such patent would afford the respective product and any competitive advantage such patent may provide. For more information, see the section entitled “Risk Factors—Risks Related to Intellectual Property.”

In addition to patents, we rely upon trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. However, trade secrets and know-how can be difficult to protect. We take measures to protect and maintain the confidentiality of proprietary information in order to protect aspects of the business that are not amenable to, or that we do not consider appropriate for, patent protection. It is our policy to require employees, consultants, outside scientific partners, sponsored researchers and other advisors (non-Talaris individuals) to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to non-Talaris individuals during the course of the relationship between us and non-Talaris individuals is to be kept confidential and not disclosed to third parties except in specific circumstances. The agreements we maintain with employees and consultants also provide that all inventions conceived by the employee or consultant in the course of employment or consulting relationships with us, or from the employee’s or consultant’s use of our confidential information, are our exclusive property and require such employees and consultants to assign their right, title and interest in such inventions to us. Although we take steps to protect our proprietary information and trade secrets, including through such contractual means with employees and consultants, we cannot guarantee that we have executed such agreements with all applicable counterparties, such agreements will not be breached, or that these agreements will afford us adequate protection of our intellectual property and proprietary rights. For more information, see the section entitled “Risk Factors—Risks Related to Intellectual Property.”

We have filed and obtained U.S. Registration No. 6180755 for the TALARIS THERAPEUTICS character mark for “biological preparations in the nature of allogeneic cell therapies for use in treating organ transplant patients” in International Class 5 and “providing laboratory services to hospitals and transplant centers involving manipulation of allogeneic cells used for cell therapy treatment of organ transplant patients” in International Class 42. We plan to register trademarks in connection with future products.

Commercialization

Subject to receiving marketing approvals, we expect to commence commercialization activities by building a focused sales and marketing organization in the United States to sell our products. Outside the United States, we expect to enter into distribution and other marketing arrangements with third parties for any of our product candidates that obtain marketing approval.

We also plan to build a marketing and sales management organization to create and implement marketing strategies for any products that we market through our own sales organization and to oversee and support our sales force. The responsibilities

of the marketing organization would include developing educational initiatives with respect to approved products and establishing relationships with researchers and practitioners in relevant fields of medicine.

Manufacturing

Our manufacturing strategy is designed to meet the high quality and demand needs of clinical supply and commercial launch of any approved product, while also pursuing the goal of carefully managing our cost structure, maximizing optionality, and optimizing long-term cost of goods. Execution of our strategy includes the following three major features:

- **In-House Manufacturing Facility:** All finished product development and manufacturing is performed in-house in our GMP Cell Processing Facility, which we believe has sufficient capacity for all contemplated clinical trials.
- **Reliable Processing:** Our one-day manufacturing process is robust, reliable and has remained substantially unchanged from Phase 2 to Phase 3, and we believe it is sufficiently scalable to meet future commercial needs without substantial modification.
- **Robust Analytical Testing:** We have developed and qualified in-process assays to support our process, and potency assays required to for the timely release of our product.

Manufacturing Facility

We believe that operating our own manufacturing facility provides us with enhanced control of material supply and enables the more rapid implementation of process enhancements. We believe this approach positions us to support our multicenter clinical trials and potential future commercialization. Our GMP Cell Processing Facility is located in Louisville, Kentucky. The overall facility is approximately 20,000 square feet and includes two identical cleanroom GMP manufacturing suites, two identical quality control testing labs, gowning, changing and supply rooms, clean corridor, material warehouse, accessioning/ shipping rooms, freezer room and other support spaces.

Manufacturing Process and Analytical Testing

The manufacture of FCR001 involves complex processes, including detailed in-process analysis of cell types required for custom patient dosing, separation of the appropriate cells from the starting material with fast and efficient processing to maintain viability, and controlled cryopreservation designed to allow stable product storage until use. Our FCR001 process is substantially unchanged from Phase 2 to Phase 3, and we have manufactured and released multiple lots of clinical trial material for our Phase 2 and Phase 3 clinical trials.

The manufacturing process takes one day and does not require the costly and difficult cell expansion or genetic manipulation necessary for gene therapy and CAR-T manufacturing. The starting material, donated mobilized apheresed peripheral blood, is shipped to our GMP Cell Processing Facility and brought to the accessioning room, where it is inspected and received into the system, and then transported to one of the two dedicated manufacturing suites. Detailed analysis of the incoming apheresis product is performed during initial processing to precisely determine the HSC, FC, and αßTCR+ T-cell content, in order to set the requirements for downstream processing. The manufacturing process is carried out on semi-automated systems which use pre-sterilized, single-use, disposable kits. In order to meet the prescribed dose, our process removes a calculated amount of αßTCR+ T-cells and relatively enriches the product for HSCs and FCs. Samples of the product are then transported to the adjacent dedicated quality control lab for release testing. The final product is cryopreserved in a controlled rate freezer and stored in liquid nitrogen freezers. After testing for all finished product specifications and review of GMP requirements, the product is released by our in-house quality unit, and is later shipped in liquid nitrogen dry shippers to the transplant center, where it is stored until the transplant date.

Government Regulation

In the United States, biological products are subject to regulation under the Federal Food, Drug, and Cosmetic Act, (FD&C Act), the Public Health Service Act (PHS Act) and other federal, state, local and foreign statutes and regulations. Both the FD&C Act and the PHS Act and their corresponding regulations govern, among other things, the research, development, clinical trial, testing, manufacturing, quality control, safety, efficacy, labeling, packaging, storage, record keeping, distribution, reporting, marketing, promotion, advertising, post-approval monitoring, and post-approval reporting involving biological products. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources and we may not be able to obtain the required regulatory approvals.

U.S. Biological Products Development Process

The process required by the FDA before a biological product may be marketed in the United States generally involves the following:

- completion of nonclinical laboratory tests and animal studies according to good laboratory practices (GLPs) and applicable requirements for the humane use of laboratory animals or other applicable regulations;
- submission to the FDA of an application for an investigational new drug application (IND) which must become effective before human clinical trials may begin;
- approval of the protocol and related documentation by an independent institutional review board (IRB) or ethics committee at each clinical trial site before each study may be initiated;
- performance of adequate and well-controlled human clinical trials according to the FDA's regulations commonly referred to as good clinical practices (GCPs) and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed biological product for its intended use;
- preparation of and submission to the FDA of a biologics license application (BLA) for marketing approval that includes sufficient evidence of establishing the safety, purity, and potency of the proposed biological product for its intended indication, including from results of nonclinical testing and clinical trials;
- payment of user fees for FDA review of the BLA (unless a fee waiver applies);
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biological product is produced to assess compliance with current good manufacturing practices (cGMPs) to assure that the facilities, methods and controls are adequate to preserve the biological product's identity, strength, quality and purity and, if applicable, the FDA's current good tissue practices (CGTPs) for human cellular and tissue products;
- potential FDA audit of the nonclinical study and clinical trial sites that generated the data in support of the BLA;
- review of the product candidate by an FDA advisory committee, where appropriate and if applicable; and
- FDA review and approval of the BLA, resulting in the licensure of the biological product for commercial marketing.

Before testing any biological product candidate, in humans, the product candidate enters the preclinical testing stage. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of product biological characteristics, chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLPs.

Prior to beginning the first clinical trial with a product candidate in the United States, an IND must be submitted to the FDA and the FDA must allow the IND to proceed. An IND is an exemption from the FD&C Act that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA allowance that such investigational product may be administered to humans in connection with such trial. Such authorization must be secured prior to interstate shipment and administration. In support of a request for an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, must be submitted to the FDA as part of an IND. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold or partial clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin. Submission of an IND therefore may or may not result in FDA allowance to begin a clinical trial.

Clinical trials involve the administration of the biological product candidate to healthy volunteers or patients under the supervision of qualified investigators which generally are physicians not employed by, or under, the control of the trial sponsor. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical trial will be stopped if certain adverse events should occur.

An IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee (DSMB). This group provides authorization as to whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study.

Certain information about certain clinical trials must also be submitted within specific timeframes to the NIH for public dissemination on its *clinicaltrials.gov* website.

Clinical trials typically are conducted in three sequential phases that may overlap or be combined:

- *Phase 1*. The investigational product is initially introduced into healthy human subjects and tested for safety. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- *Phase 2*. The investigational product is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.
- *Phase 3*. The investigational product is administered to an expanded patient population to further evaluate dosage, clinical efficacy, potency, and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for approval and product labeling.

In some cases, FDA may require, or firms may voluntary pursue, post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, after initial marketing approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up. During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical trial investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA and the investigators for serious and unexpected adverse events, any findings from other studies, tests in laboratory animals or in vitro testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor, acting on its own or based on a recommendation from the sponsor's data safety monitoring board may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the biological product has been associated with unexpected serious harm to patients.

Concurrent with clinical trials, companies usually complete additional animal studies and also must develop additional information about the physical characteristics of the biological product as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP and as applicable CGTP requirements. To help reduce the risk of the introduction of adventitious agents with use of biological products, the PHS Act emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final biological product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the biological product candidate does not undergo unacceptable deterioration over its shelf life.

U.S. Review and Approval Processes

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, nonclinical studies and clinical trials are submitted to the FDA as part of a BLA requesting approval to market the product for one or more indications. The BLA must include results of product development, laboratory and animal studies, human studies, information on the manufacture and composition of the product, proposed labeling and other relevant information.

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the FDA accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review to determine if it is substantially complete before the FDA accepts it for filing. In most cases, the submission of a BLA is subject to a substantial application user fee, although the fee may be waived under certain circumstances. Under the performance goals and policies implemented by the FDA under the Prescription Drug User Fee Act (PDUFA) for original BLAs, the FDA targets ten months from the filing date in which to complete its initial review of a standard application and respond to the applicant, and six months from the filing date for an application with priority review. The FDA does not always meet its PDUFA goal dates, and the review process is often significantly extended by FDA requests for additional information or clarification.

Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the BLA. The FDA reviews the BLA to determine, among other things, whether the proposed product is safe, pure and potent, for its intended use, and whether the product is being manufactured in accordance with cGMP to ensure its continued safety, purity and potency. The FDA may refer applications for novel biological products or biological products that present difficult or novel questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the biological product approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy (REMS) is necessary to assure the safe use of the biological product. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS; the FDA will not approve the BLA without a REMS, if required.

Before approving a BLA, the FDA typically will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Where applicable, the FDA also will not approve the product if the manufacturer is not in compliance with the CGTPs. These are FDA regulations that govern the methods used in, and the facilities and controls used for, the manufacture of human cells, tissues, and cellular and tissue-based products (HCT/Ps), which are human cells or tissue intended for implantation, transplant, infusion, or transfer into a human patient. The primary intent of the CGTP requirements is to ensure that cell and tissue-based products are manufactured in a manner designed to prevent the introduction, transmission and spread of communicable disease. FDA regulations also require tissue establishments to register and list their HCT/Ps with the FDA and, when applicable, to evaluate donors through appropriate screening and testing. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND study requirements and GCP requirements. To assure cGMP, CGTP and GCP compliance, an applicant must incur significant expenditure of time, money and effort in the areas of training, record keeping, production and quality control.

Under the Pediatric Research Equity Act (PREA), a BLA or supplement to a BLA for a novel product (e.g., new active ingredient, new indication, etc.) must contain data to assess the safety and effectiveness of the biological product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan designation has been granted.

After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response Letter will describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the Complete Response Letter without first conducting required inspections, testing submitted product lots, and/or reviewing proposed labeling. In issuing the Complete Response Letter, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse

approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, including to subpopulations of patients, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings precautions or interactions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a REMS, or otherwise limit the scope of any approval. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase IV post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making a drug or biological product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan product designation must be requested before submitting a BLA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full BLA, to market the same biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA application user fee.

A designated orphan drug many not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or, as noted above, if the second applicant demonstrates that its product is clinically superior to the approved product with orphan exclusivity or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Orphan drug designation may also entitle a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers.

Expedited Development and Review Programs

The FDA has various programs, including Fast Track designation, breakthrough therapy designation, accelerated approval and priority review, that are intended to expedite or simplify the process for the development and FDA review of drugs and biologics that are intended for the treatment of serious or life-threatening diseases or conditions. To be eligible for fast track designation, new drugs and biological product candidates must be intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new drug or biologic may request the FDA to designate the drug or biologic as a fast track product at any time during the clinical development of the product. One benefit of fast track designation, for example, is that the FDA may consider for review sections of the marketing application on a rolling basis before the complete application is submitted if certain conditions are satisfied, including an agreement with the FDA on the proposed schedule for submission of portions of the application and the payment of applicable user fees before the FDA may initiate a review.

Under the FDA's breakthrough therapy program, a sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the product candidate is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that it may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Breakthrough therapy designation comes with all of the benefits of fast track designation, which means that the sponsor may file sections of the BLA for review on a rolling basis if certain conditions are satisfied, including an agreement with the FDA on the proposed schedule for submission of portions of the application and the payment of applicable user fees before the FDA may initiate a review. The FDA may take other actions appropriate to expedite the development and review of the product candidate, including holding meetings with the sponsor and providing timely advice to, and interactive communication with, the sponsor regarding the development program.

A product candidate is eligible for priority review if it treats a serious or life-threatening disease or condition and, if approved, would provide a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention of a serious disease or condition. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug or biological product designated for priority review in an effort to facilitate the review. Under priority review, the FDA's goal is to review an application in six months once it is filed, compared to ten months for a standard review. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

Additionally, a product candidate may be eligible for accelerated approval. Drug or biological products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, which means that they may be approved on the basis of adequate and well-controlled clinical trials establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on an intermediate clinical endpoint other than survival or irreversible morbidity, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA generally requires that a sponsor of a drug or biological product receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials to verify the clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. The FDA may withdraw approval of a drug or indication approved under accelerated approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product.

RMAT Designation

As part of the 21st Century Cures Act, enacted in December 2016, Congress created the Regenerative Medicine Advanced Therapy (RMAT) designation to facilitate an efficient development program for, and expedite review of, a product candidate that meets the following criteria: (1) it qualifies as a RMAT, which is defined as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, with limited exceptions; (2) it is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and (3) preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such a disease or condition. A sponsor may request that the FDA designate a drug as a RMAT concurrently with or at any time after submission of an IND. The FDA has 60 calendar days to determine whether the drug meets the criteria. A BLA for a regenerative medicine therapy that has received RMAT designation may be eligible for priority review or accelerated approval through use of surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites. Benefits of RMAT designation also include early interactions with FDA to discuss any potential surrogate or intermediate endpoint to be used to support accelerated approval. A regenerative medicine therapy with RMAT designation that is granted accelerated approval and is subject to post-approval requirements may, as appropriate, fulfill such requirements through the submission of clinical evidence from clinical trials, patient registries, or other sources of real world evidence, such as electronic health records; the collection of larger confirmatory data sets; or post-approval monitoring of all patients treated with such therapy prior to its approval. Like some of FDA's other expedited development programs, RMAT designation does not change the standards for approval but may help expedite the development or approval process.

Post-Approval Requirements

Rigorous and extensive FDA regulation of biological products continues after approval, particularly with respect to cGMP requirements, as well as requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. We currently rely, and may continue to rely, on third parties for the production of clinical and commercial quantities of any products that we may commercialize.

Manufacturers of our products are required to comply with applicable requirements in the cGMP regulations, including quality control and quality assurance and maintenance of records and documentation. Other post-approval requirements applicable to biological products, include reporting of cGMP deviations that may affect the identity, potency, purity and overall safety of a distributed product, record-keeping requirements, reporting of adverse effects, reporting updated safety and efficacy information, and complying with electronic record and signature requirements. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. After a BLA is approved for a biological product, the product also may be subject to official lot release. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot. The FDA also may perform certain confirmatory tests on lots of some products before releasing the lots for distribution by the manufacturer. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of biological products.

Manufacturers also must comply with the FDA's advertising and promotion requirements, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities, and promotional activities involving the internet. Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions.

Failure to comply with the applicable United States requirements at any time during the product development process, approval process or after approval, may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical holds, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, product detentions or refusal to permit the import or export of the product, restrictions on the marketing or manufacturing of the product, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors or other stakeholders, debarment, restitution, disgorgement of profits, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Biological product manufacturers and other entities involved in the manufacture and distribution of approved biological products are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved BLA, including withdrawal of the product from the market. In addition, changes to the manufacturing process or facility generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

Marketing Exclusivity

Depending upon the timing, duration and specifics of the FDA approval of the use of our product candidates, some of our United States patents may be eligible for limited patent term extension under the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of a BLA plus the time between the submission date of a BLA and the approval of that application. Only one patent applicable to an approved biological product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. In addition, a patent can only be extended once and only for a single product. The U.S. PTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the Affordable Care Act), signed into law on March 23, 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 (BPCIA), which created an abbreviated approval pathway for biological products shown to be biosimilar to, or interchangeable with, an FDA-licensed reference biological product. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical trial or trials. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce

the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product, and FDA will not approve an application for a biosimilar or interchangeable product based on the reference biological product until twelve years after the date of first licensure of the reference product. “First licensure” typically means the initial date the particular product at issue was licensed in the United States. Date of first licensure does not include the date of licensure of (and a new period of exclusivity is not available for) a biological product if the licensure is for a supplement for the biological product or for a subsequent application by the same sponsor or manufacturer of the biological product (or licensor, predecessor in interest, or other related entity) for a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength, or for a modification to the structure of the biological product that does not result in a change in safety, purity, or potency.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation, and impact of the BPCIA is subject to significant uncertainty.

In addition to exclusivity under the BPCIA, a biological product can obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods, including some regulatory exclusivity periods tied to patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued “Written Request” for such a study.

Additional Regulation

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations.

U.S. Foreign Corrupt Practices Act, U.K. Bribery Act and Other Laws

The U.S. Foreign Corrupt Practices Act of 1977 (FCPA) prohibits companies and their employees, agents, and intermediaries from engaging in certain activities to obtain or retain business or secure any improper advantage, or to influence a person working in an official capacity. It is illegal to pay, offer to pay or authorize, directly or indirectly, the payment of anything of value to any employee or official of a foreign government or public international organization, or political party, political party official, or political candidate in an attempt to obtain or retain business or to otherwise influence the recipient working in an official capacity. The scope of the FCPA also includes employees and officials of state- owned or controlled enterprises, which may include healthcare professionals in many countries.

Equivalent laws have been adopted in other non-U.S. countries that impose similar obligations, including the U.K. Bribery Act 2010 (Bribery Act). As with the FCPA, these laws generally prohibit us and our employees and intermediaries from authorizing, promising, offering, or providing, directly or indirectly, improper or prohibited payments, or anything else of value, to government officials or other persons to obtain or retain business or gain some other business advantage. The Bribery Act also imposes liability for failing to prevent a person associated with us from committing a bribery offense.

There also are other laws and regulations governing international operations, including regulations administered by the governments of the United Kingdom and the United States and authorities in the European Union, including applicable export control regulations, economic sanctions and embargoes on certain countries and persons, anti-money laundering laws, import and customs requirements and currency exchange regulations, collectively referred to as trade control laws.

Failure to comply with the Bribery Act, the FCPA and other anti-corruption laws and trade control laws could subject us to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, where applicable.

Other Healthcare Laws and Compliance Requirements

In the United States, our current and future operations are subject to regulation by various federal, state and local authorities in addition to the FDA, including but not limited to, the Centers for Medicare & Medicaid Services (CMS), other divisions of the U.S. Department of Health and Human Services (HHS) (such as the Office of Inspector General, Office for Civil Rights and the Health Resources and Service Administration), the U.S. Department of Justice (DOJ), and individual U.S. attorney offices within the DOJ, and state and local governments. For example, our clinical research, sales, marketing and scientific/educational grant programs may have to comply with the anti-fraud and abuse provisions of the Social Security Act, the false claims laws, the privacy and security provisions of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), and similar state laws, each as amended, as applicable:

- the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order, arrangement or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs; a person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act or federal civil money penalties statute;
- the federal civil and criminal false claims laws, including the False Claims Act, and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, false or fraudulent claims for payment to, or approval by Medicare, Medicaid, or other federal healthcare programs, knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim or an obligation to pay or transmit money to the federal government, or knowingly concealing or knowingly and improperly avoiding or decreasing or concealing an obligation to pay money to the federal government. Manufacturers can be held liable under the False Claims Act even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The False Claims Act also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the False Claims Act and to share in any monetary recovery;
- the anti-inducement law, which prohibits, among other things, the offering or giving of remuneration, which includes, without limitation, any transfer of items or services for free or for less than fair market value (with limited exceptions), to a Medicare or Medicaid beneficiary that the person knows or should know is likely to influence the beneficiary's selection of a particular supplier of items or services reimbursable by a federal or state governmental program;
- HIPAA, which created new federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false, fictitious, or fraudulent statements or representations in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH) and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses and their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information as well as their covered subcontractors, relating to the privacy, security and transmission of individually identifiable health information;
- the federal transparency requirements under the Affordable Care Act, including the provision commonly referred to as the Physician Payments Sunshine Act, and its implementing regulations, which requires applicable manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare,

Medicaid or the Children's Health Insurance Program to report annually to the CMS information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made during the previous year to certain non-physician providers, including physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives;

- federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs; and
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.

In addition to the above, on November 20, 2020, the Office of Inspector General (OIG) finalized further modifications to the federal Anti-Kickback Statute. Under the final rules, OIG added safe harbor protections under the Anti-Kickback Statute for certain coordinated care and value-based arrangements among clinicians, providers, and others. The effective date of the new safe harbors has been delayed by the Biden administration until January 1, 2023. We continue to evaluate what effect, if any, these rules will have on our business.

Additionally, we are subject to state and foreign equivalents of each of the healthcare laws and regulations described above, among others, some of which may be broader in scope and may apply regardless of the payor. Many U.S. states have adopted laws similar to the federal Anti-Kickback Statute and False Claims Act, and may apply to our business practices, including, but not limited to, research, distribution, sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental payors, including private insurers. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America's Code on Interactions with Healthcare Professionals. Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state. There are ambiguities as to what is required to comply with these state requirements and if we fail to comply with an applicable state law requirement, we could be subject to penalties. Finally, there are state and foreign laws governing the privacy and security of health information (e.g., the California Consumer Privacy Act), many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws.

Violations of fraud and abuse laws may be punishable by criminal and/or civil sanctions, including penalties, fines, imprisonment and/or exclusion or suspension from federal and state healthcare programs such as Medicare and Medicaid and debarment from contracting with the U.S. government. In addition, private individuals have the ability to bring actions on behalf of the U.S. government under the federal False Claims Act as well as under the false claims laws of several states.

Law enforcement authorities are increasingly focused on enforcing fraud and abuse laws, and it is possible that some of our practices may be challenged under these laws. Efforts to ensure that our current and future business arrangements with third parties, and our business generally, will comply with applicable healthcare laws and regulations will involve substantial costs. If our operations, including our arrangements with physicians and other healthcare providers, are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs (such as Medicare and Medicaid), and imprisonment, any of which could adversely affect our ability to operate our business and our financial results. The approval and commercialization of any of our other cell therapies outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

If any of the physicians or other healthcare providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs, which may also adversely affect our business.

The risk of our being found in violation of these laws is increased by the fact that many of these laws have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain a robust system to comply with multiple jurisdictions with different compliance and reporting requirements increases the possibility that a healthcare company may violate one or more of the requirements. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial cost.

Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products. For example, in March 2010, the Affordable Care Act was enacted, which, among other things, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; introduced a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care plans; imposed mandatory discounts for certain Medicare Part D beneficiaries as a condition for manufacturers' outpatient drugs coverage under Medicare Part D; subjected drug manufacturers to new annual, nondeductible fees based on pharmaceutical companies' share of sales to federal healthcare programs; imposed a new federal excise tax on the sale of certain medical devices; expanded healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers and enhanced penalties for non-compliance; expanded eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability; expanded the entities eligible for discounts under the PHS Act's pharmaceutical pricing program, also known as the 340B Drug Pricing Program; created new requirements to report financial arrangements with physicians and teaching hospitals, commonly referred to as the Physician Payments Sunshine Act; created a new requirement to annually report the identity and quantity of drug samples that manufacturers and authorized distributors of record provide to physicians; created a new Patient Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research; and established the Center for Medicare Innovation at the CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending.

There have been executive, legal and political challenges to certain aspects of the Affordable Care Act. During his presidency, former President Trump signed several executive orders and numerous other directives designed to delay, circumvent, or loosen certain requirements mandated by the Affordable Care Act.

Concurrently, Congress considered legislation that would repeal or repeal and replace all or part of the Affordable Care Act. While Congress has not passed comprehensive repeal legislation, several bills affecting the implementation of certain taxes under the Affordable Care Act have been signed into law. For example, on January 22, 2018, former President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain Affordable Care Act-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices; however, on December 20, 2019, former President Trump signed into law the Further Consolidated Appropriations Act (H.R. 1865), which repealed the Cadillac tax, the health insurance provider tax, and the medical device excise tax. Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. The Bipartisan Budget Act of 2018 (BBA), among other things, amends the Affordable Care Act, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." In addition, the Tax Cuts and Jobs Act of 2017 (Tax Act), included a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On December 14, 2018, a federal district court in Texas ruled the individual mandate is a critical and inseverable feature of the Affordable Care Act, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the Affordable Care Act are invalid as well. On December 18, 2019, the Fifth Circuit U.S. Court of Appeals held that the individual mandate is unconstitutional, and remanded the case to the lower court to reconsider its earlier invalidation of the full Affordable Care Act. The United States Supreme Court is currently reviewing this case, but it is unknown when a decision will be reached. Although the U.S. Supreme Court has yet ruled on the constitutionality of the Affordable Care Act, on February 10, 2021, the Biden administration withdrew the federal government's support for overturning the Affordable Care Act. Further, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the

Affordable Care Act marketplace, which began February 15, 2021 and will remain open through August 15, 2021. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the Affordable Care Act. It is unclear how the Supreme Court ruling, other such litigation, and the healthcare reform measures of the Biden administration will impact the Affordable Care Act and our business.

Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. For example, in August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee on Deficit Reduction did not achieve a targeted deficit reduction of at least $1.2 trillion for fiscal years 2012 through 2021, triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect beginning on April 1, 2013 and, due to legislation amendments to the statute, including the BBA, will stay in effect through 2030 unless additional Congressional action is taken. However, COVID-19 relief legislation suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2021. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the former Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives.

For example, on July 24, 2020 and September 13, 2020, former President Trump signed several Executive Orders aimed at lowering drug pricing that seek to implement several of the administration's proposals. In response, the FDA released a final rule on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20 2020 CMS issued an Interim Final Rule implementing the Most Favored Nation (MFN) Model under which Medicare Part B reimbursement rates will be calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. The MFN Model regulations mandate participation by identified Part B providers and will apply in all U.S. states and territories for a seven-year period and was scheduled to begin on January 1, 2021 and end on December 31, 2027. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. Additionally, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers the implementation of which have also been delayed until January 1, 2023. However, it is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives.

Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Further, it is possible that additional governmental action is taken in response to the COVID-19 pandemic.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any cell therapies for which we obtain regulatory approval. In the United States and markets in other countries, sales of any cell therapies for which we receive regulatory approval for commercial sale will depend, in part, on the availability of coverage and reimbursement from payors.

Payors include government authorities, managed care providers, private health insurers and other organizations. Patients who are prescribed treatments for their conditions and providers generally rely on these third-party payors to reimburse all or part of the associated healthcare. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. Payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication. A decision by a payor not to cover our cell therapies could reduce physician utilization of our products once approved and have a material adverse effect on our sales, results of operations and financial condition. Moreover, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development and manufacturing costs. Further, due to the COVID-19 pandemic, millions of individuals have lost or will be losing employer-based insurance coverage, which may adversely affect our ability to commercialize our products.

In addition, coverage and reimbursement for products can differ significantly from payor to payor. One payor's decision to cover a particular medical product or service does not ensure that other payors will also provide coverage for the medical product or service, or will provide coverage at an adequate reimbursement rate. In the United States, the principal decisions about reimbursement for new medicines are typically made by the CMS. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree.

Additionally, the coverage determination process will require us to provide scientific and clinical support for the use of our products to each payor separately and will be a time-consuming process. Payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain and maintain coverage and reimbursement for any product, we may need to conduct expensive evidence generation studies in order to demonstrate the medical necessity and cost-effectiveness of such a product, in addition to the costs required to obtain regulatory approvals. If payors do not consider a product to be cost-effective compared to current standards of care, they may not cover the product as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to cover its costs or make a profit.

Employees and Human Capital Resources

We believe our employees are vital to the advancement of our product pipeline, and critical to the safety of patients enrolled in our on-going and future clinical trials. We focus on attracting innovative and collaborative employees who can lead and participate in teams that will advance our Facilitated Allo-HSCT Therapy for the ultimate long-term benefit of patients.

Our People

As of December 31, 2021, we had 112 employees and 15 consultants. A total of 22 employees hold doctoral degrees including MD, PhD or PharmD degrees. Within our workforce, 99 employees are engaged in research and development and 21 are engaged in business development, finance, project and information management, and general management and administration. Our human capital resources objectives include identifying, recruiting, retaining, incentivizing and integrating our existing and new employees, advisors and consultants. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Diversity and Inclusion

We believe that a diverse workforce fosters innovation and cultivates a culture that leverages the unique perspectives of every team member to advance our pipeline. The Company's Board of Directors and executive management team includes diverse individuals based on gender and race, and benefit from the diverse experiences of our directors and management that individually and collectively create an innovative and productive workplace culture. We also believe diversity and inclusion helps the Company attract the best talent to continue to advance our pipeline for the ultimate benefit of patients. Within the broader community, both locally and among our patient communities, we foster diversity and inclusion through our work with charities, patient advocacy organizations, and health related non-profits.

Talent Acquisition, Development and Retention

We invest in attracting, developing, and retaining our employees. Our philosophy is to communicate a clear organizational mission, purpose and strategy, to set challenging goals, to drive accountability, and to continuously assess, develop, and advance talent. Our Company provides employees opportunities to grow in their current roles as well as to have opportunities to build new skills, while also considering diversity in gender, race, and life experience.

Compensation, Benefits, and Safety

We strive to offer a comprehensive benefits program that provides resources to help employees manage their health, finances and life outside of work. Compensation for our employees includes market competitive salaries and wages, equity participation to drive an ownership culture, comprehensive health and welfare benefits, and retirement plan contributions. Our commitment to the safety of our employees, particularly those who work in our laboratory and manufacturing facilities, is also a priority and we have safety programs at all our properties to facilitate safe working practices.

Corporate Information

We were incorporated under the laws of the state of Delaware February 2002. Our mailing address is 350 E. Market Street, Suite 350, Louisville, Kentucky 40202 and our executive offices are located at 570 S. Preston Street, Suite 400, Louisville, Kentucky 40202 and our telephone number at that address is (502) 398-9250. We maintain an Internet website at the following address: www.talaristx.com. The information on our website is not incorporated by reference in this Annual Report on Form 10-K or in any other filings we make with the Securities and Exchange Commission, or SEC.

Available Information

We make available on or through our website certain reports and amendments to those reports that we file with or furnish to the SEC in accordance with the Exchange Act of 1934. These include our annual reports on Form 10-K, our quarterly reports on Form 10-Q, and our current reports on Form 8-K, exhibits and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act. We make this information available on or through our website free of charge the same day we electronically file the information with, or furnish it to, the SEC.

A copy of our Corporate Governance Guidelines, Code of Business Conduct and the charters of the Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee are posted on our website, www.talaristx.com, under “Investors – Corporate Governance.”

The SEC maintains an Internet website that contains reports, proxy and information statements, and other information regarding us and other issuers that file electronically with the SEC. The SEC’s Internet website address is www.sec.gov.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Annual Report, including our financial statements and the related notes thereto and the section of this Annual Report titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" before you make an investment decision. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and prospects. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations. As a result, the market price of our common stock could decline, and you may lose all or part of your investment in our common stock. The risks described below are not intended to be exhaustive and are not the only risks facing the Company. New risk factors can emerge from time to time, and it is not possible to predict the impact that any factor or combination of factors may have on our business, prospects, financial condition or results of operations.

Risks Related to Our Business and Product Candidates

Risks Related to Clinical Development

Our business substantially depends upon the successful development and regulatory approval of FCR001, our lead product candidate. If we are unable to obtain regulatory approval for FCR001, our business may be materially harmed.

We currently have no products approved for sale and are investing substantially all of our efforts and financial resources in the development of our Facilitated Allo-HSCT Therapy, specifically in our lead product candidate, FCR001. Successful continued development and ultimate regulatory approval of FCR001 for our initial and potential additional indications is critical to the future success of our business. We will need to raise sufficient funds for, and successfully enroll and complete, our clinical development programs of FCR001 for living donor kidney transplantation ("LDKT") and additional indications.

There is no guarantee that any of our product candidates will proceed in clinical development or achieve regulatory approval. The process for obtaining marketing approval for any product candidate is very long and risky and there will be significant challenges for us to address in order to obtain marketing approval as planned or, if at all. The potential regulatory approval of FCR001 or any other product candidate we may develop is subject to a number of risks, including the following:

- successful initiation and completion of clinical trials;
- successful patient enrollment in clinical trials;
- successful data from our clinical trials that supports an acceptable risk-benefit profile of our product candidates in the intended populations; and
- receipt and maintenance of marketing approvals from applicable regulatory authorities.

Furthermore, negative results in the development of FCR001 for our lead indication may also impact our ability to obtain regulatory approval of FCR001 for other current and potential indications since the underlying platform, manufacturing process. development process, and cell therapy is the same for all of our current programs in development. Accordingly, a failure in any one program may affect the ability to obtain regulatory approval to continue or conduct our other clinical programs.

In addition, because we have limited financial and personnel resources and are placing significant focus on the development of our lead product candidate and our lead indications, we may forgo or delay pursuit of opportunities with other future product candidates and indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and other future product candidates for specific indications may not yield any commercially viable future product candidates. If we do not accurately evaluate the commercial potential or target market for a particular future product candidate or indication, we may relinquish valuable rights to those future product candidates or indications through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such future product candidates or indications.

Many of these risks are beyond our control, including the risks related to clinical development, our proprietary manufacturing process and the regulatory submission process. If we are unable to develop and receive regulatory approval for FCR001 for the indications we are developing it for, or if we experience delays as a result of any of these risks or otherwise, our business could be materially harmed.

We may not successfully identify, develop or commercialize new indications for FCR001 or identify any additional product candidates and may be unable to expand our product pipeline through acquisition or in-licensing.

A key part of our business strategy is to leverage FCR001 by identifying and validating new indications, including other transplant settings and patients with autoimmune or immune-mediated diseases. In the event that FCR001 does not receive regulatory approval or is not successfully commercialized in our currently planned indications, then the success of our business will depend on our ability to expand FCR001 into additional indications or our product pipeline to include other product candidates through our own internal research and discovery efforts, in-licensing or other acquisitions. We may be unable to identify relevant product candidates or indications. If we do identify such product candidates or indications, we may be unable to develop these programs for a number of reasons, including insufficient capital or other resources.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and the inability to successfully and timely conduct clinical trials and obtain regulatory approval for our product candidates would substantially harm our business.

We cannot commercialize product candidates in the United States without first obtaining regulatory approval from the U.S. Food and Drug Administration ("FDA"); similarly, we cannot commercialize product candidates outside of the United States without obtaining regulatory approval from comparable foreign regulatory authorities. Before obtaining regulatory approvals for the commercial sale of any product candidate for a target indication, we must demonstrate with substantial evidence gathered in preclinical studies and clinical trials, that the product candidate is safe and effective for use for that target indication and that the manufacturing facilities, processes and controls are adequate with respect to such product candidate to assure safety, purity and potency.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and clinical trials.

The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of preclinical studies and clinical trials and depends upon numerous factors, including the study designs and substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and it is possible that none of our existing product candidates or any future product candidates will ever obtain regulatory approval.

Our product candidates could fail to receive regulatory approval from the FDA or a comparable foreign regulatory authority for many reasons, including:

- disagreement with the design or conduct of our clinical trials;
- failure to demonstrate to the satisfaction of regulatory agencies that FCR001, our lead product candidate, is safe and effective, or has a positive benefit/risk profile for its proposed indications;
- failure of clinical trials to meet the level of statistical significance required for approval;
- disagreement with our interpretation of data from preclinical studies or clinical trials;
- the insufficiency of data collected from clinical trials of our product candidates to support the submission and filing of a Biologics License Application ("BLA") or other submission or to obtain regulatory approval;

- failure to obtain approval of our manufacturing processes, our own manufacturing facility, or facilities of third-party manufacturers with whom we may in the future contract for clinical and commercial supplies; or

- changes in the approval policies or regulations that render our preclinical and clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of future clinical trial results, may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations and prospects. The FDA or a comparable foreign regulatory authority may require more information, including additional preclinical or clinical data to support approval, which may delay or prevent approval and our commercialization plans, or we may decide to abandon the development program. If we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request (including failing to approve the most commercially promising indications), may grant approval contingent on the performance of costly post-marketing clinical studies, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate.

If we experience delays or difficulties in the enrollment of patients in clinical trials, development of our product candidate may be delayed or prevented, which would have a material adverse effect on our business.

We may not be able to initiate or continue clinical trials for our product candidate if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or comparable foreign regulatory authorities. Patient enrollment is a significant factor in the timing of clinical trials. In particular, because certain of our clinical trials are focused on indications with relatively small patient populations, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate. For example, our initial indications focus on orphan diseases, which affect fewer than 200,000 individuals in the United States. Specifically, approximately 6,500 LDKT are performed on an annual basis in the United States and, in addition, we have prioritized development of FCR001 in a severe form of scleroderma known as diffuse cutaneous systemic sclerosis with a prevalence of approximately 70,000 to 80,000 individuals in the United States.

Patient enrollment may be affected if our competitors have ongoing clinical trials for product candidates that are under development for the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials instead enroll in clinical trials of our competitors' product candidates.

Furthermore, because we are investigating the treatment of complex indications that require specialized medical care by means of an HSCT procedure, which is itself a complex procedure performed by specialized physicians and treatment centers, we face inherent challenges in recruiting clinical trial sites to participate in our trials and to complete our trials on a timely basis. For LDKT, each site that participates in our trial will need to identify a lead clinician from each of the solid organ transplant and HSCT departments, who are willing and able to coordinate closely on the care and follow-up of our patients. We rely on our relationships with transplant centers of excellence to assist in identifying eligible patients and carrying out our clinical trials, and any inability to secure or deterioration of those relationships could impede our ability to successfully enroll patients in a timely manner, if at all.

Patient enrollment may also be affected by other factors, including:

- size and nature of the patient population;

- severity of the disease under investigation;

- patient eligibility criteria for the trial in question;

- nature of the trial protocol;

- our ability to recruit clinical trial investigators with the appropriate competencies and experience;

- perceived risks and benefits of the product candidate under study;

- the occurrence of adverse events attributable to our lead product candidate;
- efforts to facilitate timely enrollment in clinical trials;
- the number and nature of competing products or product candidates and ongoing clinical trials of competing product candidates for the same indication;
- patient referral practices of physicians;
- risk that enrolled subjects will drop out or die before completion;
- competition for patients from other clinical trials;
- the ability to monitor patients adequately during and after treatment;
- travel restrictions and other potential limitations by federal, state, or local governments affecting the workforce or affecting clinical research site policies implemented in response to the COVID-19 pandemic;
- delays in or temporary suspension of the enrollment of patients in our ongoing and planned clinical trials due to the ongoing and evolving COVID-19 pandemic;
- proximity and availability of clinical trial sites for prospective patients; and
- continued enrollment of prospective patients by clinical trial sites.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our clinical trials may be delayed or terminated. We have already experienced meaningful delays to our clinical trials as a result of the impact of COVID-19 on both our clinical sites and the willingness of stem cell donors and transplant recipients to travel to our clinical sites. Even if we are able to enroll a sufficient number of patients in our clinical trials, if the pace of enrollment is slower than we expect, the development costs for our product candidates may increase and the completion of our trials may be delayed or our trials could become too expensive to complete. Any delays in completing our clinical trials will increase our costs, delay or prevent our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenue. Any delays in completing our clinical studies for our product candidates may also decrease the period of commercial exclusivity. Any of these occurrences may significantly harm our business, financial condition and prospects.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

We face competition from numerous pharmaceutical and biotechnology enterprises, as well as from academic institutions, government agencies and private and public research institutions. Our commercial opportunities will be significantly impacted if our competitors develop and commercialize products that are safer, more effective, have fewer side effects, are less expensive or obtain more significant acceptance in the market than any product candidates that we develop. Additionally, our commercial opportunities will be significantly impacted if novel upstream products or changes in treatment protocols reduce the overall incidence or prevalence of diseases in our current or future target population. Competition could result in reduced sales and pricing pressure on our product candidates, if approved by applicable regulatory authorities. In addition, significant delays in the development of our product candidates could allow our competitors to bring products to market before us and impair any ability to commercialize our product candidates.

While there are currently no FDA- or EMA-approved cell-based therapies for the indications we are currently targeting, other approved or commonly used drugs and therapies for our current or future target diseases, such as use of tacrolimus and MMF for prevention of organ transplant rejection, or nintedanib to slow the rate of decline in lung function in patients with scleroderma-associated interstitial lung disease, are more well established and are accepted by physicians, patients and third-party payors. Some of these drugs are branded and subject to patent protection, and other drugs are available on a generic basis. Insurers and other third-party payors may encourage the use of generic products or specific branded products. In addition, a number of companies, academic institutions and government agencies are seeking to address limitations of existing therapies that we are also seeking to address. For example, a number of third parties, such as Jasper Therapeutics, Inc., bluebird bio, Inc. and Magenta Therapeutics, Inc., are seeking to develop conditioning regimens for HSCT that have lower toxicities, morbidities and mortalities than the current standard of care. Similarly, Johns Hopkins University and the Fred Hutchinson Cancer Center have previously administered non-myeloablative conditioning treatments. A number of other companies are also seeking to decrease the incidence and severity of graft vs. host disease ("GvHD") in HSCT. If any of these endeavors prove to be successful, the anticipated advantages of our Facilitated Allo-HSCT Therapy in comparison to the then existing standard of care could be eliminated and the demand for our Facilitated Allo-HSCT Therapy could be materially impacted.

We expect that, if our one-time investigational therapy is approved, it will be priced in a manner that will reflect its long-term clinical, economic, and humanistic value. Such a pricing model may entail a single upfront cost or multiple installments contingent upon demonstration of continued benefit that will likely be more expensive than the upfront cost or initial annual costs of competitive generic products that must be taken chronically. Absent differentiated and compelling clinical evidence, pricing premiums may impede the adoption of our products over currently approved or commonly used therapies, which may adversely impact our business. In addition, many companies are developing new therapeutics, and we cannot predict what the standard of care will become as our products continue in clinical development. Many of our competitors or potential competitors have significantly greater market presence, financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do, and as a result may have a competitive advantage over us. Smaller or early-stage companies may also prove to be significant competitors, including through collaborative arrangements or mergers with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific, commercial and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies and technology licenses complementary to our programs or advantageous to our business.

As a result of these factors, these competitors may obtain regulatory approval of their products before we are able to, which will limit our ability to develop or commercialize our product candidates. Our competitors may also develop products that are safer, more effective, more widely used and cheaper than ours, and may also be more successful than us in manufacturing and marketing their products. These appreciable advantages could render our product candidates obsolete or noncompetitive before we can recover the expenses of development and commercialization.

Delays in the clinical development or delays in or our ability to achieve regulatory approval, if at all, and commercialization of our product candidates, if approved, would have a material adverse effect on our business.

We may experience delays in our ongoing or future clinical trials and we do not know whether clinical trials will begin or enroll subjects on time, will need to be redesigned or will be completed on schedule, if at all, such as on account of the ongoing COVID-19 pandemic and its impact at clinical trials sites or on the third-party service providers on whom we rely. Clinical trials may be delayed, suspended or prematurely terminated for a variety of reasons, such as:

- delay or failure in reaching agreement with the FDA or a comparable foreign regulatory authority on the design and implementation of clinical trials;

- delay or failure in obtaining authorization to commence a trial, including the delay or ability to generate sufficient preclinical data to support initiation of clinical trials, or inability to comply with conditions imposed by a regulatory authority regarding the scope or design of a trial;

- delay or failure in reaching agreement on acceptable terms with prospective contract research organizations ("CROs") and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

- the inability of CROs to perform under these agreements, including due to impacts from the COVID-19 pandemic on their workforce;

- delay or failure in obtaining institutional review board ("IRB") approval or the approval of other reviewing entities, including comparable foreign regulatory authorities, to conduct a clinical trial at each site;
- withdrawal of clinical trial sites from our clinical trials or the ineligibility of a site to participate in our clinical trials;
- delay or failure in recruiting and enrolling suitable subjects to participate in a trial;
- delay or failure in subjects completing a trial or returning for post-treatment follow-up;
- inability to identify and maintain a sufficient number of trial sites, including because potential trial sites may not have the capabilities required for the indication that we are treating;
- failure of our third-party clinical trial managers to satisfy their contractual duties, meet expected deadlines or return trustworthy data;
- delay or failure in adding new trial sites, including due to changes in policies of the clinical research sites or local IRBs;
- interim results or data that are ambiguous or negative or are inconsistent with earlier results or data;
- feedback from the FDA, the IRB, data safety monitoring boards ("DSMBs") or comparable foreign authorities, or results from earlier stage or concurrent preclinical studies and clinical trials, that might require modification to the protocol for a trial;
- unacceptable benefit/risk profile, unforeseen safety issues or adverse side effects;
- failure to demonstrate a benefit from using a product candidate;
- lack of adequate funding to continue a trial, including the incurrence of unforeseen costs due to enrollment delays, requirements to conduct additional trials or increased expenses associated with the services of our CROs and other third parties; or
- changes in governmental regulations or administrative actions, failure by us or third parties to comply with regulatory requirements, or lack of adequate funding to continue a clinical trial.

Furthermore, clinical trials may be delayed, suspended or prematurely terminated for a variety of reasons, including as a result of clinical sites, investigators or other third parties deviating from the trial protocol, failing to conduct the trial in accordance with regulatory and contractual requirements, and/or dropping out of a trial. For example, we rely on a single clinical investigator at Northwestern Medical Center ("Northwestern") to provide ongoing data from our Phase 2 clinical trial. This investigator is our lead principal investigator for FREEDOM-1, and we anticipate that this investigator and site will be our highest enroller in our FREEDOM-1 and FREEDOM-2 clinical trials. In the event that our lead investigator at Northwestern or that site deviates materially from our trial protocol or our or the clinical site's regulatory or contractual obligations, our clinical trials could be adversely affected**.**

In addition, disruptions caused by the COVID-19 pandemic, including any current or future emerging variants of the virus, may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials. We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by a DSMB for such trial or by the FDA or comparable

foreign regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial.

Risks Related to the Results of our Preclinical Studies and/or Clinical Trials

The results of preclinical studies or earlier clinical trials are not necessarily predictive of future results. Our existing product candidates in clinical trials, and any other product candidate we advance into clinical trials, may not have favorable results in later clinical trials or receive regulatory approval.

Success in preclinical studies and our Phase 2 trial in LDKT does not ensure that later clinical trials, including our ongoing Phase 3 clinical trial of FCR001 in LDKT, will generate findings consistent with our Phase 2 trial including adequate data to demonstrate the efficacy and safety of FCR001 or any of other product candidates we may develop. Likewise, a number of companies in the pharmaceutical and biotechnology industries, including those with greater resources and experience than us, have suffered significant setbacks in clinical trials, even after seeing promising results in earlier preclinical studies or clinical trials. Despite the results reported in earlier preclinical studies or clinical trials for our product candidates, to date, results may not be replicated in subsequent trials, and we do not know whether the clinical trials we may conduct will demonstrate adequate efficacy and safety to result in regulatory approval of FCR001 or any future product candidates we develop. Moreover, later audits of our earlier clinical data, such as from our Phase 2 clinical trial, may reveal inaccuracies or deviations impacting the integrity of those data. Additionally, certain of our clinical trial endpoints also may not be adequately powered in a particular subpopulation of our trial population. Our Phase 2 trial was a “single arm” trial for which there was no comparator arm to permit a comparison of our investigational therapy against standard of care treatment. Furthermore, all of our ongoing and planned clinical trials to date have been or will be open-label trials. This means that both the patient and investigator know whether the patient is receiving our FCR001 therapy or standard of care therapy. Open-label clinical trials can be subject to various limitations that may exaggerate any therapeutic effect, as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a “patient bias.” Moreover, patients selected for early clinical studies often include the most severe sufferers and their symptoms may have been bound to improve notwithstanding the new treatment. In addition, open-label clinical trials may be subject to an “investigator bias” where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. Given that each of our planned and ongoing clinical trials include an open-label dosing design, while we believe our trials utilize objective assessment measures for measuring our primary endpoints and therefore are unlikely to be influenced in any manner by patient or investigator bias, our trials may utilize secondary endpoint patient reported outcome measures and, it is unknown whether the open-label design may not be predictive of future clinical trial results with this or other product candidates for which we conduct an open-label clinical trial when studied in a controlled environment or with only objective endpoints. In addition, clinical data obtained from a clinical trial with an allogeneic product candidate such as FCR001 may not yield the same or better results on certain relevant outcome measures as compared to an autologous product candidate. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in such trials nonetheless failed to obtain FDA, EMA or other necessary regulatory agency approval.

If later-stage clinical trials such as our FREEDOM-1 trial do not produce comparable or favorable results, our ability to achieve regulatory approval for any of our product candidates may be adversely impacted. Even if we believe that we have adequate data to support an application for regulatory approval to market any of our product candidates, no therapies for inducing immune tolerance to a transplanted organ or restoring tolerance to self in an autoimmune disease have been approved to date, and the FDA or other regulatory authorities may not agree with our interpretation and may require that we conduct additional clinical trials to support the regulatory approval of our product candidates. If we fail to obtain results in our planned and future preclinical and clinical activities and studies sufficient to meet the requirements of the relevant regulatory agencies, the development timeline and regulatory approval and commercialization prospects for any potential product candidate, and, correspondingly, our business and financial prospects, would be materially adversely affected.

Interim, “top line” or preliminary data from our clinical trials that we may announce or share with regulatory authorities from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we expect to announce clinical updates or share with regulatory authorities interim "top line" or preliminary data from our clinical trials, which is based on a preliminary analysis of then-available data. The outcome of preclinical development testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. For example, in November 2021, we announced preliminary interim results from our Phase 3 FREEDOM-1 trial, including limited efficacy and safety data for the first five patients dosed. While we believe the limited efficacy and safety data observed to date is positive, the trial is in its early stages and additional data from subsequent patients may not be comparable or positive with respect to efficacy, safety or target engagement. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their product candidates. These data and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data.

As a result, the top-line or preliminary results that we report may differ from future results of the same trials, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. Preliminary or "top line" data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously announced. As a result, interim, "top-line," and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary, "top-line," or interim data and final data could impact the regulatory approval of, and significantly harm the prospects for any product candidate that is impacted by the applicable data.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our business in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the clinical updates, or the interim, "top-line," or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for and commercialize our product candidates, our business, operating results, prospects or financial condition may be harmed.

Risks Related to Potential Side Effects and the Safety and Efficacy Profile of our Product Candidates

Our product candidates, or associated conditioning regimens or treatment protocols, may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label or result in significant negative consequences following any regulatory approval.

Undesirable side effects caused or risks exacerbated by our product candidates or associated conditioning regimens or treatment protocols could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authority. As a result of safety or toxicity issues that we may experience in our clinical trials, we may not receive approval to market any product candidates, which could prevent us from ever generating revenues or achieving profitability. Results of our trials could reveal an unacceptably high severity and incidence of side effects, or side effects outweighing the benefits of our product candidates. Such side effects could include known side effects or safety risks that are exacerbated by the combination of HSCT and LDKT in our clinical trials. In such an event, our trials could be delayed, suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. Additionally, during the course of our product development programs, FDA or comparable foreign regulatory authority review teams may change and new agency personnel may view the risk-benefit profile of any product candidates we may develop differently than prior agency review teams. Any negative views as to the risk-benefit profile of FCR001 or any product candidates we may develop in the future could lead FDA or comparable foreign regulatory authorities to require that we conduct additional clinical trials or could require more onerous clinical trial designs for any ongoing or future clinical trials. The drug-related side effects could affect patient recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. In addition, while we note the summary of safety findings we have gathered

to date, certain populations of patients receiving our Facilitated Allo-HSCT Therapy may experience side effects in greater frequency or severity than others who may receive our product candidates and additional clinical research is planned to more fully understand the safety profile of our product candidates in our patient populations and indications of focus. Furthermore, we or others may later identify undesirable side effects caused by our products, including during any long-term follow-up observation period, such as that involved in our FREEDOM-1 trial and previous trials of FCR001 in LDKT.

In particular, LDKT and HSCT involve certain known potential post-procedure complications that may manifest several weeks or months after a transplant and which may be more common in certain patient populations. For example, up to 20% of patients with inherited metabolic diseases treated with HSCT experience primary engraftment failure, resulting in severe complications, including death. GvHD also accounts for approximately 10% of deaths following allogeneic HSCT. In LDKT, certain severe complications, such as severe infection requiring discontinuation of immunosuppression, graft rejection or loss, or even death, can occur. If these or other serious adverse events, undesirable side effects, or unexpected characteristics are identified during the development of any of our product candidates, it may be difficult to determine whether these complications were or were not related to our investigational therapy, and we may need to limit, delay or abandon our further clinical development of those product candidates, even if such events, effects or characteristics were potentially the result of HSCT, LDKT or related procedures generally, and not directly or specifically caused or exacerbated by our product candidates. All serious adverse events or unexpected side effects are continually monitored per the clinical trial's approved protocol. If serious adverse events are determined to be directly or specifically caused or exacerbated by our product candidates, we would follow the trial protocol's requirements, which include certain pre-specified stopping requirements, and which call for our DSMB to review all available clinical data in making a recommendation regarding the trial's continuation. However, there may be a failure by trial sites to effectively execute our clinical trial protocols, including during any long-term follow-up period for our clinical trials during the conduct of future clinical trials or following any product approval we may receive. In addition, HSCT is associated with an increased risk of cancer. Among the likely causes of this increased risk is the total body irradiation and high-dose chemotherapy used in myeloablative conditioning regimens. We believe non-myeloablative conditioning regimens have the potential to help obviate this increased risk, however, patients receiving Facilitated Allo-HSCT Therapy in clinical trials after non-myeloablative conditioning have developed cancer after transplant. For example, a patient, a lifelong smoker, in our Phase 2 clinical trial developed non-small cell carcinoma of the lung approximately four years after HSCT.

Additionally, if any of our product candidates receives regulatory approval, and we or others later identify undesirable side effects caused or risks exacerbated by such product, a number of potentially significant negative consequences could result. For example, the FDA could require us to adopt a Risk Evaluation and Mitigation Strategy ("REMS") to ensure that the benefits of treatment with such product candidate outweigh the risks for each potential patient, which may include, among other things, a communication plan to health care practitioners, patient education, extensive patient monitoring or distribution systems and processes that are highly controlled, restrictive and more costly than what is typical for the industry. We or our collaborators may also be required to adopt a REMS or engage in similar actions, such as patient education, certification of health care professionals or specific monitoring, if we or others later identify undesirable side effects caused by any product that we develop alone or with collaborators. Other potentially significant negative consequences include that:

- we may be forced to suspend marketing of that product, or decide to remove the product form the marketplace;
- regulatory authorities may withdraw or change their approvals of that product;
- regulatory authorities may require additional warnings on the label or limit access of that product to selective specialized centers with additional safety reporting and with requirements that patients be geographically close to these centers for all or part of their treatment;
- we may be required to create a medication guide outlining the risks of the product for patients, or to conduct post-marketing studies;
- we may be required to change the way the product is administered;
- we could be subject to fines, injunctions, or the imposition of criminal or civil penalties, or to sued and held liable for harm caused to subjects or patients; and
- the product may become less competitive, and our reputation may suffer.

Any of these events could diminish the usage or otherwise limit the commercial success of our product candidates and prevent us from achieving or maintaining market acceptance of the affected product candidate, if approved by applicable regulatory authorities.

If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of the FDA or similar regulatory authorities outside the United States or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of such product candidates.

Before obtaining regulatory approval for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of such product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and the outcome is uncertain. Despite preclinical and early clinical trial data, any product candidate can unexpectedly fail at any stage of further development. The historical failure rate for product candidates is high. The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Even if our clinical trials are completed as planned, we cannot be certain that their results will support our proposed indications. In particular, we have conducted a Phase 2 trial of FCR001 in LDKT. We do not know whether FCR001 will perform in our subsequent planned clinical trials, including in diffuse systemic sclerosis and deceased donor kidney transplant, as it has performed in our initial LDKT Phase 2 trial. In addition, if our clinical results are not successful, we may terminate clinical trials for a product candidate and abandon any further research or studies of the product candidate. Any delay in, or termination of, our clinical trials will delay and possibly preclude the filing of any BLAs with the FDA and, ultimately, our ability to commercialize our product candidates and generate product revenues.

Risks Related to Combination Therapies

We intend to develop FCR001, and potentially future product candidates, in other indications and in combination with other therapies, which exposes us to additional risks. Combination therapies and additional indications involve additional complexity and risk that could delay or cause our programs to stall or fail; development of such programs may be more costly, may take longer to achieve regulatory approval and may be associated with unanticipated adverse events.

We intend to develop FCR001, and may develop future product candidates, for use in combination with nonmyeloablative conditioning and related conditioning drugs, and in our LDKT trials, we will administer FCR001 to patients taking standard of care immunosuppressive therapies. Clinical development and commercialization of combination therapies involve additional complexity and risk, including without limitation, those involving drug-drug interactions, dose selection, unanticipated adverse events, clinical design and approvals of regulatory bodies and therapeutic development networks of patient advocacy groups. Even if any product candidate we develop were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to bear the risks that the FDA or similar foreign regulatory authorities could revoke approval of the therapy used in combination with our product candidate or that safety, efficacy, manufacturing or supply issues could arise with these existing therapies. If we are unable to manage the additional complexities and risks of the development and commercialization of combination therapies, the development of FCR001 or any other current or future product candidate could be delayed, halted or otherwise fail to receive or maintain approval and may be less successful commercially.

We also intend to develop FCR001 or related product candidates for a number of different indications, including solid organ transplant, severe autoimmune diseases and other severe disorders for which allo-HSCT has previously been observed to provide potential clinical benefit. Depending on the indication, patients may manifest a variety of differing co-morbidities, may be more or less vulnerable to our conditioning regimen, and may be more or less susceptible to certain severe adverse events or complications in the near or longer term, including cancer, infection, blood disorders and other life-threatening conditions. If any of these conditions or complications were to affect a patient who is participating in one of our clinical trials, it may be difficult or impossible to determine whether these adverse events or complications are related to the original or underlying condition or to our Facilitated Allo-HSCT Therapy. Given that our trials will enroll a relatively small number of patients, even a small number of severe adverse events or serious complications could result in the delay or halt of development of our product candidates in one or more of our targeted indications.

Risks Related to Regulatory Matters and Approvals

Our product candidates represent a novel therapeutic approach that could result in heightened regulatory scrutiny. The regulatory landscape that applies to our Facilitated Allo-HSCT Therapy is rigorous, complex, uncertain and subject to change.

Given that our single-dose cell therapy represents a novel combination of nonmyeloablative conditioning, our investigational FCR001 product, and stem cell transplant-oriented treatment protocols, developing and commercializing our product candidates subjects us to a number of challenges, including obtaining regulatory approval from the FDA and other regulatory authorities, which have limited experience with regulating the development and commercialization of stem cell therapies.

Regulatory requirements governing the development of cell therapy products have changed frequently and may continue to change in the future. The FDA has established the Office of Tissues and Advanced Therapies within the Center for Biologics Evaluation and Research ("CBER"), to consolidate the review of cell therapy, and related products, and to advise the CBER on its review. Moreover, serious adverse events or developments in clinical trials of cell therapy product candidates conducted by others may cause the FDA or other regulatory bodies to initiate a clinical hold on our clinical trials or otherwise change the requirements for approval of any of our product candidates. Although the FDA decides whether individual cell therapy protocols may proceed, the review process and determinations of other reviewing bodies can impede or delay the initiation of a clinical trial, even if the FDA has reviewed the trial and approved its initiation. Adverse developments in preclinical studies or clinical trials conducted by others in the field of cell therapy may cause the FDA, the European Medicines Agency ("EMA"), and other regulatory bodies to amend the requirements for approval of any product candidates we may develop or limit the use of products utilizing cell therapies, either of which could harm our business. In addition, the clinical trial requirements of the FDA, the EMA, and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty, and intended use and market of the potential products. The regulatory approval process for product candidates such as ours can be more expensive and take longer than for other, better known, or more extensively studied pharmaceutical or other product candidates. Further, as we are developing novel potential treatments for conditions in which there is little clinical experience with new endpoints and methodologies, there is heightened risk that the FDA, the EMA or other regulatory bodies may not consider the clinical trial endpoints to provide clinically meaningful results, and the resulting clinical data and results may be more difficult to analyze. For example, we are utilizing transplant recipient chimerism as a surrogate marker for long-term immune tolerance in our ongoing Phase 3 trial of FCR001 in LDKT. We are evaluating this as a secondary endpoint, but it has not yet been validated by the FDA, EMA or other regulatory agencies, and as result, such agencies could reject such an endpoint or interpret its significance differently than we do. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of products utilizing cell therapies in a timely manner or under technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in expenses, delays, or other impediments to our research programs or the commercialization of resulting products.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved, or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for biologics or modifications to approved biologics to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

In response to the COVID-19 pandemic, on March 10, 2020, the FDA announced its intention to postpone most inspections of foreign manufacturing facilities while local, national and international conditions warrant. Since March 2020, when foreign and domestic inspections have largely been on hold, the FDA has been working to resume routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis. Since April 2021, the FDA has conducted limited inspections and employed remote interactive evaluations, using risk management methods, to meet user fee commitments and goal dates. Ongoing travel restrictions and other uncertainties continue to impact oversight operations both domestic and abroad and it is unclear when standard operational levels will resume. The FDA is continuing to complete mission-critical work, prioritize other higher-tiered inspectional needs (e.g., for-cause inspections), and carry out surveillance inspections using risk-based approaches for evaluating public health. Should FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive

evaluation to be adequate, the agency has stated that it generally intends to issue, depending on the circumstances, a complete response letter or defer action on the application until an inspection can be completed. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the ongoing COVID-19 pandemic and may experience delays in their regulatory activities.

Additionally, as of May 26, 2021, the FDA noted it is continuing to ensure timely reviews of applications for medical products during the ongoing COVID-19 pandemic in line with its user fee performance goals. However, the FDA may not be able to continue its current pace and approval timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to the ongoing COVID-19 pandemic and travel restrictions FDA is unable to complete such required inspections during the review period. During the COVID-19 public health emergency, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications.

We may not be able to maintain orphan drug designation for FCR001 or obtain orphan drug designation for our future product candidates, or to obtain and maintain the benefits associated with orphan drug designation.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs or therapies for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. In the European Union, the prevalence of the condition must not be more than five in 10,000. The FDA has granted FCR001 orphan drug designation for the prophylaxis of organ rejection without the need for chronic immunosuppression in patients receiving LDKT. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

If a product that has orphan drug designation from the FDA subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a BLA, to market the same biologic for the same indication, for seven years, except in limited circumstances such as a showing of clinical superiority to the product with orphan product exclusivity or if FDA finds that the holder of the orphan exclusivity has not shown that it can ensure the availability of sufficient quantities of the orphan product to meet the needs of patients with the disease or condition for which the product was designated. Even if we or our collaborators obtain orphan designation to a product candidate, we may not be the first to obtain marketing approval for any particular orphan indication due to the uncertainties associated with developing pharmaceutical products. The scope of exclusivity is limited to the scope of any approved indication, even if the scope of the orphan designation is broader than the approved indication. Additionally, exclusive marketing rights may be limited if we or our collaborators seek approval for an indication broader than the orphan designated indication and may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if a product obtains orphan drug exclusivity, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve a product with the same active moiety for the same condition if the FDA concludes that the later product is safer, more effective, or makes a major contribution to patient care. Furthermore, the FDA can waive orphan exclusivity if we or our collaborators are unable to manufacture sufficient supply of the product. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Similarly, in Europe, a medicinal product may receive orphan designation under Article 3 of Regulation (EC) 141/2000. This applies to products that are intended for a life-threatening or chronically debilitating condition and either (1) such condition affects no more than five in 10,000 persons in the E.U. when the application is made, or (2) the product, without the benefits derived from orphan status, would be unlikely to generate sufficient returns in the E.U. to justify the necessary investment. Moreover, in order to obtain orphan designation in the E.U. it is necessary to demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the E.U. or, if such a method exists, the product will be of significant benefit to those affected by the condition. In the E.U., orphan medicinal products are eligible for financial incentives such as reduction of fees or fee waivers and applicants can benefit from specific regulatory assistance and scientific advice. Products receiving orphan designation in the E.U. can receive ten years of market exclusivity, during which time no similar medicinal product for the same indication may be placed on the market. An orphan product can also obtain an additional two years of market exclusivity in the E.U. for pediatric studies. However, the ten-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for

orphan designation-for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if:

- the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior;
- the first applicant consents to a second orphan medicinal product application; or
- the first applicant cannot supply enough orphan medicinal product.

If we do not receive or maintain orphan drug designation to product candidates for which we seek such designation, it could limit our ability to realize revenues from such product candidates.

The incidence and prevalence of the target patient population for FCR001 are based on estimates and third-party sources. If the market opportunity for FCR001 or our other product candidates is smaller than we estimate or if any approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability might be materially and adversely affected.

Periodically, we make estimates regarding the incidence and prevalence of target patient populations based on various third-party sources and internally generated analysis. These estimates may be inaccurate or based on imprecise data. For example, the total addressable market opportunity for FCR001 in any given indication will depend on, among other things, acceptance of FCR001 by the medical community and patient access, drug pricing and reimbursement. The number of patients in the addressable markets may turn out to be lower than expected, patients may not be otherwise amenable to treatment with FCR001, or new patients may become increasingly difficult to identify or gain access to, all of which may significantly harm our business, financial condition, results of operations and prospects.

We have received Regenerative Medicine Advanced Therapy ("RMAT") designation for FCR001 for LDKT. This designation may not necessarily lead to a faster development or regulatory review or approval process, and will not necessarily increase the likelihood that FCR001 will receive marketing approval.

We have received RMAT designation from the FDA for FCR001 for the prophylaxis of organ rejection without the need for chronic immunosuppression in patients receiving LDKT. A company may request RMAT designation of its product candidate, which designation may be granted if the product meets the following criteria: (1) it is a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, with limited exceptions; (2) it is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and (3) preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such a disease or condition. RMAT designation provides potential benefits that include more frequent meetings with FDA to discuss the development plan for the product candidate, and potential eligibility for rolling review and priority review. Products granted RMAT designation may also be eligible for accelerated approval on the basis of a surrogate or intermediate endpoint reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites, including through expansion to additional sites post-approval, if appropriate. RMAT-designated products that receive accelerated approval may, as appropriate, fulfill their post-approval requirements through the submission of clinical evidence, clinical studies, patient registries, or other sources of real world evidence (such as electronic health records); through the collection of larger confirmatory data sets; or via post-approval monitoring of all patients treated with such therapy prior to approval of the therapy.

RMAT designation does not change the standards for product approval, and there is no assurance that any such designation or eligibility will result in expedited review or approval or that the approved indication will not be narrower than the indication covered by the RMAT designation. Additionally, RMAT designation can be revoked if the criteria for eligibility cease to be met as clinical data emerges.

We may never obtain FDA approval for any of our product candidates in the United States, and even if we do, we may never obtain approval for or commercialize any of our product candidates in any other jurisdiction, which would limit our ability to realize their full market potential.

In addition to regulations in the United States, to market and sell our product candidates in the European Union, many Asian countries and other jurisdictions, we must obtain separate regulatory approvals and comply with numerous and varying regulatory requirements, both from a clinical and manufacturing perspective. The approval procedure varies among countries

and can involve additional testing and validation and additional administrative review periods. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. Clinical trials accepted in one country may not be accepted by regulatory authorities in other countries. In addition, many countries outside the United States require that a product be approved for reimbursement before it can be approved for sale in that country. A product candidate that has been approved for sale in a particular country may not receive reimbursement approval in that country. We may not be able to obtain approvals from regulatory authorities or payor authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory or payor authorities in other countries or jurisdictions, and approval by one regulatory or payor authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our products in any market. If we are unable to obtain approval of any of our product candidates by regulatory or payor authorities in the European Union, Asia or elsewhere, the commercial prospects of that product candidate may be significantly diminished. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our products will be unrealized.

Even if our product candidates receive regulatory approval, we will still face extensive ongoing regulatory requirements and continued regulatory review, which may result in significant additional expense, and our products may still face future development and regulatory difficulties.

Even if we obtain regulatory approval for a product candidate, it would be subject to ongoing requirements by the FDA and comparable foreign regulatory authorities governing the manufacture, quality control, further development, labeling, packaging, storage, distribution, adverse event reporting, safety surveillance, import, export, advertising, promotion, recordkeeping and reporting of safety and other post-marketing information. These requirements include submissions of safety and other post-marketing information and reports, establishment registration and product listing, as well as continued compliance by us and/or any future contract manufacturing organizations ("CMOs") and CROs for any post-approval clinical trials that we conduct. The safety profile of any product will continue to be closely monitored by the FDA and comparable foreign regulatory authorities after approval. If the FDA or comparable foreign regulatory authorities become aware of new safety information after approval of any of our product candidates, they may require labeling changes or establishment of a REMS, impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance.

In addition, manufacturers of cell therapies and their facilities are subject to initial and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with current good manufacturing practices ("cGMP"), Good Clinical Practices ("GCP"), current good tissue practices ("cGTP"), and other regulations. For certain commercial prescription and biologic products, manufacturers and other parties involved in the supply chain must also meet chain of distribution requirements and build electronic, interoperable systems for product tracking and tracing and for notifying the FDA of counterfeit, diverted, stolen and intentionally adulterated products or other products that are otherwise unfit for distribution in the United States. If we or a regulatory agency discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. If we, our product candidates or the manufacturing facilities for our product candidates fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters or untitled letters;
- mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners, or require other restrictions on the labeling or marketing of such products;
- require us to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- seek an injunction or impose civil or criminal penalties or monetary fines;

- suspend, withdraw or modify regulatory approval;
- suspend or modify any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications filed by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of products, or require us to initiate a product recall.

The occurrence of any event or penalty described above may inhibit our ability to successfully commercialize our products.

Advertising and promotion of any product candidate that obtains approval in the United States will be heavily scrutinized by the FDA, the U.S. Federal Trade Commission, the Department of Justice ("DOJ"), the Office of Inspector General ("OIG") of the U.S. Department of Health and Human Services ("HHS"), state attorneys general, members of the U.S. Congress and the public. Additionally, advertising and promotion of any product candidate that obtains approval outside of the United States will be heavily scrutinized by comparable foreign entities and stakeholders. Violations, including actual or alleged promotion of our products for unapproved or off-label uses, are subject to enforcement letters, inquiries and investigations, and civil and criminal sanctions by the FDA or comparable foreign bodies. Any actual or alleged failure to comply with labeling and promotion requirements may result in fines, warning letters, mandates to corrective information to healthcare practitioners, injunctions, or civil or criminal penalties.

The FDA and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of any current or future product candidate. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or to the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained. Non-compliance by us or any future collaborator with regulatory requirements, including safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population can also result in significant financial penalties.

Risks Related to Healthcare Legislation

Our relationships with customers, third-party payors, physicians and healthcare providers will be subject to applicable anti-kickback, fraud and abuse, and other laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, and diminished profits.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain regulatory approval. Physicians, hospitals and third-party payors are often slow to adopt new products, technologies and treatment practices that require additional upfront costs and training. Additionally, third-party payors may not cover, or provide adequate reimbursement for, long-term follow-up evaluations required following the use of our products. Patients are unlikely to use our product candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our product candidates. Because our product candidates have a higher cost of goods than conventional therapies, and may require long-term follow-up evaluations, the risk that coverage and reimbursement rates may be inadequate for us to achieve profitability may be greater. Based on these and other factors, hospitals, physicians and payors may decide that the benefits of this new therapy do not or will not outweigh its costs. Our current and future arrangements with third-party payors and customers may expose us to broadly applicable federal and varied state fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we conduct research as well as market, sell and distribute our products. As a pharmaceutical company, even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are, and will be, applicable to our business. Restrictions under applicable federal and state healthcare laws and regulations that may affect our ability to operate include, but are not limited to, the following:

- the federal healthcare Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving, paying or providing remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order, arrangement, or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under a federal healthcare program such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act or federal civil monetary penalties. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand, and prescribers, purchasers and formulary managers, among others, on the other;

- federal civil and criminal false claims laws, including the False Claims Act, and the civil monetary penalties law, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, false or fraudulent claims for payment to, or approval by, Medicare, Medicaid, or other federal healthcare programs, knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government, or knowingly concealing or knowingly and improperly avoiding or decreasing or concealing an obligation to pay money to the federal government. Manufacturers can be held liable under the False Claims Act even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act. The False Claims Act also permits a private individual acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the False Claims Act and to share in any monetary recovery;

- the federal beneficiary inducement statute, includes, without limitation, any transfer of items or services for free or for less than fair market value (with limited exceptions), to a Medicare or Medicaid beneficiary that the person knows or should know is likely to influence the beneficiary’s selection of a particular supplier of items or services reimbursable by a federal or state governmental program;

- the federal Health Insurance Portability and Accountability Act of 1996 (“HIPAA”) which created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious, or fraudulent statements in connection with the delivery of or payment for healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (“HITECH”) and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates, independent contractors or agents of covered entities, that perform services for them that involve the creation, maintenance, receipt, use, or disclosure of, individually identifiable health information as well as their covered subcontractors relating to the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys’ fees and costs associated with pursuing federal civil actions. In addition, there may be additional federal, state and non-U.S. laws which govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;

- the federal transparency requirements under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the "ACA"), including the provision commonly referred to as the Physician Payments Sunshine Act, and its implementing regulations, which requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the Centers for Medicare & Medicaid Services ("CMS") information related to payments or other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. As of January 1, 2022, these reporting obligations now extend to include transfers of value by manufacturers that are made to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives during the previous year;

- federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs;

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and

- analogous state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers or patients; state laws that require pharmaceutical companies to comply with the industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state and local laws that require the licensure of sales representatives; and state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and pricing information. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America's Code on Interactions with Healthcare Professionals.

In addition to the above, on November 20, 2020, OIG finalized further modifications to the federal Anti-Kickback Statute. Under the final rules, OIG added safe harbor protections under the Anti-Kickback Statute for certain coordinated care and value-based arrangements among clinicians, providers, and others. These rules (with exceptions) were scheduled to become effective January 19, 2021, but their effective date has been delayed by the Biden administration until January 1, 2026. We continue to evaluate what effect, if any, these rules will have on our business.

Efforts to ensure that our current and future business arrangements with third parties, and our business generally, continue to comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with any such laws and regulations. If our operations, including our arrangements with physicians and other healthcare providers, are found to be in violation of any such laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, reputational harm, exclusion from government-funded healthcare programs, such as Medicare and Medicaid, disgorgement, additional reporting requirements, and/or the curtailment or restructuring of our operations, as well as additional reporting obligations oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws. If any physicians or other healthcare providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to similar penalties.

Risks Related to Privacy and Data Security Laws

We are subject to stringent and changing privacy and data security laws, contractual obligations, self-regulatory schemes, government regulation, and standards related to data privacy and security. The actual or perceived failure by us, our

collaborators, vendors or other relevant third parties to comply with such obligations could harm our reputation, subject us to significant fines and liability, or otherwise adversely affect our business, operations and financial performance.

We collect, receive, store, process, use, generate, transfer, disclose, make accessible, protect and share personal information and other information, including information we collect about patients and healthcare providers in connection with clinical trials.

There are numerous federal, state, local and international laws, regulations and guidance regarding privacy, information security and processing, the number and scope of which is changing, subject to differing applications and interpretations, and which may be inconsistent among jurisdictions, or in conflict with other rules, laws or data protection obligations. Data protection laws and data protection worldwide is, and is likely to remain, uncertain for the foreseeable future, and our failure or perceived failure to address or comply with these laws could: increase our compliance and operational costs; expose us to regulatory scrutiny, actions, fines and penalties; result in reputational harm; lead to a loss of customers; reduce the use of our products; result in litigation and liability; and otherwise result in other material harm to our business.

For example, in the United States, HIPAA, as amended by HITECH, imposes privacy, security and breach reporting obligations with respect to individually identifiable health information upon “covered entities” (health plans, health care clearinghouses and certain health care providers), and their respective business associates, individuals or entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity, as well as their covered subcontractors. HIPAA mandates the reporting of certain breaches of health information to HHS, affected individuals and, if the breach is large enough, the media. Entities that are found to be in violation of HIPAA as the result of a breach of unsecured protected health information, a complaint about privacy practices or an audit by HHS, may be subject to significant civil, criminal and administrative fines and penalties and/or additional reporting and oversight obligations if required to enter into a resolution agreement and corrective action plan with HHS to settle allegations of HIPAA non-compliance. Even when HIPAA does not apply, according to the Federal Trade Commission (“FTC”), failing to take appropriate steps to keep consumers’ personal information secure constitutes unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act (“FTCA”), 15 U.S.C. § 45(a). The FTC expects a company’s data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards. The FTC’s guidance for appropriately securing consumers’ personal information is similar to what is required by the HIPAA security regulations.

Additionally, U.S. States have begun introducing privacy legislation. For example, California recently enacted the California Consumer Privacy Act (“CCPA”), which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA, which went into effect on January 1, 2020, will require covered companies to provide certain disclosures to consumers about its data collection, use and sharing practices, and to provide affected California residents with ways to opt-out of certain sales or transfers of personal information. The CCPA also provides for civil penalties for violations, as well as a private right of action for data breaches that may increase our risk to data breach class action litigation. The CCPA will be expanded substantially on January 1, 2023, when the California Privacy Rights Act of 2020 (“CPRA”) becomes fully operative. The CPRA will, among other things, give California residents the ability to limit use of certain sensitive personal information, establish restrictions on the retention of personal information, expand the types of data breaches subject to the CCPA’s private right of action, and establish a new California Privacy Protection Agency to implement and enforce the new law. The CCPA and the CPRA could substantially impact our business.

Additionally, some observers have noted that the CCPA and CPRA could mark the beginning of a trend toward more stringent privacy legislation in the U.S., which could increase our potential liability and adversely affect our business. Already, in the United States, we have witnessed significant developments at the state level. For example, on March 2, 2021, Virginia enacted the Consumer Data Protection Act (the "CDPA") and, on July 8, 2021, Colorado's governor signed the Colorado Privacy Act ("CPA"), into law. The CDPA and the CPA will both become effective January 1, 2023. While the CDPA and CPA incorporate many similar concepts of the CCPA and CPRA, there are also several key differences in the scope, application, and enforcement of the law that will change the operational practices of regulated businesses. The new laws will, among other things, impact how regulated businesses collect and process personal sensitive data, conduct data protection assessments, transfer personal data to affiliates, and respond to consumer rights requests.

We may also be subject to additional privacy restrictions in various foreign jurisdiction around the world in which we operate or process personal information. The collection, use, storage, disclosure, transfer, or other processing of personal information regarding individuals in the European Economic Area (“EEA”), including personal health data, is subject to the General Data Protection Regulation 2016/679 (“GDPR”). The GDPR is wide-ranging and imposes numerous requirements on companies

that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR is a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities.

In addition, further to the UK's exit from the EU on January 31, 2020, the GDPR ceased to apply in the UK at the end of the transition period on December 31, 2020. However, as of January 1, 2021, the UK's European Union (Withdrawal) Act 2018 incorporated the GDPR (as it existed on December 31, 2020 but subject to certain UK specific amendments) into UK law, referred to as the UK GDPR. The UK GDPR and the UK Data Protection Act 2018 set out the UK's data protection regime, which is independent from but aligned to the EU's data protection regime. Non-compliance with the UK GDPR may result in monetary penalties of up to £17.5 million or 4% of worldwide revenue, whichever is higher. Complying with these laws, if enacted, would require significant resources and leave us vulnerable to possible fines and penalties if we are unable to comply.

In addition, GDPR prohibits the transfer of personal data from the EU to the U.S. and other countries in respect of which the European Commission or other relevant regulatory body has not issued a so-called “adequacy decision” (known as “third countries”), unless the parties to the transfer have implemented specific safeguards to protect the transferred personal data. One of the primary safeguards used for transfers of personal data to the U.S. was the EU-U.S. Privacy Shield framework administered by the U.S. Department of Commerce. However, certain recent EU court decisions cast doubt on the ability to use one of the primary alternatives to the EU-U.S. Privacy Shield, namely the European Commission’s Standard Contractual Clauses, to lawfully transfer personal data to the U.S. and other third countries. In addition, the European Commission has recently published new versions of the Standard Contractual Clauses, which must be used for all new transfers of personal data from the EEA to third countries (including the United States) starting in September 2021, and all existing transfers of personal data from the EU to third countries relying on the existing versions of the Standard Contractual Clauses must be replaced by December 2022. The implementation of the new Standard Contractual Clauses will necessitate significant contractual overhaul of our data transfer arrangements with customers, sub-processors and vendors. Use of both the existing and the new Standard Contractual Clauses must now be assessed on a case-by-case basis taking into account the legal regime applicable in the destination country, in particular applicable surveillance laws and rights of individuals, and additional supplementary technical, organizational and/or contractual measures and/or contractual provisions may need to be put in place.

At present, there are few if any viable alternatives to the Standard Contractual Clauses, and there remains some uncertainty with respect to the nature and efficacy of such supplementary measures in ensuring an adequate level of protection of personal data. As supervisory authorities issue further guidance on personal data export mechanisms (including circumstances where the Standard Contractual Clauses can and cannot be used) and/or start taking enforcement action, we could suffer additional costs, complaints and/or regulatory investigations or fines. In addition, if we are unable to transfer personal data between and among countries and regions in which we operate and/or engage providers and/or otherwise transfer personal data, this could affect the manner in which we receive and/or provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results and generally increase compliance risk as a result. Additionally, other countries outside of Europe have enacted or are considering enacting similar cross-border data transfer restrictions and laws requiring local data residency, which could increase the cost and complexity of operating our business.

Furthermore, following Brexit, the relationship between the U.K. and the EEA in relation to certain aspects of data protection law remains somewhat uncertain. In June 2021, the European Commission issued an adequacy decision under the GDPR which allows transfers (other than those carried out for the purposes of U.K. immigration control) of personal data from the EEA to the U.K. to continue without restriction for a period of four years. After that period, the adequacy decision may be renewed only if the U.K. continues to ensure an adequate level of data protection. During these four years, the European Commission will continue to monitor the legal situation in the U.K. and could intervene at any point if the U.K. deviates from the level of data protection in place at the time of issuance of the adequacy decision. If the adequacy decision is withdrawn or not renewed, transfers of personal data from the EEA to the U.K. will require a valid “transfer mechanism” and we may be required to implement new processes and put new agreements in place, such as Standard Contractual Clauses, to enable transfers of personal data from the EEA to the U.K. to continue, which could disrupt our operations.

In addition, while the U.K. data protection regime currently permits data transfers from the U.K. to the EEA and other third countries covered by a European Commission adequacy decision, and currently includes a framework to permit the continued use of the existing version of the Standard Contractual Clauses for personal data transfers from the U.K. to third countries, this is subject to change in the future, and any such changes could have implications for our transfers of personal data from the U.K. to the EEA and other third countries. In particular, the U.K. Information Commissioner's Office has stated that it is working on its own bespoke version of the Standard Contractual Clauses and it is not clear whether the new Standard Contractual Clauses published by the European Commission will be accepted as a valid mechanism to permit the transfer of personal data from the U.K. to third countries and/or whether any U.K. version of the Standard Contractual Clauses will supersede the existing and/or new EU version of the Standard Contractual Clauses. This could necessitate the implementation of both U.K. and EU versions of Standard Contractual Clauses, which would require significant resources and result in significant cost to implement and manage.

We are also subject to the terms of our external and internal privacy and security policies, representations, certifications, standards, publications and frameworks, and contractual obligations to third parties related to privacy, information security and processing.

With applicable data protection laws, privacy policies and data protection obligations imposing complex and burdensome obligations, and with substantial uncertainty over the interpretation and application of these requirements, we have faced and may face additional challenges in addressing and complying with them, and making necessary changes to our privacy policies and practices, and may incur material costs and expenses in an effort to do so, any of which could materially adversely affect our business operations and financial results, and may reduce the overall demand for our products.

We strive to comply with applicable data protection laws, privacy policies and data protection obligations to the extent possible, but we may at times fail to do so, or may be perceived to have failed to do so. Moreover, despite our efforts, we may not be successful in achieving compliance if our personnel, collaborators or vendors do not comply with applicable data protection laws, privacy policies and data protection obligations. Any failure or perceived failure by us or our collaborators, service providers and contractors to comply with federal or foreign laws or regulation, our internal policies and procedures, representations or our contracts governing the processing of personal data could result in negative publicity, disruptions or interruptions in our operations, fines, penalties, lawsuits, liability, inability to process personal data, diversion of time and effort, proceedings against us by governmental entities, or other adverse effects to our business.

Risks Related to Our Dependence on Third Parties

We are dependent on a limited number of suppliers and, in some cases sole suppliers, for some of our components and materials used in our product candidates.

Our manufacturing process, like that of a number of other cell therapy companies, is characterized by limited numbers of suppliers, and in some cases sole source suppliers, with the manufacturing capabilities and know-how to create or source the reagents, materials and equipment necessary for the production of our product candidates. For example, like many other cell therapy companies, our manufacturing process for FCR001 depends on certain cell manipulation equipment and related reagents, all of which are available from Miltenyi Biotec, or "Miltenyi," as the sole supplier.

We cannot be sure that our suppliers will remain in business, or that they will not be purchased by one of our competitors or another company that decides not to continue producing these materials for us. Additionally, since the beginning of the COVID-19 pandemic, three vaccines for COVID-19 have received Emergency Use Authorization by the FDA and two of those later received marketing approval. Additional vaccines may be authorized or approved in the future. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or reagents for our current and any future product candidates for our clinical trials or for commercial production, if approved, which could lead to delays in these trials or issues with our commercial supply. Our use of a sole or a limited number of suppliers of raw materials, components and finished goods exposes us to several risks, including disruptions in supply, price increases, late deliveries and an inability to meet customer demand. While we try to mitigate these risks by purchasing excess supplies, some of these components, such as reagents, typically expire after approximately four to six months. This short expiration period means that stocking the reagents in large quantities for future needs would not be an effective strategy to mitigate against the risk of shortage due to disruption of the supply chain or termination of our business relationship. We also pursue multiple sources for the critical components of our manufacturing process, but there are, in general, relatively few alternative sources of supply for these components and we may not be successful in securing these additional sources at all or on a timely basis. These vendors may be unable or unwilling to meet our future demands for our clinical trials or commercial sale. If we are able to find a replacement supplier, the

replacement supplier would need to be qualified and may require additional regulatory authority approval, which could result in further delay. For example, the FDA or EMA could require additional supplemental data, manufacturing data and comparability data up to and including clinical trial data if we rely upon a new supplier. Any disruption in supply from any supplier or manufacturing location, including as a result of or impact from the COVID-19 pandemic, could lead to supply delays or interruptions which would damage our business, financial condition, results of operations and prospects. If we are required to switch to a replacement supplier, the manufacture and delivery of our product candidates could be interrupted for an extended period, adversely affecting our business. Establishing additional or replacement suppliers may not be accomplished quickly. While we seek to maintain adequate inventory of the components and materials used in our product candidates, any interruption or delay in the supply of components or materials, or our inability to obtain components or materials from alternate sources at acceptable prices in a timely manner, could impair our ability to conduct our clinical trials and, if our product candidates are approved, to meet the demand of our customers and cause them to cancel orders.

In addition, as part of the FDA's approval of our product candidates, the FDA must review and approve the individual components of our production process, which includes raw materials, the manufacturing processes and facilities of our suppliers and CMOs. Some of our current suppliers may not have undergone this process, and may not have had any components included in any product approved by the FDA.

Our reliance on external suppliers subjects us to a number of risks that could harm our reputation, business, and financial condition, including, among other things:

- the interruption of supply resulting from modifications to or discontinuation of a supplier's operations;
- delays in product shipments resulting from uncorrected defects, reliability issues, or a supplier's variation in a component;
- a lack of long-term commercial supply arrangements for key components with our suppliers;
- the inability to obtain adequate supply in a timely manner, or to obtain adequate supply on commercially reasonable terms;
- difficulty and cost associated with locating and qualifying alternative suppliers for our components in a timely manner;
- production delays related to the evaluation and testing of products from alternative suppliers, and corresponding regulatory qualifications;
- a delay in delivery due to our suppliers prioritizing other customer orders over ours; and
- fluctuation in delivery by our suppliers due to changes in demand from us or their other customers.

If any of these risks materialize, costs could significantly increase and our ability to conduct our clinical trials and, if our product candidates are approved, to meet demand for our products could be impacted. Some of these events could be the basis for FDA or other regulatory authority action, including injunction, recall, seizure, or total or partial suspension of production of our product candidates.

We rely on third parties to conduct our clinical trials and perform some of our research and preclinical studies. If these third parties do not satisfactorily carry out their contractual duties or fail to meet expected deadlines, our development programs may be delayed or subject to increased costs, each of which may have an adverse effect on our business and prospects.

We do not have the ability to conduct all aspects of our clinical trials ourselves. As a result, we are, and expect to remain, dependent on third parties to conduct our ongoing clinical trials and any future clinical trials of our product candidates, including but not limited to governmental agencies and university laboratories, CMOs, CROs, distribution and supply

(logistics) services organizations, contract testing organizations ("CTOs"), consultants or consultant organization with specialized knowledge-based expertise. The timing of the initiation and completion of these trials will therefore be partially controlled by such third parties and may result in delays to our development programs. Specifically, we expect CROs, clinical investigators, and consultants to play a significant role in the conduct of these trials and the subsequent collection and analysis of data. However, we will not be able to control all aspects of their activities. Nevertheless, we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on the CROs, CTOs, and other third parties does not relieve us of our regulatory responsibilities. For example, we rely on a single third-party investigator to provide ongoing data from our Phase 2 clinical trial. We, our CROs and clinical sites are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for all of our current product candidates and any future product candidates in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, clinical trial investigators and clinical trial sites. If we or any of our CROs, and in particular, our single third-party investigator for our Phase 2 company-sponsored trial, or clinical trial sites fail to adhere to our clinical trial protocols or to comply with applicable GCP requirements, the data generated in our clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to stop and/or repeat clinical trials, which would delay the marketing approval process. Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the trial. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of our product candidates.

There is no guarantee that any such CROs, clinical trial investigators or other third parties on which we rely will devote adequate time and resources to our development activities or perform as contractually required. Further, the performance of our CROs has been, and may again in the future be interrupted by the ongoing COVID-19 pandemic, including due to travel or quarantine policies, heightened exposure of CRO staff who are healthcare providers to COVID-19 or prioritization of resources toward the pandemic. If any of these third parties fail to meet expected deadlines, adhere to our clinical protocols or meet regulatory requirements, otherwise performs in a substandard manner, or terminates its engagement with us, the timelines for our development programs may be extended or delayed or our development activities may be suspended or terminated. If any of our clinical trial sites terminates for any reason, we may experience the loss of follow-up information on subjects enrolled in such clinical trials unless we are able to transfer those subjects to another qualified clinical trial site, which may be difficult or impossible. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA or comparable foreign regulatory authorities concludes that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any marketing application we submit by the FDA or any comparable foreign regulatory authority. Any such delay or rejection could prevent us from commercializing our current product candidates and any future product candidates.

We may not realize the benefits of strategic alliances that we may form in the future or of potential future product acquisitions or licenses.

We may desire to form strategic alliances, create joint ventures or collaborations, enter into licensing arrangements with third parties or acquire products or businesses, in each case that we believe will complement or augment our existing business. These relationships or transactions, or those like them, may require us to incur nonrecurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders, reduce the potential profitability of the products that are the subject of the relationship or disrupt our management and business. In addition, we face significant competition in seeking appropriate strategic alliances and transactions and the negotiation process is time-consuming and complex and there can be no assurance that we can enter into any of these transactions even if we desire to do so. Moreover, we may not be successful in our efforts to establish a strategic alliance or other alternative arrangements for any future product candidates and programs because our research and development pipeline may be insufficient, our product candidates and programs may be deemed to be at too early a stage of development for collaborative effort and third parties may not view our product candidates and programs as having the requisite potential to demonstrate a positive risk profile. Any delays in entering into new strategic alliances agreements related to our product candidates could also delay the development and commercialization of our product candidates and reduce their competitiveness even if they reach the market.

If we license products or acquire businesses, we may not be able to realize the benefit of these transactions if we are unable to successfully integrate them with our existing operations and company culture. We cannot be certain that, following an acquisition or license, we will achieve the financial or strategic results that would justify the transaction.

Risks Related to Manufacturing

Risks Related to our Manufacturing Facility

We currently operate our own manufacturing facility and intend to scale-up our manufacturing and processing approaches to appropriately address our anticipated commercial needs for FCR001, which will require significant resources. We may fail to successfully operate our facility, which could adversely affect our clinical trials and the commercial viability of our product candidates.

We operate our own dedicated cGMP cell processing facility, located on the campus of the University of Louisville, where we manufacture our product candidates for our current and planned clinical trials. Although we are currently operating our manufacturing facility, our operations remain subject to review and oversight by the FDA, and the FDA could object to our use of our manufacturing facility or the processes used therein.

We have begun to scale-up our manufacturing and processing approaches to appropriately address our anticipated commercial needs for FCR001 for LDKT. In order to scale-up our manufacturing capabilities and facility, we will require substantial additional funds and will need to hire and retain significant additional personnel and comply with extensive cGMP regulations applicable to a commercial facility. If we fail to complete any construction in an efficient manner, recruit the required personnel and generally manage our growth effectively, the development and production of our product candidates could be curtailed or delayed. Our manufacturing facility would also need to be licensed for the production of our product candidates by the FDA. Even if our manufacturing facility is approved by the FDA, we would be subject to ongoing periodic unannounced inspection by the FDA, corresponding state agencies and potentially third party collaborators to ensure strict compliance with cGMPs and other government regulations. Our license to manufacture product candidates will be subject to continued regulatory review.

We expect to use the same manufacturing process and starting material for future programs as those that we have used in our Phase 2 and Phase 3 trials of FCR001 for LDKT, except that our starting materials and process may be different for programs where we derive our component cells from a deceased donor. However, our use of this manufacturing process in our Phase 2 and Phase 3 trials may not be successfully replicated in subsequent trials, which could adversely affect our ability to scale-up our manufacturing processes or obtain or maintain the requisite licenses and approvals from the FDA to commercialize our product candidates.

We believe that our manufacturing processes can be scaled-up to address our commercial needs. However, there can be no assurance that we will not encounter difficulties in scaling out our manufacturing processes. Significant scale-up of manufacturing may result in unanticipated technical challenges and may require additional FDA approvals. We may encounter difficulties in scaling out production, including problems involving raw material suppliers, production yields, technical difficulties, scaled-up product characteristics, quality control and assurance, shortage of qualified personnel, capacity constraints, compliance with FDA and foreign regulations, environmental compliance, production costs and development of advanced manufacturing techniques and process controls. The actual cost to manufacture and process our product candidates could also be greater than we expect and could materially and adversely affect the commercial viability of our product candidates. Any of these difficulties, if they occur and are not overcome to the satisfaction of the FDA or other regulatory agency, could lead to significant delays and possibly the termination of the development program for such product candidate. These risks become more acute as we scale-up for commercial quantities, where a reliable source of product becomes critical to commercial success. The commercial viability of any of our product candidates, if approved, will depend on our ability to produce our personalized cell therapy at a large scale. Failure to achieve this level of supply could jeopardize the successful commercialization of our therapy.

The manufacture of a cell therapy is complex and requires significant expertise, including the development of advanced manufacturing techniques and process controls. Manufacturers of cell therapy products often encounter difficulties in production, particularly in scaling out and validating initial production and ensuring the absence of contamination. These problems include difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, operator error, shortages of qualified personnel, shortages of raw materials, as well as compliance with strictly enforced federal, state and foreign regulations. For example, in late 2021, we were required to undertake an additional apheresis of a donor when quality testing revealed that the product prepared from that donor’s stem cells was contaminated. While there can be no assurance at what point the donor blood product was contaminated, whether at the point of apheresis or

during the manufacturing process, we nonetheless have reviewed and enhanced our quality control procedures and believe the risk of future contamination to be low. Furthermore, if contaminants are discovered in our cell therapy or in the manufacturing facilities, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. We cannot ensure that any stability or other issues relating to the manufacture of our product candidates will not occur in the future.

We may fail to manage the logistics of collecting and shipping donor cell material to the manufacturing site and shipping the product candidate to the patient. Logistical and shipment delays and problems caused by us, our vendors or other factors not in our control, such as weather, could cause breakage or contamination of our products and prevent or delay the delivery of product candidates to patients. Additionally, we have to maintain a complex chain of identity and chain of custody with respect to donor material as it moves to the manufacturing facility, through the manufacturing process, and to the recipient. Failure to maintain chain of identity and chain of custody could result in patient death, loss of product or regulatory action.

Though our supply chain has not been materially impacted by the COVID-19 pandemic to date, our manufacturing capabilities could be affected by cost-overruns, resource constraints, unexpected delays, equipment failures, labor shortages or disputes, natural disasters, power failures and numerous other factors that could prevent us from realizing the intended benefits of our manufacturing strategy, jeopardize our ability to provide our product candidates to patients, and have a material adverse effect on our business, financial condition, results of operations and prospects. For example, since the beginning of the COVID-19 pandemic, three vaccines for COVID-19 have received Emergency Use Authorization by the FDA and two of those later received marketing approval. Additional vaccines may be authorized or approved in the future. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing supplies for, or timely manufacture, the products needed for our clinical trials, which could lead to delays in these trials.

If our manufacturing facility is damaged or destroyed or production at our manufacturing facility is otherwise interrupted, our business would be negatively affected.

Damage to our manufacturing facility or disruption to our operations for any reason, including due to natural disaster (such as earthquake, wildfires and other fires or extreme weather), power loss, communications failure, cyberattack, unauthorized entry or other events, such as a flu or other health epidemic (such as the COVID-19 pandemic, including any current and future variants), could affect our manufacturing processes.

In particular, our manufacturing facility, located on the Health Science Center campus of the University of Louisville, supplies all of our clinical needs, and any damage or disruption to that facility could cause a loss of products or materials or otherwise adversely affect our ability to manufacture our current and any future product candidates in support of our clinical trials. It may require substantial lead time to repair, and we may not have control over such repairs. The property damage and business interruption insurance coverage on our facility that we maintain might not cover all losses under such circumstances, and we may not be able to renew or obtain such insurance in the future on acceptable terms with adequate coverage or at reasonable costs.

Any damage or disruption to the University of Louisville's operations, including the foregoing events, may also adversely affect our business. For example, disruption to any of the utilities provided to our facility by University of Louisville (HVAC, electrical, water, etc.) could inhibit or prevent us from being able to manufacture our product candidates. Moreover, if we are unable to obtain key inputs used in our manufacturing process, disinfectants or other materials required to maintain "clean room" sterility in our manufacturing facility, we may be unable to manufacture products entirely. Any failure of our building systems could also adversely affect our operations, including but not limited to equipment malfunctions, failure to follow specific protocols and procedures, and issues relating to air handling and other utilities. Any significant disruption to our manufacturing facility or processes would likely have an adverse impact on our business.

Any adverse developments affecting manufacturing operations for our current and any future product candidates may result in lot failures, inventory shortages, shipment delays, product losses or other interruptions in the supply of our product candidates for an undetermined period of time. We may also have to write off raw material and drug product inventory, incur other charges and expenses for key manufacturing inputs that fail to meet specifications, undertake costly remediation efforts, or seek more costly manufacturing alternatives. Inability to meet the clinical demand for our product candidates could damage our reputation and the reputation of our products among physicians, healthcare payors, patients or the medical community that supports our product development efforts, including hospitals and outpatient clinics.

Our manufacturing process needs to comply with regulations relating to the quality and reliability of such processes. Any failure to comply with relevant regulations could result in delays in or termination of our clinical programs and suspension or withdrawal of any regulatory approvals. Further, as our preclinical and clinical programs and the manufacture of our product candidates are dependent on human donor material, we are or could be subject to additional regulations and requirements.

The FDA, EMA and comparable foreign regulatory authorities require that our product candidates and any products that we may eventually commercialize be manufactured according to cGMP, cGTP and similar jurisdictional standards. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation. The FDA and comparable foreign regulatory agencies may also implement new standards at any time, or change their interpretations and enforcement of existing standards, including for the manufacture, packaging or testing of biological products.

We may encounter difficulties in achieving quality control and quality assurance or meeting regulatory expectations. Our facilities are subject to inspections by the FDA and comparable foreign regulatory authorities to confirm compliance with applicable regulatory requirements. Any failure to follow cGMP, cGTP or other regulatory requirements or delay, interruption or other issues that arise in the manufacture, packaging, or storage of our product candidates as a result of our failure to comply with regulatory requirements or pass any regulatory authority inspection could significantly impair our ability to develop and commercialize our product candidates, including leading to significant delays in the availability of our product candidates for our clinical trials or the termination of or suspension of a clinical trial, or the delay or prevention of a filing or approval of marketing applications for our product candidates. Significant non-compliance could also result in the imposition of sanctions, including warning or untitled letters, fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could damage our reputation and our business.

In addition, our clinical programs and the manufacture of our product candidates are dependent on human donor material. Procurement of certain human organs for transplantation is subject to the National Organ Transplant Act of 1984 (“NOTA”), which prohibits the acquisition, receipt, or transfer of any human organ for valuable consideration for use in human transplantation. We depend on third parties who arrange for living donor kidney transplants to comply with applicable NOTA requirements and we do not know whether any failure by such third parties to comply with NOTA requirements could impact the integrity or usability of data in our clinical trials.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers’ compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials with a policy limit that we believe is customary for similarly situated companies and adequate to provide us with insurance coverage for foreseeable risks, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological or hazardous materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions, which could adversely affect our business, financial condition, results of operations and prospects.

The process for treatment using cell therapies is subject to human and systemic risks.

The “vein-to-vein” cycle for treating patients using our Facilitated Allo-HSCT Therapeutic Approach and other cell-based targeted therapies typically takes approximately four to twelve weeks and involves a large number of steps, as well as human

participants. In the United States, samples of the final product are subjected to several release tests which must fulfill specified criteria for the drug product to be released for infusion. These include sterility, identity, purity, potency and other tests. We are subject to stringent regulatory and quality standards in the course of our cell therapy treatment process. We cannot assure you that our quality control and assurance efforts will be successful or that the risk of human or systemic errors in these processes can be eliminated. Our cell therapies are uniquely manufactured for each recipient, so they must be administered only to the recipient matched to the donor from which the cellular source material was collected. While we implement specific identifiers, lot numbers and labels with cross checks for our products and operations from collection of cellular source material, through manufacture of drug product, transport of product to the clinical site up to thawing and administration of the product, it is possible that a product may be administered into the wrong patient. If our cell therapies were to be administered into the wrong recipient, the recipient could suffer harm, including experiencing a severe adverse immune reaction and this event, should it happen, could adversely affect our business, financial condition, results of operations and prospects.

Risks Related to the Manufacturing of our Product Candidates

Our product candidates are uniquely manufactured for each patient and we may encounter difficulties in production, particularly with respect to scaling our manufacturing capabilities.

The manufacturing process used to produce our product candidates is novel and has not been validated for commercial production. Our product candidates comprise a composition of hematopoietic stem cells ("HSCs"), facilitating cells ("FCs") and Alpha Beta T-cell Receptor Cells ("αßTCR+ T cells"), the dose of each of which is tailored to the recipient using our proprietary manufacturing process. Due to the personalized nature of the product candidate, we expect the cost to manufacture our product candidates to be high.

Although we have qualified and obtained positive initial FDA feedback on our potency assays for each of our active cell components in FCR001, we must validate the potency assays prior to submission of a marketing application for FCR001. Potency assays have traditionally proven difficult to develop for cell-based products and must be validated prior to approval. There can be no assurance that we will be able to validate our potency assays to FDA's satisfaction, or that FDA will not want us to develop different or alternative potency assays for FCR001 or other product candidates. Any such development could delay or prevent approval of FCR001 or our other product candidates.

There is a risk of manufacturing issues associated with the differences in donor starting materials, interruptions in the manufacturing process, contamination, equipment or reagent failure, improper installation or operation of equipment, vendor or operator error, and variability in product characteristics. Even minor deviations from our normal manufacturing processes could result in reduced production yields, lot failures, product defects, product delays, product recalls, product liability claims and other supply disruptions. If for any reason we lose a donor's starting material or one of our custom-manufactured products at any point in the process, the manufacturing process for that recipient will need to be restarted and the resulting delay may adversely affect that recipient's outcome. Because our product candidate is manufactured for each particular patient, we will be required to maintain a chain of identity with respect to materials as they move from the donor to the manufacturing facility, through the manufacturing process and on to the patient. Further, as our product candidate is developed through preclinical to later-stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, are altered in an effort to optimize processes and results. If we make these types of changes, we may not achieve our intended objectives and any of these changes could cause our product candidates to perform differently than we expect, potentially affecting the results of clinical trials.

Although we continually attempt to optimize our manufacturing process, doing so is a difficult and uncertain task and there are risks associated with scaling to the level required for advanced clinical trials or commercialization, including, among others, cost overruns, potential problems with process scale-up, process reproducibility, stability issues, lot consistency and timely availability of reagents or raw materials. If we are unable to adequately validate or scale-up our manufacturing processes, we may encounter lengthy delays in commercializing our product candidates. We may continue to manufacture our product ourselves or we may ultimately decide to outsource our manufacturing to a third party CMO. We may not be successful in transferring our production system to such manufacturer, or the manufacturer(s) on whom we rely may not have the necessary capabilities to complete the implementation and development process. If we are able to adequately validate and scale-up the manufacturing processes for our product candidates with a contract manufacturer, we will still need to negotiate an agreement for commercial supply with that contract manufacturer and it is not certain we will be able to come to agreement on terms acceptable to us. As a result, we may ultimately be unable to reduce the cost of goods for our product candidates to levels that will allow for an attractive return on investment if and when those product candidates are approved and commercialized.

The manufacturing process for any products that we may develop is subject to the FDA and foreign regulatory authority approval processes and, if we choose to outsource our commercial production, we will need to contract with manufacturers who we believe can meet applicable FDA and foreign regulatory authority requirements on an ongoing basis. If we are unable to reliably produce our cell therapy candidate to specifications acceptable to the FDA or other regulatory authorities, we may not obtain or maintain the approvals we need to commercialize our products. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that either we or any CMOs we may contract with in the future will be able to manufacture the approved product to specifications and under cGMPs acceptable to the FDA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product, or to meet potential future demand. Any of these challenges could delay completion of clinical trials, require bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates, impair commercialization efforts, increase our cost of goods and have an adverse effect on our business, financial condition, results of operations and growth prospects.

Our future success depends on our ability to manufacture our products on a timely basis with acceptable manufacturing costs, while at the same time maintaining good quality control and complying with applicable regulatory requirements. Our inability to do so could have a material adverse effect on our business, financial condition, prospects and results of operations. In addition, we could incur higher manufacturing costs if manufacturing processes or standards change and we could need to replace, modify, design or build and install equipment, all of which would require additional capital expenditures.

In addition, the FDA, the EMA and other foreign regulatory authorities may require us to submit samples of any personalized product lot, together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA, the EMA or other foreign regulatory authorities may require that we not distribute a specific product lot until the relevant agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. Lot failures or product recalls could cause us to delay product launches or clinical trials, which could be costly to us and otherwise harm our business, financial condition, results of operations and prospects. Problems in our manufacturing process could restrict our ability to meet market demand for our products.

Any problems in our manufacturing process or facilities could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs.

Our product candidate requires specific shipping, storage, handling and administration at the clinical sites, including cold-chain logistics, which could subject our product candidates to risk of loss or damage.

Our product candidates are sensitive to temperature, storage and handling conditions. They must be stored at very low temperatures in specialized freezers or specialized shipping containers until immediately prior to use. For administration, the cryopreserved product container must be carefully removed from storage, and rapidly thawed under controlled temperature conditions in an area proximal to the patient's bedside and administered into the patient. The handling, thawing and administration of the cryopreserved therapy product must be performed according to specific instructions, typically using specific disposables, specific bags and in some steps within specific time periods. Failure to correctly handle our product, including the potential breakage of the cryopreservation bags or to follow the instructions for thawing and administration and or failure to administer our product within the specified period post-thaw could negatively impact the efficacy and or safety of our product, or cause a loss of product.

In addition, our product candidates must be cryopreserved/frozen using specialized equipment and following specific procedures in order to be stored without damage in a cost-efficient manner and without degradation. We may encounter difficulties in further optimization of freezing and thawing methodologies, and also in obtaining the necessary regulatory approvals for using such methodologies in treatment. If we cannot adequately demonstrate similarity of our frozen product to the unfrozen or thawed form to the satisfaction of the FDA, we could face substantial delays in our regulatory approvals. If we are unable to freeze FCR001 or other cell-based therapies we may develop for storage and shipping purposes, our ability to promote adoption and standardization of our products, as well as achieve economies of scale by centralizing production facilities, will be limited.

Even if we are able to successfully freeze and thaw FCR001 without damage in a cost-efficient manner and without degradation to the satisfaction of the FDA to support regulatory approval, we will still need to scale-up a cost-effective and reliable cold-chain distribution and logistics network, which we may be unable to accomplish. Failure to effectively scale-up our cold-chain supply logistics, by us or third parties, could in the future lead to additional manufacturing costs and delays in our ability to

supply required quantities for commercial supply. For these and other reasons, we may not be able to manufacture FCR001 or other cell-based therapies we may develop at commercial scale or in a cost-effective manner.

The process of manufacturing cell therapies is inherently susceptible to contamination. If microbial, viral or other contaminations are discovered in any product candidate or in our manufacturing facility, our manufacturing facility may need to be closed for an extended period of time to allow us to investigate and remedy the contamination. Because our cell therapy product candidates are manufactured from the cells of third-party donors, the process of manufacturing is susceptible to the availability of the third-party donor material. The process of developing products that can be commercialized may be particularly challenging, even if they otherwise prove to be safe and effective. The manufacture of these product candidates involves complex processes. Some of these processes require specialized equipment and highly skilled and trained personnel. The process of manufacturing these product candidates will be susceptible to additional risks, given the need to maintain aseptic conditions throughout the manufacturing process. Contamination with viruses or other pathogens in either the donor material or materials utilized in the manufacturing process or ingress of microbiological material at any point in the process may result in contaminated or unusable product. These types of contaminations could result in manufacturing delays which could result in delays in the development of our product candidates. These contaminations could also increase the risk of adverse side effects.

Risks Related to Our Intellectual Property

Risks Related to our Intellectual Property Licensed from ULRF

We depend substantially on intellectual property licensed from the ULRF, and termination of this license could result in the loss of significant rights, which would materially harm our business.

We depend substantially on the ULRF License for our intellectual property, data and know-how. The ULRF License, imposes, and we expect that future license agreements will impose, various development, diligence, commercialization and other obligations on us. This license may be terminated upon certain conditions. Any termination of this license could result in the loss of significant rights and could harm our ability to commercialize our product candidate. In the future, we may also enter into additional license agreements that are material to the development of our product candidates.

Disputes may also arise between us and our licensors regarding intellectual property subject to a license agreement, including those related to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our collaborators.

If disputes over intellectual property that we have licensed, or license in the future, prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. In addition, the resolution of any such disputes could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We may rely on third parties from whom we license proprietary technology to file and prosecute patent applications and maintain patents and otherwise protect the intellectual property we license from them. We may have limited control over these activities or any other intellectual property that may be related to our in-licensed intellectual property. For example, we cannot be certain that such activities by these licensors will be conducted in compliance with applicable laws and regulations or will

result in valid and enforceable patents and other intellectual property rights. We may have limited control over the manner in which our licensors initiate an infringement proceeding against a third-party infringer of the intellectual property rights, or defend certain of the intellectual property that may be licensed to us. It is possible that the licensors' infringement proceeding or defense activities may be less vigorous than if we conduct them ourselves.

We are generally also subject to all of the same risks with respect to protection of intellectual property that we license, as we are for intellectual property that we own, which are described below. If we or our licensors fail to adequately protect such licensed intellectual property, our ability to commercialize products could suffer.

Risks Related to our Intellectual Property Protection

If we are unable to obtain and maintain sufficient intellectual property protection for our product candidates and manufacturing process, or if the scope of the intellectual property protection is not sufficiently broad, our ability to commercialize our product candidates successfully and to compete effectively may be adversely affected.

We rely upon a combination of patents, trademarks, trade secrets and confidentiality agreements-both that we own or possess or that are owned or possessed by our collaborators that are in-licensed to us under licenses, including the ULRF License, to protect the intellectual property related to our technology and product candidates. When we refer to "our" technologies, inventions, patents, patent applications or other intellectual property rights, we are referring to both the rights that we own or possess as well as those that we in-license, many of which are critical to our intellectual property protection and our business. For example, our product candidates and Facilitating Allo-HSCT Therapy are protected by patents or patent applications of ULRF that we have licensed and as confidential know-how and trade secrets. Additionally, our earlier stage product candidates are not yet protected by any patents or patent applications. If the intellectual property that we rely on is not adequately protected, competitors may be able to use our technologies and erode or negate any competitive advantage we may have.

The patentability of inventions and the validity, enforceability and scope of patents in the biotechnology field is highly uncertain because it involves complex legal, scientific and factual considerations, and it has in recent years been the subject of significant litigation. Moreover, the standards applied by the U.S. Patent and Trademark Office ("USPTO") and non-U.S. patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology patents.

There is no assurance that all potentially relevant prior art relating to our patents and patent applications is known to us or has been found in the instances where searching was done. Further, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all. Thus, we may be unaware of prior art that could be used to invalidate an issued patent or prevent a pending patent application from issuing as a patent. There also may be prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim of one of our patents or patent applications, which may, nonetheless, ultimately be found to affect the validity or enforceability of such claim. As a consequence of these and other factors, our patent applications may fail to result in issued patents with claims that cover our product candidates in the United States or in other countries.

Even if patents have issued or do successfully issue from patent applications, and even if these patents cover our product candidates, third parties may challenge the validity, ownership, enforceability or scope thereof, which may result in these patents being narrowed, invalidated, circumvented, or held to be unenforceable. No assurance can be given that if challenged, our patents would be declared by a court to be valid or enforceable.

Even if unchallenged, our patents and patent applications or other intellectual property rights may not adequately protect our intellectual property, provide exclusivity for our product candidates or prevent others from designing around our claims. The possibility exists that others will develop products on an independent basis which have the same or similar effect as our product candidates and which do not infringe our patents or other intellectual property rights, or that others will design around the claims of patents that we have had issued that cover our product candidates. If the breadth or strength of protection provided by our patents and patent applications with respect to our product candidates is threatened, it could jeopardize our ability to commercialize our product candidates and dissuade companies from collaborating with us.

We may also desire to seek a license from a third party who owns intellectual property that may be necessary or useful for providing exclusivity for our product candidates, or for providing the ability to develop and commercialize a product candidate in an unrestricted manner. There is no guarantee that we will be able to obtain a license from such a third party on commercially reasonable terms, or at all.

Obtaining and enforcing biopharmaceutical patents is costly, time consuming and complex, and we may not be able to file and prosecute all necessary or desirable patent applications, or maintain, enforce and license any patents that may issue from such patent applications, at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. We may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain patents licensed from third parties. We may have limited control over the manner in which our licensors initiate an infringement proceeding against a third-party infringer of the intellectual property rights, or defend certain of the intellectual property that may be licensed to us. It is possible that the licensors' infringement proceeding or defense activities may be less vigorous than if we conduct them ourselves. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

We and our collaborators have filed a number of patent applications covering our product candidates or methods of using or making those product candidates. We cannot offer any assurances about which, if any, patents will be issued with respect to these pending patent applications, the breadth of any such patents that are ultimately issued or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. Because patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we or our collaborators were the first to file any patent application related to a product candidate. We or our collaborators may also become involved in proceedings regarding our patents, including patent infringement lawsuits, interference or derivation proceedings, oppositions, reexaminations, and *inter partes* and post-grant review proceedings before the USPTO, the European Patent Office and other non-U.S. patent offices.

Even if granted, patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent generally occurs 20 years after the earliest U.S. non-provisional application is filed. Although various extensions may be available if certain conditions are met, the life of a patent and the protection it affords is limited. If we encounter delays in our clinical trials or in obtaining regulatory approvals, the period of time during which we could exclusively market any of our product candidates under patent protection, if approved, could be reduced. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be vulnerable to competition from biosimilar products, as we may be unable to prevent competitors from entering the market with a product that is similar or identical to our product candidates.

In the United States, a patent that covers an FDA-approved drug or biologic may be eligible for a term extension designed to restore the period of the patent term that is lost during the premarket regulatory review process conducted by the FDA. Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 ("Hatch-Waxman Act"), which permits a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and only claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. In the European Union, our product candidates may be eligible for term extensions based on similar legislation. In either jurisdiction, however, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Even if we are granted such extension, the duration of such extension may be less than our request. If we are unable to obtain a patent term extension, or if the term of any such extension is less than our request, the period during which we can enforce our patent rights for that product will be in effect shortened and our competitors may obtain approval to market competing products sooner. The resulting reduction of years of revenue from applicable products could be substantial.

In addition, the United States federal government retains certain rights in inventions produced with its financial assistance under the Bayh-Dole Act. The federal government retains a "nonexclusive, nontransferable, irrevocable, paid-up license" for its own benefit. The Bayh-Dole Act also provides federal agencies with "march-in rights". March-in rights allow the government, in specified circumstances, to require the contractor or successors in title to the patent to grant a "nonexclusive, partially exclusive, or exclusive license" to a "responsible applicant or applicants." If the patent owner refuses to do so, the government may grant the license itself. Some of our licensed patents are subject to the provisions of the Bayh-Dole Act.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting, enforcing and defending patents on all of our product candidates in all countries throughout the world would be prohibitively expensive. Our intellectual property rights in certain countries outside the United States may be less extensive than those in the United States. In addition, the laws of certain foreign countries do not protect intellectual property

rights to the same extent as laws in the United States. Consequently, we and our future collaborators may not be able to prevent third parties from practicing our inventions in countries outside the United States, or from selling or importing infringing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection or where we do not have exclusive rights under the relevant patents to develop their own products and, further, may export otherwise-infringing products to territories where we and our collaborators have patent protection but where enforcement is not as strong as that in the United States. These infringing products may compete with our product candidates in jurisdictions where we or our future collaborators have no issued patents or where we do not have exclusive rights under the relevant patents, or our patent claims and other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us and our collaborators to stop the infringement of our patents or marketing of competing products in violation of our intellectual property rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us or our future collaborators. We or our future collaborators may not prevail in any lawsuits that we or our collaborators initiate, and even if we or our collaborators are successful, the damages or other remedies awarded, if any, may not be commercially meaningful.

In some jurisdictions, including European Union countries, compulsory licensing laws compel patent owners to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our future collaborators are forced to grant a license to third parties under patents relevant to our business, or if we or our future collaborators are prevented from enforcing patent rights against third parties, our competitive position may be substantially impaired in such jurisdictions.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we employ an outside firm and rely on our outside counsel to pay these fees due to non-U.S. patent agencies. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

If we are unable to protect the confidentiality of our trade secrets and other proprietary information, the value of our technology could be materially adversely affected and our business could be harmed.

In addition to seeking the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce, and other elements of our technology, discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, including by enabling them to develop and commercialize products substantially similar to or competitive with our product candidates, thus eroding our competitive position in the market.

Trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements and invention assignment agreements with our employees, consultants, and outside scientific advisors, contractors and collaborators. These agreements are designed to protect our proprietary information. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, collaborators, or outside scientific

advisors might intentionally or inadvertently disclose our trade secrets or confidential, proprietary information to our competitors. In addition, our competitors may otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. If any of our confidential proprietary information were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position.

Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, the laws of certain foreign countries do not protect proprietary rights such as trade secrets to the same extent or in the same manner as the laws of the United States. Misappropriation or unauthorized disclosure of our trade secrets to third parties could impair our competitive advantage in the market and could materially adversely affect our business, results of operations and financial condition.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential collaborators or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our unregistered trademarks or trade names. Over the long term, if we are unable to successfully register our trademarks and trade names and establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

Risks Related to Potential Third Party Claims

If we are sued for infringing the intellectual property rights of third parties, the resulting litigation could be costly and time-consuming and could prevent or delay our development and commercialization efforts.

Our commercial success depends, in part, on us and our future collaborators not infringing the patents and proprietary rights of third parties. However, our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. There is a substantial amount of litigation and other adversarial proceedings, both within and outside the United States, involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interference or derivation proceedings, oppositions, reexaminations, and *inter partes* and post-grant review proceedings before the USPTO and non-U.S. patent offices. Numerous U.S. and non-U.S. issued patents and pending patent applications owned by third parties exist in the fields in which we are developing and may develop our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of third parties' patent rights, as it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform or predictable. For example, we are aware of certain issued patents that may cover some of our product candidates, and while we believe these patent claims are not valid and would not establish a basis for our operations to be enjoined, we may be subject to litigation and be obligated to pay reasonable royalties to the patent owners. In addition, many companies in intellectual property-dependent industries, including the biotechnology and pharmaceutical industries, have employed intellectual property litigation as a means to gain an advantage over their competitors. Some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us.

Third parties may assert infringement claims against us based on existing or future intellectual property rights, alleging that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacturing of our product candidates that we failed to identify. For example, patent applications covering our product candidates could have been filed by others without our knowledge, since these applications generally remain confidential for some period of time after their filing date. Even pending patent applications that have been published, including some of which we are aware, could be

later amended in a manner that could cover our product candidates or their use or manufacture. After issuance, the scope of patent claims remains subject to construction as determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. In addition, we may have analyzed patents or patent applications of third parties that we believe are relevant to our activities and believe that we are free to operate in relation to any of our product candidates, but our competitors may obtain issued claims, including in patents we consider to be unrelated, which may block our efforts or potentially result in any of our product candidates or our activities infringing their claims.

If we or our future collaborators are sued for patent infringement, we would need to demonstrate that our product candidates, products and methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving that a patent is invalid or unenforceable is difficult and even if we are successful in the relevant proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted from other activities. If any issued third-party patents were held by a court of competent jurisdiction to be valid and enforceable and cover aspects of our materials, formulations, methods of manufacture or methods for treatment, we could be forced, including by court order, to cease developing, manufacturing or commercializing the relevant product candidate until the relevant patent expires. Alternatively, we may desire or be required to obtain a license from such third party in order to use the infringing technology and to continue developing, manufacturing or marketing the infringing product candidate. However, we may not be able to obtain any required license on commercially reasonably terms, or at all. Even if we were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property licensed to us. Additionally, in the event of a successful intellectual property claim against us, we may have to pay substantial damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent, or to redesign our infringing product candidates, which may be impossible or technically infeasible, or require substantial time and monetary expenditure. In addition to paying monetary damages, we may lose valuable intellectual property rights or personnel and the parties making claims against us may obtain injunctive or other equitable relief, which could impose limitations on the conduct of our business.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industry, we employ individuals who are or were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. In particular, our founder and Chief Scientific Officer, Suzanne T. Ildstad, MD, is the Jewish Hospital Distinguished Professor of Transplantation Research, Director of the Institute for Cellular Therapeutics, and a Professor in the Department of Surgery with associate appointments in the Departments of Physiology & Biophysics and Microbiology & Immunology at the University of Louisville School of Medicine. Our Chief Technology Officer, Michael Zdanowski, and certain other employees or consultants were previously employed at Medeor Therapeutics, Inc. ("Medeor Therapeutics"), which is developing a cell therapy similar to ours. Although we try to ensure that our employees, consultants and independent contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of our employee's former employer or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We may face claims that we misappropriated, or otherwise acted unjustly or in bad faith with respect to, the confidential information or trade secrets of third parties, including collaborators or former collaborators. If we are found to have misappropriated a third party's trade secrets, or otherwise to have acted unjustly or in bad faith with respect to such trade secrets, we may be prevented from further using these trade secrets, which could limit our ability to develop our product candidates, or may be otherwise subject to monetary damages.

We may face claims that we misappropriated, or otherwise acted unjustly or in bad faith with respect to, the confidential information or trade secrets of third parties, including collaborators or former collaborators. Defending against intellectual property claims could be costly and time consuming, regardless of the outcome. Thus, even if we were to ultimately prevail, or to settle before a final judgment, any litigation could burden us with substantial unanticipated costs. Parties making claims against us may be able to sustain the costs of litigation more effectively than we can because they have substantially greater resources. In addition, litigation or threatened litigation could result in significant demands on the time and attention of our management team, distracting them from the pursuit of other company business. During the course of any intellectual property litigation, there could be public announcements of the results of hearings, rulings on motions, and other interim proceedings in

the litigation and these announcements may have negative impact on the perceived value of our product candidates, programs or intellectual property. Any uncertainties resulting from the initiation and continuation of any litigation could have material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects. As a result of all of the foregoing, any actual or threatened intellectual property claim, including claims that we acted unjustly or in bad faith with respect to the intellectual property of others, could prevent us from developing or commercializing a product candidate, subject us to monetary damages, or force us to cease some aspect of our business operations.

We cannot ensure that additional patent rights relating to inventions described and claimed in our pending patent applications will issue or that patents based on our patent applications will not be challenged and rendered invalid and/or unenforceable.

We have issued and pending U.S. and foreign patent applications in our portfolio, however, we cannot predict:

- if and when additional patents may issue based on our patent applications;
- the scope of protection of any patent issuing based on our patent applications;
- whether the claims of any patent issuing based on our patent applications will provide protection against competitors;
- whether or not third parties will find ways to invalidate or circumvent our patent rights;
- whether or not others will obtain patents claiming aspects similar to those covered by our patents and patent applications;
- whether we will need to initiate litigation or administrative proceedings to enforce and/or defend our patent rights which will be costly whether we win or lose; and
- whether the patent applications that we own or in-license will result in issued patents with claims that cover our product candidates or uses thereof in the United States or in other foreign countries.

We cannot be certain that the claims in our pending patent applications directed to our product candidates and/or technologies will be considered patentable by the USPTO or by patent offices in foreign countries. One aspect of the determination of patentability of our inventions depends on the scope and content of the "prior art," information that was or is deemed available to a person of skill in the relevant art prior to the priority date of the claimed invention. There may be prior art of which we are not aware that may affect the patentability of our patent claims or, if issued, affect the validity or enforceability of a patent claim. The examination process may require us to narrow our claims, which may limit the scope of patent protection that we may obtain. Even if the patents are issued based on our patent applications, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, patents in our portfolio may not adequately exclude third parties from practicing relevant technology or prevent others from designing around our claims. If the breadth or strength of our intellectual property position with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop and threaten our ability to commercialize our product candidates. In the event of litigation or administrative proceedings, we cannot be certain that the claims in any of our issued patents will be considered valid by courts in the United States or foreign countries.

We may become involved in lawsuits to protect or enforce our intellectual property, which could be expensive, time-consuming and unsuccessful and have a material adverse effect on the success of our business.

Third parties may infringe our patents or misappropriate or otherwise violate our intellectual property rights. Our patent applications cannot be enforced against third parties practicing the technology claimed in these applications unless and until a patent issues from the applications, and then only to the extent the issued claims cover the technology. In the future, we or our collaborators may elect to initiate legal proceedings to enforce or defend our or our collaborators' intellectual property rights, to protect our or our collaborators' trade secrets or to determine the validity, ownership, enforceability or scope of our intellectual property rights. Any claims that we or our collaborators assert against perceived infringers could also provoke these

parties to assert counterclaims against us or our collaborators alleging that we or our collaborators infringe their intellectual property rights or that our intellectual property rights are invalid or unenforceable.

Interference or derivation proceedings provoked by third parties, brought by us or our collaborators, or declared by the USPTO may be necessary to determine the priority of inventions or matters of inventorship with respect to our patents or patent applications. We or our collaborators may also become involved in other proceedings, such as reexamination or opposition proceedings, *inter partes* review, post-grant review or other pre-issuance or post-grant proceedings before the USPTO or in non-U.S. jurisdictions relating to our intellectual property or the intellectual property of others. An unfavorable outcome in any of these proceedings could result in us losing our valuable intellectual property rights, require us or our collaborators to cease using the related technology and commercializing our product candidates, or require us to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us or our collaborators a license on commercially reasonable terms if any license is offered at all. Even if we or our licensors obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us or our collaborators. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Any intellectual property proceedings can be expensive and time-consuming. Our or our collaborators' adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we or our collaborators can. Accordingly, despite our or our collaborators' efforts, we or our collaborators may not be able to prevent third parties from infringing upon or misappropriating our intellectual property rights, particularly in countries where the laws may not protect our rights as fully as in the United States. Even if we are successful in the relevant proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted from other activities. In addition, in an infringement proceeding, a court may decide that one or more of our patents is invalid or unenforceable, in whole or in part, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and if securities analysts or investors view these announcements in a negative light, the price of our common stock could be adversely affected.

Risks Related to Intellectual Property Laws and Regulations

Some intellectual property has been discovered through government-funded programs and thus may be subject to federal regulations such as certain reporting requirements, a preference for U.S.-based companies, and the possibility of "march-in" rights. Compliance with such regulations or the inability to obtain a waiver for meeting such requirements may limit our ability to contract with non-U.S. manufacturers, or, in the unlikely event of the government exercising their "march-in" rights, may limit our exclusive rights.

Some of our intellectual property rights were generated through the use of U.S. government funding and are therefore subject to certain federal regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in certain of our current or future product candidates pursuant to the Bayh-Dole Act of 1980 ("Bayh-Dole Act"). These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right, under certain limited circumstances, to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). To our knowledge, however, the U.S. government has, to date, not exercised any march-in rights on any patented technology that was generated using U.S. government funds. The U.S. government also has the right to take title to these inventions if we or the applicable grantee fail to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources. In addition, the U.S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential

licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. To the extent any of our current or future intellectual property is generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply.

Changes in U.S. or foreign patent laws could diminish the value of patents in general, thereby impairing our ability to protect our products.

Changes in either the patent laws or interpretation of the patent laws in the United States or non-U.S. jurisdictions could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith America Invents Act (the "America Invents Act"), enacted in September 2011, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013, but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant of the time from invention to filing of a patent application and be diligent in filing patent applications, but circumstances could prevent us from promptly filing patent applications on our inventions. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors were the first to either (i) file any patent application related to our product candidates or (ii) invent any of the inventions claimed in our or our licensor's patents or patent applications.

The America Invents Act also included a number of significant changes that affect the way patent applications are prosecuted and also affects patent litigation. These include allowing third party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post-grant review and, *inter partes* review, and derivation proceedings. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned or in-licensed patent applications and the enforcement or defense of our owned or in-licensed issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

Risks Related to Our Financial Condition and Capital Needs

We are a late-stage clinical biotechnology company and we have incurred net losses since our inception. We anticipate that we will continue to incur significant net losses for the foreseeable future, and may never achieve or maintain profitability.

We are a late-stage clinical biotechnology company with a limited operating history. Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain regulatory approval and become commercially viable. We have no products approved for commercial sale and have not generated any revenue to date, and we will continue to incur significant research and development and other expenses related to our clinical development and ongoing operations. As a result, we are not profitable and have incurred net losses in each period since our inception. Since our inception, we have devoted substantially all of our resources to developing our lead product, FCR001, building our intellectual property portfolio, business planning, raising capital and providing general and administrative support for these operations. Our financial condition and operating results, including net losses, may fluctuate significantly from quarter to

quarter and year to year. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance. Additionally, net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital. Our net loss was $47.8 million for the year ended December 31, 2021 and $22.7 million for year ended December 31, 2020. As of December 31, 2021, we had an accumulated deficit of $90.8 million. We expect to continue to incur net losses for the foreseeable future, and we expect our research and development expenses, general and administrative expenses and capital expenditures to continue to increase.

We anticipate that our expenses will increase substantially if and as we:

- continue to initiate and conduct clinical trials for our lead product candidate, FCR001, in our initial and potential additional indications;
- seek to identify additional product candidates and initiate research, preclinical and clinical development efforts for any future product candidates;
- seek regulatory approvals for FCR001 or any future product candidates that successfully complete clinical development;
- scale our in-house manufacturing process to address anticipated commercial needs;
- seek to meet regulatory requirements for our in-house manufacturing process;
- add operational, financial and management information systems and personnel, including personnel to help us comply with our obligations as a public company;
- hire and retain additional personnel, such as clinical, quality control, scientific, manufacturing, commercial and administrative personnel, to support our product candidate development;
- maintain, expand and protect our intellectual property portfolio;
- establish sales, marketing, distribution, manufacturing, supply chain and other commercial infrastructure in the future to commercialize any product candidates for which we may obtain regulatory approval;
- adapt our regulatory compliance efforts to incorporate requirements applicable to marketed products;
- add equipment and physical infrastructure to support our research and development; and
- acquire or in-license other product candidates and technologies.

Our expenses could increase beyond our expectations if we are required by the FDA or other regulatory authorities to perform clinical trials in addition to those that we currently expect, if there are any delays in establishing appropriate manufacturing arrangements for our product candidates, or if we experience delays in the initiation or completion of our clinical trials or the development of any of our product candidates for any reason, including as a result of the COVID-19 pandemic.

We have not yet completed any registrational trials and have no history of commercializing products, which may make it difficult to evaluate the success of our business to date and to assess our future viability.

We were first formed in February 2002 under the name Regenerex LLC, and engaged in operations with non-dilutive funding, or in collaboration with Novartis International AG ("Novartis") from 2013 to 2016, until October 2018 when we closed our first external financing round, converted into a corporation and changed our name to Regenerex, Inc. and subsequently to Talaris Therapeutics, Inc. Since we commenced our operations, we have devoted substantially all of our resources to raising capital, organizing and staffing our company, business planning, conducting discovery and research activities, establishing and

protecting our intellectual property portfolio, developing and progressing FCR001 and preparing for clinical trials, and manufacturing initial quantities of FCR001. As an organization, we have not yet demonstrated an ability to successfully complete any Phase 3 clinical trials, obtain regulatory approval, consistently manufacture a commercial scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for the successful commercialization of any of our product candidates. In addition, our Facilitated Allo-HSCT Therapy is novel and has only been evaluated in a limited number of patients to date. Any predictions about our future success, performance or viability, particularly in view of the rapidly evolving immunotherapy field, may not be accurate given the limits of our operating history and lack of approved products.

In addition, given the limits of our operating history, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition from a company with a research and development focus to a company capable of supporting commercial activities and may not be successful in such a transition. We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, our financial results for any quarterly or annual periods may not be indicative of future operating performance.

We will require substantial additional funding to develop and commercialize our product candidates and identify and invest in new product candidates. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product discovery and development programs or commercialization efforts.

Developing biopharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. We expect to continue to spend substantial amounts of capital to continue the preclinical and clinical development of our current and future programs. If we are able to gain marketing approval for any product candidate we develop, including for any indication for which we are developing or may develop FCR001, we will require substantial additional funding in order to launch and commercialize such product candidates, to the extent that such launch and commercialization are not the responsibility of a collaborator that we may contract with in the future. We may also invest in preparations for launch and commercialization in advance of receiving regulatory approval for a product candidate, and such approval may not be received on a timely basis or at all. In addition, other unanticipated costs may arise in the course of our development efforts. Because the design and outcome of our planned and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of any product candidate we develop. Additionally, any COVID-19-related program setbacks or delays due to changes in federal, state, or local laws and regulations or clinical site policies could impact the timing and cost of the development of our product candidates. Under the terms of the ULRF License Agreement, we are also obligated to make payments upon the achievement of certain development, regulatory and commercial milestones.

Our future capital requirements depend on many factors, including:

- the scope, progress, results and costs of researching and developing FCR001 for our initial and potential additional indications, as well as any other product candidates we may develop, including any COVID-19-related delays or other effects on our development programs;
- the timing of, and the costs involved in, obtaining marketing approvals for FCR001 for our initial and potential additional indications, and any other product candidates we may develop;
- if approved, the costs of commercialization activities for FCR001 for any approved indications, or any other product candidate that receives regulatory approval to the extent such costs are not the responsibility of a collaborator that we may contract with in the future, including the costs and timing of scaling our manufacturing and establishing product sales, marketing, distribution and manufacturing capabilities;
- subject to receipt of regulatory approval, revenue, if any, received from commercial sales of FCR001 for any approved indications or any other product candidates;
- the extent to which we in-license or acquire rights to other products, product candidates or technologies;
- our headcount growth and associated costs as we expand our research and development, increase our office space, and establish a commercial infrastructure;

- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights, including enforcing and defending intellectual property related claims; and

- the ongoing costs of operating as a public company.

As of December 31, 2021, we had cash, cash equivalents and marketable securities of approximately $244.0 million. We cannot be certain that additional funding will be available on acceptable terms, or at all. Further, our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and the recent disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic. If we are unable to raise sufficient additional capital, we could be forced to curtail our planned operations and the pursuit of our growth strategy. We have no committed source of additional capital and if we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of our product candidates or other research and development initiatives. Any of our current or future license agreements may also be terminated if we are unable to meet the payment or other obligations under the agreements.

We believe that our cash, cash equivalents and marketable securities as of December 31, 2021 will enable us to fund our operating expenses and capital expenditure requirements for more than 12 months from the date of the accompanying financial statements. This estimate may prove to be wrong, and we could use our available capital resources earlier than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds earlier than planned.

Raising capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our product candidates on terms that are unfavorable to us.

We may seek additional capital through a variety of means, including through private and public equity offerings and debt financings. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of existing stockholders will be diluted, and the terms may include liquidation or other preferences that adversely affect the rights of stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take certain actions, including incurring additional debt, making capital expenditures, entering into licensing arrangements or declaring dividends. If we raise additional funds from third parties, we may have to relinquish valuable rights to our technologies or product candidates or grant licenses on terms that are not favorable to us. Market volatility resulting from the COVID-19 pandemic or other factors may further adversely impact our ability to access capital as and when needed. If we are unable to raise additional funds through equity or debt financing when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts for our product candidates, grant to others the rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves or take other actions that are adverse to our business.

Risks Related to Our Business, Growth and Industry

Risks Related to the COVID-19 Pandemic

Our business has been adversely affected by the ongoing COVID-19 pandemic, and could be further adversely affected by the effects this and other of public health epidemics in regions where we, or third parties on which we rely have significant research, development or production facilities, concentrations of clinical trial sites or other business operations.

Our business has been adversely affected by the COVID-19 pandemic, and could be further adversely affected by this and other public health epidemics in regions where we, and third parties on which we rely, such as CROs or suppliers, have concentrations of clinical trial sites or other business operations, and could cause significant disruption in the operations of those third-parties, and adversely affect our business. For example, enrollment in our Phase 3 FREEDOM-1 clinical trial has consistently lagged both our original and revised enrollment projections, significantly limiting the data which we are able to report at periodic medical conferences. In November 2021, when we provided the first interim data in connection with the American Association of Nephrology meeting, we reported data on five dosed patients, only three of whom had met the three-month post-transplant milestone. We believe the COVID-19 pandemic significantly impacted the ability of our clinical trial sites to attract and enroll clinical trial subjects. Furthermore, the performance of our CROs may also be delayed or disrupted by the ongoing COVID-19 pandemic and current and future variants of the virus, including due to travel or quarantine policies, availabilities of staff, exposure of CRO staff to COVID-19 or re-prioritization of CRO resources as a result of the pandemic.

Quarantines, shelter-in-place and similar government orders, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could impact personnel at our manufacturing facilities, including our ability to manufacture FCR001, or the availability or cost of materials, which would disrupt our supply chain. Any manufacturing supply interruption of materials could adversely affect our ability to conduct ongoing and future research and manufacturing activities.

In addition, our clinical trials have been and may be further affected by the COVID-19 pandemic, particularly as viral variants, such as the COVID-19 delta and omicron variants, continue to proliferate in areas where we have clinical trials. Clinical site initiation and patient enrollment has been and may be further delayed due to prioritization of healthcare system resources toward the COVID-19 pandemic. For example, some of our patients may not be able to comply with clinical trial protocols and follow-ups if quarantines impede patient movement, interrupt healthcare services, reduce patient access to trial investigators, hospitals and trial sites, and limit on-site personnel support at various trial sites. Similarly, COVID-19 and current and evolving variants may adversely impact our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19, thereby adversely impacting our clinical trial operations and enrollment timelines.

The spread of COVID-19, which has caused a broad impact globally, may materially affect us economically. While the potential economic impact brought by, and the duration of, COVID-19 may be difficult to assess or predict, a widespread pandemic could result in significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common stock.

The global COVID-19 pandemic continues to rapidly evolve. The ultimate impact of the COVID-19 pandemic is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, healthcare systems or the global economy as a whole. However, these potential effects could have a material impact on our operations, and we will continue to monitor the COVID-19 situation closely.

Risks Related to Employee and Growth Matters

We are highly dependent on our key personnel and anticipate hiring new key personnel. If we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, scientific and medical personnel, including Scott Requadt, our Chief Executive Officer; Suzanne T. Ildstad, MD, our founder and Chief Scientific Officer; Nancy Krieger, MD, our Chief Medical Officer; Michael Zdanowski, our Chief Technology Officer; and Mary Kay Fenton, our Chief Financial Officer. While we expect to engage in an orderly transition process as we integrate newly appointed officers and managers, we face a variety of risks and uncertainties relating to management transition, including diversion of management attention from business concerns, failure to retain other key personnel or loss of institutional knowledge. In addition, the loss of the services of any of our executive officers, other key employees and other scientific and medical advisors, and an inability to find suitable replacements could result in delays in product development and harm our business.

We conduct our main operations at our cell processing facility in Louisville, Kentucky, we maintain a corporate office in Wellesley, Massachusetts and a laboratory in Houston, Texas. Competition for skilled personnel, particularly in the rapidly growing cell and gene therapy (“CGT”) market, is intense, particularly in Massachusetts, which serves as headquarters to many other biopharmaceutical companies and many academic and research institutions, and may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all. Changes to U.S. immigration and work authorization laws and regulations, including those that restrain the flow of scientific and professional talent, can be significantly affected by political forces and levels of economic activity. Our business may be materially adversely affected if legislative or administrative changes to immigration or visa laws and regulations impair our hiring processes and goals or projects involving personnel who are not U.S. citizens.

To encourage valuable employees to remain at our company, in addition to salary and cash incentives, we have provided stock options that vest over time. The value to employees of stock options that vest over time may be significantly affected by movements in our stock price that are beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies. Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us on short notice. Although we have employment agreements with our key employees, these employment agreements provide for at-will employment, which means that any of our employees

could leave our employment at any time, with or without notice. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level and senior managers as well as junior, mid-level and senior scientific and medical personnel. It may be difficult or time-consuming to recruit all the qualified personnel that we need in order to scale-up our manufacturing operations in Louisville.

We may need to grow the size of our organization, and we may experience difficulties in managing this growth.

As of December 31, 2021, we had 112 employees, five of whom worked less than full-time, and 15 consultants. As our development and commercialization plans and strategies develop, and as we transition into operating as a public company, or as a result of any future acquisitions, we expect to need additional managerial, operational, manufacturing, sales, marketing, financial and other personnel, as well as additional facilities to expand our operations to support this future growth. Our management, personnel and systems currently in place may not be adequate to support this future growth. Future growth would impose significant added responsibilities on members of management, including:

- managing our preclinical studies and clinical trials effectively;
- identifying, recruiting, maintaining, motivating and integrating additional employees;
- managing our internal development efforts effectively while complying with our contractual obligations to licensors, licensees, contractors and other third parties;
- improving our managerial, development, operational, information technology, and finance systems; and
- expanding our facilities.

As our operations expand, we will also need to manage additional relationships with various strategic collaborators, suppliers and other third parties. Our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our development efforts and preclinical and clinical studies effectively and hire, train and integrate additional management, research and development, manufacturing, administrative and sales and marketing personnel. Our failure to accomplish any of these tasks could prevent us from successfully growing our company.

Our employees, principal investigators, consultants and collaborators may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of employee and third party fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions, litigation and serious harm to our reputation. It is not always possible to identify and deter employee and third-party misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of noncompliance with these laws, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business, financial condition and results of operations.

Risks Related to Business Disruptions

If our security measures are compromised now, or in the future, or the security, confidentiality or integrity or availability of our information technology, software, services, communications or data is compromised, limited, or fails, this could result in a materially adverse impact, including without limitation, damage to our reputation, significant financial and legal exposure, breach or triggering of data protection laws, privacy policies and data protection obligations, disruption to our clinical trial or administrative activities, or loss of customers or collaborators.

We rely on information technology systems that we or our third-party providers operate to process, transmit and store electronic information in our day-to-day operations. In connection with our business, we may collect and use a variety of personal data, such as name, mailing address, email addresses, phone number and clinical trial information, as well as intellectual property, trade secrets, and proprietary business information owned or controlled by ourselves or other parties.

Despite the implementation of security measures, our internal computer systems and those of our current and future CROs and other contractors, consultants and relevant third parties are vulnerable to several threats, including without limitation damage from computer viruses, unauthorized access, terrorism, war, natural disasters, and telecommunication and electrical failures. We exercise little or no control over these third parties, which increases our vulnerability to problems with their systems. A successful cyberattack could result in the theft or destruction of intellectual property, data, or other misappropriation of assets, or otherwise compromise our confidential or proprietary information and disrupt our operations. Cyberattacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyberattacks could include wrongful conduct by hostile foreign governments, industrial espionage, wire fraud and other forms of cyber fraud, the deployment of harmful malware, phishing attacks, denial-of-service, social engineering fraud or other means to threaten data security, confidentiality, integrity and availability. Although we have not, to our knowledge, experienced a material security incident, we realize that cyberattacks are a threat, and there can be no assurance that our efforts will prevent information security breaches.

We may be required to expend significant resources, fundamentally change our business activities and practices, or modify our services, software, operations or information technology in an effort to protect against security breaches and to mitigate, detect, and remediate actual and potential vulnerabilities. Applicable data protection laws, privacy policies and other data protection obligations may require us to implement specific security measures or use industry-standard or reasonable measures to protect against security breaches.

If we, our service providers, collaborators, or other relevant third parties have experienced or in the future experience, any security incident(s) that result in any data loss, deletion or destruction, unauthorized access to, loss of, unauthorized acquisition or disclosure of, or inadvertent disclosure of sensitive information or compromise related to the security, confidentiality, integrity or availability of our (or their) information technology, software, services, communications or data, it may result in a material adverse impact, including without limitation, legal liability, government investigations an inability to conduct our clinical trials, regulatory investigations, enforcement actions, indemnity obligations, the disruption of our operations, delays to the development and commercialization of our product candidates, negative publicity and financial loss. A failure by us or relevant third parties to detect, anticipate, measure or detect such security incidents could result in similar material adverse impacts.

Additionally, applicable data protection laws, privacy policies and data protection obligations may require us to notify relevant stakeholders of security breaches, including affected individuals, customer and regulators. Such disclosures are costly, and the disclosures or the failure to comply with such requirements could lead to material adverse impacts, including without limitation, negative publicity, a loss of customer confidence in our products or security measures or a breach of contract claim. There can be no assurances that the limitations of liability in our contract would be enforceable or adequate or would otherwise protect us from liabilities or damages.

Failures or significant downtime of our information technology or telecommunication systems or those used by our third-party service providers could cause significant interruptions in our operations and adversely impact the confidentiality, integrity and availability of sensitive or confidential information. While we have not experienced any such material system failure or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of data from completed or future preclinical studies and clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

While we maintain general liability insurance coverage and coverage for errors or omissions, we cannot assure that such coverage will be adequate or otherwise protect us from or adequately mitigate liabilities or damages with respect to claims, costs, expenses, litigation, fines, penalties, business loss, data loss, regulatory actions or other material adverse impacts arising out of our privacy and security actions we may experience, or that such coverage will continue to be available on acceptable

terms or at all. The successful assertion of one or more large claims against us that exceeds our available insurance coverage, or that results in changes to our insurance policies (including premium increases or the imposition of large deductible or co-insurance requirements), could have an adverse effect on our business. In addition, we cannot be sure that our existing insurance coverage and coverage for errors and omissions will continue to be available on acceptable terms or that our insurers will not deny coverage as to any future claim.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our manufacturing operations, and those of our CROs, suppliers and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or man-made disasters or business interruptions, for which we are predominantly self-insured. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.

Global credit and financial markets have experienced extreme volatility and disruptions in the past several years, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment or continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, or do not improve, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive.

Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other collaborators may not survive these difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget.

Furthermore, our stock price may decline due in part to the volatility of the stock market and the general economic downturn.

Global economic uncertainty and weakening product demand caused by political instability, changes in trade agreements and conflicts, such as the conflict between Russia and Ukraine, could adversely affect our business and financial performance.

Economic uncertainty in various global markets caused by political instability and conflict and economic challenges caused by the COVID-19 pandemic has resulted, and may continue to result, in weakened demand for our products and services and difficulty in forecasting our financial results and managing inventory levels. Political developments impacting government spending and international trade, including current or potential government-imposed sanctions, potential government shutdowns and trade disputes and tariffs, may negatively impact markets and cause weaker macro-economic conditions. The effects of these events may continue due to potential U.S. government shutdowns and the transition in administrations, and the United States' ongoing trade disputes with China and other countries. The continuing effect of any or all of these events could adversely impact demand for our products, harm our operations and weaken our financial results.

Risks Related to Laws and Regulations that May Affect our Business

Legislation or other changes in U.S. tax law could adversely affect our business and financial condition.

The rules dealing with U.S. federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many changes have been made to applicable tax laws and changes are likely to continue to occur in the future.

It cannot be predicted whether, when, in what form, or with what effective dates, new tax laws may be enacted, or regulations and rulings may be enacted, promulgated or issued under existing or new tax laws, which could result in an increase in our or our shareholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law or in the interpretation thereof.

Our ability to use our U.S. net operating loss carryforwards and certain other U.S. tax attributes may be limited.

Our ability to use our U.S. federal and state net operating losses to offset potential future taxable income and related income taxes that would otherwise be due is dependent upon our generation of future taxable income, and we cannot predict with certainty when, or whether, we will generate sufficient taxable income to use all of our net operating losses.

Under current law, unused U.S. federal net operating losses generated for tax years beginning after December 31, 2017 are not subject to expiration and may be carried forward indefinitely. Such U.S. federal net operating losses generally may not be carried back to prior taxable years, except that, net operating losses generated in 2018, 2019 and 2020 may be carried back to each of the five tax years preceding the tax years of such losses. Additionally, for taxable years beginning after December 31, 2020, the deductibility of such U.S. federal net operating losses is limited to 80% of our taxable income in any future taxable year. In addition, both our current and our future unused U.S. federal net operating losses and tax credits may be subject to limitation under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the "Code"), if we undergo an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a rolling three-year period. We may have experienced such ownership changes in the past, and we may experience ownership changes in the future as a result of shifts in our stock ownership, some of which are outside our control. Our net operating losses and tax credits may also be impaired or restricted under state law. As of December 31, 2021, we had U.S. federal net operating loss carryforwards of approximately $78.0 million, and our ability to utilize those net operating loss carryforwards could be limited by an "ownership change" as described above, which could result in increased tax liability to us.

We are subject to U.S. anti-corruption laws and regulations and can face serious consequences for violations.

We are subject to anti-corruption laws, including the U.S. domestic bribery statute contained in 18 U.S.C. 201, the U.S. Travel Act, and the U.S. Foreign Corrupt Practices Act of 1977, as amended. These anti-corruption laws generally prohibit companies and their employees, agents, and intermediaries from authorizing, promising, offering, or providing, directly or indirectly, corrupt or improper payments or anything else of value to recipients in the public or private sector. We can be held liable for the corrupt or illegal activities of our agents and intermediaries, even if we do not explicitly authorize or have actual knowledge of such activities. Violations of anti-corruption laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences. Likewise, any investigation of potential violations of anti-corruption laws could also have an adverse impact on our reputation, our business, results of operations and financial condition.

If product liability lawsuits are brought against, we may incur substantial liabilities and may be required to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. Product liability claims may be brought against us by subjects enrolled in our clinical trials, patients, healthcare providers or others using, administering or selling our products. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- termination of clinical trial sites or entire trial programs;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to study subjects or patients;
- loss of revenue;

- exhaustion of any available insurance and our capital resources;
- diversion of management and scientific resources from our business operations;
- the inability to commercialize any products that we may develop; and
- a decline in our share price.

We currently hold product liability insurance coverage at a level that we believe is customary for similarly situated companies and adequate to provide us with insurance coverage for foreseeable risks, but which may not be adequate to cover all liabilities that we may incur. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. We intend to expand our insurance coverage for products to include the sale of commercial products if we obtain regulatory approval for our product candidate in development, but we may be unable to obtain commercially reasonable product liability insurance for any products that receive regulatory approval. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us, particularly if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

Risks Related to Ownership of Our Common Stock

Risks Related to our Common Stock

The price of our stock may be volatile, and you could lose all or part of your investment.

The trading price of our common stock is likely to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. In addition to the factors discussed in this “Risk Factors” section and elsewhere in this Annual Report, these factors include:

- actual or anticipated variations in quarterly operating results;
- our cash position;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- publication of research reports about us or our industry, or cell therapy in particular, or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- changes in the market valuations of similar companies;
- overall performance of the equity markets;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;
- changes in accounting practices;

- ineffectiveness of our internal controls;
- disputes or other developments relating to intellectual property or proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including intellectual property or stockholder litigation;
- changes in the structure of health care payment systems;
- general political and economic conditions, including impacts from the COVID-19 pandemic; and
- other events or factors, many of which are beyond our control.

In addition, the stock market in general, and the market for biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company's securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management's attention and resources, which would harm our business, financial condition, results of operation and future prospects.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant influence over matters subject to stockholder approval.

Our executive officers, directors, and 5% stockholders beneficially owned approximately 79.1% of our outstanding voting common stock as of December 31, 2021. The voting power of this group may increase to the extent they convert shares of non-voting common stock they hold into common stock. Therefore, these stockholders will have the ability to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders.

The dual class structure of our capital stock may limit your ability to influence corporate matters and may limit your visibility with respect to certain transactions.

The dual class structure of our capital stock may limit your ability to influence corporate matters. Holders of our common stock are entitled to one vote per share, while holders of our non-voting common stock are not entitled to any votes. Nonetheless, each share of our non-voting common stock may be converted at any time into one share of our common stock at the option of its holder by providing written notice to us, subject to the limitations provided for in our amended and restated certificate of incorporation. Citadel Multi-Strategy Equities Master Fund Ltd. holds an aggregate of 1,150,000 shares of our non-voting common stock. This entity could convert a portion of these shares of non-voting common stock until it and its affiliates beneficially own up to an aggregate of 9.9% of our shares of common stock at any time upon written notice. Consequently, if this holder of our non-voting common stock exercises its option to make this conversion, this will have the effect of increasing the relative voting power of the prior holder of our non-voting common stock, and correspondingly decreasing the voting power of the holders of our common stock, which may limit your ability to influence corporate matters.

Risks Related to our Filer Status

We are an emerging growth company and a smaller reporting company, and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies and smaller reporting companies will make our common stock less attractive to investors.

We are an emerging growth company, as defined in the JOBS Act, enacted in April 2012. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended (the "Sarbanes-Oxley Act"), reduced disclosure obligations regarding executive compensation in this Annual Report and our periodic reports and proxy statements, and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We could be an emerging growth company for up to five years following the completion of our offering in May 2021, although circumstances could cause us to lose that status earlier. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the closing of our initial public offering, (b) in which we have total annual gross revenue of at least $1.07 billion or (c) in which we are deemed to be a large accelerated filer, which requires the market value of our common stock and non-voting common stock that are held by non-affiliates to exceed $700 million as of the prior June 30th, and (2) the date on which we have issued more than $1 billion in non-convertible debt during the prior three-year period.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to not "opt out" of this exemption from complying with new or revised accounting standards and, therefore, we will adopt new or revised accounting standards at the time private companies adopt the new or revised accounting standard and will do so until such time that we either (i) irrevocably elect to "opt out" of such extended transition period or (ii) no longer qualify as an emerging growth company.

Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company," which would allow us to continue to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements.

We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions applicable to emerging growth companies and smaller reporting companies. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

Risks Related to our Certificate of Incorporation and Bylaws

Anti-takeover provisions under our certificate of incorporation and bylaws and Delaware law could delay or prevent a change of control, which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management.

Our amended and restated certificate of incorporation and our amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of stockholders be called only by the board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors;

- a requirement of approval of not less than two-thirds of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our certificate of incorporation; and

- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval and which preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These anti-takeover provisions and other provisions in our amended and restated certificate of incorporation and amended and restated bylaws could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors and could also delay or impede a merger, tender offer, or proxy contest and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

Our bylaws designate certain courts as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, or employees.

Our bylaws provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any state law claims for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of fiduciary duty owed by any of our directors, officers, and employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws or (iv) any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein (the "Delaware Forum Provision"). The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act or the Exchange Act. Our amended and restated bylaws further provide that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall be the sole and exclusive forum for resolving any complaint asserting a cause or causes of action arising under the Securities Act (the "Federal Forum Provision"). In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our common stock is deemed to have notice of and consented to the foregoing provisions; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

The Delaware Forum Provision and the Federal Forum Provision in our amended and restated bylaws may impose additional litigation costs on stockholders in pursuing any such claims. Additionally, the forum selection clauses in our amended and restated bylaws may limit our stockholders' ability to bring a claim in a forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders. In addition, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court were "facially valid" under Delaware law, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert that the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware and the federal district courts of the United States may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

General Risk Factors

We will incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a public company, we will incur significant legal, accounting, and other expenses that we did not incur as a private company. We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), which will require, among other things, that we file with the Securities and Exchange Commission (the "SEC"), annual, quarterly,

and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and The Nasdaq Global Market to implement provisions of the Sarbanes-Oxley Act, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, in July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act (the "Dodd-Frank Act") was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas, such as "say on pay" and proxy access. Recent legislation permits emerging growth companies to implement many of these requirements over a longer period and up to five years from the pricing of our initial public offering. We intend to take advantage of this new legislation but cannot guarantee that we will not be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment, and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

We expect the rules and regulations applicable to public companies to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition, and results of operations. The increased costs will decrease our net income or increase our net loss and may require us to reduce costs in other areas of our business or increase the prices of our products or services. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain the same or similar coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees, or as executive officers.

If we fail to establish and maintain proper and effective internal control over financial reporting, our operating results and our ability to operate our business could be harmed.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles. We have begun the process of documenting, reviewing, and improving our internal controls and procedures for compliance with Section 404 of the Sarbanes-Oxley Act, which will require annual management assessment of the effectiveness of our internal control over financial reporting. We have begun recruiting additional finance and accounting personnel with certain skill sets that we will need as a public company.

Implementing any appropriate changes to our internal controls may distract our officers and employees, entail substantial costs to modify our existing processes, and take significant time to complete. These changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase our operating costs and harm our business. In addition, investors' perceptions that our internal controls are inadequate or that we are unable to produce accurate financial statements on a timely basis may harm our stock price and make it more difficult for us to effectively market and sell our service to new and existing customers.

We do not intend to pay dividends on our common stock, so any returns will be limited to the value of our stock.

We currently anticipate that we will retain future earnings for the development, operation, and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. In addition, we may enter into agreements that prohibit us from paying cash dividends without prior written consent from our contracting parties, or which other terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Any return to stockholders will therefore be limited to the appreciation of their stock, which may never occur.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. In the event one or more of the analysts who cover us downgrades our stock or publishes inaccurate

or unfavorable research about our business, our stock price may decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

We may be at an increased risk of securities class action litigation.

Historically, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years. If we were to be sued, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our corporate headquarters is located in Louisville, Kentucky, where we lease and occupy 19,585 square feet of office and laboratory space. The current term of our Louisville lease expires in November 2023 with an option to extend the term by three successive one-year renewal periods in each case upon six months' prior written notice. We also lease additional corporate space in Louisville, Kentucky, where we lease and occupy 6,130 square feet of office space. The current term of this lease expires in November 2023. We maintain additional corporate office space in Wellesley, Massachusetts, where we currently lease 1,040 square feet. We have executed an amendment for an expanded suite in the same location totaling 7,410 square feet. This lease is anticipated to begin in June 2022 and expire in September 2025. We also lease additional space in Houston, Texas, where we lease and occupy 6,000 square feet of office and laboratory space. The current term of our Houston lease expires in January 2025. We believe our existing facilities in Louisville, Wellesley and Houston are sufficient for our needs for the foreseeable future. To meet the future needs of our business, we may lease additional or alternate space, and we believe suitable additional or alternative space will be available in the future on commercially reasonable terms.

Item 3. Legal Proceedings.

From time to time, we may become involved in litigation or other legal proceedings. As of December 31, 2021, we are not currently a party to any litigation or legal proceedings that, in the opinion of our management, are probable to have a material adverse effect on our business, financial position, results of operations or cash flow. Regardless of outcome, litigation can have an adverse impact on our business, financial condition, results of operations and prospects because of defense and settlement costs, diversion of management resources and other factors.

Item 4. Mine Safety Disclosures.

Not Applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market for Common Stock

On May 7, 2021, our common stock began trading on the Nasdaq Global Market under the symbol "TALS". Prior to such time, there was no public market for our common stock.

Stockholders

As of March 1, 2022, there were 28 stockholders of record of our common stock. The actual number of holders of our common stock is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers or held by other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividends

We currently intend to retain all available funds and any future earnings to fund the growth and development of our business. We have never paid or declared any cash dividends on our common stock and do not intend to pay cash dividends to our stockholders in the foreseeable future. Any future determination to declare dividends will be made at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements, general business conditions and other factors that our board of directors may deem relevant.

Unregistered Sales of Equity Securities and Use of Proceeds

Set forth below is information regarding stock options granted by us and exercised during the period covered by this Annual Report on Form 10-K that were not registered under the Securities Act of 1933, as amended, or the Securities Act. Included is the consideration, if any, we received for such shares and options and information relating to the section of the Securities Act under which exemption from registration was claimed.

From January 1, 2021 to the closing of our IPO on May 11, 2021, we granted options to purchase an aggregate of 737,319 shares of common stock, with exercise prices ranging from $5.72 to $6.79 per share, to directors, employees and consultants pursuant to our Second Amended and Restated 2018 Equity Incentive Plan, as amended (the "2018 Plan"). During such period, 24,442 shares of common stock were issued for gross proceeds of $0.0 million upon the exercise of stock options pursuant to the 2018 Plan.

No underwriters were involved in the foregoing issuances of securities. The issuances of the securities described above were deemed to be exempt from registration pursuant to Section 4(a)(2) of the Securities Act as transactions by an issuer not involving a public offering or Rule 701 promulgated under the Securities Act as transactions pursuant to compensatory benefit plans. All recipients either received adequate information about us or had access, through employment or other relationships, to such information. On May 6, 2021, we filed a registration statement on Form S-8 under the Securities Act to register all of the shares of our common stock subject to outstanding options and all shares of our common stock otherwise issuable pursuant to our equity compensation plans.

Use of Proceeds from Initial Public Offering

On May 11, 2021, we completed our initial public offering, (our "IPO"), in which we issued and sold 8,825,000 shares of common stock, $0.0001 par value per share, at a price to the public of $17.00 per share. The offer and sale of the shares in the IPO was registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-255316) that was filed with the Securities and Exchange Commission (the "SEC") on May 3, 2021 and declared effective on May 6, 2021. The underwriters of the offering were Morgan Stanley & Co. LLC, SVB Leerink LLC, Evercore Group L.L.C. and Guggenheim Securities, LLC. Our IPO commenced on May 7, 2021.

We raised approximately $137.2 million in net proceeds after deducting underwriting discounts and commissions of $10.5 million and other offering expenses of approximately $2.4 million payable by us. No underwriting discounts and commissions or offering expenses were paid directly or indirectly to any of our directors

or officers (or their affiliates) or persons owning ten percent or more of any class of our equity securities or to any other affiliates.

We are holding a significant portion of the balance of the net proceeds in a variety of capital preservation investments, including money market funds, short-term investment-grade, interest bearing instruments and U.S. government securities. There has been no material change in the planned proceeds from our IPO, as described in our final prospectus filed with the SEC on May 10, 2021 pursuant to Rule 424(b) under the Securities Act.

Securities Authorized for Issuance under Equity Compensation Plans

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report.

Issuer Purchases of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report.

Item 6. Reserved.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

You should read the following discussion and analysis of our financial condition and results of operations together with the "Selected Financial Data" section of this prospectus and our financial statements and the related notes appearing elsewhere in this prospectus. This discussion and other parts of this prospectus contain forward-looking statements that involve risks and uncertainties, such as statements regarding our plans, objectives, expectations, intentions and projections. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the "Risk Factors" section of this prospectus.

Overview

We are a late-clinical stage, cell therapy company developing an innovative method of allogeneic hematopoietic stem cell transplantation ("**allo-HSCT**") that we believe has the potential to transform the standard of care in solid organ transplantation, certain severe autoimmune diseases and certain severe blood, immune and metabolic disorders. In the organ transplant setting, which is our initial focus, we believe our proprietary therapeutic approach, which we call "**Facilitated Allo-HSCT Therapy**", could prevent organ rejection without the morbidity and mortality that has been associated with the use of lifelong immunosuppression. Beyond the organ transplant setting, our Facilitated Allo-HSCT Therapy also has the potential to treat a range of severe blood, immune and metabolic disorders, in each case with potential for similar outcomes to what has previously been observed with HSCT, while mitigating the toxicities, morbidities and extended hospital stay associated with the fully myeloablative conditioning typically required by HSCT. We believe that these indications, individually and collectively, represent a significant unmet need and commercial opportunity.

We were incorporated as Regenerex, Inc. in 2018 under the laws of the State of Delaware, having converted from a limited liability company under the name Regenerex LLC. In 2019, we changed our corporate name from Regenerex, Inc. to Talaris Therapeutics, Inc.

Since our inception, we have devoted substantially all of our resources to developing our lead product candidate, FCR001, building our intellectual property portfolio, business planning, raising capital and providing general and administrative support for these operations. To date, we have principally financed our operations through private placements of convertible preferred stock, payments under a former research collaboration with Novartis, Inc., research grants and most recently, our IPO. Through December 31, 2021, we had received net proceeds of $186.2 million from sales of our convertible preferred stock and net proceeds of $137.2 million, after deducting underwriting discounts and commissions and other expenses, from our IPO.

We have incurred significant operating losses since inception. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of our product and any future product candidates. Our net losses were $47.8 million and $22.7 million for the years ended December 31, 2021 and December 31, 2020. As of December 31, 2021, we had an accumulated deficit of $90.8 million. We expect to continue to incur net losses for the foreseeable future, and we expect our research and development expenses, general and administrative expenses and capital expenditures to continue to increase. In particular, we expect our expenses to increase as we continue our development of, and seek regulatory approvals for, our product candidates, as well as hire additional personnel, pay fees to outside consultants, lawyers and accountants, and incur other increased costs associated with being a public company. In addition, if we obtain marketing approval for any product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. We may also incur expenses in connection with the in-licensing or acquisition of additional product candidates. Furthermore, we expect to incur additional costs associated with operating as a public company, including significant legal, accounting, investor relations, compliance and other expenses that we did not incur as a private company. As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through the sale of equity, debt financings, or other capital sources, which may include collaborations with other companies or other strategic transactions. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as and when needed, we may have to significantly delay, reduce

or eliminate the development and commercialization of one or more of our product candidates or delay our pursuit of potential in-licenses or acquisitions.

Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

Based upon our current operating plan, we believe that our existing cash and cash equivalents and marketable securities of $244.0 million as of December 31, 2021 will be sufficient to fund our operating expenses and capital expenditure requirements for more than 12 months from the date of issuance. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect.

Impact of COVID-19 on Our Business

In December 2019, a novel strain of coronavirus ("COVID-19") was reported in China. Since then, COVID-19 has spread globally. Efforts to contain the spread of COVID-19 have intensified and are evolving. As a result, the COVID-19 pandemic has caused significant disruptions to the U.S., regional and global economies and has contributed to significant volatility and negative pressure in financial markets.

The worldwide COVID-19 pandemic and emergence of the delta and omicron variants of the virus have affected and may continue to affect in the future our ability to initiate and complete preclinical studies, delay the initiation and completion of our current and planned clinical trials, disrupt regulatory activities or have other adverse effects on our business, results of operations, financial condition and prospects. In addition, the pandemic has caused substantial disruption in the financial markets and may adversely impact economies worldwide, both of which could adversely affect our business, operations and ability to raise funds to support our operations.

We are following, and plan to continue to follow, recommendations from federal, state and local governments regarding workplace policies, practices and procedures. We have a mandatory COVID-19 vaccination policy in place for our workforce, and to the extent necessary, we limit access to our facility to those employees and vendors who are vaccinated or have received negative COVID-19 tests before entering our site. We will continue to monitor and follow masking and other COVID-19 related guidance from state and local authorities in the jurisdictions in which we operate.

Timely enrollment in planned clinical trials is dependent upon clinical trial sites which have been adversely affected by global health matters, such as the COVID-19 pandemic. For example, screening and enrollment in our ongoing FREEDOM-1 Phase 3 clinical trial, as well as our recently initiated FREEDOM-2 and FREEDOM-3 Phase 2 clinical trials, have been adversely impacted by the COVID-19 pandemic. In addition, we and the third-party manufacturers, CROs, and academic collaborators that we engage may face future disruptions that could affect our ability to initiate and complete preclinical studies or clinical trials, including disruptions in procuring items that are essential for our research and development activities, such as, for example, raw materials used in the manufacture of our product candidates and laboratory supplies for our preclinical studies and clinical trials, in each case, for which there may be shortages because of ongoing efforts to address the COVID-19 pandemic.

Notwithstanding the foregoing, the future impact of the COVID-19 pandemic on our industry, the healthcare system and our current and future operations and financial condition will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the scope, severity and duration of the pandemic, the impact of new strains of the virus, the effectiveness and availability of vaccines and antiviral medications, the pace of these efforts, the actions taken to contain the pandemic or mitigate its impact, any additional preventative and protective actions that governments may direct, and the direct and indirect economic effects of the pandemic and containment measures, among others. See “Item 1A. Risk Factors” for a discussion of the potential adverse impact of COVID-19 on our business, results of operations and financial condition

License Agreement

In October 2018, we entered an amended and restated exclusive license agreement ("ULRF License Agreement") with University of Louisville Research Foundation ("ULRF") related to certain licensed patent rights and know-how related to human facilitating cells for our Facilitated Allo-HSCT Therapy approach. Pursuant to the ULRF License Agreement, ULRF granted us an exclusive, worldwide license under such patents and a nonexclusive royalty-bearing, worldwide license for such know-how to research, develop, commercialize and manufacture FCR001 and products containing FCR001 in all fields, without limitation. ULRF also granted us the right to grant sublicenses in accordance with the ULRF License Agreement. Under the terms of the ULRF License Agreement, the Company is obligated to compensate ULRF three percent of net sales of all licensed products sold, one third of any non-royalty sublicensing income, and up to $1.625 million in regulatory and sales milestones on each licensed product upon the occurrence of specific events as outlined in the ULRF License Agreement; and annual license maintenance fees. As of December 31, 2021, we have paid ULRF $0.1 million in milestone payments and $0.1 million in annual maintenance fees, for a total of $0.2 million.

In addition, upon execution of the ULRF License Agreement, we granted contingent equity consideration equal to 65,186 shares of common stock to ULRF. Pursuant to the ULRF License Agreement, on or prior to our first underwritten public offering or any transaction that is treated as a deemed liquidation event, we are required to either issue to ULRF the 65,186 shares in common stock or make a cash payment equal to the 65,186 shares of common stock multiplied by either the price per share of common stock in the underwritten public offering or by the price per share of common stock received in connection with such deemed liquidation event. Coincident with the completion of our IPO in May 2021, we issued to ULRF 48,889 shares of common stock in addition to $0.3 million in a cash payment to fully satisfy the contingent stock liability to ULRF (see Note 8 in the accompanying financial statements). As of December 31, 2021, we had no liability to ULRF for contingent common stock. As of December 31, 2020, we measured the fair value of the contingent equity consideration and recorded a contingent stock liability of $0.4 million in other liabilities (see Note 3 in accompanying audited financial statements).

Components of Our Results of Operations

Revenue

We have not generated any revenue since our inception and do not expect to generate any revenue from the sale of products in the future, if at all. If our product candidates we are currently developing and that we may develop in the future are successful and result in marketing approval or if we enter into collaboration or license agreements with third parties, we may generate revenue in the future from a combination of product sales or payments from such collaboration or license agreements.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred in connection with the development and research of our novel cell therapy, as well as unrelated discovery program expenses. We expense research and development costs as incurred. These expenses include:

- employee-related expenses, including salaries, related benefits and stock-based compensation expense, for employees engaged in research and development functions;
- external research and development expenses incurred under arrangements with third parties, such as CROs, investigational sites, and consultants;
- the cost of acquiring, developing, and manufacturing clinical study materials;
- costs associated with preclinical and clinical activities and regulatory operations;
- costs incurred in development of intellectual property; and
- an allocated portion of facilities and other infrastructure costs associated with our research and development activities.

We enter into consulting, research, and other agreements with commercial entities, researchers, universities, and others for the provision of goods and services. Such arrangements are generally cancelable upon reasonable notice and payment of costs incurred. Costs are considered incurred based on an evaluation of the progress to completion of specific tasks under each contract using information and data provided by the respective vendors, including our clinical sites. These costs consist of direct and indirect costs associated with specific projects, as well as fees paid to various entities that perform certain research on behalf of us. Depending upon the timing of payments to the service providers, we recognize prepaid expenses or accrued expenses related to these costs. These accrued or prepaid expenses are based on management's estimates of the work performed under service agreements, milestones achieved, and experience with similar contracts. We monitor each of these factors and adjust estimates accordingly.

The successful clinical development and subsequent commercialization of product candidates is highly uncertain. This is due to the numerous risks and uncertainties with product development and commercialization, including significant variations in our clinical development costs as well as the following factors:

- per patient trial costs;
- the number of trials required for approval;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;
- the number of patients that participate in the trials;
- the length of hospitalization of patients in our clinical trials
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring requested by regulatory agencies;
- the duration of patient participation in the trials and follow-up;
- the cost and timing of manufacturing our product candidates;
- the phase of development of our product candidates;
- the efficacy and safety profile of our product candidates. the timing and progress of nonclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- raising necessary additional funds;
- the progress of the development efforts of parties with whom we may enter into collaboration arrangements;
- our ability to maintain our current development program and to establish new ones;
- our ability to establish new licensing or collaboration arrangements;
- the successful initiation and completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to the FDA or any comparable foreign regulatory authority;
- the receipt and related terms of regulatory approvals from applicable regulatory authorities;
- the availability of drug substance and drug product for use in production of our product candidate;
- the development of commercial scale manufacturing and distribution processes for our product candidates;
- establishing and maintaining agreements with third-party manufacturers for commercial manufacturing, if we pursue a third party manufacturing strategy outside of the United States, and if our product candidate is approved;

- our ability to obtain and maintain patents, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- our ability to protect our rights in our intellectual property portfolio;
- the commercialization of our product candidate, if and when approved;
- obtaining and maintaining third-party insurance coverage and adequate reimbursement;
- the acceptance of our product candidate, if approved, by patients, the medical community and third-party payors;
- competition with other products; and
- a continued acceptable safety profile of our therapies following approval.

We may never succeed in obtaining regulatory approval for any of our current and future product candidates, including FCR001. We may obtain unexpected results from our preclinical studies and clinical trials including FREEDOM-1, FREEDOM-2, and FREEDOM-3. We may elect to discontinue, delay or modify clinical trials of some product candidates or focus on others. A change in the outcome of any of these factors could mean a significant change in the costs and timing associated with the development of our current and future preclinical and clinical product candidates. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials for FCR001 beyond those that we currently anticipate will be required for the completion of clinical development, or if we experience significant delays in execution of any of our preclinical studies or execution or enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of preclinical and clinical development. A change in the outcome of any of these variables with respect to the development of our product candidates could significantly change the costs and timing associated with the development of that product candidate. We may never succeed in obtaining regulatory approval for any of our product candidates.

Research and development activities account for a significant portion of our operating expenses. We expect our research and development expenses to increase for the foreseeable future as we continue to implement our business strategy, which includes advancing FCR001 through clinical development of FREEDOM-1, FREEDOM-2 and FREEDOM-3 as well as other product candidates into clinical development, expanding our research and development efforts, including hiring additional personnel to support our research efforts, our clinical and product development efforts, and seeking regulatory approvals for our product candidates that successfully complete clinical trials.

We use our personnel and infrastructure resources across multiple research and development programs directed toward identifying and developing product candidates. Our direct research and development expenses are tracked on a program-by-program basis and consist primarily of external costs, including fees paid to consultants, contractors and CROs in connection with our development activities and the cost of acquiring, developing, and manufacturing clinical study materials. At this time, we do not fully allocate personnel costs to individual programs as many of our personnel are deployed across multiple programs.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs for personnel in executive, finance, corporate and business development, human resources and administrative functions. General and administrative expenses also include legal fees relating to patent and corporate matters, professional fees for accounting, auditing, tax and administrative consulting services, insurance costs and other operating costs, including an allocated portion of facilities and other infrastructure costs associated with our general and administrative activities.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support development of our product candidates and our continued research activities. We also anticipate that we will incur increased accounting, audit, legal, regulatory, compliance and director and officer insurance costs as well as investor and public relations expenses associated with being a public company.

Other Income (Expense), Net

Other income (expense), net is comprised of interest income earned on cash reserves in our operating account and on our marketable securities, amortization expense and accretion income on our marketable securities and expense incurred in relation to the change in fair value of our contingent stock liability with ULRF.

Results of Operations

Comparison of Years Ended December 31, 2021 and 2020

The following table summarizes our results of operations for the years ended December 31, 2021 and 2020:

	Years ended December 31,		
	2021	2020	Change
		(in thousands)	
Operating expenses			
Research and development	$ 34,245	$ 15,278	$ 18,967
General and administrative	13,262	7,406	5,856
Total operating expenses	47,507	22,684	24,823
Loss from operations	(47,507)	(22,684)	(24,823)
Interest and other income (expense), net	(326)	(23)	(303)
Net loss	$ (47,833)	$ (22,707)	$ (25,126)

Research and development expenses

	Years ended December 31,		
	2021	2020	Change
		(in thousands)	
Direct research and development program expense:			
FCR001 clinical and pre-clinical programs	$ 8,843	$ 4,340	$ 4,503
Indirect research and development expenses:			
Personnel related (including stock-based compensation)	18,140	8,572	9,568
Facilities and other operating costs	7,262	2,366	4,896
Total research and development expenses	$ 34,245	$ 15,278	$ 18,967

Research and development activities are central to our business model. We expect that our research and development expenses will continue to increase substantially for the foreseeable future as we advance FCR001 through clinical trials, including our FREEDOM- 1 Phase 3 clinical trial, our FREEDOM-2 and FREEDOM-3 Phase 2 clinical trials, and we continue to develop additional product candidates.

Research and development expenses were $34.3 million for the year ended December 31, 2021, compared to $15.3 million for the year ended December 31, 2020. The increase of $19.0 million was primarily due to:

- An increase of $9.6 million in personnel costs related to the need for additional staff to conduct our FREEDOM-1 Phase 3 clinical trial, start-up and progress our FREEDOM-2 and FREEDOM-3 Phase 2 clinical trials, and to advance other pre-clinical activities. We also incurred additional personnel costs as we invested in hiring regulatory, medical affairs and process development personnel to further advance our pipeline programs;
- An increase of $4.9 million in external consulting, medical affairs, and patient advocacy related costs in support of ongoing and planned clinical trials; and
- An increase of $4.5 million in direct clinical trial expenses related to our FREEDOM-1 Phase 3 trial as additional clinical sites were activated and additional subjects were enrolled, as compared to the same period in 2020 when COVID-19 related delays limited such activity from March to December. This increase also includes direct start-up costs in our FREEDOM-2 and FREEDOM-3 Phase 2 clinical trials.

General and Administrative Expenses

The following table summarizes our general and administrative expenses to support our business activities for the years ended December 31, 2021 and 2020:

	Years ended December 31,		
	2021	2020	Change
		(in thousands)	
Personnel related (including stock-based compensation)	$ 5,525	$ 3,031	$ 2,494
Professional and consulting fees	2,859	1,981	878
Facility-related and other	4,878	2,394	2,484
Total general and administrative expenses	$ 13,262	$ 7,406	$ 5,856

General and administrative expenses were $13.3 million for the year ended December 31, 2021, compared to $7.4 million for the year ended December 31, 2020. The increase in general and administrative costs of $5.9 million was primarily due to:

- An increase of $2.5 million in personnel costs primarily due to the hiring of personnel in our finance, human resources and other administrative functions in support the growing organization, and increased stock compensation expense stemming from additional option grants as well as higher valuations for grants;
- An increase of $2.5 million in facility-related costs as well as other operating costs, primarily increased director and officer insurance expense following our IPO in May 2021; and
- An increase of $0.9 million of professional fees primarily due to increased legal and accounting fees in support of additional quarterly and annual reporting requirements.

Other Income (Expense), Net

Other income, net in the year ended December 31, 2021 was comprised of $0.8 million in interest income from our marketable securities and operating cash balance, $(0.4) million of net amortization expense on our marketable securities and $(0.7) million in expense related to a fair value adjustment of our contingent stock liability. Other income, net in the year ended December 31, 2020 was comprised of $0.4 million in interest income from our marketable securities and operating cash balance, $(0.1) million of net amortization expense on our marketable securities and $(0.3) million in expense related to a fair value adjustment of our contingent stock liability.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses. We have not yet commercialized any products and we do not expect to generate revenue from sales of products for several years, if at all. Since 2018, we have funded our operations primarily with proceeds from the sale of our convertible preferred stock. Through December 31, 2021, we had received net proceeds of $186.2 million from sales of our convertible preferred stock and net proceeds of $137.2 million, after deducting underwriting discounts and commissions and other expenses, from our IPO.

Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation. Our primary use of cash is to fund operating expenses, which consist primarily of research and development expenditures, and to a lesser extent, general and administrative expenditures. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses. As of December 31, 2021, we had cash and cash equivalents of $18.6 million and marketable securities of $225.4 million.

Contractual Obligations

We are currently a party to four operating leases for our manufacturing facility in Louisville, Kentucky, laboratory space in Houston, Texas, corporate office space in Wellesley, Massachusetts, and additional corporate

office space in Louisville, Kentucky. The future minimum lease obligations for these leases total $4.0 million over the next four years.

Furthermore, as described above, we are party to the ULRF License Agreement. Under the terms of the ULRF License Agreement, the Company is obligated to compensate ULRF three percent of net sales of all licensed products sold, one third of any non-royalty sublicensing income, and up to $1.625 million in regulatory and sales milestones on each licensed product upon the occurrence of specific events as outlined in the ULRF License Agreement; and annual license maintenance fees.

We have also entered into other contracts in the normal course of business with certain CROs and other third parties for nonclinical research studies and testing, as well as clinical trials. These contracts do not contain any minimum purchase commitments and are cancelable by us upon prior notice and, as a result, are not included in the table of contractual obligations and commitments above. Payments due upon cancellation consist only of payments for services provided and expenses incurred, including non-cancelable obligations of our service providers, up to the date of cancellation.

Cash Flows

The following table summarizes our sources and uses of cash for each of the periods presented:

	Years ended December 31,		
	2021	2020	Change
		(in thousands)	
Net cash used in operating activities	$ (39,988)	$ (19,212)	$ (20,776)
Net cash used in investing activities	(96,387)	(133,300)	36,913
Net cash provided by financing activities	137,400	131,123	6,277
Net increase (decrease) in cash and cash equivalents and restricted cash	$ 1,025	$ (21,389)	$ 22,414

Cash Flow from Operating Activities

During the year ended December 31, 2021, operating activities used $40.0 million of cash, due to our net loss of $47.8 million, partially offset by non-cash charges of $5.5 million and net cash provided by changes in our operating assets and liabilities of $2.3 million. Non-cash charges primarily consisted of $3.8 million of stock-based compensation expense, $1.0 million of depreciation on fixed assets and amortization of marketable securities and $0.7 million of expense related to the fair value adjustment of our contingent stock liability. Net cash provided by changes in our operating assets and liabilities primarily consisted of a $3.7 million increase in accounts payable and accrued expenses related to timing, offset by a $1.3 million increase in prepaids and other current assets driven by director and officer insurance premiums and a $0.1 million increase in other assets driven by security deposits for new leases.

During the year ended December 31, 2020, operating activities used $19.2 million of cash, due to our net loss of $22.7 million, partially offset by non-cash charges of $1.9 million and net cash provided by changes in our operating assets and liabilities of $1.6 million. Non-cash charges primarily consistent of $1.0 million of stock-based compensation expense, $0.6 million of depreciation on fixed assets and amortization of marketable securities and $0.3 million of expense related to the fair value adjustment of our contingent stock liability. Net cash provided by changes in our operating assets and liabilities primarily consisted of a $1.0 million increase in accounts payable and accrued expenses related to timing and a decrease in current assets of $0.6 million driven by a decrease in our prepaid balances with contract research organizations.

Cash Flow from Investing Activities

During the year ended December 31, 2021, investing activities used $96.4 million of cash, due to purchases of marketable securities of $275.9 million and purchases of property and equipment of $2.4 million, partially offset by maturities of marketable securities of $181.9 million.

During the year ended December 31, 2020, investing activities used $133.3 million of cash, due to purchases of marketable securities of $158.2 million and purchases of property and equipment of $1.3 million, partially offset by maturities of marketable securities of $26.2 million.

Cash Flow from Financing Activities

During the year ended December 31, 2021, net cash provided by financing activities was $137.4 million, primarily consisting of net proceeds after deducting underwriting discounts and commissions, of $139.5 million from our IPO, $0.3 million of proceeds from exercise of stock options and $0.2 million of proceeds from purchases of shares in our Employee Stock Purchase Plan, partially offset by $2.4 million paid for other IPO expenses $0.3 million paid in partial satisfaction of ULRF contingent stock liability.

During the year ended December 31, 2020, net cash provided by financing activities was $131.1 million, primarily consisting of proceeds from our issuances of Series B preferred stock in September 2020 of $114.5 million, net of issuance costs, issuances of Series A-1 preferred stock in August 2020 of $15.0 million, net of issuance costs, early exercise of stock options of $1.0 million and issuances of common stock from exercise of stock options of $0.6 million.

Future Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the late-stage clinical development of our product candidates. In addition, we expect to incur additional costs associated with operating as a public company. The timing and amount of our operating expenditures will depend largely on:

- the initiation, progress, timing, costs and results of preclinical studies and clinical trials for our product candidates or any future product candidates we may develop;
- the outcome, timing and cost of seeking and obtaining regulatory approvals from the FDA and comparable foreign regulatory authorities, including the potential for such authorities to require that we perform more preclinical studies or clinical trials than those that we currently expect or change their requirements on studies that had previously been agreed to;
- the cost to establish, maintain, expand, enforce and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with licensing, preparing, filing, prosecuting, defending and enforcing any patents or other intellectual property rights;
- the effect of competing technological and market developments;
- the costs of continuing to grow our business, including hiring key personnel and maintaining or acquiring operating space;
- market acceptance of any approved product candidates, including product pricing, as well as product coverage and the adequacy of reimbursement by third-party payors;
- the cost of acquiring, licensing or investing in additional businesses, products, product candidates and technologies;
- the cost and timing of selecting, auditing and potentially validating or expanding a manufacturing site for commercial-scale manufacturing;
- the cost of establishing sales, marketing and distribution capabilities for any product candidates for which we may receive regulatory approval and that we determine to commercialize; and
- our need to implement additional internal systems and infrastructure, including financial and reporting systems.

We believe that our existing cash and cash equivalents and marketable securities as of December 31, 2021, will enable us to fund our operating expenses and capital expenditure requirements for more than 12 months from the date

of issuance. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. We expect that we will require additional funding to (i) further develop FCR001 in our ongoing Phase 3 registrational trial, FREEDOM-1, through evaluation of its primary endpoint, including in-house manufacturing and quality assurance of clinical trial material, third-party clinical trials costs, clinical development and trial management, and personnel associated with each; (ii) continue research and development of FCR001 in additional pipeline programs such as living donor kidney transplant delayed tolerance induction and scleroderma in our FREEDOM-2 and FREEDOM-3 trials, respectively, through evaluation of their primary endpoints, including in-house manufacturing and quality assurance of clinical trial material, third-party clinical trials costs, clinical development and trial management, and personnel associated with each; (iii) develop expanded CMC operations to facilitate scale-up and commercialization of FCR001, or to engage a third-party manufacturer to undertake such commercialization; and (iv) develop our preclinical programs towards IND filings and/or into clinical trials. If we receive regulatory approval for any of product candidates, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution, depending on where we choose to commercialize those product candidates ourselves.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval for any product candidates or generate revenue from the sale of any product candidate for which we may obtain marketing approval. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of drugs that we do not expect to be commercially available for many years, if ever. Accordingly, we will need to obtain substantial additional funds to achieve our business objectives.

Adequate additional funds may not be available to us on acceptable terms, or at all. We do not currently have any committed external source of funds. Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, royalty-based financings, debt financings, collaborations, strategic alliances, and marketing, distribution or licensing arrangements with third parties. To the extent that we raise additional capital through the sale of equity or convertible debt securities, ownership interest may be materially diluted, and the terms of such securities could include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing, royalty-based financing and preferred equity financing, if available, may involve agreements that include restrictive covenants that limit our ability to take specified actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise funds through royalty-based financings, collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, reduce or eliminate our product development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Critical Accounting Policies and Estimates

Our financial statements are prepared in accordance with generally accepted accounting principles (GAAP) in the United States. The preparation of our financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, costs and expenses, and the disclosure of contingent assets and liabilities in our financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 2 to our financial statements appearing at the end of this Annual Report, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our financial statements.

Research and Development Contract Costs and Accruals

As part of the process of preparing our financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advance payments. We make estimates of our accrued expenses as of each balance sheet date in the financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of these estimates with the service providers and make adjustments, if necessary. Examples of estimated accrued research and development expenses include fees paid to:

- vendors in connection with clinical development activities; and
- CROs and investigative sites in connection with pre-clinical, non-clinical, and human clinical trials

We base the expense recorded related to external research and development on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple CROs that supply, conduct and manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or the amount of prepaid expenses accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

Stock-Based Compensation Expense

We measure stock-based awards granted to employees, directors, and nonemployees based on their fair value on the date of the grant and recognize compensation expense for those awards over the requisite service period, which is generally the vesting period of the respective award. For stock-based awards with service-based vesting conditions, we recognize compensation expense using the straight-line method. The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model, which requires inputs based on certain subjective assumptions, including the expected stock price volatility, the expected term of the option, the risk-free interest rate for a period that approximates the expected term of the option, and our expected dividend yield. The fair value of each option to purchase common stock award is estimated on the date of grant based on the fair value of our common stock on that same date.

Determination of the Fair Value of Common Stock

As there had been no public market for our common stock prior to the closing of our IPO, the estimated fair value of our common stock was determined by our board of directors as of the date of each option grant with input from management, considering our most recently available third-party valuations of common stock, and our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. These independent third-party valuations of our equity instruments were performed contemporaneously with identified value inflection points. Our common stock valuation was prepared using the option-pricing method ("OPM"), which used a market approach to estimate our enterprise value, as well as the probability-weighted expected return method ("PWERM") and the hybrid method, a combination of OPM and PWERM.

These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation. We account for equity-based compensation in accordance with ASC 718, *Compensation-Stock Compensation* ("ASC 718"). In accordance with ASC 718, compensation cost is measured at

estimated fair value and is included as compensation expense over the vesting period during which service is provided in exchange for the award. Our common stock valuation was prepared using the OPM, which used a market approach to estimate our enterprise value.

The OPM treats common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common stock has value if the funds available for distribution to stockholders exceed the value of the liquidation preferences at the time of a liquidity event, such as a strategic sale or merger. The common stock is modeled as a call option on the underlying equity value at a predetermined exercise price. In the model, the exercise price is based on a comparison with the total equity value rather than, as in the case of a regular option, a comparison with a per share stock price. Thus, common stock is considered to be a call option with a claim on the enterprise at an exercise price equal to the remaining value immediately after the preferred stock liquidation preference is paid. The OPM uses the Black-Scholes option pricing model to price the call options. This model defines the fair value of securities as functions of the current fair value of a company and uses assumptions such as the anticipated timing of a potential liquidity event and the estimated volatility of the equity securities.

The PWERM is a scenario-based analysis that estimates the value per share of common stock based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes considered by the Company, as well as the economic and control rights of each share class. The OPM, PWERM and/or the hybrid methods were used for our January 2021 valuations.

The assumptions used to determine the fair values of stock options granted to employees and directors during the years ended December 31, 2021 and December 31, 2020, are presented as follows:

	December 31,	
	2021	2020
Fair value of common stock	$5.72-17.00	$1.44-5.72
Dividend yield	—%	—%
Volatility	80.6%-91.25%	72.8%-80.6%
Risk-free interest rate	0.50%-1.33%	0.31%-1.46%
Expected term (years)	6.25	6.25

The assumptions underlying these valuations were highly complex and subjective and represented management's best estimates, which involved inherent uncertainties and the application of management's judgment. As a result, if we had used significantly different assumptions or estimates, the fair value of our common stock and our stock-based compensation expense could be materially different.

Once a public trading market for our common stock was established in connection with the completion of our IPO, our board of directors no longer have to estimate the fair value of our common stock in connection with our accounting for granted stock options and other such awards we may grant, as the fair value of our common stock is now determined based on the quoted market price of our common stock.

Emerging Growth Company and Smaller Reporting Status

In April 2012, the Jumpstart Our Business Startups Act of 2012 ("JOBS Act") was enacted. Section 107 of the JOBS Act provides that an "emerging growth company" ("EGC") can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended (Securities Act), for complying with new or revised accounting standards. Thus, an EGC can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to use the extended transition period for new or revised accounting standards during the period in which we remain an emerging growth company; however, we may adopt certain new or revised accounting standards early to the extent allowed by the standard.

We will remain an emerging growth company until the earliest to occur of: (i) the last day of the fiscal year in which we have more than $1.07 billion in annual revenue; (ii) the date we qualify as a "large accelerated filer," with at least $700.0 million of equity securities held by non-affiliates; (iii) the date on which we have issued more than

$1.0 billion in non-convertible debt securities during the prior three-year period; and (iv) the last day of the fiscal year ending after the fifth anniversary of our initial public offering.

We are also a “smaller reporting company” meaning that the market value of our stock held by non-affiliates is less than $700 million and our annual revenue was less than $100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than $250 million or (ii) our annual revenue was less than $100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the Securities and Exchange Commission

Recently Issued and Adopted Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2 to our financial statements appearing at the end of this Annual Report.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Our primary exposure to market risk relates to changes in interest rates. As of December 31, 2021 and 2020, we had cash and cash equivalents of $18.6 million and $17.6 million, respectively. As of December 31, 2021 and 2020, we had marketable securities of $225.4 million and $131.9 million, respectively. Our exposure to interest rate sensitivity is affected by changes in the general level of U.S. interest rates. If market interest rates were to increase immediately and uniformly by 100 basis points, or one percentage point, the net fair value of our interest sensitive marketable securities would not experience a material change in fair market value.

All of our employees and our operations are currently located in the United States. We have, from time to time, engaged in contracts with contractors or other vendors in a currency other than the U.S. dollar. To date, we have had minimal exposure to fluctuations in foreign currency exchange rates as the time period between the date that transactions are initiated, and the date of payment or receipt of payment is generally of short duration. Accordingly, we believe we do not have a material exposure to foreign currency risk.

Inflation generally affects us by increasing our cost of labor. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the years ended December 31, 2021 or 2020.

Item 8. Financial Statements and Supplementary Data.

Our consolidated financial statements, together with the reports of our independent registered public accounting firms, appear beginning on page F-1 of this Annual Report for the years ended December 31, 2021 and December 31, 2020.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

The Company has established disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the under the Exchange Act) designed to ensure that information required to be disclosed in the reports that the Company files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and is accumulated and communicated to management, including the principal executive officer (our Chief Executive Officer) and principal financial officer (our Chief Financial Officer), to allow timely decisions regarding required disclosure. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2021. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, mean controls and other procedures of a company that are designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosures.

Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgement in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2021 our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at a reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding our internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) or an attestation report of our independent registered accounting firm due to a transition period established by rules of the SEC for newly public companies.

Changes in Internal Control over Financial Reporting

There has been no change in our internal controls over financial reporting as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Securities Exchange Act of 1934 during the fiscal year ended December 31, 2021 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

As of the date of this Annual Report on Form 10-K, we intend to hold our 2022 Annual Meeting of Stockholders (the "2022 Annual Meeting") on or about June 9, 2022 at 1 P.M. local time, at 93 Worcester Street, Wellesley, Massachusetts 02481. We are providing the following disclosure in accordance with our Amended and Restated Bylaws (the "Bylaws") and Rule 14a-8 under the Securities Exchange Act of 1934, as amended (the "Exchange Act").

Bylaws Advance Notice Deadline for Submission of Stockholder Proposals and Director Nominations

Pursuant to our Bylaws, since the 2022 Annual Meeting is the first Annual Meeting following our initial public offering, for notice of stockholder proposals submitted outside of Rule 14a-8 of the Exchange Act and director nominations to be timely, they must be so received not later than the later of (A) the close of business on the 90thday before the 2022 Annual Meeting; or (B) the close of business on the 10thday following the day on which public announcement of the date of the 2022 Annual Meeting is first made by us. As this is our first public disclosure of the date of the 2022 Annual Meeting, to be considered timely, stockholder proposals submitted outside of Rule 14a-8 of the Exchange Act and director nominations, in each case intended to be brought before the 2022 Annual Meeting, must be received no later than the close of business on March 27, 2022. Any such stockholder proposals and director nominations must be directed to our Corporate Secretary at our corporate offices at 570 S. Preston St., Louisville, KY 40202. Such stockholder proposals and director nominations must also comply with the advance notice provisions contained in Section 2 of our Bylaws.

Rule 14a-8 Deadline for Submission of Stockholder Proposals

As we did not hold an annual meeting in 2021, pursuant to Rule 14a-8(e)(2) under the Exchange Act, the deadline for the receipt of any stockholder proposals submitted pursuant to Rule 14a-8 of the Exchange Act for inclusion in the Company's proxy materials for the 2022 Annual Meeting would be a reasonable time before the company begins to print and send its proxy materials. We have determined that March 27, 2022 is a reasonable time before we expect to begin to print and distribute its proxy materials for the 2022 Annual Meeting, and that any stockholder proposals must be received on or before the close of business on that day. Such proposals must be directed to our Corporate Secretary at our corporate offices at 570 S. Preston St., Louisville, KY 40202. Such proposals must also comply with Rule 14a-8 of the Exchange Act.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the SEC in connection with our 2022 Annual Meeting of Stockholders not later than 120 days after the close of the Company's fiscal year ended December 31, 2021.

We have adopted a Code of Business Conduct and Ethics for all of our directors, officers and employees as required by Nasdaq governance rules and as defined by applicable SEC rules. Stockholders may locate a copy of our Code of Business Conduct and Ethics on our website at www.talaristx.com or request a copy without charge from:

Talaris Therapeutics, Inc.
Attention: Investor Relations
570 S. Preston St.
Louisville, KY 40202

We will post to our website any amendments to the Code of Business Conduct and Ethics, and any waivers that are required to be disclosed by the rules of either the SEC or Nasdaq.

Item 11. Executive Compensation.

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the SEC in connection with our 2022 Annual Meeting of Stockholders not later than 120 days after the close of the Company's fiscal year ended December 31, 2021.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the SEC in connection with our 2022 Annual Meeting of Stockholders not later than 120 days after the close of the Company's fiscal year ended December 31, 2021.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2021.

Item 14. Principal Accounting Fees and Services.

Information about aggregate fees billed to us by our independent principal accountant, Deloitte & Touche LLP (PCAOB ID No. 34), located in Boston, Massachusetts, will be presented in our definitive proxy statement to be filed with the SEC with respect to our 2022 Annual Meeting of Stockholders under the caption "Audit Committee Matters — Principal Accounting Firm Fees" and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(1) For a list of the financial statements included herein, see Index to the Consolidated Financial Statements on page F-1 of this Annual Report on Form 10-K, incorporated into this Item by reference.

(2) Financial statement schedules have been omitted because they are either not required or not applicable or the information is included in the consolidated financial statements or the notes thereto.

(3) The exhibits required by Item 601 of Regulation S-K and Item 15(b) of this Annual Report on Form 10-K are set forth on the Exhibit Index immediately preceding the signature page of this Annual Report on Form 10-K. The Exhibit Index is incorporated herein by reference.

Exhibit Number	Description
3.1	Third Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Form 8-K (File No. 001-40384) filed on May 11, 2021)
3.2	Second Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's Form 8-K (File No. 001-40384) filed on May 11, 2021)
4.1	Specimen Common Stock Certificate (incorporated by reference to Exhibit 4.1 to our Registration Statement on Form S-1/A (File No. 333-255316) filed with the SEC on May 3, 2021)
4.2	Amended and Restated Investors' Rights Agreement among the Registrant and certain of its stockholders, effective as of September 22, 2020 (incorporated by reference to Exhibit 4.2 of the Registrant's Registration Statement on Form S-1 (File No. 333-255316) filed on April 16, 2020)
4.3*	Description of Securities
10.1#	2021 Stock Option and Incentive Plan and form of award agreements thereunder (incorporated by reference to Exhibit 10.2 to our Registration Statement on Form S-1/A (File No. 333-255316) filed with the SEC on May 3, 2021)
10.2#	2021 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.3 to our Registration Statement on Form S-1/A (File No. 333-255316) filed with the SEC on May 3, 2021)
10.3#	Forms of Indemnification Agreement between the Registrant and each of its directors and executive officers (incorporated by reference to Exhibit 10.4 to our Registration Statement on Form S-1/A (File No. 333-255316) filed with the SEC on May 3, 2021)
10.4#	Senior Executive Cash Incentive Bonus Plan (incorporated by reference to Exhibit 10.5 to our Registration Statement on Form S-1/A (File No. 333-255316) filed with the SEC on May 3, 2021)
10.5#	Severance and Change in Control Plan (incorporated by reference to Exhibit 10.6 to our Registration Statement on Form S-1/A (File No. 333-255316) filed with the SEC on May 3, 2021)
10.6#	Non-Employee Director Compensation Policy (incorporated by reference to Exhibit 10.7 to our Registration Statement on Form S-1/A (File No. 333-255316) filed with the SEC on May 3, 2021)
10.7	Lease Agreement between the Registrant and the University of Louisville, dated as of November 1, 2018, as amended on July 1, 2019, February 1, 2020, and May 15, 2020 (incorporated by reference to Exhibit 10.8 to our Registration Statement on Form S-1/A (File No. 333-255316) filed with the SEC on May 3, 2021)
10.8#	Employment Agreement, by and between the Registrant and Scott Requadt, dated November 1, 2018 (incorporated by reference to Exhibit 10.9 to our Registration Statement on Form S-1/A (File No. 333-255316) filed with the SEC on May 3, 2021)
10.9#	Employment Agreement, by and between the Registrant and Suzanne T. Ildstad, dated November 1, 2018 (incorporated by reference to Exhibit 10.10 to our Registration Statement on Form S-1/A (File No. 333-255316) filed with the SEC on May 3, 2021)
10.10#	Offer Letter, by and between the Registrant and Nancy Krieger, dated November 1, 2018 (incorporated by reference to Exhibit 10.11 to our Registration Statement on Form S-1/A (File No. 333-255316) filed with the SEC on May 3, 2021)
10.11#	Offer Letter, by and between the Registrant and Michael Zdanowski, dated September 29, 2020 (incorporated by reference to Exhibit 10.12 to our Registration Statement on Form S-1/A (File No. 333-255316) filed with the SEC on May 3, 2021)

10.12#	Offer Letter, by and between the Registrant and Mary Kay Fenton, as amended, dated January 21, 2021 (incorporated by reference to Exhibit 10.13 to our Registration Statement on Form S-1/A (File No. 333-255316) filed with the SEC on May 3, 2021)
10.13†	Amended and Restated Exclusive License Agreement, by and between the Registrant and University of Louisville Research Foundation, Inc., dated October 31, 2018 (incorporated by reference to Exhibit 10.14 to our Registration Statement on Form S-1/A (File No. 333-255316) filed with the SEC on May 3, 2021)
10.14#	Deferred Compensation Plan for Non-Employee Directors of the Registrant (incorporated by reference to Exhibit 10.15 to our Registration Statement on Form S-1/A (File No. 333-255316) filed with the SEC on May 3, 2021)
21.1*	List of Subsidiaries of the Registrant
23.1*	Consent of Deloitte & Touche LLP, independent registered public accounting firm.
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2*	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS*	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104*	Cover Page Interactive Data File (embedded within the Inline XBRL document)

# Indicates a management contract or any compensatory plan, contract or arrangement.
* Filed herewith.
† Portions of this exhibit (indicated by asterisks) were omitted pursuant to Item 601(b)(10) of Regulation S-K.
+ The certifications furnished in Exhibit 32.1 hereto are deemed to be furnished with this Annual Report on Form 10-K and will not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.

Item 16. Form 10-K Summary

The Company has elected not to include summary information.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

Talaris Therapeutics, Inc.

Date: March 17, 2022 By: /s/ Scott Requadt

Scott Requadt
President and Chief Executive Officer
(Principal Executive Officer)

Each person whose individual signature appears below hereby authorizes and appoints Scott Requadt and Mary Kay Fenton, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this annual report on Form 10-K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Scott Requadt **Scott Requadt**	President, Chief Executive Officer and Director (Principal Executive Officer)	March 17, 2022
/s/ Mary Kay Fenton **Mary Kay Fenton**	Chief Financial Officer (Principal Financial and Accounting Officer)	March 17, 2022
/s/ Francois Nader **Francois Nader**	Chairman of the Board	March 17, 2022
/s/ Sandip Agarwala **Sandip Agarwala**	Director	March 17, 2022
/s/ Nicholas Galakatos **Nicholas Galakatos**	Director	March 17, 2022
/s/ Suzanne Ildstad **Suzanne Ildstad**	Chief Scientific Officer and Director	March 17, 2022
/s/ Geoff MacKay **Geoff MacKay**	Director	March 17, 2022
/s/ Mark McDade **Mark McDade**	Director	March 17, 2022
/s/ Gaurav Shah **Gaurav Shah**	Director	March 17, 2022
/s/ Sapna Srivastava **Sapna Srivastava**	Director	March 17, 2022

INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the shareholders and the Board of Directors of Talaris Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Talaris Therapeutics, Inc. (the "Company") as of December 31, 2021 and 2020, the related statements of operations and comprehensive loss, convertible preferred stock and shareholders' deficit, and cash flows, for each of the two years in the period ended December 31, 2021, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2021, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Deloitte & Touche LLP

Boston, Massachusetts

March 17, 2022

We have served as the Company's auditor since 2019.

TALARIS THERAPEUTICS, INC.

BALANCE SHEETS
(in thousands, except share and per share amounts)

	As of December 31,	
	2021	**2020**
Assets		
Current assets:		
Cash and cash equivalents	$ 18,614	$ 17,589
Marketable securities	225,357	131,899
Prepaid and other current assets	2,543	1,263
Total current assets	246,514	150,751
Property and equipment, net	4,804	2,013
Other assets	104	14
Total assets	$ 251,422	$ 152,778
Liabilities and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 2,556	$ 767
Accrued expenses	5,431	2,637
Total current liabilities	7,987	3,404
Share repurchase liability	593	996
Contingent stock liability	—	373
Other liabilities	33	—
Total liabilities	8,613	4,774
Commitments and contingencies (Note 8)		
Convertible preferred stock		
Series A convertible preferred stock, $0.0001 par value, no shares authorized, issued and outstanding as of December 31, 2021 and 40,000,000 shares authorized, issued and outstanding (liquidation preference of $40,000) as of December 31, 2020	—	37,383
Series A-1 convertible preferred stock, $0.0001 par value, no shares authorized, issued and outstanding as of December 31, 2021 and 28,000,000 shares authorized, issued and outstanding (liquidation preference of $35,000) as of December 31, 2020	—	34,272
Series B convertible preferred stock, $0.0001 par value, no shares authorized, issued and outstanding as of December 31, 2021 and 62,499,993 shares authorized, issued and outstanding (liquidation preference of $114,994) as of December 31, 2020	—	114,496
Total convertible preferred stock	—	186,151
Stockholders' equity (deficit)		
Common stock, $0.0001 par value, 140,000,000 shares authorized and 39,763,049 issued and outstanding and 10,000,000 non-voting shares authorized and 1,150,000 issued and outstanding as of December 31, 2021 and 36,366,101 shares authorized and 7,087,130 issued and outstanding as of December 31, 2020	4	1
Additional paid-in-capital	333,730	4,879
Accumulated deficit	(90,847)	(43,014)
Accumulated other comprehensive loss	(78)	(13)
Total stockholders' equity (deficit)	242,809	(38,147)
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$ 251,422	$ 152,778

The accompanying notes are an integral part of these financial statements.

TALARIS THERAPEUTICS, INC.

STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(in thousands, except share and per share amounts)

	Years Ended December 31,	
	2021	2020
Operating expenses		
Research and development	$ 34,245	$ 15,278
General and administrative	13,262	7,406
Total operating expenses	47,507	22,684
Loss from operations	(47,507)	(22,684)
Interest and other income (expense), net	(326)	(23)
Net loss	$ (47,833)	$ (22,707)
Unrealized loss on marketable securities	(65)	(13)
Total other comprehensive loss	(65)	(13)
Total comprehensive loss	$ (47,898)	$ (22,720)
Net loss attributable to common stockholders	$ (47,833)	$ (22,707)
Net loss per common share, basic and diluted	(1.64)	$ (3.40)
Weighted average number of common shares outstanding used in computation of net loss per common share, basic and diluted	29,126,373	6,685,066

The accompanying notes are an integral part of these financial statements.

TALARIS THERAPEUTICS, INC.

STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' DEFICIT
(in thousands, except share amounts)

	Series A Convertible Preferred Stock		Series A-1 Convertible Preferred Stock		Series B Convertible Preferred Stock		Common Stock		Additional		Accumulated Other	Total
	Outstanding Shares	Amount	Outstanding Shares	Amount	Outstanding Shares	Amount	Outstanding Shares	Amount	Paid-in Capital	Accumulated Deficit	Comprehensive Income (Loss)	Stockholders' Deficit
Balance at December 31, 2019	40,000,000	$ 37,383	16,000,000	$ 19,307	—	$ —	6,390,137	$ 1	$ 3,204	$ (20,307)	$ —	$ (17,102)
Issuance of Series A-1 convertible preferred stock, net of issuance costs	—	—	12,000,000	14,966	—	—	—	—	—	—	—	—
Issuance of Series B convertible preferred stock, net of issuance costs	—	—	—	—	62,499,993	114,496	—	—	—	—	—	—
Issuance of common stock upon exercise of stock options	—	—	—	—	—	—	696,993	0	653	—	—	653
Stock-based compensation expense	—	—	—	—	—	—	—	—	1,022	—	—	1,022
Net loss	—	—	—	—	—	—	—	—	—	(22,707)	—	(22,707)
Unrealized loss on marketable securities	—	—	—	—	—	—	—	—	—	—	(13)	(13)
Balance at December 31, 2020	40,000,000	$ 37,383	28,000,000	$ 34,272	62,499,993	$ 114,496	7,087,130	$ 1	$ 4,879	$ (43,014)	$ (13)	$ (38,147)
Issuance of common stock, net of underwriting discounts and issuance costs of $12,858,764	—	—	—	—	—	—	8,825,000	1	137,165	—	—	137,166
Conversion of convertible preferred stock to common stock	(40,000,000)	(37,383)	(28,000,000)	(34,272)	(62,499,993)	(114,496)	24,392,498	2	186,149	—	—	186,151
Issuance of contingent common stock	—	—	—	—	—	—	48,889	—	831	—	—	831
Issuance of common stock upon exercise of stock options	—	—	—	—	—	—	543,649	—	721	—	—	721
Issuance of common stock under 2021 employee stock purchase plan	—	—	—	—	—	—	15,883	—	207	—	—	207
Stock-based compensation expense	—	—	—	—	—	—	—	—	3,778	—	—	3,778
Net loss	—	—	—	—	—	—	—	—	—	(47,833)	—	(47,833)
Unrealized loss on marketable securities	—	—	—	—	—	—	—	—	—	—	(65)	(65)
Balance at December 31, 2021	$ —	$ —	$ —	$ —	$ —	$ —	$ 40,913,049	$ 4	$ 333,730	$ (90,847)	$ (78)	$ 242,809

The accompanying notes are an integral part of these financial statements.

TALARIS THERAPEUTICS, INC.

STATEMENTS OF CASH FLOWS
(in thousands)

	Years Ended December 31,	
	2021	2020
Cash flows from operating activities:		
Net loss	$ (47,833)	$ (22,707)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	623	447
Accretion and amortization of marketable securities, net	427	95
Stock-based compensation expense	3,778	1,022
Fair value adjustment of contingent stock liability	735	310
Gain on disposal of property and equipment	(33)	—
Other	—	7
Changes in operating assets and liabilities:		
Prepaid and other current assets	(1,280)	553
Other assets	(90)	6
Accounts payable	1,323	100
Accrued expenses	2,329	955
Other liabilities	33	—
Net cash used in operating activities	(39,988)	(19,212)
Cash flows from investing activities:		
Purchases of property and equipment	(2,437)	(1,286)
Purchases of marketable securities	(275,879)	(158,237)
Maturities of marketable securities	181,929	26,224
Net cash used in investing activities	(96,387)	(133,300)
Cash flows from financing activities:		
Proceeds from issuances of Series A-1 convertible preferred stock	—	15,000
Proceeds from issuances of Series B convertible preferred stock	—	115,000
Preferred stock issuance costs	—	(526)
Proceeds from issuance of common stock	139,523	—
Common stock issuance costs	(2,369)	—
Payment of partial settlement of contingent stock liability	(277)	—
Proceeds from exercise of stock options	317	1,649
Proceeds from issuance of common stock under 2021 employee stock purchase plan	206	—
Net cash provided by financing activities	137,400	131,123
Net increase (decrease) in cash and cash equivalents	1,025	(21,389)
Cash and cash equivalents at beginning of period	17,589	38,978
Cash and cash equivalents at end of period	$ 18,614	$ 17,589
Supplemental disclosure of non-cash investing and financing activities:		
Property and equipment additions included in accounts payable and accrued expenses	$ 1,028	$ 86
Preferred stock issuance costs included in accounts payable and accrued expenses	$ —	$ 11

The accompanying notes are an integral part of these financial statements.

1. Nature of Business and Liquidity

Talaris Therapeutics, Inc. (“Talaris” or the “Company”) is a late-clinical stage, cell therapy company developing an innovative method of allogeneic hematopoietic stem cell transplantation ("allo-HSCT"), called "Facilitated Allo-HSCT Therapy", that the Company believes has the potential to transform the standard of care in solid organ transplantation, certain severe autoimmune diseases and certain severe blood, immune and metabolic disorders. The Company believes that these indications, individually and collectively, represent a significant unmet need and commercial opportunity. The Company maintains corporate offices in Boston, Massachusetts, a laboratory in Houston, Texas and its cell processing facility in Louisville, Kentucky.

Initial Public Offering

The Company completed an initial public offering (“IPO”) on May 11, 2021 in which the Company issued and sold 8,825,000 shares of its common stock at a public offering price of $17.00 per share. The Company’s aggregate gross proceeds from the sale of shares in the IPO was $150.0 million before underwriting discounts and commissions and other expenses of approximately $12.9 million. Upon completion of the offering, the Company’s outstanding convertible preferred stock was automatically converted into shares of common stock and non-voting common stock. Following the IPO, there were no shares of preferred stock outstanding. Prior to the IPO, on April 30, 2021, the Company’s board of directors and shareholders approved a one-for-5.35 reverse share split of issued and outstanding common shares and incentive shares and a proportional adjustment to the existing conversion ratios for the Company’s convertible preferred stock.

Liquidity

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. Management has evaluated whether there are conditions and events that raise substantial doubt about the Company’s ability to continue as a going concern within one year after the date the financial statements are issued. Since its inception, the Company has incurred net losses and negative cash flows from operations. During the years ended December 31, 2021 and 2020, the Company incurred a net loss of $47.8 million and $22.7 million, respectively, and used $40.0 million and $19.2 million in cash for operations, respectively. In addition, as of December 31, 2021, the Company had an accumulated deficit of $90.8 million. The Company expects to continue to generate operating losses and negative cash flows for the foreseeable future. The Company currently expects the cash and cash equivalents of $18.6 million and marketable securities of $225.4 million as of December 31, 2021, will be sufficient to fund its operating expenses and capital requirements for more than 12 months from the date the financial statements are available to be issued.

Additional funding will be needed to finance future clinical, pre-clinical, manufacturing and commercial activities. There is no assurance the Company will be successful in obtaining such additional financing on terms acceptable to it, if at all, and it may not be able to enter into other arrangements. If the Company is unable to obtain funding, it could be forced to delay, reduce or eliminate our research and development programs, portfolio expansion or commercialization efforts, which could adversely affect its business prospects and ability to continue operations.

The Company is subject to risks common to companies in the biopharmaceutical industry. There can be no assurance that the Company’s research and development will be successfully completed, that adequate protection for its intellectual property will be maintained, that any products developed will obtain required regulatory approval, or that any approved products will be commercially viable. Even if the development efforts are successful, it is uncertain when, if ever, the Company will generate significant product sales and ultimately net income.

Coronavirus Pandemic

In March 2020, the World Health Organization declared the COVID-19 outbreak a pandemic. The worldwide COVID-19 pandemic has affected and may affect in the future the Company’s ability to initiate and complete preclinical studies, delay the initiation and completion of its current and planned clinical trials, disrupt regulatory activities or have other adverse effects on its business, results of operations, financial condition and prospects. In addition, the pandemic has caused substantial disruption in the financial markets and may adversely impact economies worldwide, both of which could adversely affect the Company’s business, operations and ability to raise funds to support its operations.

The Company cannot be certain what the overall impact of the COVID-19 pandemic will be on its business, and it has the potential to adversely affect its business, financial condition, results of operations and prospects.

2. Summary of Significant Accounting Policies

Basis of Presentation

The financial statements have been prepared in accordance with generally accepted accounting principles in the United States of America (US GAAP).

Use of Estimates

The preparation of financial statements in conformity with US GAAP requires management to make judgments, assumptions, and estimates that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of financial statements, and the reported amounts of income and expense during the reporting period. The most significant estimates relate to the determination of fair value of the Company's common stock, determination of the fair value of stock option grants and estimates related to the amount of accrued research and development expenses as of the balance sheet date. Management evaluates its estimates and assumptions on an ongoing basis using historical experience and other factors, including the current economic environment, and makes adjustments when the facts and circumstances dictate. These estimates are based on information available as of the date of the financial statements; therefore, actual results could differ from those estimates.

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of three months or less at the date of purchase to be cash equivalents. As of December 31, 2021 and 2020, cash consists primarily of checking and savings deposits and money market fund holdings.

Marketable Securities

The Company classifies its marketable securities as available-for-sale securities, which are carried at their fair value based on the quoted market prices of the securities. Unrealized gains and losses are reported as accumulated other comprehensive loss, a separate component of stockholders' deficit. Realized gains and losses on available-for-sale securities are included in net loss in the period earned or incurred.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation. Depreciation expense is recognized using the straight-line method over the estimated useful life of each asset. Equipment and furniture and fixtures are depreciated over five or seven year lives. Leasehold improvements are amortized over the shorter of the lease term or the five-year estimated useful life of the asset. Computer equipment and computer software are depreciated over three years. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is included in loss from operations. Expenditures for repairs and maintenance are expensed as incurred.

Impairment of Long-Lived Assets

The Company evaluates its long-lived assets, which consist primarily of property and equipment, for impairment whenever events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to the future undiscounted net cash flows expected to be generated by the asset. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the carrying amount of the asset exceeds the fair value of the asset. No impairments have been identified as of December 31, 2021 and 2020.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to significant concentration of credit risk consist primarily of cash and cash equivalents. The Company's investment policy includes guidelines regarding the quality of the financial institutions and financial instruments and defines allowable investments that it believes minimizes the exposure to

concentration of credit risk. The Company may invest in money market funds (minimum of $1 billion in assets), U.S. Treasury securities, corporate debt, bank debt, U.S. government-related agency securities, other sovereign debt, municipal debt and commercial paper. These deposits may exceed federally insured limits. The Company has not experienced any losses historically in these accounts and believes that it is not exposed to significant credit risk as our deposits are held at financial institutions that management believes to be of high credit quality.

Fair Value of Financial Instruments

Fair value is defined as the price that the Company would receive to sell an investment in a timely transaction or pay to transfer a liability in a timely transaction with an independent buyer in the principal market, or in the absence of a principal market, the most advantageous market for the investment or liability. A framework is used for measuring fair value utilizing a three-tier hierarchy that prioritizes the inputs to valuation techniques used to measure fair value. The hierarchy gives the highest priority to unadjusted quoted prices in active markets for identical assets or liabilities (Level 1 investments) and the lowest priority to unobservable inputs (Level 3 investments).

The three levels of the fair value hierarchy are as follows:

- ***Level 1 inputs:*** Unadjusted quoted prices in active markets that are accessible at the measurement date for identical, unrestricted assets or liabilities;
- ***Level 2 inputs:*** Quoted prices in markets that are not considered to be active or financial instrument valuations for which all significant inputs are observable, either directly or indirectly; and,
- ***Level 3 inputs:*** Prices or valuations that require inputs that are both significant to the fair value measurement and unobservable.

Financial instruments are categorized in their entirety based on the lowest level of input that is significant to the fair value measurement. The assessment of the significance of a particular input to the fair value measurement requires judgment and considers factors specific to the investment.

The Company’s money market funds and marketable securities are carried at fair value determined according to the fair value hierarchy described above (Level 1 and Level 2, respectively).

The Company’s contingent stock liability as of December 31, 2020 (see Note 3) is carried at fair value determined according to the fair value hierarchy described above (Level 3).

Research and Development Expenses

Research and development expenses include (i) employee-related expenses, including salaries, benefits, travel and stock-based compensation expense; (ii) external research and development expenses incurred under arrangements with third parties, such as contract research organization agreements, investigational sites, and consultants; (iii) the cost of acquiring, developing, and manufacturing clinical study materials; (iv) costs associated with preclinical and clinical activities and regulatory operations; (v) costs incurred in development of intellectual property; and (vi) an allocated portion of facilities and other infrastructure costs associated with our research and development activities. Costs incurred in connection with research and development activities are expensed as incurred.

The Company enters into consulting, research, and other agreements with commercial entities, researchers, universities, and others for the provision of goods and services. Such arrangements are generally cancelable upon reasonable notice and payment of costs incurred. Costs are considered incurred based on an evaluation of the progress to completion of specific tasks under each contract using information and data provided by the respective vendors, including the Company’s clinical sites. These costs consist of direct and indirect costs associated with specific projects, as well as fees paid to various entities that perform certain research on behalf of the Company. Depending upon the timing of payments to the service providers, the Company recognizes prepaid expenses or accrued expenses related to these costs. These accrued or prepaid expenses are based on management’s estimates of the work performed under service agreements, milestones achieved, and experience with similar contracts. The Company monitors each of these factors and adjusts estimates accordingly.

Stock-Based Compensation

The Company measures all stock options and other stock-based awards granted to employees, nonemployees, and directors based on the fair value on the date of the grant and recognizes stock-based compensation expense of those awards over the requisite service period, which is generally the vesting period of the respective award. Generally, the Company issues stock option awards with only service-based vesting conditions and records the expense for these awards using the straight-line method. The Company's policy is to account for forfeitures when they occur.

The Company classifies stock-based compensation expense in its statement of operations in the same manner in which the award recipient's payroll costs are classified or in which the award recipients' service payments are classified.

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model. The Company recently completed its IPO and lacks company-specific historical and implied volatility information. Therefore, it estimates its expected stock volatility based on the historical volatility of a publicly traded set of peer companies and expects to continue to do so until it has adequate historical data regarding the volatility of its own traded stock price. The expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The expected term of stock options granted to non-employees is equal to the contractual term of the option award. The risk-free interest rate is determined by reference to the US Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is zero because the Company has never paid cash dividends on common stock and does not expect to pay any cash dividends in the foreseeable future.

Prior to the Company's IPO, the Company considered the estimated fair value of the common stock as of the measurement date in determining the exercise price for options granted. The estimated fair value of the common stock was determined at each grant date based upon a variety of factors, including the illiquid nature of the common stock, arm's-length sales of the Company's capital stock (including convertible preferred stock), the effect of the rights and preferences of the preferred shareholders, and the prospects of a liquidity event. Among other factors are the Company's financial position and historical financial performance, forecasted future operations of the Company, an evaluation or benchmark of the Company's competition, and the current business climate in the marketplace. Significant changes to the key assumptions underlying the factors used could result in different fair values of common stock at each valuation date. The fair value for options granted since the Company's IPO are based on the closing stock price on grant date.

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the financial statements or in the Company's tax returns. Deferred tax assets and liabilities are determined on the basis of the differences between the financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

The Company accounts for uncertainty in income taxes recognized in the financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more likely than not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the financial statements. The amount of the benefit that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

The Company provides reserves for potential payments of tax to various tax authorities related to uncertain tax positions. These reserves are based on a determination of whether and how much of a tax benefit taken by the Company in its tax filings or positions is more likely than not to be realized following resolution of any potential contingencies present related to the tax benefit. Potential interest and penalties associated with such uncertain tax positions are recorded as a component of income tax expense. The Company had no significant uncertain tax positions as of December 31, 2021 and December 31, 2020.

Basic and Diluted Net Loss Per Share

The Company calculates basic and diluted net loss per share using the two-class method. The two-class method requires income available to common stockholders for the period to be allocated between common stock and participating securities based upon their respective rights to receive dividends as if all income for the period had been distributed. The Company's Series A convertible preferred stock, Series A-1 convertible preferred stock and Series B convertible preferred stock are participating securities. These participating securities do not contractually require the holders of such shares to participate in the Company's losses. As such, net losses for the years presented were not allocated to the Company's participating securities. Accordingly, basic net loss per share is computed by dividing the net loss by the weighted average number of common shares outstanding during the period, without consideration of potential dilutive securities. Diluted net loss per share is computed by dividing the net loss by the sum of the weighted average number of common shares outstanding during the period plus the dilutive effects of potentially dilutive securities outstanding during the period. Potentially dilutive securities include vested and unexercised stock options, restricted stock issued upon early exercise of stock options, convertible preferred shares and contingent stock liabilities. The dilutive effect of stock options and contingent stock liabilities are computed using the treasury stock method and the dilutive effect of convertible preferred shares is calculated using the if-converted method. The Company has generated a net loss for all periods presented, therefore diluted net loss per share is the same as basic net loss per share since the inclusion of potentially dilutive securities would be anti-dilutive.

Segments

Operating segments are defined as components of an entity for which separate financial information is made available and is regularly evaluated by the chief operating decision maker ("CODM") in making decisions regarding resource allocation and assessing performance. The Company's CODM is the chief executive officer and operations are managed as a single segment for the purposes of assessing performance and making operating decisions.

Comprehensive Loss

Comprehensive loss represents net loss for the period plus the results of certain other changes in stockholders' equity (deficit). The Company's comprehensive loss included unrealized gains related to marketable securities for the years ended December 31, 2021 and 2020.

Recently Issued Accounting Pronouncements

In June 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2016-13, *Financial Instruments—Credit Losses*, ("ASC 326"), which introduces a new model for recognizing credit losses on financial instruments based on an estimate of current expected credit losses. The new model will apply to (1) loans, accounts receivable, trade receivables, and other financial assets measured at amortized cost; (2) loan commitments and certain other off-balance-sheet credit exposures; (3) debt securities and other financial assets measured at fair value through other comprehensive income; and (4) beneficial interests in securitized financial assets. The adoption of ASC 326 in January 2021 had no material impact on the Company's financial statements.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*, which eliminates the current tests for lease classification under U.S. GAAP and requires lessees to recognize the right-to-use assets and related lease liabilities in the balance sheet. The new standard provides for a modified retrospective application. ASU 2016-02 is effective for interim and annual period beginning after December 15, 2021.

The Company plans to adopt ASU 2016-02 on January 1, 2022. The Company expects to elect the package of practical expedients permitted under the transition guidance within the new standard, which, among other things, allows the Company to carry forward historical lease classification. The Company is completing its evaluation of the impact of adoption of ASU 2016-02 on its financial statements and expects to recognize a lease liability and related right-of-use assets on its balance sheet of approximately $3.4 million. The Company does not expect the standard to have a material impact on its results of operations or cash flows. In addition, the Company is currently implementing changes to processes and controls to support lease accounting and related disclosures under the new standard.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (ASC 820): Disclosure Framework-Changes to the Disclosure Requirements for Fair Value Measurement*. ASU No. 2018-13 removes certain disclosures, modifies certain disclosures, and adds additional disclosures. ASU No. 2018-13 is effective for annual periods, including interim periods within those annual periods, beginning after December 15, 2019. The adoption of ASU 2018-13 in January 2020 had no material impact on the Company's financial statements.

3. Fair Value of Financial Assets and Liabilities

The following table presents information about the Company's financial instruments that are measured at fair value on a recurring basis and indicates the fair value hierarchy of the inputs the Company utilized to determine such fair value *(in thousands)*:

	December 31, 2021			
	Total	Level 1	Level 2	Level 3
Financial assets:				
Money market funds (cash equivalents)	$ 10,319	$ 10,319	$ —	$ —
Marketable securities	225,357	27,186	198,171	—
Total financial assets measured at fair value	$ 235,676	$ 37,505	$ 198,171	$ —

	December 31, 2020			
	Total	Level 1	Level 2	Level 3
Financial assets:				
Money market funds (cash equivalents)	$ 13,943	$ 13,943	$ —	$ —
Marketable securities	131,899	11,169	120,730	—
Total financial assets measured at fair value	$ 145,842	$ 25,112	$ 120,730	$ —
Financial liabilities:				
Contingent stock liability	$ 373	$ —	$ —	$ 373
Total financial liabilities measured at fair value	$ 373	$ —	$ —	$ 373

The contingent stock liability in the table above represents the fair value of contingent equity consideration equal to 65,186 shares of common stock contingently issuable to the University of Louisville Research Foundation Inc. (ULRF) in connection with its amended and restated exclusive license agreement with the Company (see Note 8). In conjunction with the Company's IPO, the Company issued 48,889 shares of common stock and paid the cash equivalent fair value of 16,297 shares, or $0.3 million, to ULRF in May 2021 (see note 8). A rollforward of the contingent common stock liability, which is measured at fair value for the years ended December 31, 2021 and 2020, is represented as follows *(in thousands)*:

Fair value as of January 1, 2020	$ 63
Change in fair value	310
Fair value as of December 31, 2020	373
Change in fair value	735
Share issuance in partial settlement of contingent stock	(831)
Cash payment in partial settlement of contingent stock	(277)
Fair value as of December 31, 2021	$ —

Valuation techniques used to measure fair value maximize the use of relevant observable inputs and minimize the use of unobservable inputs. Prior to the Company's IPO, the Company's contingent stock liability was classified within Level 3 of the fair value hierarchy because its fair value measurement is based, in part, on significant inputs not observed in the market, which incorporates assumptions and estimates to value the Company's common stock. As there was no public market for the Company's common stock prior to May 2021, the estimated fair value was determined by the Company's board of directors with input from management, considering the most recently available third-party valuations of common stock, and the board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of each valuation. Historically, these third-party valuations of the Company's common stock were performed contemporaneously when events occurred which management believed would have an impact on the valuation of the Company. The Company's common stock valuation was prepared using the option-pricing method, ("OPM"), which uses a market approach to estimate enterprise value. The fair value of the Company's common stock used to value the contingent stock liability as of December 31, 2020 was $5.72. The Company's IPO price of $17.00 was used to determine the contingent stock value prior to settlement in cash and share issuance.

4. Marketable Securities

The fair value of the Company's marketable securities as of December 31, 2021 and December 31, 2020 is based on level 1 and level 2 inputs. The Company's investments consist mainly of U.S. government and agency securities, government-sponsored bond obligations and certain other corporate debt securities. Fair value is determined by taking into consideration valuations obtained from third-party pricing services. The third-party pricing services utilize industry standard valuation

models, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include reported trades of and broker/dealer quotes on the same or similar securities; issuer credit spreads; benchmark securities; and other observable inputs. There were no transfers between levels within the hierarchy during the years ended December 31, 2021 and December 31, 2020. The Company has assessed U.S. government treasuries as level 1 and all other marketable securities as level 2 within the fair value hierarchy of ASC 820. The Company classifies its entire investment portfolio as available-for-sale as defined in ASC 320, *Debt Securities*. Securities are carried at fair value with the unrealized gains (losses) reported in other comprehensive loss.

As of December 31, 2021 and December 31, 2020, none of the Company's investments were determined to be other than temporarily impaired.

The following table summarizes the Company's investments *(in thousands)*:

	December 31, 2021			
	Amortized Cost	Unrealized Gain	Unrealized (Loss)	Estimated Fair Value
Commercial paper	$ 179,151	$ 38	$ (47)	$ 179,142
Corporate debt securities	31,244	—	(58)	31,186
Government and agency securities	15,040	—	(11)	15,029
Total	$ 225,435	$ 38	$ (116)	$ 225,357

5. Prepaid and Other Current Assets

Prepaid and other current assets consisted of the following *(in thousands)*:

	December 31,	
	2021	2020
Prepaid insurance	$ 1,121	$ 102
Prepaid research and development expenses	782	702
Other current assets	640	459
Total prepaid and other current assets	$ 2,543	$ 1,263

6. Property and Equipment, Net

Property and equipment, net consisted of the following *(in thousands)*:

	December 31,	
	2021	2020
Equipment	$ 4,449	$ 2,666
Leasehold improvements	821	580
Computer equipment	953	264
Furniture and fixtures	426	255
Construction in progress	952	491
Total property and equipment	7,601	4,256
Less accumulated depreciation	(2,797)	(2,243)
Property and equipment, net	$ 4,804	$ 2,013

Depreciation expense was $0.6 million and $0.4 million for the years ended December 31, 2021 and 2020, respectively.

7. Accrued Expenses

Accrued expenses consisted of the following *(in thousands)*:

	December 31,	
	2021	2020
Compensation and benefit costs	$ 3,320	$ 1,400
Research and development expenses	854	788
Professional fees, consulting and other	1,257	449
Total accrued expenses	$ 5,431	$ 2,637

8. Commitments and Contingencies

Leases

The Company currently has six active lease agreements for office and laboratory space and related equipment. The primary lease is located on the University of Louisville campus in Louisville, Kentucky (the "Louisville Lease"). This lease has a termination date in November 2023, with an option to extend for three additional years at the Company's discretion. In May 2020, the Company added additional office and laboratory space to the Louisville Lease. In September 2021, the Company entered into a sublease agreement for additional office space in Louisville, Kentucky. This sublease has a termination date in November 2023. The Company maintained a third lease for ancillary office space in Louisville, Kentucky. This lease was terminated in December 2021.

The Company maintains a lease for office space in Wellesley, Massachusetts, that had an original termination date in March 2021. The Company entered into a month-to-month lease agreement for the office space in Wellesley effective as of April 2021 and in June 2021, finalized an amended lease agreement. The amended lease commencement date will be the later of September 2021 or the date the landlord substantially completes agreed-upon renovations. The term of the lease will be 39 months from the commencement date. The Company will maintain its current office space in Wellesley until the commencement of the amended lease agreement. The amended lease had not commenced as of December 31, 2021.

In July 2021, the Company entered into a lease agreement for laboratory space in Houston, Texas. The agreement has a term of five months with the option to extend on a month-to-month basis at the end of the original term. The Company utilized the space under this lease on a temporary basis while construction of a permanent lease was completed. This lease was terminated in December 2021. In July 2021, the Company entered into a second lease agreement for laboratory space in Houston, Texas (the "Houston Lease"). The Houston Lease commencement date will be the later of September 2021 or the date the landlord substantially completes agreed-upon renovations. The term of the lease will be 36 months from the commencement date. The Houston lease commenced in January 2022.

The future minimum rent payments relating to all four of the Company's ongoing facility operating leases under the terms and conditions existing as of December 31, 2021, as well as amendments the Company has entered into between the date of these financial statements and the date they were available to be issued (as described in Note 16), are summarized as follows *(in thousands)*:

Years Ending December 31,	
2022	$ 907
2023	$ 1,065
2024	$ 937
2025	$ 700
2026 and beyond	$ 437
Total	$ 4,046

The Company incurred rent expense of $0.7 million and $0.6 million for the years ended December 31, 2021 and 2020, respectively.

License Agreement

In October 2018, the Company entered an amended and restated exclusive license agreement with the ULRF related to certain licensed patent rights and know-how related to human facilitating cells for its Facilitated Allo-HSCT Therapy approach.

Pursuant to the ULRF License Agreement, ULRF granted the Company an exclusive, worldwide license under such patents and a nonexclusive royalty-bearing, worldwide license for such know-how to research, develop, commercialize and manufacture FCR001 and products containing FCR001 in all fields, without limitation. ULRF also granted the Company the right to grant sublicenses in accordance with the ULRF License Agreement. Under the terms of the agreement, the Company is obligated to compensate ULRF three percent of net sales of all licensed products sold, one third of any non-royalty sublicensing income, and up to $1.625 million in regulatory and sales milestones on each licensed product upon the occurrence of specific events as outlined in the license agreement; and annual license maintenance fees.

In addition, upon execution of the ULRF License Agreement, the Company granted contingent equity consideration equal to 65,186 shares of common stock to ULRF. On or prior to the Company's first underwritten public offering or any transaction that is treated as a deemed liquidation event, the Company may either issue to ULRF the 65,186 shares in common stock or make a cash payment equal to the 65,186 shares of common stock multiplied by either the price per share of common stock in the underwritten public offering or by the price per share of common stock received in connection with such deemed liquidation event.

Coincident with the completion of the Company's IPO, the Company issued 48,889 shares of common stock to ULRF and provided a cash payment of approximately $0.3 million in lieu of issuing the remaining 16,297 shares of common stock. As of December 31, 2021, the contingent stock liability was fully satisfied. As of December 31, 2020, the Company measured the fair value of the contingent equity consideration and recorded a contingent stock liability of $0.4 million in other liabilities (see Note 3).

The Company incurred $0.1 million in expense in February 2021 related to an annual maintenance fee pursuant to the license agreement for the year ended December 31, 2021. The Company incurred a $0.1 million milestone payment to ULRF in June 2020 which was recorded as research and development expense. The Company also incurred $0.1 million in expense in February 2020 related to the annual maintenance fee for the year ended December 31, 2020.

Legal Proceedings

The Company is not currently a party to any material legal proceedings. At each reporting date, the Company evaluates whether a potential loss amount or a potential range of loss is probable and reasonably estimable under the provisions of the authoritative guidance that addresses accounting for contingencies. The Company expenses as incurred the costs related to its legal proceedings.

9. Convertible Preferred Stock

Issuances of Convertible Preferred Stock

In November 2018, the Company issued 22,500,000 shares of Series A Convertible Preferred Stock at $1.00 per share for gross cash proceeds of $22.5 million. The Company incurred issuance costs of $2.0 million, which have been recorded as a reduction to the value of Series A Convertible Preferred Stock in mezzanine equity in the accompanying balance sheets. In connection with the initial issuance of the Series A Convertible Preferred Stock, the purchasers received the right to purchase, and the Company had the obligation to sell, additional shares of Series A Convertible Preferred Stock at $1.00 per share and a unit, comprised of one share of Series A-1 Convertible Preferred Stock and one product interest right (each a "Unit"), at $1.25 per Unit (together, the "Tranche Rights") upon achieving certain milestones related to the Company's research and clinical developments in a series of tranches (the "Tranche 2," "Tranche 3," and "Tranche 4") milestones.

In December 2019, the Tranche 2 milestone was met and the Company issued an additional 17,500,000 shares of Series A Convertible Preferred Stock at $1.00 per share for gross cash proceeds of $17,500,000 and 16,000,000 Units (consisting of 16,000,000 shares of Series A-1 Convertible Preferred Stock and 16,000,000 shares of product interest rights) at $1.25 per Unit for gross cash proceeds of $20.0 million. The Company incurred issuance costs of $1.3 million in relation to Tranche 2, which have been recorded as a reduction to the value of Series A-1 Convertible Preferred Stock in mezzanine equity in the accompanying balance sheets.

In August 2020, the holders of Series A-1 Convertible Preferred Stock voted to amend the Preferred Stock and Unit Purchase Agreement ("SPA") and waive the requirements of the Tranche 3 milestone. The Company issued an additional 12,000,000 Units (consisting of 12,000,000 shares of Series A-1 Convertible Preferred stock and 12,000,000 shares of product interest rights) at $1.25 per Unit for gross cash proceeds of $15.0 million.

In September 2020, the Company issued 62,499,993 shares of Series B Convertible Preferred Stock at $1.84 per share for gross cash proceeds of $115.0 million. The Company incurred issuance costs of $0.5 million in relation to the issuance of Series B Convertible Preferred Stock, which have been recorded as a reduction to the value of Series B Convertible Preferred Stock in mezzanine equity in the accompanying balance sheets.

In conjunction with the Series B Convertible Preferred Stock financing in September 2020, all holders of the Company's preferred stock entered into an amendment to the SPA to terminate all rights, liabilities and obligations in respect to the Tranche 4 milestone.

Tranche Rights

The Company determined that the Tranche Rights did not meet the definition of a freestanding financial instrument because the Tranche Rights are not legally detachable from the initial Series A Convertible Preferred Stock issued. The Company made this determination due to the express prohibition of the transfer of the Tranche Rights. Further, the Company determined that the Tranche Rights do not meet the definition of an embedded derivative that would require bifurcation from the initial Series A Preferred Stock issued. Therefore, at the initial issuance of the Series A Convertible Preferred Stock in November 2018, there was no separate recognition of the Tranche Rights.

Product Interest Rights

After the first commercial sale of product, the product interest right entitles the holders to a product interest payment for each product interest right held equal to 1/48,000,000 multiplied by 9% of net product sales on a territory-by-territory basis. If the Company enters into a license of rights to develop and/or commercialize a product, the holder is entitled to a product interest payment for each product interest right equal to 1/48,000,000 multiplied by 30% of licensing income. If the holder does not participate or events occur in which the holder transfers its ownership, it must determine to transfer either its shares or the unit purchase right. If the holder elects to receive a product interest payment, then a corresponding total number of Series A-1 Convertible Preferred Stock initially underlying a Unit (the "Unit Share"), will be canceled and forfeited. The total number of Unit Shares canceled and forfeited will be determined by dividing the product interest payment received by the fair value of the Unit Share at such time. The product interest right payment term shall commence upon the first commercial sale of product, on a territory-by-territory basis, and continue until the fifteenth anniversary thereafter, or any earlier date that there are no remaining product interest rights outstanding.

If at any time, the Unit is transferred, the holder must elect to transfer either (i) the Unit Share underlying the Unit or (ii) the product interest right underlying the Unit. If the holder elects to transfer the Unit Share, the corresponding product interest right underlying the Unit shall be automatically canceled, forfeited, and extinguished for no consideration. If the holder elects to transfer the product interest right, the corresponding Unit Share unit shall be automatically canceled and forfeited for no consideration.

The Company determined the product interest rights did not meet the definition of a freestanding financial instrument because the product interest rights are not legally detachable or separately exercisable from the Unit Shares. Further, the Company determined that the product interest rights do not meet the definition of an embedded derivative that would require bifurcation from the Unit Share. Therefore, upon issuance of Units in December 2019, there was no separate recognition of the product interest rights.

In March 2021, the Company entered into a termination agreement with the holders of Series A and Series A-1 Convertible Preferred Stock to terminate the Product Interest Rights Agreement between the parties effective immediately prior to, but subject to the closing of the Company's initial public offering. The termination agreement cancelled all product interest rights associated with the Series A-1 Convertible Preferred Stock. There was no value offered in exchange for the cancellation.

Rights and Privileges of Convertible Preferred Stock

The rights and privileges of the Series A, Series A-1 and Series B Convertible Preferred Stock (together, "Convertible Preferred Stock") are as follows:

Voting Rights—The holders of each series of Convertible Preferred Stock are entitled to vote on all matters and shall have the number of votes equal to the number of shares of common stock into which the preferred stock is convertible.

Dividends—The Company shall not declare, pay, or set aside any dividends on shares of any other class or series of capital stock (other than dividends on shares of common stock payable in shares of common stock), unless the holders of the Convertible Preferred Stock receive a dividend on each outstanding share of Convertible Preferred Stock in an amount at least equal to (i) in the case of a dividend on common stock or any class or series that is convertible into common stock, that dividend per share of Convertible Preferred Stock as would equal the product of (A) the dividend payable on each share of such class or series determined, if applicable, as if all shares of such class or series had been converted into common stock and (B) the number of shares of common stock issuable upon conversion of a share of the applicable series of Convertible Preferred Stock or (ii) in the case of a dividend on any class or series that is not convertible into common stock, at a rate per share of the applicable series of Convertible Preferred Stock determined by (A) dividing the amount of the dividend payable on each share of such class or series of capital stock by the original issuance price of such class or series of capital stock and (B) multiplying such fraction by an amount equal to the original issue price of the applicable series of Convertible Preferred Stock. No dividends were declared or paid during the years ended December 31, 2021 and December 31, 2020.

Liquidation Preference—In the event of any voluntary or involuntary liquidation, dissolution, or winding-up of the Company, the holders of shares of Convertible Preferred Stock will receive, in preference to any distribution to the holders of common stock an amount per share equal to the greater of (i) the applicable original issue price of such series of Convertible Preferred Stock, plus any dividends declared but unpaid thereon, or (ii) such amount per share as would have been payable had all shares of Convertible Preferred Stock been converted into common stock immediately prior to such liquidation, dissolution, winding-up, or deemed liquidation event. If upon any such liquidation, dissolution, or winding-up of the Company or deemed liquidation event, the assets available for distribution to the Company's stockholders are not sufficient to pay the holders of Convertible Preferred Stock the full amount to which they shall be entitled, the holders of Convertible Preferred Stock shall share ratably in any distribution of the assets available for distribution in proportion to the respective amounts, which would otherwise be payable in respect of the shares held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full.

In the event of a deemed liquidation event, if the Company does not effect a dissolution within 90 days after such deemed liquidation event, each holder of Convertible Preferred Stock has the right to require the redemption of such shares, and if voting together as a majority, has the right to require redemption of all outstanding Convertible Preferred Stock in accordance with the liquidation preferences afforded to holders of the Convertible Preferred Stock. Any shares of Convertible Preferred Stock that are redeemed or otherwise acquired by the Company or any of its subsidiaries be automatically and immediately canceled and retired and shall not be reissued, sold, or transferred. Neither the Company nor any of its subsidiaries may exercise any voting or other rights granted to the holders of Convertible Preferred Stock following redemption. A Deemed Liquidation Event shall include a merger or consolidation (other than one in which the capital stock of the Company outstanding immediately prior to such merger or consolidation continue to represent a majority by voting power of the capital stock of the surviving corporation) or a sale, lease, transfer, exclusive license, or other disposition of all or substantially all of the assets of the Company.

Conversion

Conversion Ratio—Each share of Convertible Preferred Stock shall be convertible, at the option of the holder thereof, at any time into such number of fully paid and nonassessable shares of common stock as is determined by dividing the applicable original issue price by the applicable conversion price (Series A original issue price is $1.00 per share and applicable conversion price is $5.35 per share; Series A-1 original issue price is $1.25 and applicable conversion price is $6.69 per share; Series B original issue price is $1.84 per share and applicable conversion price is $9.84 per share), subject to adjustment in the case of termination or fractional shares.

Mandatory Conversion—All outstanding shares of Convertible Preferred Stock are automatically convertible based upon either (a) the closing of a firm-commitment underwritten public offering in which the aggregate gross proceeds to the Company of at least $60,000,000 of gross proceeds to the Company and have an offering price to the public of at least $9.84 per share or (b) the vote or written consent of holders of at least a majority of the Convertible Preferred Stock outstanding at that time with respect to the conversion of the Convertible Preferred Stock then all outstanding shares of Convertible Preferred Stock shall automatically be converted into shares of common stock at the then effective conversion rate and such shares may not be reissued. Upon the completion of the Company's IPO in May 2021, all Convertible Preferred Stock was converted to shares of common stock or non-voting common stock. Series A Convertible Preferred Stock was converted into 7,476,632 shares of common stock, Series A-1 Convertible Preferred Stock was converted into 5,233,637 shares of common stock and Series B Convertible Preferred Stock was converted into 10,532,229 shares of common stock and 1,150,000 shares of non-voting common stock.

10. Common Stock

Common Stock

On April 30, 2021, the Company's stockholders approved the third amended and restated certificate of incorporation of the Company, which included the authorization of 10,000,000 shares of undesignated preferred stock with a par value of $0.0001, authorization of 140,000,000 shares of voting common stock and 10,000,000 shares of non-voting common stock. As of December 31, 2021, no undesignated preferred stock was outstanding.

Common Stock Reserved

The number of shares of common stock that have been reserved for the potential conversion of Preferred Stock, outstanding stock options granted and stock options available for grant under the Company's 2021 Stock Option and Incentive Plan (the "2021 Plan") and the 2018 Equity Incentive Plan (the "2018 Plan") and shares reserved for issuance under the Company's 2021 Employee Stock Purchase Plan (the "2021 ESPP") are as follows:

	December 31,	
	2021	2020
Conversion of Series A Preferred Stock	—	7,476,632
Conversion of Series A-1 Preferred Stock	—	5,233,637
Conversion of Series B Preferred Stock	—	11,682,229
Restricted stock related to early exercise of common stock options	538,340	932,279
Outstanding common stock options	3,643,796	2,745,185
Shares reserved for issuance under equity incentive plans	2,702,995	1,143,820
Shares reserved for issuance under the 2021 Employee Stock Purchase Plan	837,088	—
Contingent stock	—	65,186
Total	7,722,219	29,278,968

11. Stock-Based Compensation

2021 Employee Stock Purchase Plan

In April 2021, the Company's board of directors and stockholders approved the 2021 ESPP. The 2021 ESPP became effective immediately prior to the effectiveness of the Company's registration statement on Form S-1 for its IPO. The 2021 ESPP provides employees the opportunity to purchase shares at a 15% discount at the lower of the share price at the beginning or end of six-month offering periods. 852,971 shares have been reserved and approved for this purpose for the 2021 plan year. The number of shares reserved and available for issuance under the plan will increase on January 1, 2022, and each January 1 thereafter through January 1, 2031, by the lesser of (A) 3,000,000 shares of common stock, (B) 1% of the cumulative number of shares of common stock issued and outstanding on the immediately preceding December 31st or (C) such lesser number of shares of common stock as determined by the Board. The expense incurred under this plan for the year ended December 31, 2021 was not material to the financial statements. The amounts have been included in the total stock-based compensation line items in the accompanying financial statements and disclosures.

Equity Incentive Plans

The April 2021, the Company's board of directors and stockholders approved the 2021 Plan and terminated the 2018 Plan with respect to any unissued awards. The 2021 Plan became effective immediately prior to the effectiveness of the Company's registration statement on Form S-1 for its IPO. The 2021 Plan provides for the issuance of up to 3,015,907 new share-based awards, as well as the 3,381,382 options to purchase common stock then outstanding under the 2018 Plan, for a total of 6,397,289 shares. To the extent outstanding options granted under the 2018 Plan are cancelled, forfeited, or otherwise terminated without being exercised and would otherwise have been returned to the share reserve under the 2018 Plan, the number of shares underlying such awards will be available for future grant under the 2021 Plan.

As of December 31, 2021, 2,702,995 shares remained available for future grant under the 2021 Plan. 3,569,030 options were outstanding under the 2021 Plan and 2018 Plan as of December 31, 2021.

The Company's 2021 Plan provides for the Company to sell or issue common stock or restricted common stock or to grant incentive stock options or nonqualified stock options for the purchase of common stock, to employees, nonemployees and members of the board of directors of the Company. The 2021 Plan is administered by the board of directors or at the discretion of the board of directors by the compensation committee of the board. The exercise prices, vesting periods, and other

restrictions are determined at the discretion of the compensation committee of the board of directors, except that the exercise price per share of stock options may not be less than 100% of the fair market value of the share of common stock on the date of grant and the contractual term of stock option may not be greater than 10 years. Stock options granted to date typically vest over four years.

Stock Option Valuation

The assumptions used to determine the fair values of stock options granted to employees and directors are presented as follows:

	For the years ended December 31,	
	2021	2020
Fair value of common stock	$5.72-17.00	$1.44-5.72
Dividend yield	—%	—%
Volatility	80.6%-91.25%	72.8%-80.6%
Risk-free interest rate	0.50%-1.33%	0.31%-1.46%
Expected term (years)	6.25	6.25

Summary of Option Activity

The Company's stock option activity regarding employees, directors, and nonemployees is summarized as follows (*in thousands excepts share and per share amounts)*:

	Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (in years)	Aggregate intrinsic value
Options outstanding—January 1, 2020	1,536,428	$ 1.12	8.96	$ —
Granted	2,939,809	3.92		
Exercised	(1,629,276)	1.00		
Cancelled	(1,809)	0.93		
Forfeited	(99,961)	0.93		
Options outstanding—December 31, 2020	2,745,185	$ 4.20	9.40	$ 4,183
Granted	1,076,022	9.19		
Exercised	(149,707)	2.12		
Cancelled	(7,605)	1.38		
Forfeited	(20,099)	5.79		
Options outstanding—December 31, 2021	3,643,796	$ 5.75	8.69	$ 34,754
Options exercisable—December 31, 2021	958,921	$ 3.90	8.19	
Options vested and expected to vest—December 31, 2021	2,203,488	$ 2.32	7.69	

Additional information with regard to stock option activity involving employees and directors is as follows (*in thousands except per share amounts)*:

	For the years ended December 31,	
	2021	2020
Weighted-average grant-date fair value per option of total options granted	$ 6.69	$ 2.77
Aggregate intrinsic value of stock options exercised	1,616	961

As of December 31, 2021, total unrecognized compensation cost related to the unvested awards to employees, directors, and nonemployees is $11.5 million, which is expected to be recognized over a weighted-average period of 2.9 years.

Stock-Based Compensation

The Company recorded stock-based compensation expense regarding its employees, directors, and nonemployees as follows *(in thousands)*:

	For the years ended December 31,	
	2021	2020
Research and development expense	$ 1,848	$ 357
General and administrative expense	1,930	665
Total	$ 3,778	$ 1,022

12. Income Taxes

The Company recorded no income tax benefit for the net loss incurred for the years ended December 31, 2021 and December 31, 2020, due to its uncertainty of realizing a benefit from such losses. All of the Company's operating losses since inception have been generated in the United States.

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective tax rate is as follows:

	For the years ended December 31,	
	2021	2020
Federal statutory rate	21.0%	21.0%
Federal research tax credit/orphan drug credit	(0.6)%	(0.5)%
Permanent items, including stock compensation	2.4%	4.2%
Change in valuation allowance	(21.9)%	(26.8)%
Other	(0.9)%	2.2%
	0.0%	0.0%

Significant components of the Company's deferred tax assets are included in the table below *(in thousands)*:

	For the years ended December 31,	
	2021	2020
Deferred tax assets:		
Net operating loss and capital loss carryforwards	$ 20,815	$ 10,586
Research and development credit carryforwards	2,359	1,196
Accrued expenses	1,377	400
Stock-based compensation	876	171
Total deferred tax assets	25,427	12,353
Deferred tax liabilities—depreciation	(80)	(206)
Less valuation allowance	(25,347)	(12,147)
Net deferred tax assets	$ —	$ —

The Company's management has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which are composed primarily of net operating loss (NOL) carryforwards and research and development credit carryforwards. Management has considered the Company's history of net losses incurred since inception and probability of future losses to conclude it is more likely than not that the Company will not recognize the benefits of federal and state deferred tax assets. As a result, the Company has established a valuation allowance for the full amount of the net deferred tax assets as of December 31, 2021 and December 31, 2020. The valuation allowance increased by $13.2 million and $6.5. million during the years ended December 31, 2021 and December 31, 2020, respectively.

As of December 31, 2021, the Company has $78.0 million of US federal NOLs and $80.2 million of Kentucky state NOL carryforwards that have no expiration dates. The Company has $0.1 million in US federal and state capital loss carryforwards that expire in 2023. In addition, the Company had a US federal research and development tax credit carryforward of $2.4 million, which may be available to reduce future tax liabilities which start to expire in 2039.

Through December 31, 2021, the Company has generated research and development tax credits but has not conducted a study to document the qualified activities. Such study may result in an adjustment to the Company's research and development credit carryforwards. Since a full valuation allowance has been provided against the Company's research and development

credits, any reduction in the gross deferred tax asset established for the research and development credit carryforwards would not result in any net impact to the Company's financial statements.

Realization of the future tax benefits is dependent on many factors, including the Company's ability to generate taxable income within the NOL carryforward period. Under the provisions of Sections 382 and 383 of the Internal Revenue Code ("IRC"), and corresponding provisions of state law, certain substantial changes in the Company's ownership, including a sale of the Company or significant changes in ownership due to sales of equity, may have limited, or may limit in the future, the amount of NOL carryforwards, which could be used annually to offset future taxable income. No study has been completed as of the date of these financial statements to determine whether a change in control, as defined by Section 382 of the IRC, has occurred. If it is determined the Company has experienced a change in control at any time since inception, realization of the NOL carryforwards or research and development tax credit carryforwards may be subject to an annual limitation. Any limitation may result in the expiration of a portion of NOL or research and development tax credit carryforwards before they are realized.

The Company files US federal and state tax returns in the United States. All tax years since incorporation remain open to examination by the major taxing jurisdictions (state and federal) to which the Company is subject, as carryforward attributes generated in years past may still be adjusted upon examination by the Internal Revenue Service (IRS) or other authorities if they have or will be used in a future period. The Company is not currently under examination by the IRS or any other jurisdictions for any tax year.

13. Defined Contribution Plan

The Company established a defined contribution savings plan under Section 401(k) of the Internal Revenue Code. This plan covers substantially all employees who meet minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pretax basis. Company contributions to the plan are made to employees who meet minimum service requirements in the amount of 3% of gross pay, subject to certain limitations. For the years ended December 31, 2021 and December 31, 2020, the Company made contributions in the amount of $0.4 million and $0.2 million, respectively.

14. Net Loss Per Share Attributable to Common Stockholders

Net Loss Per Share

The following table summarizes the computation of basic and diluted net loss per share attributable to common stockholders of the Company *(in thousands except share and per share amounts*).

	For the years ended December 31,	
	2021	**2020**
Net loss and net loss attributable to common stockholders	$ (47,833)	$ (22,707)
Net loss per share attributable to common stockholders, basic and diluted	$ (1.64)	$ (3.40)
Weighted average number of common shares outstanding used in computation of net loss per common share, basic and diluted	29,126,373	6,685,066

The Company's potential dilutive securities, which include convertible preferred stock, contingent stock liabilities, restricted stock related to early exercise of common stock options and common stock options, have been excluded from the computation of diluted net loss per share as the effect would be antidilutive. Therefore, the weighted average number of common shares outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same. The following potential dilutive securities, presented on an as converted basis, were excluded from the calculation of net loss per share due to their anti-dilutive effect:

	For the years ended December 31,	
	2021	**2020**
Convertible preferred shares (as converted to common stock and non-voting common stock)	—	24,392,498
Options to purchase common stock	3,643,796	2,745,185
Restricted stock related to early exercise of options to purchase common stock	538,340	932,279
Contingent common stock (as converted to common stock)	—	65,186
	4,182,136	28,135,148

15. Related Party Transactions

The Company engaged a firm managed by a former executive of the company for professional services related to accounting, finance and other administrative functions. The costs incurred under this arrangement totaled $0.1 million and $0.4 million for the years ended December 31, 2021 and 2020, respectively, which were recorded as general and administrative expense in the accompanying statements of operations. As of December 31, 2021, there were no amounts owed under this arrangement.

16. Subsequent Events

The Company has evaluated subsequent events through March 17, 2022, the date the financial statements were available to be issued. The Company has concluded no subsequent events have occurred that require disclosure, except for those referenced below.

Leases

On February 28, 2022, the Company entered into an amended lease agreement for office space in Wellesley, Massachusetts on substantially the same terms as reflected in Note 8, but for minor alterations to the improvements to be completed by the landlord. These alterations will be an additional obligation for the Company. These are not expected to be material to the financial statements.

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

The summary of the general terms and provisions of the registered securities of Talaris Therapeutics, Inc. (the "Company," "we," "us," and "our") set forth below does not purport to be complete. It is subject to and qualified in its entirety by reference to our Third Amended and Restated Certificate of Incorporation ("certificate of incorporation") and our Amended and Restated Bylaws ("bylaws"), each of which are incorporated by reference as an exhibit to the Annual Report on Form 10-K of which this Exhibit 4.3 is a part, and by applicable law. We encourage you to read our certificate of incorporation, our bylaws and the applicable provisions of the Delaware General Corporation Law for additional information.

General

Our authorized capital stock consists of 140,000,000 shares of common stock, par value $0.0001 per share ("common stock"), 10,000,000 shares of non-voting common stock, par value $0.0001 per share ("non-voting common stock"), and 10,000,000 shares of preferred stock, par value $0.0001 per share ("preferred stock"), all of which shares of preferred stock are undesignated.

Common Stock and Non-Voting Common Stock

The holders of our common stock and non-voting common stock have identical rights subject to two exceptions. First, except as otherwise expressly provided in our certificate of incorporation or as required by applicable law, on any matter that is submitted to a vote by our stockholders, holders of our common stock are entitled to one vote per share of common stock, and holders of our non-voting common stock are not entitled to any votes per share of non-voting common stock, including for the election of directors. Second, holders of our common stock have no conversion rights, while holders of our non-voting common stock shall have the right to convert each share of our non-voting common stock held into one share of common stock at such holder's election, provided that as a result of such conversion, such holder, together with its affiliates and any members of a Schedule 13(d) group with such holder, would not beneficially own in excess of 9.9% of our common stock following such conversion, unless otherwise expressly provided for in our certificate of incorporation. However, this ownership limitation may be increased to any other percentage designated by such holder of non-voting common stock upon 61 days' notice to us or decreased at any time. Holders of our non-voting common stock are also permitted to make certain transfers to non-affiliates upon which, such transferred shares would immediately convert to shares of our common stock.

Holders of our common stock and non-voting common stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock and non-voting common stock have no preemptive rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock and non-voting common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock.

Preferred Stock

Our board of directors have the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive

dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our Company or other corporate action.

No shares of preferred stock are outstanding as of the date of our Annual Report on Form 10-K with which this Exhibit 4.3 is filed as an exhibit.

Registration Rights

Certain holders of our voting common stock and non-voting common stock are entitled to rights with respect to the registration of these securities under the Securities Act of 1933, as amended (the "Securities Act"). These rights are provided under the terms of an investors' rights agreement between us and the holders of our preferred stock. The investors' rights agreement includes demand registration rights, short-form registration rights and piggyback registration rights. All fees, costs and expenses of underwritten registrations under this agreement will be borne by us and all selling expenses, including underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

Demand Registration Rights

Beginning six months after our initial public offering, certain holders of our voting common stock and non-voting common stock are entitled to demand registration rights. Under the terms of the investors' rights agreement, we will be required, upon the written request of a majority of holders of the registerable securities then outstanding that would result in an aggregate offering price of at least $10 million, to file a registration statement on Form S-1 with respect to at least 30% of the registrable securities then outstanding and to use commercially reasonable efforts to effect the registration of all or a portion of these shares for public resale.

Short-Form Registration Rights

Certain holders of our voting common stock and non-voting common stock are also entitled to short-form registration rights. Pursuant to the investors' rights agreement, if we are eligible to file a registration statement on Form S-3, upon the written request of at least 20% in interest of these holders to sell registrable securities at an aggregate price of at least $5 million, we will be required to use commercially reasonable efforts to effect a registration of such shares. We are required to effect only two registrations in any twelve month period pursuant to this provision of the investor rights agreement.

Piggyback Registration Rights

Certain holders of our voting common stock and non-voting common stock are entitled to piggyback registration rights. If we register any of our securities either for our own account or for the account of other security holders, the holders of these shares are entitled to include their shares in the registration. Subject to certain exceptions contained in the investors' rights agreement, we and the underwriters may limit the number of shares included in the underwritten offering to the number of shares which we and the underwriters determine in our sole discretion will not jeopardize the success of the offering.

Indemnification

Our investors' rights agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expiration of Registration Rights

The demand registration rights and short-form registration rights granted under the investor rights agreement will terminate on the third anniversary of the completion of our initial public offering.

Anti-Takeover Effects of Our Certificate of Incorporation and Bylaws and Delaware Law

Our certificate of incorporation and bylaws include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board Composition and Filling Vacancies

Our certificate of incorporation provides for the division of our board of directors into three classes serving staggered three-year terms, with one class being elected each year. Our certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of two-thirds or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum. The classification of directors, together with the limitations on removal of directors and treatment of vacancies, has the effect of making it more difficult for stockholders to change the composition of our board of directors.

No Written Consent of Stockholders

Our certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our bylaws or removal of directors by our stockholders without holding a meeting of stockholders.

Meetings of Stockholders

Our certificate of incorporation and bylaws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance Notice Requirements

Our bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. Our bylaws specify the requirements as to form and content of all stockholders' notices. These requirements may preclude stockholders from bringing matters before the stockholders at an annual or special meeting.

Amendment to Certificate of Incorporation and Bylaws

Any amendment of our certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our certificate of incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, board composition, and limitation of liability must be approved by not less than two-thirds of the outstanding shares entitled to vote on the amendment, and not less than two-thirds of the outstanding shares of each class entitled to vote thereon as a class. Our bylaws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the bylaws; and may also be amended by the affirmative vote of a majority of the outstanding shares entitled to vote on the amendment, voting together as a single class, except that the amendment of the provisions relating to notice of stockholder business and nominations and special meetings

must be approved by not less than two-thirds of the outstanding shares entitled to vote on the amendment, and not less than two-thirds of the outstanding shares of each class entitled to vote thereon as a class, or, if our board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Undesignated Preferred Stock

Our certificate of incorporation provides for 10,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock and non-voting common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Choice of Forum

Our bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for any state law claims for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, and employees to us or our stockholders, (3) any action asserting a claim arising pursuant to the Delaware General Corporation Law, our certificate of incorporation or our bylaws, (4) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws, or (5) any action asserting a claim that is governed by the internal affairs doctrine; provided, however, that the this provision shall not apply to any causes of action arising under the Securities Act or Exchange Act. In addition, our bylaws provide that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall be the sole and exclusive forum for resolving any complaint asserting a cause or causes of action arising under the Securities Act, including all causes of action asserted against any defendants to such complaint. For the avoidance of doubt, this provision is intended to benefit and may be enforced by us, our officers and directors, the underwriters to any offering giving rise to such complaint, and any other professional entity whose profession gives authority to a statement made by that person or entity and who has prepared or certified any part of the documents underlying the offering. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions, and there can be no assurance that such provisions will be enforced by a court in those other jurisdictions. Any person or entity purchasing or otherwise acquiring any interest in our securities shall be deemed to have notice of and consented to these forum provisions. These forum provisions may impose additional costs on stockholders, may limit our stockholders' ability to bring a claim in a forum they find favorable, and the designated courts may reach different judgments or results than other courts.

Section 203 of the Delaware General Corporation Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;

- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or

- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;

- any sale, transfer, lease, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;

- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;

- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; and

- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges, or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Nasdaq Global Market Listing

Our common stock is listed on the Nasdaq Global Market under the trading symbol “TALS.” The non-voting common stock is not listed for trading on any securities exchange and we do not plan to list the non-voting common stock on any securities exchange.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock and non-voting common stock will be Computershare Trust Company, N.A. The transfer agent and registrar’s address is 250 Royall Street, Canton, Massachusetts 02021, and its telephone number is (800) 962-4284.

Exhibit 21.1

List of Subsidiaries of Company

None.

ACTIVE/115803178.1

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement No. 333-255835 on Form S-8 of our report dated March 17, 2022, relating to the consolidated financial statements of Talaris Therapeutics, Inc. appearing in this Annual Report on Form 10-K for the year ended December 31, 2021.

/s/ DELOITTE & TOUCHE LLP

Boston, Massachusetts
March 17, 2022

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) OR 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Scott Requadt, certify that:

1. I have reviewed this Annual Report on Form 10-K for the period ended December 31, 2021 of Talaris Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 17, 2022

By: /s/ Scott Requadt

Scott Requadt
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) OR 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Mary Kay Fenton, certify that:

1. I have reviewed this Annual Report on Form 10-K for the period ended December 31, 2021 of Talaris Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 17, 2022

By: /s/ Mary Kay Fenton

Mary Kay Fenton
Chief Financial Officer
(Principal Accounting Officer and Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Talaris Therapeutics, Inc. (the "Company") on Form 10-K for the period ending December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 17, 2022

By: /s/ Scott Requadt
Scott Requadt
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Talaris Therapeutics, Inc. (the "Company") on Form 10-K for the period ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 17, 2022

By: /s/ Mary Kay Fenton
Mary Kay Fenton
Chief Financial Officer
(Principal Accounting Officer and Principal Financial Officer)