FATE THERAPEUTICS INC
Form 10-K
March 17, 2014

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2013

o **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 001-36067

FATE THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**65-1311552**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
3535 General Atomics Court, Suite 200, San Diego, CA	**92121**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code:
(858)-875-1800

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

Title of each class	**Name of each exchange on which registered**
Common Stock, $0.001 par value	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 o or No ý

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes o or No ý

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 ý or No o

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Website, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§229.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ý No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ý

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

Large accelerated filer o	Accelerated filer o	Non-accelerated filer o (Do not check if a smaller reporting company)	Smaller reporting company ý

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes o No ý

The registrant did not have a public float on the last business day of its most recently completed second fiscal quarter because there was no public market for the registrant's common equity as of such date.

The number of outstanding shares of the registrant's common stock, par value $0.001 per share, as of March 13, 2014 was 20,435,676.

INCORPORATION BY REFERENCE

Portions of the registrant's definitive proxy statement to be filed with the Securities and Exchange Commission, or SEC, pursuant to Regulation 14A in connection with the registrant's 2014 Annual Meeting of Stockholders, to be filed subsequent to the date hereof, are incorporated by reference into Part III of this annual report on Form 10-K. Such proxy statement will be filed with the SEC not later than 120 days after the conclusion of the registrant's fiscal year ended December 31, 2013.

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FATE THERAPEUTICS, INC.

Annual Report on Form 10-K

For the Fiscal Year Ended December 31, 2013

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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"). Such forward-looking statements, which represent our intent, belief or current expectations, involve risks and uncertainties and other factors that could cause actual results and the timing of certain events to differ materially from future results expressed or implied by such forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "may," "will," "expect," "anticipate," "estimate," "intend," "plan," "predict," "potential," "believe," "should" and similar expressions. Forward-looking statements in this Annual Report on Form 10-K include, but are not limited to, statements about:

- our projected timing of initiation, rate of enrollment and duration of our clinical trials for our product candidates;
- our plans to resume enrollment in our Phase 2 clinical trial, or to commence other clinical trials, of ProHema;
- our ability and our timing to incorporate the use of, and our ability to continue to use once incorporated, our nutrient-rich media, or NRM, formulation in our Phase 2 clinical trial of ProHema in adults undergoing double umbilical cord blood transplant, or UCBT, and in any subsequent clinical trials of ProHema;
- any review comments, or additional requirements, by FDA based upon our submission of ProHema manufacturing and product data generated using our NRM formulation with materials intended for clinical use;
- our expectations of safety and improved potency and efficacy of ProHema, arising from the use of our NRM formulation in the product's manufacture, in our Phase 2 clinical trial of ProHema in adults undergoing double UCBT, and in any subsequent clinical trials of ProHema;
- our plans to complete the preclinical development of, and to submit an Investigational New Drug, or IND, application for, and to conduct and generate data from the first clinical trials of, our Wnt7a analogs, and the timing of these activities;
- our ability to satisfy regulatory requirements with respect to ProHema and our other product candidates, many of which are new and still evolving;
- the ability of cell processing facilities operated by transplant centers to consistently manufacture ProHema under the proper conditions;
- the performance of third-party service providers and independent contractors, upon whom we rely to conduct our preclinical studies and clinical trials and to manufacture our product candidates and certain components of our product candidates;
- our ability to discover, develop and commercialize innovative therapeutics using our proprietary platforms;
- our ability to develop sales and marketing capabilities or to enter into strategic partnerships to develop and commercialize ProHema or any of our other product candidates;
- the timing and success of the commercialization of ProHema or any of our other product candidates;

the potential price and degree of market acceptance of stem cell-based therapeutics in general and our product candidates in particular;

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the size and growth of the potential markets for our product candidates and our ability to serve those markets;

regulatory developments and approval pathways in the United States and foreign countries for stem cell-based therapeutics in general and our product candidates in particular;

our ability to obtain, maintain, defend and enforce intellectual property rights protecting our product candidates, and our ability to develop and commercialize our product candidates without infringing the proprietary rights of third parties;

the accuracy of our estimates regarding revenues, expenses and capital requirements; and

the additional risks and other factors described under the caption "Risk Factors" under Item 1A of this Annual Report on Form 10-K.

In this Annual Report on Form 10-K, unless the context requires otherwise, "Fate Therapeutics," "Company," "we," "our," and "us" means Fate Therapeutics, Inc. and its subsidiaries.

PART I

ITEM 1. Business

General Development of Our Business

Fate Therapeutics, Inc., incorporated under the laws of the State of Delaware in April 2007, is a clinical-stage biopharmaceutical company engaged in the discovery and development of pharmacologic modulators of adult stem cells. Based on our understanding of key biological mechanisms that guide the fate of adult stem cells, we have built two platforms that optimize the activity and enhance the therapeutic potential of adult stem cells: our hematopoietic stem cell, or HSC, modulation platform and our muscle satellite stem cell, or Satellite Cell, modulation platform.

We believe that the product candidates generated by our stem cell modulation platforms have significant potential as life-changing or curative therapeutics across a broad range of orphan indications. We are pursuing the development of pharmacologically optimized HSC therapeutics for the treatment of hematologic malignancies and certain lysosomal storage disorders, or LSDs. In addition, we are pursuing the pharmacologic activation of muscle satellite stem cells using Wnt7a-based protein analogs, and we are initially focused on developing Wnt7a-based protein analogs for the treatment of muscular dystrophies. The following table summarizes key information about our platforms and our product candidates:

Product Candidate	Targeted Orphan Disorders(1)	Status
HSC Modulation Platform		
ProHema	Adult hematologic malignancies	Phase 2
ProHema	Pediatric hematologic malignancies	Preclinical
ProHema	LSDs	Preclinical
Second Generation HSC Therapeutic	LSDs	Preclinical
Satellite Cell Modulation Platform		
Wnt7a Protein Analogs	Muscular dystrophies	Preclinical
Wnt7a Protein Analogs	Neuromuscular disorders	Preclinical

(1) We have been granted orphan designation in the United States for human allogeneic HSCs *ex vivo* modulated with 16, 16-dimethyl prostaglandin E2, which we refer to as FT1050, for the enhancement of stem cell engraftment and in the European Union for ProHema for the treatment of acute myelogenous leukemia through the *ex vivo* modulation of allogeneic umbilical cord blood cells.

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We plan to continue the validation of our two platforms by demonstrating the clinical benefit of our initial product candidates over the next two years in three orphan disease settings: hematologic malignancies, LSDs and muscular dystrophy. Our lead product candidate from our HSC modulation platform, ProHema, is presently undergoing Phase 2 clinical development for the treatment of adult patients with hematologic malignancies. We expect to generate full data on the primary and major secondary endpoints from this trial in mid-2015. We are also pursuing the development of ProHema for the treatment of pediatric patients with hematologic malignancies and certain demyelinating LSDs, and we plan to initiate our first clinical trials of ProHema in these clinical settings in 2014 with the goal of generating data from these trials in 2015. Our most advanced product candidates from our Satellite Cell modulation platform are Wnt7a protein analogs, which are presently undergoing IND-enabling development. We plan to initiate a Phase 1 clinical trial of an injectable analog of a Wnt7a-based recombinant human protein in 2015 with the goal of generating data from this clinical trial in 2015.

We believe both of our platforms have the ability to generate additional products with therapeutic utility beyond their initial target indications. We also intend to expand our initial indications across a broader spectrum of orphan diseases, including those where allogeneic HSCT holds curative potential and those where muscle regeneration holds disease-modifying potential.

Description of Our Business

We are a clinical-stage biopharmaceutical company engaged in the discovery and development of pharmacologic modulators of adult stem cells to treat orphan diseases, including certain hematologic malignancies, lysosomal storage disorders, or LSDs, and muscular dystrophies. Our novel approaches utilize established pharmacologic modalities, including small molecules and therapeutic proteins, and target well-characterized biological mechanisms to enhance the therapeutic potential of adult stem cells. Adult stem cells play a key role in the growth, maintenance and repair of many tissues and organ systems in the body. Due to their natural ability to self-renew, and to regenerate and repair diseased or damaged tissue, adult stem cells also hold considerable therapeutic promise.

Based on our deep understanding of key biological mechanisms that guide the fate of adult stem cells, we have built two modulation platforms that optimize the activity of adult stem cells using techniques that operate both outside of the body, or *ex vivo*, and within the body, or *in vivo*. We believe that the product candidates generated by our stem cell modulation platforms have significant potential as life-changing or curative therapeutics across a broad range of orphan indications.

Our HSC modulation platform focuses on the *ex vivo* pharmacologic optimization of hematopoietic stem cells, which are adult stem cells that regenerate all types of blood cells throughout a person's lifespan. HSCs have been used for decades in a potentially curative procedure called hematopoietic stem cell transplant, or HSCT. This procedure is most commonly used in patients with hematologic malignancies to replace a diseased hematopoietic system with a healthy one. While over one million HSCT procedures have been performed to date, we believe HSCs have not been pharmacologically optimized to improve patient outcomes. Our HSC modulation platform has the potential to generate products that will improve patient outcomes in orphan indications by enhancing hematopoietic reconstitution through accelerated, durable engraftment, permitting greater donor matching flexibility, reducing the risk of major side effects and enabling the use of less toxic conditioning regimens.

Our lead product candidate, ProHema, is a pharmacologically-modulated HSC therapeutic derived from umbilical cord blood. We have established human proof-of-concept for ProHema in the clinical setting by demonstrating enhanced and durable engraftment of HSCs within the bone marrow. Engraftment, which is the localization and integration of HSCs within a targeted tissue where they can produce new cells, is an important determinant of patient outcomes in HSCT. We are presently advancing ProHema in Phase 2 clinical development for hematologic malignancies. We are also pursuing the development of pharmacologically optimized HSC therapeutics for the treatment of

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certain LSDs, where HSCs have demonstrated the ability to home, or migrate, to and engraft within the central nervous system, or CNS.

Our Satellite Cell modulation platform focuses on the *in vivo* pharmacologic activation of muscle satellite stem cells, which are adult stem cells that regenerate muscle throughout a person's lifespan. The regenerative capacity of satellite cells in skeletal muscle is exhausted both in the natural aging process and in degenerative conditions, such as muscular dystrophies. We have identified Wnt7a as a natural promoter of satellite cells to drive muscle regeneration, and we are initially focused on developing Wnt7a analogs for the treatment of muscular dystrophies.

Using our expertise in Wnt protein chemistry, we have engineered pharmacologically optimized analogs of the Wnt protein class. Wnts comprise a family of 19 secreted proteins known to play a key physiological role in developmental and regenerative processes. We have developed injectable analogs of Wnt7a as recombinant human protein therapeutics with muscle regenerative activity. In preclinical models of muscular dystrophies, our Wnt7a protein analogs demonstrated an expansion of the satellite cell population, an increase in muscle hypertrophy, a reduction in disease-specific muscle fiber necrosis and inflammation and an increase in muscle strength, all of which were statistically significant. We are presently advancing our Wnt7a analogs in preclinical development. Subject to the completion of IND-enabling studies and the filing of an IND application, we plan to initiate a Phase 1 clinical trial of an injectable analog of a Wnt7a-based recombinant human protein in 2015 with the goal of generating data from this clinical trial in 2015.

Our platforms and product candidates are based on the research of our scientific founders, all of whom are internationally recognized experts in the field of adult stem cell biology and have contributed significant intellectual capital to our efforts. Our stem cell modulation platforms and our proprietary product candidates are protected by a strong intellectual property position. We have retained worldwide therapeutic rights to product candidates generated by each of our platforms.

Our Novel Approach to *Ex Vivo* HSC Modulation

While over one million HSCT procedures have been performed to date with curative intent, we believe HSCs administered to patients undergoing HSCT have not been pharmacologically optimized to improve patient outcomes. Our HSC modulation platform pioneers a novel approach to improving patient outcomes in HSCT: we enhance the biological properties of HSCs *ex vivo* to drive well-understood biological mechanisms *in vivo* that are critical to the success of the procedure.

We believe our product candidates can significantly improve and enable the curative potential of HSCT in patients with orphan hematologic malignancies and rare genetic disorders. Our HSC modulation platform encompasses the following advantages:

We optimize HSCs ex vivo to enhance their biological properties. Our strategies and methods of optimizing HSCs *ex vivo* are designed to specifically enhance the ability of HSCs to achieve desired therapeutic effects *in vivo*. Our proprietary processes induce profound changes in gene expression that are critical to HSC homing and engraftment, which are required for successful patient outcomes.

Our platform is applicable across different stem cell sources and a broad range of diseases. We believe that our approach to the pharmacological enhancement of certain biological properties of HSCs can be applied across various sources of HSCs, such as mobilized peripheral blood, bone marrow and umbilical cord blood. Furthermore, we believe our technology can be employed in both the allogeneic and autologous HSCT settings, independent of the underlying cause of disease. Accordingly, we believe our HSC modulation platform will enable us to develop additional HSC therapeutics for the treatment of a broad spectrum of hematologic malignancies and rare genetic diseases.

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Our proprietary HSC optimization process can be readily adopted into the HSCT standard of care. We believe we can efficiently optimize HSCs in a rapid *ex vivo* treatment process conducted on site at the clinical center. Following this process, the enhanced cells are washed to remove the modulators and can be immediately infused into the patient within the established framework of HSCT.

Our Novel Approach to *In Vivo* Muscle Satellite Stem Cell Modulation

We are applying our knowledge of stem cell modulation to develop novel biologic therapeutics based on the natural signals that stimulate muscle satellite stem cells *in vivo*. Our Satellite Cell modulation platform enables us to evaluate multiple opportunities in skeletal muscle biology and neuromuscular disease. Our initial focus is on the treatment of muscular dystrophies. We believe we are the first company to demonstrate in preclinical studies that satellite cells can be pharmacologically modulated *in vivo* to improve muscle regeneration.

Our Satellite Cell modulation platform seeks to stimulate the intrinsic regenerative capacity of skeletal muscle. While several promising product candidates have emerged for the treatment of genetically distinct subtypes of muscular dystrophies, such as Duchenne muscular dystrophy, these therapeutics are generally focused on preventing further muscle degeneration. We are not aware of any clinical-stage programs focused on driving the natural regenerative process to increase muscle strength. We believe that our approach is novel and applicable across multiple forms of muscular dystrophies.

We believe that our proprietary Wnt7a analogs validate our therapeutic strategy for the pharmacologic modulation of satellite cells and represent a novel and promising approach for the treatment of muscular dystrophies. The advantages of our approach include:

Our means of satellite cell intervention are receptor-mediated and highly-specific. We leverage the inherent specificity conferred by the endogenous protein Wnt7a and its receptor, Fzd7, which is selectively expressed in muscle tissue. We believe this inherent specificity will enable us to develop therapeutics with a low risk of off-target effects.

Our Satellite Cell modulation platform is enabled by our expertise in the development of Wnt-based therapeutics. The therapeutic and regenerative potential of the Wnt protein family is well known. However, Wnt proteins have not been developed as therapeutics because their molecular characteristics prevent their scaled production, formulation, functional specificity and administration for human use. We have systematically applied structural prediction, rational design and protein engineering techniques to overcome these challenges. We believe we are the first company to produce Wnt protein analogs that are amenable to therapeutic development and *in vivo* administration.

We drive muscle regeneration through a unique dual mechanism of action. We have established preclinical proof-of-concept for our Wnt7a protein analogs in models of muscular dystrophy. These studies demonstrate that a single injection of our Wnt7a analogs induced an expansion of the satellite cell population, an increase in muscle hypertrophy and a decrease in muscle inflammation and damage, all of which were statistically significant. We have demonstrated in preclinical studies that these profound effects result in a significant increase in muscle strength. We believe the ability of our Wnt7a protein analogs to both activate satellite cell population expansion and increase muscle hypertrophy is a unique dual mechanism of action for the treatment of muscular dystrophies.

Our Wnt7a analogs have therapeutic potential as stand-alone or complementary treatments across a broad spectrum of muscular dystrophies. Most approaches to treat muscular dystrophies seek to slow the degeneration of muscle in genetically distinct subtypes of the disease. In contrast, because our Wnt7a protein analogs enable muscular regeneration, they have

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the potential to treat a broader spectrum of muscular dystrophies either as stand-alone or complementary therapeutics. We believe that our Wnt-based protein analogs are the only therapeutics in development that actively promote the regeneration of muscle for the treatment of muscular dystrophies.

Our Satellite Cell modulation platform has potential beyond muscular dystrophies. Our Wnt7a analogs target the biological mechanisms underlying the body's intrinsic muscle regenerative process. We believe that enhancing these mechanisms can restore the balance between muscle degeneration and regeneration for other neuromuscular disorders. Accordingly, our Wnt protein analogs have the potential to treat a wide range of conditions, such as cachexia, atrophy, trauma and sarcopenia.

Our Strategy

Our goal is to realize the therapeutic potential of our two stem cell modulation platforms across a broad range of orphan diseases through the discovery, development and commercialization of first-in-class products. The key elements of our strategy are to:

Validate the transformative therapeutic potential of our platforms. We plan to validate our two stem cell modulation platforms over the next two years by demonstrating the clinical benefit of our initial product candidates in three orphan disease settings: hematologic malignancies, LSDs and muscular dystrophy. We believe the data generated from our planned clinical trials will enable us to establish stem cell modulation as a new treatment modality with application across a broad range of orphan diseases.

Efficiently develop and commercialize our orphan therapeutic candidates. We plan to pursue a fast-to-market strategy through efficient clinical development and expedited regulatory pathways. Due to the nature of our target indications, we believe our pivotal clinical trials will generally require relatively small numbers of patients and measure relatively short-term efficacy endpoints. We also intend to pursue, where possible, expedited regulatory pathways such as fast track or breakthrough therapy designations, which are available for therapies that address serious conditions and provide a major advance in treatment. In addition, because our target markets are highly specialized and concentrated within a limited number of centers of excellence, we intend to build our own focused sales and marketing capabilities to commercialize any products that we may successfully develop in a cost-efficient manner.

Leverage lifecycle opportunities. We believe that our therapeutic approach provides a unique opportunity for strategic lifecycle management and indication expansion. First, because our product candidates have broad therapeutic utility, clinical validation in their initial target indications may allow for the development of these product candidates for the treatment of additional diseases. Second, we intend to leverage both of our platforms to generate additional product candidates to further exploit the therapeutic potential of hematopoietic and muscle satellite stem cell modulation.

We may also seek partners who can bring therapeutic, development and commercialization capabilities, geographical expertise and financial resources that allow us to leverage the potential of our product platforms within or beyond our initial clinical and commercial focus.

Our HSC Modulation Platform and Product Candidates

Background on Hematopoietic Stem Cells

HSCs are adult stem cells that have the ability to regenerate all types of blood cells throughout a person's lifespan. HSCs have been used for decades in HSCT, a potentially curative or life-saving procedure that is most commonly performed in patients with hematologic malignancies to replace a

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diseased hematopoietic system with a healthy one. There are two types of HSCT procedures, autologous and allogeneic transplant. In the autologous setting, a patient's own HSCs are recovered from bone marrow aspirates or are mobilized and recovered from peripheral blood for transplant. In the allogeneic setting, matched HSCs are recovered from a related or unrelated donor, or from umbilical cord blood. The standard of care for HSCT in both of these settings uses HSCs that have not been pharmacologically optimized.

The number of HSCT procedures performed annually has increased steadily over the past two decades and continues to grow. According to a global survey conducted by the Worldwide Network for Blood and Marrow Transplantation, a total of 56,739 HSCT procedures were performed worldwide in 2010, including 26,241 such procedures in the allogeneic setting. It is estimated that approximately 95% of HSCT procedures are performed for the treatment of hematologic malignancies. Additionally, it is estimated that allogeneic HSCT procedures have been used in the treatment of over 50 rare genetic disorders, many of which are life-threatening and lack alternative therapeutic options.

Limitations of Allogeneic HSCT

While allogeneic HSCT is a proven therapeutic intervention strategy with curative potential, it is associated with significant treatment-related limitations and 100-day mortality rates between 20% and 30%. Treatment-related morbidity and mortality for patients undergoing allogeneic HSCT are significantly influenced by several key factors, including:

HLA matching. The ability to achieve human leukocyte antigen, or HLA, matching, or the degree to which a donor's and recipient's tissues are immunologically compatible, is a critical determinant of clinical outcomes. If the donor-derived immune system is not sufficiently compatible with the recipient's tissue, a serious complication known as graft-versus-host disease, or GvHD, may occur. Chronic GvHD occurs in 25-50% of patients who undergo HSCT procedures. Greater HLA mismatch also increases the risk of failure to engraft.

Cell dose. Successful transplants require an adequate dose of HSCs in order to ensure timely reconstitution. While a sufficient number of HSCs can usually be collected from healthy adults donating bone marrow or mobilized peripheral blood, some HSC collections may be suboptimal, which increases the risk of delayed or failed engraftment. Despite many advantages, cord blood units generally contain fewer HSCs than traditional HSC sources, which translates into delayed engraftment and a higher risk of failed engraftment. Graft failure rates can be as high as 23% after double umbilical cord blood unit transplant and 27% after single umbilical cord blood unit transplant in adults. As a result, many of the banked cord blood units are deemed to contain an insufficient number of HSCs for adult transplant.

Patient conditioning. Prior to allogeneic HSCT, chemotherapy or radiation therapy and immunotherapy are administered to eradicate a patient's diseased hematopoietic system and enable donor-derived HSCs to reconstitute a healthy hematopoietic system. HSCT has traditionally required intense myeloablative conditioning, or MAC, which is highly toxic and associated with high rates of transplant-related morbidity. As a result, only younger and healthier patients are typically considered eligible for MAC. More recently, investigators have developed reduced-intensity conditioning, or RIC, regimens that employ significantly lower doses of chemotherapy or radiation and are less toxic. Despite their safety advantages, RIC regimens are associated with lower rates of engraftment and higher rates of relapse.

Reconstitution. The process by which a patient's hematopoietic system reconstitutes, which occurs over the course of several weeks and months after HSCT, is also critical to patient outcomes. Importantly, the components of the hematopoietic system do not return to normal levels at the same rate. Time to engraftment, particularly as measured by time to the engraftment of neutrophils, a type of white blood cell involved in fighting bacterial infections,

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correlates with key clinical outcomes including the length of hospital stays, rates of serious infections and overall transplant-related morbidity and mortality.

Advantages of Our HSC Modulation Platform

Our HSC modulation platform is designed to address the current limitations of allogeneic HSCT and enhance its curative potential across a broad range of orphan hematologic malignancies and rare genetic disorders. Since our inception, we have worked closely with our scientific founders, who are internationally-recognized leaders in HSC biology, to gain a deep understanding of the molecular pathways involved in homing and engraftment. Extensive genome-wide expression studies have provided key insights that allow us to modulate these signaling networks using a proprietary pathway screening approach. We have also developed sophisticated assays to characterize the molecular and functional properties of HSCs following the *ex vivo* modulation process. These tools have enabled us to optimize the *ex vivo* modulation process by systematically and precisely evaluating key parameters of the incubation conditions, including time, dose, temperature and media. Our HSC modulation platform also utilizes established *in vivo* models of hematopoiesis to rapidly assess and quantify the enhanced properties of our product candidates.

Our scientific founders were the first to demonstrate preclinical proof-of-concept for the *ex vivo* pharmacologic modulation of HSCs using prostaglandin E2 receptor agonists in 2007. Dr. Leonard Zon identified FT1050 to be a potent regulator of hematopoiesis. Since then, we have systematically applied our HSC modulation platform to translate this initial academic discovery into the clinical setting. This involved optimizing the incubation conditions and performing extensive preclinical characterization studies. By modulating HSCs derived from human umbilical cord blood with FT1050, we generated our initial product candidate, which we refer to as ProHema. The figure below shows the enhanced homing and engraftment properties of the *ex vivo* modulated human HSCs in a sub-lethally irradiated NSG mouse model of HSCT:

Homing **Engraftment**

We also performed a series of mouse transplantation experiments to determine whether the improved homing and engraftment properties of ProHema translated into improved survival outcomes following transplants with suboptimal HSC numbers. The figure below shows that the majority of lethally irradiated mice in the control group (seven out of ten) died during the 30-day observation period due to insufficient HSC dose, while all of the mice in the ProHema group survived.

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Survival

Our HSC modulation platform has the potential to enhance the biological properties of HSCs from any source, including umbilical cord blood, peripheral blood and bone marrow, and addresses many of the limitations of the current standard of care for HSCT as follows:

Expand the pool of HSC sources. We believe that the use of HSC sources that are immunologically naïve, such as umbilical cord blood, can increase the likelihood of identifying an HLA-compatible HSC source for allogeneic HSCT and reduce the incidence and severity of GvHD. It is believed that most patients have the chance to rapidly find a well HLA-matched umbilical cord blood unit for use in allogeneic HSCT, given that there are currently over 600,000 publicly-banked cord blood units available worldwide. Enhancing the biological properties of cord blood derived HSCs has the potential to significantly broaden the pool of viable banked cord blood units, and thereby improve the odds of finding the best or a better HLA-matched unit.

Overcome cell dose limitations. We believe that the optimization of HSCs can improve the engraftment potential of allogeneic HSCT, particularly when performed with umbilical cord blood, in which the HSC dose is lower than with other allogeneic HSC sources. As a result, we believe this will enable patients who are potential candidates for HSCT to have greater access to HSC sources, such as umbilical cord blood units that previously would have been considered to contain HSC doses insufficient for HSCT.

Enable the use of less toxic conditioning regimens. By enhancing the biological properties of HSCs, we believe that we can improve the rate of engraftment in the safer RIC setting as compared to MAC. We believe that improving the viability of RIC regimens will widen the adoption of, and broaden the eligible patient populations for, allogeneic HSCT.

Enhance HSC engraftment and reconstitution. We believe that the pharmacologic modulation of HSCs can improve patient outcomes across HSCT by increasing engraftment success rates, accelerating the time to reconstitution and improving the durability of engraftment. In addition, we believe that improving engraftment success rates and accelerating the time to reconstitution will lead to improved patient outcomes and the broader adoption of allogeneic HSCT.

We believe ProHema is the first *ex vivo* pharmacologically-modulated HSC product candidate to be evaluated in a clinical trial in patients undergoing HSCT. We have established human proof-of-concept for ProHema in the clinical setting by demonstrating enhanced and durable engraftment, which are important determinants of patient outcomes. The HSC modulation process used in the manufacture of ProHema takes only two hours, can be performed directly in the transplant center, does not require significant changes to existing infrastructure and is compatible with standard of care treatment modalities.

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Phase 1b Clinical Proof-of-Concept for ProHema

In September 2011, we completed a Phase 1b clinical trial of ProHema in adult patients with hematologic malignancies undergoing double UCBT after a RIC regimen. The primary objective of our Phase 1b clinical trial, referred to as the ProHema-01 trial, was to evaluate the safety of allogeneic HSCT using ProHema plus an unmanipulated cord blood unit. Secondary objectives of the trial included the assessment of time to engraftment and 100-day survival.

The ProHema-01 trial consisted of two cohorts of patients with acute leukemia, non-Hodgkin's lymphoma and myelodysplastic syndrome:

- an inactive cohort of nine patients who received an unmanipulated cord blood unit and a cord blood unit modulated with FT1050 under biologically inactive conditions; and
- the ProHema cohort of 12 patients who received ProHema and an unmanipulated cord blood unit.

The trial was conducted at the Dana Farber Cancer Institute and the Massachusetts General Hospital, and the results were compared against recent historical results from a control group of 53 adult patients with hematologic malignancies undergoing double UCBT at these same institutions.

Key Clinical Observations

We observed the following potential clinical benefits in our ProHema-01 trial:

- Treatment with ProHema demonstrated a statistically significant improvement in time to neutrophil engraftment, as compared to the historical control (p=0.043). Neutrophil engraftment was defined as peripheral blood neutrophil count above 500 cells per microliter. A p-value is a probability with a value ranging from 0 to 1, which indicates the likelihood that the results of a study are different between treatment and control groups. P-values below 0.05 are typically referred to as statistically significant;
- ProHema improved the cumulative incidence of neutrophil engraftment and the cumulative incidence of platelet engraftment, as defined by peripheral blood platelet count above 20,000 platelets per microliter;
- 100-day survival in the ProHema cohort compared favorably to both the inactive cohort and the historical control;
- there was a low incidence of acute and chronic GvHD in the ProHema cohort; and
- ProHema contributed to durable long-term hematopoietic reconstitution in a significant majority of the patients in the ProHema cohort and compared favorably to the historical control.

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The following table shows the results observed in the ProHema-01 trial with respect to the key measures of time to engraftment, cumulative incidence of neutrophil engraftment, rate of failure to achieve neutrophil engraftment and 100-day survival:

Cohort	Median Time to Engraftment	Cumulative Incidence of Neutrophil Engraftment by Day 26	Rate of Failure to Achieve Neutrophil Engraftment	100-Day Survival
ProHema	17.5 days (range 14 - 31 days)	83%	0%	100%
Inactive	22.0 days (range 14 - 40 days)	67%	11%	89%
Historical	20.5 days (range 13 - 70 days)	70%	6%	87%

The ProHema cohort also compared favorably to both the inactive cohort and the historical control in other measures of engraftment, including the cumulative incidence of platelet engraftment by Day 100 and the rate and incidence of cumulative engraftment as defined by absolute neutrophil count and platelet count. The following graphs show the rate and incidence of absolute neutrophil count and platelet count in the ProHema cohort, as compared to the historical control:

Rate and Incidence of Neutrophil Engraftment

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Rate and Incidence of Platelet Engraftment

We also evaluated the incidence of GvHD and observed a low incidence of acute GvHD in the twelve patients in the ProHema cohort. By Day 100, there was an 8% incidence of Grade II-IV acute GvHD in the ProHema cohort, as compared to 17% in the historical control group. One patient in the ProHema cohort experienced mild chronic GvHD.

Additionally, we performed an assessment of the ProHema cohort and the historical control to determine which of the two cord blood units contributed to long-term hematopoietic reconstitution. This analysis determined that, at Day 100, 83% of patients (10 of 12) in the ProHema cohort had achieved predominant hematopoietic reconstitution with ProHema as opposed to the unmodulated cord blood unit. In contrast, at Day 100, the profile of hematopoietic reconstitution in the historical control was substantially diverse: 34% of patients engrafted with the first cord administered to the patient; 34% of patients engrafted with the second cord administered to the patient; and 8% of patients persisted in a state referred to as dual chimerism, where both cords contributed to hematopoietic reconstitution, and the remainder of patients either experienced graft failure or died prior to Day 100. At a median follow-up among survivors of 24.6 months, no patient in the ProHema cohort experienced secondary graft failure, or graft failure following an initial period of engraftment. In addition, the one-year and two-year progression-free survival rates in the ProHema cohort were 61.7% and 31.3%, respectively. The corresponding one- and two-year overall survival rates in the ProHema cohort were 75.0% and 38.9%, respectively. Post-100 day survival rates in the inactive cohort and in the historical control were not available for analysis in the ProHema-01 trial.

Safety Assessment

The trial met all established safety criteria and demonstrated that ProHema was well tolerated. Adverse events attributed to ProHema consisted of mild to moderate infusion-related events consisting of rash, nausea, chills, flushing, abdominal pain, and cough, all of which are considered common transplant-related side effects. One patient with known coronary artery disease experienced transient myocardial ischemia that resolved promptly after completion of the infusion.

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ProHema-01 Trial Conclusion

We believe the results of our ProHema-01 trial demonstrate human proof-of-concept that the *ex vivo* pharmacologic modulation of HSCs has the potential to improve the key clinical measures of time to, and durability of, neutrophil engraftment. These improvements were demonstrated in allogeneic HSCT using a RIC regimen that is less toxic to patients and an HSC source that increases HLA compatibility and reduces the risk of GvHD.

In an End-of-Phase 1 meeting with the FDA in the first quarter of 2012, we received guidance from the FDA on potential Phase 3 clinical trial endpoints. This guidance suggested that time to engraftment of neutrophils, platelets, or both may be a sufficient primary endpoint to support approval, and that a single Phase 3 trial, enrolling both adult and pediatric subjects, may be sufficient for approval in both age groups, depending on the results.

The ProHema-01 trial was designed with safety as the primary endpoint and not efficacy. To support marketing approval, we will need to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that ProHema is safe and effective, and otherwise meets the appropriate standards required for approval for each targeted indication, in subsequent well-designed and conducted clinical trials, including our Phase 2 clinical trial and a Phase 3 registrational trial that we intend to initiate if our Phase 2 trial is successful. We may not be able to achieve or replicate the results of our Phase 1b clinical trial in our Phase 2 clinical trial or other subsequent trials for a variety of reasons. For example, the anticipated use of our NRM formulation in our Phase 2 clinical trial may not produce the efficacy or safety benefits that we currently expect; later-stage trials that enroll a larger number of patients may not produce the same or similar results as earlier trials with fewer patients; and the expansion in the number of participating clinical centers in later-stage trials may present operational and manufacturing challenges.

Improved Nutrient-Rich Media Formulation to Enhance the Potency of ProHema

In our ProHema-01 trial, ProHema was manufactured using standard processing media, which is commonly used throughout the clinical setting today for the thawing and washing of umbilical cord blood units. During the second quarter of 2013, we completed additional *in vitro* and animal studies demonstrating that the clinical potency and efficacy profile of ProHema may be significantly improved by using our new nutrient-rich media formulation, which we refer to as our NRM formulation, for clinical manufacture.

The manufacture of ProHema using our improved NRM formulation, as compared to the use of standard processing media, resulted in increased expression of PGE2-related genes and improved performance in *ex vivo* homing assays. In addition, the new manufacturing conditions also improved cell viability, as measured by HSC recovery. The homing potential of HSCs, as measured by an *in vitro* transwell migration assay, was also improved. The results of our studies using *in vitro* assays are summarized below:

Biological Measure of Activity	Standard Processing Media	NRM
Expression of relevant genes	2 - 6 fold increase	9 - 126 fold increase
Homing potential	7%	34%
Viable HSC Recovery	88%	107%
Increase in HSC population	62%	131%

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These enhanced modulation effects using our improved NRM formulation, as compared to standard processing media, translated into significantly improved homing and a more than two-fold improvement in engraftment in mouse models, as shown in the graphs below:

Homing **Engraftment**

Based on the data described above, we believe that the use of our NRM formulation will improve ProHema's potency and efficacy profile in the clinical setting. We intend to incorporate our improved NRM formulation into our clinical development program for ProHema.

Phase 2 Clinical Development in Adult Patients with Hematologic Malignancies

In March 2014, we initiated enrollment of a randomized, controlled, Phase 2 multi-center clinical trial of ProHema using our NRM formulation in adult patients undergoing double UCBT for hematologic malignancies using both MAC and RIC regimens, which we refer to as our ProHema-03 trial. Our ProHema-03 trial using our NRM formulation is currently active, and has been approved for conduct at ten major allogeneic HSCT centers in the United States. The trial is expected to enroll 60 additional adult patients across both MAC and RIC regimens. Patients in this trial will be randomized, at a ratio of 2:1, with approximately 40 patients receiving ProHema plus an unmanipulated cord blood unit and approximately 20 patients receiving two unmanipulated cord blood units. Prior to randomization, patients will be stratified based upon whether a RIC or MAC regimen will be employed. The primary endpoint of the trial is the cumulative incidence of neutrophil engraftment by a pre-specified control median, which will be adjusted based upon the median times calculated for subjects enrolled to the control arm. The study is designed to demonstrate with statistical significance that 70% of the subjects in the ProHema arm achieve neutrophil engraftment before the control median engraftment time. Secondary endpoints include additional measures of engraftment, including time to neutrophil engraftment, cumulative incidence of neutrophil engraftment by Day 42, time to platelet engraftment, cumulative incidence of platelet engraftment by Day 180, as well as rates of graft failure and of GvHD and event-free and overall survival. We expect to generate full data on the primary and major secondary endpoints from this trial in mid-2015.

In December 2012, we originally initiated the ProHema-03 trial using standard processing media for the manufacture of ProHema. In May 2013, we notified the FDA of our election to pause enrollment and our intent to generate data qualifying the optimized manufacturing process of ProHema using our NRM formulation. On August 1, 2013, we submitted to the FDA an amendment to our IND application, which contained preclinical and product development data supporting the use of our NRM formulation in the manufacture of ProHema and that its use should not result in additional safety risks. In addition, we submitted an amended protocol defining how we planned to resume the ProHema-03

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trial using our NRM formulation. Specifically, we stated that we planned to enroll the full 60 patients using our NRM formulation for the manufacture of ProHema, and that patients enrolled using standard processing media for the manufacture of ProHema prior to our election to pause enrollment would be followed and analyzed separately. In March 2014, we submitted to the FDA manufacturing and product data incorporating our NRM formulation for the manufacture of ProHema, where such data was generated using the NRM formulation intended for clinical use. Any FDA review or comments on this submission may lead the FDA to require us to generate additional preclinical or clinical data to support the use of our NRM formulation in our ProHema-03 trial or may impose additional requirements on our clinical development activities for ProHema, which may cause delays in enrollment and in the availability of full data from our ProHema-03 trial.

Prior to our election in May 2013 to pause enrollment of our ProHema-03 trial to qualify the optimized manufacturing process of ProHema using our NRM formulation, 11 patients conditioned using a MAC regimen had either consented to enrollment or been enrolled into the study. Eight of these patients were randomized to receive ProHema plus an unmanipulated cord blood unit, and three were randomized into the control arm to receive two unmanipulated cord blood units. No patients conditioned using a RIC regimen were enrolled. The three patients in the control arm engrafted at Days 30, 31 and 40, yielding a control median of 31 days. Five of the eight patients in the ProHema arm engrafted prior to the control median, at Days 14, 19, 24, 28 and 30. Two of the eight patients in the ProHema arm engrafted post the control median at Days 40 and 48, and one of the eight patients in the ProHema arm failed to engraft. Of the eight patients in the ProHema arm, six patients survived to Day 100 and two patients died before Day 100. The three patients in the control arm survived to Day 100. With a median overall follow-up for overall survival of 11.0 months, four of eight patients in the ProHema arm remain alive with a median survival that has not been reached but is greater than 9.0 months, as compared to one of three patients in the control arm who remain alive with a median survival of 6.0 months. No patients have experienced secondary graft failure. One patient in the ProHema arm experienced Grade IV acute GvHD, and one patient each in the ProHema and control arms experienced Grade III acute GvHD. Adverse events attributed to ProHema were primarily limited to common infusion-related side effects.

If our ProHema-03 trial is successful, we plan to seek additional regulatory guidance with the goal of initiating a Phase 3 registrational trial of ProHema, which may include both adult and pediatric patients undergoing UCBT for hematologic malignancies. Based on the regulatory guidance obtained to date, and preliminary statistical power calculations, we believe the Phase 3 program could consist of a single trial enrolling approximately 200 patients, with time to engraftment of neutrophils, platelets, or both as an endpoint to support approval.

Preclinical Development and Clinical Development Plans in Pediatric Patients with Hematologic Malignancies

For pediatric patients, the standard of care in UCBT for the treatment of hematologic malignancies utilizes a single cord blood unit. While the cell dose received by a pediatric patient from a single cord blood unit can be sufficient, data suggests that pediatric patients undergoing single UCBT still suffer from delayed engraftment, high rates of graft failure and high rates of transplant-related morbidity and mortality.

To explore the potential of ProHema in a pediatric patient population, we conducted a Phase 1 clinical trial to determine safety in the setting of single UCBT in adults with hematologic malignancies, which we refer to as our ProHema-02 trial. Qualifying patients received the same RIC regimen that was used in our ProHema-01 trial. After conditioning, patients received a single ProHema cord blood unit. The primary endpoint of the trial was safety. We analyzed a range of engraftment measures as well as rates of GvHD, relapse and survival.

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The trial enrolled eight patients. Of the eight patients, six patients were evaluable, age 19-64 years (median 55.9 years), with the following diagnoses: acute myelogenous leukemia (four patients), myelodysplastic syndrome (one patient) and multiple myeloma (one patient). Four of the six evaluable patients engrafted at Days 17, 19, 22 and 37, and two experienced primary graft failure. Survival at 100 days was 100%. At a median follow-up of 10.2 months, no patients experienced secondary graft failure, and there was no reported acute or chronic GvHD. Adverse events attributed to ProHema were limited to common transplant-related side effects.

Based on these results, we engaged in a preliminary review of the ProHema-02 data with the FDA and discussed our intent to conduct a Phase 1b trial in children and adolescents with hematologic malignancies. The FDA indicated that it was open to our conducting such a pediatric trial, but requested a written summary of the ProHema-02 trial as well as a synopsis of our proposed Phase 1b trial in pediatric patients with our justifications for the trial design. Subject to our submission of the requested information and FDA approval of the final study protocol, we plan to initiate a Phase 1b clinical trial in children and adolescents with hematologic malignancies, in which patients would receive a single ProHema unit. The primary endpoint of the trial is expected to be safety as defined by neutrophil engraftment. Secondary endpoints are expected to include additional measures of engraftment, including time to neutrophil engraftment, cumulative incidence of neutrophil engraftment by Day 42, time to platelet engraftment, cumulative incidence of platelet engraftment by Day 180, as well as rates of graft failure and of GvHD and event-free and overall survival. We anticipate commencing enrollment in our planned Phase 1b clinical trial in pediatric patients during 2014 and conducting the trial at one to three clinical centers in the United States. We expect to use our NRM formulation for the manufacture of ProHema in this trial. In addition, we believe we can conduct our planned Phase 1b clinical trial in pediatric patients under our current IND application for ProHema, and thus we may be able to amend our existing IND application in order to commence this planned clinical trial. Although we currently believe that amending our existing IND application will suffice, we will need to submit clinical development plans to the FDA before we can commence this trial. The FDA may disagree with our plans and require us to file a new IND application before we can commence clinical trials of ProHema for the treatment of hematologic malignancies in pediatric patients.

Our Opportunity in Rare Genetic Disorders

Overview

The steady growth in the number of HSCT procedures to treat patients with hematologic malignancies has been paralleled by an increase in the use of HSCT for rare genetic disorders. The treatment of rare genetic disorders requires allogeneic HSCT, as it provides HSCs from a healthy donor that carries a normal version of the defective gene. It is estimated that over 50 rare, genetic disorders, many of which are life-threatening and lack alternative therapeutic options, have been treated with allogeneic HSCT to date, including:

- LSDs, including Hurler syndrome, Krabbe disease and metachromatic leukodystrophy;
- peroxisomal storage disorders, including adrenoleukodystrophy;
- hemoglobinopathies, such as sickle cell disease and certain thalassemias;
- inherited bone marrow failure syndromes, such as Fanconi anemia and Diamond-Blackfan anemia; and
- inherited immune deficiencies, such as Wiskott-Aldrich syndrome.

The transformative effect of allogeneic HSCT, and UCBT in particular, across these rare genetic disorders has been demonstrated and published in numerous clinical studies, case series and

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retrospective analyses of multi-national patient registries. For instance, long-term follow up of children with LSDs and peroxisomal storage disorders who underwent allogeneic HSCT has shown that the progressive worsening of many clinical manifestations can be prevented or substantially reduced through early allogeneic HSCT intervention. These effects have been attributed to the ability of HSCs to home to and engraft within the CNS, where they give rise to microglia cells that become a permanent source of enzyme supply through a process called cross-correction.

It is well-recognized that umbilical cord blood has several important advantages over bone marrow and mobilized peripheral blood as a source of HSCs in the setting of allogeneic HSCT for LSDs. First, compared to the hematologic malignancy setting, even more patients lack a suitable related or matched unrelated donor. Second, cord blood can be readily accessed and can reduce time from diagnosis to transplant, a critical factor for patient outcomes, especially in patients with early-onset and rapidly progressing disorders, such as infantile Hurler syndrome or Krabbe disease. Furthermore, there is growing evidence that the proportion of patients achieving normal enzyme levels is higher following allogeneic HSCT with cord blood than with traditional HSC sources, which may improve the chances of reversing or halting the progressive manifestations of the disorder.

Unmet Medical Need

The key factors that determine HSCT patient outcomes in the hematologic malignancy setting are also highly relevant for rare genetic disorders and include:

Reconstitution. Timely and durable reconstitution of donor-derived HSCs is a critical success factor following allogeneic HSCT in patients with rare genetic disorders. Additionally, in patients with demyelinating LSDs, the homing of donor-derived HSCs across the blood-brain barrier is critical to arresting the degenerative effects of demyelination.

HLA matching. The degree of HLA matching is an important determinant of outcome following allogeneic HSCT in rare genetic disorders. Specifically, for certain LSDs, the rapid and irreversible progression of the disease requires urgent intervention and the immediate need to find an HLA-matched HSC source. We believe our ability to use pharmacologically optimized cord blood will reduce the time to transplant and improve patient outcomes.

Patient conditioning. Allogeneic HSCT procedures for rare genetic disorders are routinely performed using MAC regimens, because attempts to utilize RIC regimens have resulted in unacceptably high graft failure rates. The use of these highly toxic MAC regimens in infants and young children with rare genetic disorders is of significant concern. We believe the enhanced engraftment potential of our pharmacologically optimized HSCs will enable the broader adoption of RIC regimens.

Potential of Our HSC Modulation Platform in Rare Genetic Disorders

Given our preclinical findings of enhanced homing and engraftment, as well as the clinical proof-of-concept that we have achieved for our HSC modulation platform in the hematologic malignancy setting, we believe that pharmacologically-modulated HSCs have considerable potential to improve outcomes following allogeneic HSCT for rare genetic disorders. We are initially planning to study an *ex vivo* pharmacologically-modulated HSC therapeutic in pediatric patients with demyelinating LSDs. We plan to evaluate this potential both in an initial clinical trial of ProHema, as well as through a focused research program to identify other product candidates.

Preclinical Data

We have demonstrated in a preclinical model that *ex vivo* modulated cord blood increases the number of donor cells that home to and migrate across the blood-brain barrier into the CNS. We

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treated human cord blood-derived HSCs with FT1050 or vehicle control for two hours at 37°C and injected into sub-lethally irradiated NSG mice. Twenty hours following injections, genomic DNA was isolated from the brain tissue of the mice and the number of human cells in each sample was determined. The figure below shows that homing properties of HSCs derived from human cord blood to the CNS were significantly improved by *ex vivo* modulation with FT1050:

CNS Homing

In additional follow-up experiments, we treated human cord blood-derived HSCs with FT1050 or vehicle control for two hours at 37°C and injected into sub-lethally irradiated NSG mice. Eight weeks following injections, the number of human cells which had engrafted in the CNS were determined using qPCR against human specific sequences and the number of human iduronidase transcripts was measured using RT-qPCR. The figures below show that *ex vivo* modulation increases the number of donor-derived human cells engrafted in the CNS and results in higher numbers of iduronidase transcripts, which is the gene that is defective in patients with Hurler's syndrome:

CNS Engraftment

Enzyme mRNA in CNS

Clinical Plan

We plan to file an IND application in mid-2014 to initiate a first clinical trial of ProHema using our NRM formulation in pediatric patients with demyelinating LSDs later in 2014, with the goal of generating data from this trial in 2015. The primary objective of this trial is expected to evaluate the potential of *ex vivo* enhanced HSCs to enable robust engraftment under MAC and RIC regimens, where previous studies have shown that unmodulated cord blood units demonstrate higher rates of

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graft failure and longer times to engraftment as compared to their use in the treatment of hematologic malignancies. This trial is expected to enroll patients between the ages of one and 21 years. After conditioning, patients would receive a ProHema unit in combination with an unmodulated cord blood unit. The first cohort of patients would receive a conditioning regimen using a combination of high-dose chemotherapy agents that comprise a standard myeloablative regimen used for such transplants but in which one agent has been dose-reduced by 25%. Subsequent cohorts would receive conditioning regimens that are successively dose-reduced. The primary endpoint of the study is expected to be neutrophil engraftment, such that a reduced intensity dosing regimen could be identified that results in consistent and prompt engraftment. Patients would also be followed for other measures of engraftment and safety. In addition, patients would undergo regular cognitive and functional evaluations to measure the impact of the HSCT procedure on developmental milestones. We expect the trial will be conducted at one to three centers that specialize in pediatric cord blood transplantation for rare genetic disorders.

Next-Generation HSC Modulators

We are using our HSC modulation platform to develop second-generation therapeutics specifically designed to enhance biological mechanisms that are critical to improving and enabling the curative potential of HSCT in patients with orphan hematologic malignancies and rare genetic disorders, including homing of HSCs to the CNS to improve delivery of essential enzymes which are deficient in patients with LSDs.

Our Satellite Cell Modulation Platform

Therapeutic Potential of Muscle Satellite Stem Cells in Muscle Regeneration

Skeletal muscle has a potent natural regenerative capacity. Muscle satellite stem cells, or satellite cells, are regenerative precursor cells that play a key physiological role in the biological processes that drive skeletal muscle growth, maintenance and repair throughout a person's lifespan. In response to natural molecular triggers from exercise, injury or disease, satellite cells become activated, proliferate, and either differentiate into *de novo* muscle fibers or fuse with, and augment, existing muscle fibers. The regenerative capacity of muscle is exhausted both in the natural aging process and in degenerative conditions such as muscular dystrophies, where there is a constant cycle of muscle damage and compensatory repair. We are applying our knowledge of stem cell modulation to develop novel biologic therapeutics based on the natural signals that stimulate satellite cells *in vivo* to drive muscle regeneration in muscular dystrophies and other neuromuscular diseases and conditions.

Unmet Medical Need in Muscle Dystrophies

Muscular dystrophies encompass a group of rare diseases with diverse genetic bases and pathophysiological manifestations. The most prevalent and well-characterized forms are the X chromosome-linked Duchenne and Becker muscular dystrophies, or DBMDs, in which a loss or deleterious modification to the dystrophin protein results in significant and progressive muscle degeneration. There are many other distinct types of muscular dystrophies resulting from specific genetic mutations or deletions to over 30 distinct genes, including facioscapulohumeral muscular dystrophy, limb-girdle dystrophies and myotonic dystrophy. It is estimated that in the United States, DBMD occurs in one out of 3,500 live births, resulting in approximately 10,000 males living with these diseases. According to a 2007 study, over 80% of patients suffering from DBMD were wheelchair-bound by 14 years of age. In addition, DBMD patients usually do not live to the age of 30. There are no therapeutics specifically approved for the treatment of muscular dystrophies.

A core pathophysiologic phenomenon seen in muscular dystrophies is a cycle of muscle degeneration leading to continuous compensatory satellite cell activation and differentiation to affect a

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regenerative response. It is believed that the eventual exhaustion of this regenerative capacity results in accelerated tissue degeneration and, ultimately, significant loss of muscle function. Several promising therapeutics aimed at preventing further muscular degeneration through the reestablishment of dystrophin function are currently in clinical development. These include oligonucleotide exon-skipping of specific mutations in a subset of DBMD patients, stop-codon override approaches and utrophin up-regulation. To our knowledge, there are no clinical-stage programs focused on driving the natural regenerative process to reestablish muscular strength. We believe that restoring the balance between muscle degeneration and regeneration to induce tissue repair represents a promising approach for the treatment of all muscular dystrophies irrespective of the causative genetic mutation.

We have used our knowledge and systematic interrogation of satellite cell biology to identify specific natural signaling molecules that drive the muscle regenerative response. Further, we have applied our expertise in protein engineering to design protein analogs with therapeutic potential and preferred pharmaceutical development properties.

Our Proprietary Wnt7a Analogs

We have identified Wnt7a, a naturally-occurring secreted protein, as a key regulator of skeletal muscle regeneration. We have demonstrated in preclinical studies that a single administration of a Wnt7a analog resulted in a significant expansion of the satellite cell population and an increase in muscle hypertrophy. We have engineered analogs of Wnt7a and are developing them for regeneration in muscular dystrophies.

The role of Wnt7a as a potent stimulator of satellite cell population expansion and muscle hypertrophy was first identified by one of our scientific founders, Michael Rudnicki, Ph.D. This activity was shown to be dependent on a receptor known as Fzd7, which is predominantly expressed in skeletal muscle. Based on these findings, we believe that Wnt7a offers a highly-specific means to effect a regenerative response in skeletal muscle in order to treat neuromuscular diseases, irrespective of etiology. We own or have exclusively licensed worldwide rights to the use of Wnt7a in muscle regeneration.

Wnt7a is a member of a wider family of 19 secreted Wnt proteins known to play a central role in the processes of embryonic development, stem cell fate determination, tissue repair and homeostasis. Despite their widely-recognized importance throughout human physiology, to our knowledge, there are no Wnt proteins currently undergoing clinical development. This is primarily due to specific molecular characteristics that prevent their effective development as biologic therapeutics. We have systematically applied structural prediction, rational design and protein engineering techniques to overcome these challenges. We believe we are the first company to produce an analog of a Wnt protein that is amenable to manufacture, formulation and administration for *in vivo* therapeutic use. Our approach to the development of Wnt protein analogs encompasses the following advantages:

We have overcome manufacturing challenges. Natural Wnt proteins are expressed at very low levels in typical biologic manufacturing systems and are extremely difficult to purify while retaining activity. We have engineered Wnt compositions which enable effective, high level expression in commonly used host cells, thus enabling scaled recombinant manufacturing. We believe our proprietary Wnt compositions also allow scaled protein purification using methods commonly implemented by commercial biologic manufacturing organizations.

We have enabled therapeutic formulations. Natural Wnt proteins have limited solubility in preferred therapeutic excipients. Using structural biology, systematic engineering and signaling activity assessments, we have designed and produced Wnt proteins that retain activity and enable therapeutic formulation to allow *in vivo* administration.

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Our product candidates can be readily administered. Natural Wnt proteins are characterized as locally acting signaling molecules, potentially limiting their therapeutic range on administration. We have demonstrated that our Wnt7a analogs induce significant regenerative effects across a whole muscle on a single administration of protein.

Our product candidates retain a high degree of specificity. There are 19 human Wnt proteins and over 15 different receptors and co-receptors that drive a number of diverse signaling pathways and biological mechanisms in a tissue-specific manner. We have engineered Wnt7a analogs that retain specificity for the signaling pathway implicated in muscle regeneration but are inactive in other characterized Wnt signaling pathways, thereby potentially avoiding off-target activity or toxicities.

We believe that our knowledge of the role of Wnts in stem cell biology, our proprietary approaches for engineering Wnt-based analogs and their methods of formulation and manufacture represent foundational expertise that can be leveraged beyond Wnt7a. We intend to assess other Wnt-based biologic modulators for use in additional therapeutic applications. We own or have exclusively licensed worldwide rights to intellectual property pertaining to the design, composition and methods of manufacture and use of our Wnt analog proteins.

Preclinical Proof-of-Concept for Our Proprietary Wnt7a Analogs

We have demonstrated the therapeutic potential of our proprietary Wnt7a analogs in various preclinical models. They have been shown to expand the population of satellite cells, drive muscle hypertrophy, decrease disease-related muscle damage and increase muscle strength with similar potency as naturally-occurring Wnt7a in both wild-type rodents and rodent models of muscular dystrophy, or mdx. Additionally, in *in vitro* cultures of differentiated muscle cells, or myotubes, derived from healthy human subjects and from human subjects with various forms of muscular dystrophies, our proprietary Wnt7a analogs have been shown to drive muscle cell hypertrophy.

The Unique Dual Mechanism of Action of Wnt7a

In preclinical studies, we have demonstrated that a single injection of either Wnt7a or a Wnt7a analog to the *tibialis anterior* muscle of either wild type or mdx mice induces muscle hypertrophy and a significant expansion of the satellite cell population in a dose dependent manner. These effects are seen at three weeks following a single intramuscular injection of low microgram amounts of protein. In an example of these effects, we compared the hypertrophic activity of Wnt7a and a Wnt7a analog in treated muscle to both an injection of relevant formulation control and the equivalent untreated muscle on the opposite side of the body in the relevant animal model, which we refer to as the contralateral control. We demonstrated a statistically significant hypertrophic effect of Wnt7a and a Wnt7a analog relative to the contralateral control in the wild-type mouse represented by an approximately 20% increase in the median muscle fiber minimum cross-sectional diameter. We also demonstrated a statistically significant increase in the number of satellite cells, represented by an approximately three-fold increase in the number of Pax7 positive cell nuclei, a marker for satellite cells, in the treated

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muscle relative to the contralateral control. The figures below show our preclinical results demonstrating an increase in muscle hypertrophy and satellite cell population expansion:

Muscle Hypertrophy

Satellite Cell Population Expansion

Wnt7a Induced Regeneration Reduces Inflammation and Muscle Damage

Muscle fiber necrosis and inflammation are common abnormalities associated with muscular dystrophies that contribute to tissue fibrosis and a reduction in strength and regenerative capacity. Inducing muscle regeneration in the mdx mouse through a single administration of Wnt7a or a Wnt7a analog has been shown to increase muscle fiber integrity and reduce inflammatory cell infiltration of the tissue. In preclinical studies, we demonstrated a statistically significant reduction in disease-specific muscle fiber necrosis measured as the mean IgG-positive fibers per unit area of muscle and the reduction in positive staining of a cellular biomarker of inflammation, CD11b, within the muscles of mdx mice. The figures below show these results comparing Wnt7a or a Wnt7a analog to formulation control:

Improvement in Muscular Strength

The mdx rodent model of muscular dystrophy is significantly weaker than a wild-type rodent, as measured by specific force. Specific force is the normalization of force per cross-sectional area of muscle and represents a standard and accurate measure of muscular strength. In preclinical studies, we demonstrated that a single administration of Wnt7a or a Wnt7a analog protein induced a statistically significant increase of approximately 17-19% in the specific force or strength generated by the mdx

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rodent *tibialis anterior* muscle. The figures below show these results comparing Wnt7a or a Wnt7a analog to formulation control:

Specific Force Measurements

Activity on Human Dystrophic Muscle Cells

There are more than 30 distinct forms of muscular dystrophies. Each type can differ based on the muscles affected, the age of onset and genetic cause. For example, Duchenne and Becker muscular dystrophies are caused by a deficiency of the dystrophin protein due to a range of mutations in the dystrophin gene. In contrast, facioscapulohumeral dystrophies are thought to be caused by a defect in the expression of the DUX4 gene and are characterized by muscle weakness in the face, shoulders and upper arms. In *in vitro* cultures of myotubes derived from healthy human subjects and from human subjects with Duchenne, Becker and facioscapulohumeral dystrophies, our proprietary Wnt7a analogs have been shown to drive muscle cell hypertrophy. We believe these studies support the potential for our proprietary Wnt7a analogs to regenerate human skeletal muscle and to drive muscle hypertrophy across different types of muscular dystrophies irrespective of the underlying genetic cause.

Wnt7a Analog Development Strategy for Muscular Dystrophies

We are currently expanding our preclinical assessments to include dose and regimen optimization in rodent models, and are currently conducting preliminary, non-GLP toxicology assessments with dose escalation, which are intended to inform future IND-enabling toxicology studies. We also plan to initiate efficacy and pharmacokinetic assessments in a well-characterized large animal model of muscular dystrophy to assess the effects in larger muscle groups. We believe these studies of larger muscle groups may allow for a more predictable transition of dose and administration regimen to human trials.

We have identified potential Wnt7a-specific pharmacodynamic biomarkers, which can be attained through a pre- and post-treatment punch biopsy, in an effort to accelerate our clinical development process. These include both cellular effects, such as muscle hypertrophy and satellite cell population expansion, and molecular signatures based on whole genome expression analysis of Wnt7a-treated muscle. We have identified specific molecular signatures that represent potential biomarkers that may be measured in clinical trials.

Subject to the completion of IND-enabling studies and the filing of an IND application, we plan to initiate a Phase 1 clinical trial of an injectable analog of a Wnt7a-based recombinant human protein candidate in healthy volunteers in 2015, with the goal of generating data from this clinical trial in 2015. The primary objective of this trial is expected to evaluate safety and dose of a product candidate locally-administered to a targeted muscle group. We also plan to assess biological activity in this trial using histological and gene expression pharmacodynamic markers and measures of muscle strength by electromyography. Based on the results of our Phase 1 clinical trial in healthy volunteers, we expect to conduct a clinical trial to assess safety and dose, and to demonstrate human proof-of-concept, of a

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product candidate administered locally to a targeted muscle group in X chromosome-linked dystrophy patients. We believe that the combination of a Phase 1 clinical trial in healthy volunteers, a dose escalation clinical trial in an X chromosome-linked muscular dystrophy population and the establishment of effective pharmacodynamic biomarkers would allow us to efficiently assess both safety and efficacy for an injectable analog of a Wnt7a-based recombinant human protein candidate. We also believe these studies would provide a strong foundation for further discussions with the FDA regarding the path to approval in muscular dystrophies.

Indication Expansion Opportunities

We have demonstrated that Wnt7a is both a potent and a specific regulator of satellite cell population expansion and muscle hypertrophy and integrity. We have identified several Wnt7a analogs that we believe have therapeutic potential. While we are pursuing the development of a lead Wnt7a analog for the treatment of muscular dystrophies, we believe that this analog, as well as certain other Wnt7a analogs, may have potential in treating a wider range of neuromuscular degenerative conditions including cachexia, atrophy, trauma and sarcopenia. We are currently exploring therapeutic efficacy in additional preclinical models. We believe that the clinical assessment of safety and efficacy of our first Wnt7a analog in healthy volunteers and in muscular dystrophy patients can provide a basis for exploring the therapeutic benefit of Wnt7a in a wider array of neuromuscular disorders.

Additional Research and Discovery Activities

In addition to our two stem cell modulation platforms, we are advancing proprietary technologies for the industrial-scale generation, expansion and maintenance of induced pluripotent stem cells, or iPSCs. The ability to generate iPSCs is recognized to be one of the most important discoveries of the last decade. iPSCs are generated in a process by which fully-differentiated mature cells, such as skin cells or blood cells, are reprogrammed to a less-differentiated, embryonic stem cell-like state through the expression of certain pluripotency genes. Over the past five years, iPSCs have been used to produce cardiomyocytes and hepatocytes for the purposes of conducting drug toxicology testing and to produce other cell types for modeling human diseases, such as Parkinson's disease, Huntington's disease and Duchenne's muscular dystrophy. We are currently deploying our iPSC technology in the development of our stem cell modulators.

Our technology is built upon the discoveries and inventions of two of our scientific founders, Drs. Rudolf Jaenisch and Sheng Ding, both of whom are considered pioneers in the field of iPSC technology. We believe that our proprietary iPSC technology enables both the efficient, high throughput generation of stable, well-qualified iPSCs and the large-scale expansion and maintenance of iPSCs. We have exclusively licensed patents and patent applications, and developed proprietary technologies, that we believe are currently foundational to the practice of iPSC technology for commercial purposes. The key proprietary features and benefits of our iPSC technology include:

Patent-protected cellular compositions of reprogramming. One of the key pluripotency genes typically relied on for the generation of iPSCs is Oct4. The cellular composition comprising a somatic cell having an exogenous nucleic acid that encodes an Oct4 protein is a patent-protected composition of matter in the United States which we have exclusively licensed for commercial purposes.

Patent-protected small molecule combination for reprogramming. We incorporate a patent-protected small molecule in our culture systems of reprogramming. The use of these systems results in a 50-fold increase in reprogramming efficiency.

Proprietary methods for industrial-scale iPSC generation. We have developed an automated method for high-throughput iPSC generation which directly selects high-quality iPSC cells through proprietary combinations of cell surface antibodies. This method significantly enhances

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the throughput and quality of cellular reprogramming and enables industrial applications, such as disease modeling and toxicology screening from multiple genetic backgrounds.

Proprietary culture systems for iPSC expansion and maintenance. We have developed a proprietary small molecule-enhanced culture system which enables large-scale iPSC culture expansion while maintaining high quality, homogeneous cells. We believe this culture system enables commercial applications of iPSC technology, such as drug screening and, ultimately, iPSC-based cell therapies.

In September 2010, we entered into a collaboration and license agreement with Becton, Dickinson and Company, or BD, to develop and provide life science researchers and the pharmaceutical community with reliable access to certain advanced iPSC tools and technologies for use in human disease research, drug discovery and development, and the manufacture of cell-based therapies. Under the collaboration and license agreement, which concluded in September 2013, we co-developed certain stem cell reagent products with BD. BD has the right to commercialize these co-developed products on a worldwide basis. In June 2012, BD commercially launched the first stem cell product co-developed under the collaboration, BD SMC4, which is a patent-protected, pre-formulated cocktail of small molecules for improving cellular reprogramming efficiencies.

Our Intellectual Property

Overview

We strive to protect our product candidates and our stem cell modulation platforms through a variety of methods, including seeking and maintaining patents intended to cover our products and compositions, their methods of use and processes for their manufacture, our platform technologies and any other inventions that are commercially important to the development of our business. We have entered into exclusive license agreements with various academic and research institutions to obtain the rights to use certain patents for the development and commercialization of our product candidates. We also rely on know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position. We seek to obtain domestic and international patent protection and endeavor to promptly file patent applications for new commercially valuable inventions to expand our intellectual property portfolio.

As of March 12, 2014, our intellectual property portfolio is currently composed of 91 issued patents and 180 patent applications that we license from academic and research institutions and 42 patent applications that we own, and these patent and patent applications generally provide us with the rights to develop our product candidates in the United States and worldwide. This portfolio covers (i) our HSC modulation platform, including ProHema; (ii) our satellite cell modulation platform, including our Wnt7a analogs and (iii) our other technologies, such as our iPSC technology. We believe that we have a significant intellectual property position and substantial know-how relating to the modulation of adult stem cells, including HSCs and satellite cells.

We continually assess and refine our intellectual property strategy in order to fortify our position in our target market. To that end, we are prepared to file additional patent applications in any of the above fields if our intellectual property strategy requires such filings, or where we seek to adapt to competition or seize business opportunities. Further, we are prepared to file patent applications relating to new technologies we develop soon after the experimental data necessary for a strong application become available and our cost-benefit analyses justify filing such applications.

In addition to filing and prosecuting patent applications in the United States, we typically file counterpart patent applications in additional countries where we believe such foreign filing is likely to be beneficial, including Europe, Japan, Canada, Australia and China.

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We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications we may own or license in the future, nor can we be sure that any of our existing patents or any patents we may own or license in the future will be useful in protecting our technology. Please see "Risk Factors Risks Related to Our Intellectual Property" for additional information on the risks associated with our intellectual property strategy and portfolio.

Intellectual Property Relating to Our HSC Modulation Platform and ProHema

As of March12, 2014, we own six families of pending U.S. and foreign patent applications covering our HSC modulation platform. This portfolio includes 16 pending applications relating to ProHema and other therapeutic compositions of stem cells that have been pharmacologically modulated to enhance their therapeutic properties, and methods of manufacturing the cellular compositions. Applications in this portfolio include claims covering (i) a therapeutic composition of human HSCs that have been modulated *ex vivo* with an agent, such as a prostaglandin agonist, resulting in increased expression of genes associated with the beneficial biological properties of the cells and (ii) methods of improving HSCT and methods of treating patients requiring hematopoietic reconstitution, such as patients undergoing chemotherapy or radiation therapy for cancer, including hematologic malignancies, and patients with non-malignant blood disorders, as well as disclosures of methods for preparing cell populations for transplant, as well as a cell culture media, including NRM, for improved processing and modulating populations of cells *ex vivo* and methods describing a cell potency assay for determining or validating the therapeutic potential in cell populations. Any U.S. patents issued from these applications will have statutory expiration dates between 2030 and 2034.

We have an exclusive license to a portfolio consisting of two families of issued patents and pending patent applications co-owned by the Children's Medical Center Corporation and The General Hospital Corporation. We currently have exclusive rights to 19 issued patents and 26 pending patent applications in the United States and worldwide relating to methods for promoting tissue growth or regeneration (including of the hematopoietic system) using modulators that up-regulate the prostaglandin signaling pathway or its downstream mediators. These patent rights consist of an issued U.S. patent (U.S. Patent 8,168,428) claiming a method for promoting HSC engraftment through the *ex vivo* modulation of HSCs using FT1050, including HSCs obtained from cryopreserved cord blood, bone marrow and mobilized peripheral blood. Pending applications in the United States and foreign jurisdictions are directed to therapeutic compositions of HSCs derived from cord blood, wherein the cells have been modulated by increasing prostaglandin activity, methods of preparing these compositions, and methods of promoting hematopoietic reconstitution, expansion and self-renewal using modulators that increase prostaglandin signaling activity. Any patents within this portfolio that have issued or may yet issue will have a statutory expiration date in 2027.

We license exclusive rights to two families of patent applications from the Indiana University Research and Technology Corporation claiming methods of enhancing HSCT procedures by altering prostaglandin activity in HSCs and progenitor cells and methods for enhancing gene transduction efficacy in stem cell gene therapy. These applications describe methods of increasing mobilization of stem cells from a stem cell donor, and methods for increasing HSC homing and engraftment in a stem cell transplant recipient. One family of applications is directed to preferentially modulating certain receptors present on HSCs to increase the therapeutic potential of such cells for homing and engraftment. Claims in these applications specifically cover the modulation of umbilical cord blood by altering prostaglandin activity and methods for increasing gene transduction efficacy for gene therapy. These applications are currently pending in the United States and in certain foreign jurisdictions, and U.S. patents, if issued, from the applications could have terms expiring in 2029 or 2030.

We also license from the University of Rochester on exclusive terms a family of patent applications pending in the United States, Japan and the European Patent Office covering methods of expanding

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HSC populations *in vivo* or *ex vivo* using compositions comprising prostaglandin or a prostaglandin receptor agonist, including methods of selectively expanding highly proliferative short term HSCs to decrease recovery time in patients undergoing HSCT. Any U.S. patents that may issue from these applications would have a statutory expiration date in 2027.

To supplement our rights to develop and commercialize ProHema, we also have exclusive rights under additional license agreements with academic institutions to patents and patent applications that cover various methods for enhancing HSCT and modulating HSCs, including methods for increasing HSC numbers, promoting engraftment and increasing stem cell mobilization.

Intellectual Property Relating to Our Satellite Cell Modulation Platform and Wnt Analogs

In support of our program for the modulation of satellite cells using Wnt analogs, we own patent applications pending in the United States and internationally covering compositions of matter, including Wnt polypeptide analogs having production and formulation advantages, as well as formulations containing such Wnt analogs suitable for local and systemic administration, and methods of preparing such Wnt proteins and formulations. These applications specifically disclose and claim our proprietary Wnt7a analogs and formulations containing these Wnt7a analogs that have enhanced production characteristics. Our applications also describe methods of using our novel Wnt analogs for the regeneration of injured or diseased muscle tissue, and include claims to methods of treating a spectrum of diseases and conditions affecting muscle and muscle degenerative diseases, such as muscular dystrophies. Any U.S. patents that may issue from these applications will have a statutory expiration date in 2032 or 2033.

We also license exclusive rights from the Board of Trustees of the Leland Stanford Junior University, or Stanford, to a family of patent applications pending in the US and internationally directed to novel Wnt proteins that provide enhanced characteristics for producing therapeutic formulations of Wnt proteins, formulations of such proteins, and methods of manufacturing such proteins. Patent protection, to the extent it issues, would be expected to extend to 2032.

We also obtained rights, as the successor in interest to Verio Therapeutics, Inc., or Verio, to a portfolio of U.S. and international patents and patent applications owned by the Ottawa Hospital Research Institute, or OHRI, that supports our program for the treatment of muscle degeneration. These applications were licensed exclusively to Verio under a restated license agreement between Verio and OHRI effective April 2010. This portfolio includes patent applications directed to a novel population of satellite cells, enhanced Wnt protein analogs, and the modulation of satellite cells to promote muscle regeneration. These issued patents and applications include claims to compositions of novel stem cell populations and methods of treating muscle degenerative disorders by driving satellite cell population expansion and using small molecules or proteins to promote muscle tissue formation and muscle hypertrophy. These issued patents and any patents that may issue from these pending patent applications will expire on dates ranging from 2022 to 2033.

Intellectual Property Relating to iPSC Technology

We own two patent families with applications pending in the US and internationally directed to our proprietary small molecule-enhanced cell culture system which enables large-scale iPSC culture expansion while maintaining high quality, homogeneous cells. These applications also cover methods for industrial-scale iPSC generation. Any patents issued from these applications will expire in 2031 or 2036.

We have an exclusive license in commercial fields, including for drug discovery and therapeutic purposes, to a portfolio of four patent families including issued patents and pending applications broadly applicable to the reprogramming of somatic cells. This portfolio covers the generation of human pluripotent cells from somatic cells, and includes two issued patents (U.S. Patents 8,071,369 and 7,682,828) claiming compositions employed in reprogramming mammalian somatic cells to a less

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differentiated state (including to a pluripotent state). These issued patents and any patents that may issue from these pending patent applications will expire on dates ranging from 2024 to 2029.

We also have exclusive licenses to a portfolio of seven patent families relating to compositions and methods for reprogramming mammalian somatic cells, which covers non-genetic and viral-free reprogramming mechanisms, including the use of various small molecule classes and compounds and the introduction of cell-penetrating proteins to reprogram mammalian somatic cells. This portfolio includes an issued patent (U.S. Patent 8,044,201) that provides composition of matter protection for a small molecule, thiazovivin, that improves the efficiency of induction of reprogramming in somatic cells, and compositions and methods of using the small molecule. Any issued patents and any patents that may issue from patent applications pending in the US and internationally in this portfolio will have statutory expiration dates ranging from 2026 to 2032.

Our Material Technology License Agreements

Children's Medical Center Corporation

In May 2009, we entered into a license agreement with Children's Medical Center Corporation, or CMCC, for rights relating to therapeutic compositions of modulated HSCs and methods for promoting reconstitution of the hematopoietic system using modulators of the prostaglandin pathway, as described in more detail above under "Intellectual Property Relating to Our HSC Modulation Platform and ProHema." Under our agreement with CMCC, we acquired an exclusive royalty-bearing, sublicensable, worldwide license to make, use and sell products covered by the licensed patent rights, and to perform licensed processes, in each case, in all fields. CMCC retains a non-exclusive right to practice and use the patent rights for research, educational, clinical or charitable purposes, and also to license other academic and nonprofit organizations to practice the patent rights for research, educational, and charitable purposes (but excluding any clinical use and commercialization of the patent rights to the extent granted to us under the license agreement). Our license is also subject to pre-existing rights of the U.S. government and rights retained by the Howard Hughes Medical Institute and the General Hospital Corporation to use the patent rights for research purposes. Additionally, if we make any discovery or invention that is described in a patent application and is not within the scope of the licensed patent rights but would not have been made but for the licensed patent rights, we are required to disclose the invention to CMCC and enter into a non-exclusive license agreement with CMCC, for no more than a nominal fee, for CMCC to practice the invention solely for internal research purposes or clinical purposes and not for commercial purposes.

Under the terms of the license agreement, we are required to pay to CMCC a yearly license maintenance fee during the term of the agreement. We also are required to make payments to CMCC of up to $5.0 million per product in development, regulatory and sales milestones. If commercial sales of a licensed product commence, we will pay CMCC royalties at percentage rates ranging in the low to mid single digits on net sales of licensed products in countries where such product is protected by patent rights. Our obligation to pay royalties continues on a country by country basis until the expiration of all licensed patent rights covering licensed products in such country, and our royalty payments will be reduced by other payments we are required to make to third parties until a minimum royalty has been reached. In the event that we sublicense the patent rights, CMCC is also entitled to receive a percentage of the sublicensing income received by us.

Under the license with CMCC, we are obligated to use commercially reasonable efforts to bring a licensed product to market as soon as practicable, and also to use good faith and diligent efforts to manufacture and distribute a licensed product, and make licensed products reasonably available to the public during the term of the agreement. We are also required to use good faith and diligent efforts to meet the milestones set forth in development plans as part of the agreement, subject to any revisions to the development plans that may be permitted under certain circumstances. Additionally, if a third party

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expresses interest in an area under the license that we are not pursuing, under the terms of our agreement with CMCC, we may be required to sublicense rights in that area to the third party.

The agreement will continue until the last to expire of the patent rights. We may terminate the agreement by providing prior written notice to CMCC, and CMCC has the right to terminate the agreement if we fail to pay royalties or otherwise materially breach the agreement and fail to cure such breach within a specified grace period. CMCC may also terminate the agreement should we cease operations or in the event of our bankruptcy or insolvency.

The Board of Trustees of the Leland Stanford Junior University

In May 2013, we entered into an exclusive license agreement with Stanford for rights relating to novel Wnt analogs. Under our agreement, Stanford granted us an exclusive worldwide license to make, use and sell Wnt proteins and compositions of such proteins that are covered by the licensed patent rights for the treatment, prevention, and palliation of diseases, conditions, syndromes and maladies of humans and animals. The rights exclusively licensed to us under the license are described in more detail above under "Intellectual Property Related to Our Satellite Cell Modulation Platform and Wnt Analogs."

Stanford retains the right, on behalf of itself and all other non-profit academic research institutions, to practice under the patent rights for any non-profit purpose, including sponsored research and collaborations. We may grant sublicenses to third parties so long as we are actively pursuing the development or commercialization of products covered by the patent rights. We may also be required to sublicense our rights under the agreement at Stanford's request under certain conditions, including if we are unwilling or unable to serve a potential market or territory and there is a third party willing to be a sublicensee in such market or territory.

We are obligated to pay to Stanford a yearly license maintenance fee during the term of the agreement, but we may offset the maintenance fee against earned royalty payments due on net sales occurring in that year. Stanford is entitled to receive a royalty as a percentage of net sales of licensed products, ranging from the low to mid single digits. Our agreement contains provisions for royalty offsets to the extent we need to obtain any rights from third parties to make, use, or sell the licensed products, subject to a minimum floor in the single digits. We have agreed to pay Stanford a percentage of non-royalty revenue we receive from our sublicensees, with the amount owed decreasing if we enter into the applicable sublicense agreement after meeting certain clinical milestones and, should we sublicense rights under the agreement with other patent rights, with the amount owed being apportioned between the patent rights under the agreement and any other rights sublicensed with the patent rights. In addition, we are obligated to pay Stanford up to approximately $900,000 upon the achievement of specific intellectual property, clinical and regulatory milestone events.

Under the license with Stanford, we are obligated to use commercially reasonable efforts to develop, manufacture, and commercialize at least one licensed product; to develop markets for such licensed products; and to meet certain development milestones as agreed upon between us and Stanford.

The agreement terminates on a country-by-country basis upon the last to expire of the patent rights in such country. We may terminate the agreement by providing prior written notice to Stanford, and Stanford has the right to terminate the agreement if we fail to achieve certain milestones or make payments under the agreement, or are not actively pursuing development of a licensed product, or if we otherwise materially breach the agreement and fail to cure such breach within a specified grace period.

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Ottawa Hospital Research Institute

We acquired Verio in April 2010, and as the successor to Verio we acquired rights to various patents and patent applications pursuant to a restated license agreement between OHRI and Verio, which we refer to as the OHRI License. The licensed patents and patent applications under the OHRI License include issued patents and patent applications relating to the use of Wnt7a and analogs for the treatment of muscle degeneration, as described in more detail above under "Intellectual Property Relating to Our Satellite Cell Modulation Platform and Wnt Analogs."

Through the OHRI License, we obtained an exclusive, worldwide, royalty-bearing license, with the right to sublicense, to develop, make, use and sell products covered by the licensed patent rights in all fields. OHRI retains the right under the OHRI License to practice the licensed technology and patent rights for non-commercial, research and academic purposes. We are obligated to pay OHRI an annual license maintenance fee, which is creditable towards any royalties owed under the OHRI License. We are also required to make payments to OHRI of up to CDN$1.4 million per product in connection with development, regulatory and commercial milestones. OHRI is entitled to receive a royalty in the low single digit range on net sales of licensed products, and we may offset any payments made to third parties to obtain rights needed for the commercialization of a licensed product against royalties payable to OHRI, provided that such expenses in a given year may not be credited against more than a specified percentage of the royalties payable to OHRI in such year. We have the right to sublicense our rights under OHRI License, and we are obligated to pay OHRI a percentage of any sublicense income.

Under the OHRI License, we are required to use commercially reasonable efforts to exploit the licensed patent rights in countries where it is commercially reasonable to develop licensed products, and to commercialize licensed products. We must also use commercially reasonable efforts to achieve development benchmarks described in the agreement in accordance with the specified time periods. If we fail to achieve a development benchmark in accordance with its applicable timeline, and OHRI determines that we have not used commercially reasonable efforts to develop the applicable product, OHRI may convert our license to the related patent rights to a non-exclusive license or may terminate the agreement, subject to our right to cure such deficiency or extend the timeline for achieving such benchmark once upon the payment of a fee.

We may terminate the OHRI License by providing ninety days' written notice to OHRI. OHRI may terminate the OHRI License if we materially breach the license agreement and fail to cure the breach within a grace period, or if we become insolvent or bankrupt. The OHRI License otherwise expires upon the expiration of the last to expire of the licensed patents.

Manufacturing

We do not own or operate, and currently have no plans to establish, any of our own manufacturing facilities. Other than small amounts of compounds and proteins that we may synthesize ourselves for preclinical testing, we currently rely, and expect to continue to rely, on third party contract manufacturing organizations, or CMOs, for the manufacture of our required raw materials and proteins, including FT1050, the small molecule HSC modulator used in manufacturing ProHema.

ProHema Manufacturing

ProHema (formally referred to as ProHema-CB Suspension for Infusion), is a composition of pharmacologically-modulated human cord blood cells. ProHema is produced by treating qualified human umbilical cord units with FT1050 in a multistep process that is performed on the day of transplantation in relative close proximity to the recipient, such that it may be administered within minutes to one or two hours after release. The cord blood units, or CBUs, therefore never leave the vicinity of the clinical center, eliminating the risk that shipment to a distant offsite manufacturing facility may result in delivery delays.

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ProHema is manufactured on the same day as product administration, corresponding to Day 0 of the transplant regimen. A cryopreserved CBU that meets clinical protocol criteria for the manufacturing process is used as the starting cellular source material. These CBUs are identified through online search facilities that are able to identify potentially suitable CBUs from cord blood banks around the world, based upon a patient's HLA type and cell dose requirements.

The manufacturing process consists of treating the physician-selected CBU with FT1050 in our proprietary two-hour modulation process. After the cells are modulated, an automated wash is performed to reduce residual FT1050 prior to administration of ProHema. After in-lab filtration and final packaging and labeling, the final product consists of *ex vivo* modulated human cord blood cells. ProHema is then tested in a variety of ways prior to release.

ProHema is manufactured at clinical cell processing facilities operated by or affiliated with our clinical sites. Although some of these facilities may be certified GMP cell manufacturing environments, the ProHema manufacturing process consists largely of closed production, which we believe minimizes the requirement for full GMP environmental monitoring and control. One objective of our product development program is to close the ProHema manufacturing process to the point that it may be conducted by the majority of clinical cell processing facilities that are otherwise capable of handling standard HSC products for allogeneic HSCT.

In addition to FT1050, we use other components in the manufacturing of ProHema, including components used in our NRM formulation, as well as disposable materials such as bags and tubing sets. To date, we have obtained the FT1050 starting material for ProHema in our preclinical studies and clinical trials from one third-party manufacturer. We obtain our supply of FT1050 for our clinical trials from this manufacturer on a purchase order basis under a clinical supply manufacturing agreement, and do not have any current contractual relationships for the commercial manufacture and supply of bulk FT1050 substance for manufacturing ProHema. If our current third-party manufacturer of FT1050 should become unavailable to us for any reason, we believe that there are several potential replacements, although we may incur some delay in identifying and qualifying such replacements. We intend to source other components used in the manufacturing of ProHema, including those that comprise our NRM formulation, from other third-party suppliers.

Wnt7a Protein Manufacturing

Our Wnt7a analogs are recombinant proteins generated from a stably-transfected mammalian cell expression system. Our initial supply of Wnt7a analogs used in our preclinical efficacy and pharmacokinetic studies was synthesized within our laboratories by our scientists. Other than small amounts of proteins and compounds that we may synthesize ourselves for preclinical testing, we expect to rely on third parties for the manufacture of the Wnt7a analog and any other Wnt-based product candidates that we may develop. We are currently selecting the contract manufacture organization for master cell banking, process development and ultimate cGMP manufacture of our Wnt7a analog therapeutic.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technology, development experience and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

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Many of our competitors will have substantially greater financial, technical and human resources. Accordingly, our competitors may be more successful in developing or marketing products and technologies that are more effective, safer or less costly. Additionally, our competitors may obtain regulatory approval for their products more rapidly and may achieve more widespread market acceptance.

There are several clinical-stage development programs that seek to improve human UCBT through the use of *ex vivo* expansion technologies to increase the quantity of HSCs for use in HSCT or the use of *ex vivo* differentiation technologies to increase the quantity of hematopoietic progenitor cells for use in HSCT. Companies active in this area include, but are not limited to, Gamida Cell Ltd., Biotest Pharmaceuticals Corporation, Aldagen, Inc., a wholly-owned subsidiary of Cytomedix, Inc., Novartis Pharmaceuticals Corporation and Celerant Technology Corp.

Currently, there are no approved pharmaceutical products specifically developed for the treatment of muscular dystrophies. We are aware of several other companies developing therapies that are in various stages of development for the treatment of muscular dystrophies, including Prosensa Holding B.V., Sarepta Therapeutics Inc., PTC Therapeutics, Inc., Summit Corporation plc, Halo Therapeutics LLC, and Tivorsan Pharmaceuticals, Inc.

Government Regulation

In the United States, the FDA regulates biological products under the Federal Food, Drug, and Cosmetic Act, or FDCA, and the Public Health Service Act, or PHS Act, and related regulations. Biological products are also subject to other federal, state, local, and foreign statutes and regulations. The FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries impose substantial requirements upon the clinical development, manufacture and marketing of biological products. These agencies and other federal, state, local, and foreign entities regulate research and development activities and the testing, manufacture, quality control, safety, effectiveness, packaging, labeling, storage, distribution, record keeping, reporting, approval, advertising and promotion, and import and export of our products. Failure to comply with the applicable U.S. regulatory requirements at any time during the product development process, including clinical testing, approval process or after approval may subject an applicant to administrative or judicial sanctions.

Government regulation may delay or prevent marketing of product candidates for a considerable period of time and impose costly procedures upon our activities. The testing and approval process requires substantial time, effort, and financial resources, and we cannot be certain that the FDA or any other regulatory agency will grant approvals for ProHema or any future product candidates on a timely basis, if at all. The FDA's policies may change and additional government regulations may be enacted that could prevent or delay regulatory approval of ProHema or any future product candidates or approval of new disease indications or label changes. We cannot predict the likelihood, nature or extent of adverse governmental regulation that might arise from future legislative, judicial, or administrative action, either in the United States or abroad.

Marketing Approval

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

completion of nonclinical laboratory and animal tests according to good laboratory practices, or GLPs, and applicable requirements for the humane use of laboratory animals or other applicable regulations;

submission to the FDA of an IND application which must become effective before human clinical trials may begin;

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performance of adequate and well-controlled human clinical trials according to the FDA's regulations commonly referred to as good clinical practices, or 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 or uses;

submission to the FDA of a Biologics License Application, or BLA, for marketing approval that includes substantive evidence of safety, purity, and potency from results of nonclinical testing and clinical trials;

satisfactory completion of an FDA pre-approval inspection of manufacturing facilities where the biological product is produced to assess compliance with good manufacturing practices, or GMPs, 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, or GTPs, for the use of human cellular and tissue products to prevent the introduction, transmission or spread of communicable diseases;

potential FDA audit of the nonclinical study sites and clinical trial sites that generated the data in support of the BLA; and

FDA review and approval, or licensure, of the BLA which must occur before a biological product can be marketed or sold.

U.S. Biological Products Development Process

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

Prior to commencing the first clinical trial, the clinical trial sponsor must submit the results of the nonclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of an initial IND application. Some nonclinical testing may continue even after the IND application is submitted. The IND application automatically becomes effective 30 days after receipt by the FDA unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the clinical trial and places the clinical trial on a clinical hold. In such case, the sponsor of the IND application must resolve any outstanding concerns with the FDA before the clinical trial may begin. Further, an independent institutional review board, or IRB, for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial before it commences at that site. An IRB is charged with protecting the welfare and rights of study subjects and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. The FDA or IRB may impose clinical holds on a biological product candidate at any time before or during clinical trials due to safety concerns or non-compliance. If the FDA imposes a clinical hold, trials may not recommence without FDA or IRB authorization and then only under terms authorized by the FDA and IRB. Accordingly, we cannot be sure that submission of an IND application will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that will result in the suspension or termination of such trials.

Clinical trials involve the administration of the biological product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control. Clinical trials are conducted under protocols detailing, among other

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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. Each protocol and any amendments to the protocol must be submitted to the FDA as part of the IND application and to the IRB.

For purposes of BLA approval, human clinical trials are typically conducted in three sequential phases that may overlap:

Phase 1 The biological 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. These trials may also provide early evidence on effectiveness.

Phase 2 These trials are conducted in a limited number of patients in the target 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 and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.

Phase 3 Phase 3 trials are undertaken to provide statistically significant evidence of clinical efficacy and to further evaluate dosage, potency, and safety in an expanded patient population at multiple clinical trial sites. They are performed after preliminary evidence suggesting effectiveness of the product has been obtained, and are intended to establish the overall benefit-risk relationship of the investigational product, and to provide an adequate basis for product approval and labeling.

Post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials may be required by the FDA as a condition of approval and are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up. The FDA now has express statutory authority to require post-market clinical trials to address safety issues. All of these trials must be conducted in accordance with GCP requirements in order for the data to be considered reliable for regulatory purposes.

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. Regulatory authorities, a data safety monitoring board or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the participants 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.

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Our ongoing and planned clinical trials for our product candidates may not begin or be completed on schedule, if at all. Clinical trials can be delayed for a variety of reasons, including delays in:

- obtaining regulatory approval to commence a trial;
- reaching agreement with third-party clinical trial sites and their subsequent performance in conducting accurate and reliable trials on a timely basis;
- obtaining IRB approval to conduct a trial at a prospective site;
- recruiting patients to participate in a trial; and
- supply of the biological product or components required for the manufacture of the biological product.

Typically, if a biological product is intended to treat a chronic disease, as is the case with ProHema, safety and efficacy data must be gathered over an extended period of time, which can range from six months to three years or more. Success in early stage clinical trials does not ensure success in later stage clinical trials. Data obtained from clinical activities are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval.

Concurrent with clinical trials, companies usually complete additional animal studies and must also 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 GMP requirements. To help reduce the risk of the introduction of adventitious agents with the 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

In order to obtain approval to market a biological product in the United States, a BLA must be submitted to the FDA that provides data establishing to the FDA's satisfaction the safety, purity and potency of the investigational biological product for the proposed indication. The application includes all data available from nonclinical studies and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's manufacture and composition, and proposed labeling, among other things. The testing and approval processes require substantial time and effort and there can be no assurance that the FDA will accept the BLA for filing and, even if filed, that any approval will be granted on a timely basis, if at all.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each BLA must be accompanied by a user fee. The FDA adjusts the PDUFA user fees on an annual basis. According to the FDA's fee schedule, effective beginning on October 1, 2013 and in effect through September 30, 2014, the user fee for an application requiring clinical data, such as a BLA, will be $2,169,100 for fiscal year 2014. PDUFA also imposes an annual product fee for biologics ($104,060 for fiscal year 2014), and an annual establishment fee ($554,600 for fiscal year 2014) on facilities used to manufacture prescription biologics. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

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The FDA has 60 days from its receipt of a BLA to determine whether the application will be accepted for filing based on the agency's threshold determination that the application is sufficiently complete to permit substantive review. 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 before the FDA accepts it for filing. After the BLA submission is accepted for filing, the FDA reviews the BLA to determine, among other things, whether the proposed product is safe and potent, or effective, for its intended use, and has an acceptable purity profile, and whether the product is being manufactured in accordance with GMPs to assure and preserve the product's identity, safety, strength, quality, potency, and purity, and biological product standards. The FDA may refer applications for novel biological products or biological products that present difficult 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, if so, under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving a BLA, the FDA 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 GMP requirements and adequate to assure consistent production of the product within required specifications. For a human cellular or tissue product, the FDA also will not approve the product if the manufacturer is not in compliance with the GTPs. 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, or HCT/Ps, which are human cells or tissue intended for implantation, transplant, infusion, or transfer into a human recipient. The primary intent of the GTP 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 screening and testing. Additionally, before approving a BLA, the FDA may inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND study requirements and GCPs. To assure GMP, GTP and GCP compliance, an applicant must incur significant expenditure of time, money and effort. If the FDA determines the manufacturing process or manufacturing facilities are not acceptable, it typically will outline the deficiencies and often will require the facility to take corrective action and provide documentation evidencing the implementation of such corrective action. This may significantly delay further review of the application. If the FDA finds that a clinical site did not conduct the clinical trial in accordance with GCPs, the FDA may determine the data generated by the clinical site should be excluded from the primary efficacy analyses provided in the BLA, and request additional testing or data. Additionally, notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

The FDA also has authority to require a Risk Evaluation and Mitigation Strategy, or REMS, from manufacturers to ensure that the benefits of a biological product outweigh its risks. A sponsor may also voluntarily propose a REMS as part of the BLA submission. The need for a REMS is determined as part of the review of the BLA. Based on statutory standards, elements of a REMS may include "dear doctor letters," a medication guide, more elaborate targeted educational programs, and in some cases restrictions on distribution. These elements are negotiated as part of the BLA approval, and in some cases may delay the approval date. Once adopted, REMS are subject to periodic assessment and modification.

After the FDA completes its initial review of a BLA, it will communicate to the sponsor that the biological product will either be approved, or it will issue a complete response letter to communicate that the BLA will not be approved in its current form. The complete response letter usually describes

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all of the specific deficiencies in the BLA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the applicant in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, or withdraw the application.

The FDA may not grant approval on a timely basis, or at all. We may encounter difficulties or unanticipated costs in our efforts to secure necessary governmental approvals, which could delay or preclude us from marketing our products. The testing and approval process for a biological product usually takes several years to complete.

One of the performance goals agreed to by the FDA under PDUFA is to review 90% of standard BLAs in 10 months and 90% of priority BLAs in six months, whereupon a review decision is to be made. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs and its review goals are subject to change from time to time. The review process and the PDUFA goal data may be extended by three months if the FDA requests or the BLA applicant otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

Even if a product candidate receives regulatory approval, the approval may be limited to specific disease states, patient populations and dosages, or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings, or precautions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a risk management plan, or otherwise limit the scope of any approval. In addition, the FDA may require Phase 4 post-marketing clinical trials, designed to further assess a biological product's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized. Further, even after regulatory approval is obtained, later discovery of previously unknown problems with a product may result in the imposition of new restrictions on the product or even complete withdrawal of the product from the market. Delay in obtaining, or failure to obtain and maintain, regulatory approval for ProHema, or obtaining approval but for significantly limited use, would harm our business.

Expedited Development and Review Programs

The FDA has a Fast Track program that is intended to facilitate the development and expedite the review of new drugs and biological products that meet certain criteria. Specifically, new drugs and biological products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening condition or disease 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 biological 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. Unique to a Fast Track product, the FDA may consider for review sections of the marketing application on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application.

Any product submitted to the FDA for marketing, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant

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improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. 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. Additionally, a product 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 a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, 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 may require that a sponsor of a drug or biological product receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. 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. Fast Track designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process.

The Food and Drug Administration Safety and Innovation Act of 2012 also amended the FDCA to require FDA to expedite the development and review of a breakthrough therapy. A drug or biological product can be designated as a breakthrough therapy if it is intended 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. A sponsor may request that a drug or biological product be designated as a breakthrough therapy at any time during the clinical development of the product. If so designated, FDA shall act to expedite the development and review of the product's marketing application, including by meeting with the sponsor throughout the product's development, providing timely advice to the sponsor to ensure that the development program to gather nonclinical and clinical data is as efficient as practicable, involving senior managers and experienced review staff in a cross-disciplinary review, assigning a cross-disciplinary project lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor, and taking steps to ensure that the design of the clinical trials is as efficient as practicable.

U.S. Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration, and specifics of the FDA approval of the use of our product candidates, some 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, commonly referred to as the Hatch-Waxman Amendments. Patent term restoration can compensate for time lost during product development and the regulatory review process by returning up to five years of patent life for a patent that covers a new product or its use. 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 period of patent term restoration is generally one-half the time between the effective date of an IND application (falling after issuance of the patent) and the submission date of a BLA, plus the time between the submission date of the BLA and the approval of that application, provided the sponsor acted with diligence. 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. The application for patent term extension is subject to approval by the U.S. Patent and Trademark Office, or USPTO, in consultation with the FDA.

A patent term extension is only available when the FDA approves a biological product for the first time. We believe ProHema and the manner in which it modulates HSCs have not been previously