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 endpo