BIOTIME INC
Form 10-K
March 17, 2014

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

FORM 10-K

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

For the fiscal year ended December 31, 2013

OR

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 1-12830

BioTime, Inc.
(Exact name of registrant as specified in its charter)

California	94-3127919
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

1301 Harbor Bay Parkway, Suite 100
Alameda, California 94502
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code (510) 521-3390

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

Title of each class	Name of exchange on which registered
Common shares, no par value	NYSE MKT

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 No x

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 No x

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 x No o

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files).
Yes x o No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) 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 o

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.

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

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

The approximate aggregate market value of voting common shares held by non-affiliates computed by reference to the price at which common shares were last sold as of June 30, 2013 was $135,804,066. Shares held by each executive officer and director and by each person who beneficially owns more than 5% of the outstanding common shares have been excluded in that such persons may under certain circumstances be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The number of common shares outstanding as of March 5, 2014 was 69,598,709.

Documents Incorporated by Reference
Portions of the registrant's Proxy Statement for 2014 Annual Meeting of Shareholders are incorporated by reference in Part III

BioTime, Inc.

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PART I

Statements made in this Form 10-K that are not historical facts may constitute forward-looking statements that are subject to risks and uncertainties that could cause actual results to differ materially from those discussed. Words such as “expects,” “may,” “will,” “anticipates,” “intends,” “plans,” “believes,” “seeks,” “estimates,” and similar expressions identify forward-looking statements. See Note 1 to Financial Statements.

References to “we” means BioTime, Inc. and its subsidiaries unless the context otherwise indicates.

The description or discussion, in this Form 10-K, of any contract or agreement is a summary only and is qualified in all respects by reference to the full text of the applicable contract or agreement.

Item 1. Business

Overview

We are a biotechnology company focused on the emerging field of regenerative medicine. Our core technologies center on stem cells capable of becoming all of the cell types in the human body, a property called pluripotency. Products made from these "pluripotent" stem cells are being developed by us and our subsidiaries, for use in a variety of fields of medicine, including: neuroscience, oncology, orthopedics, and blood and vascular diseases. BioTime's commercial strategy targets near-term yet strategic commercial opportunities such as: Renevia™ (a product currently in clinical trials in Europe to facilitate cell transplantation); ReGlyde™ and Premvia™ for tendon and dermatological applications; PanC-Dx™ (a family of novel blood and urine-based cancer screens); our current line of research products including PureStem® cell lines, associated ESpan™ culture media, and cGMP-capable human embryonic stem cell lines; and the LifeMap Database Suite. Four of our subsidiaries, Asterias Biotherapeutics, Inc. ("Asterias"), Cell Cure Neurosciences, Ltd (Cell Cure Neurosciences"), OrthoCyte Corporation ("OrthoCyte"), and ReCyte Therapeutics, Inc. ("ReCyte Therapeutics") are focused on developing cell based therapeutic products for diseases such as neurological disorders, cancer, age related macular degeneration, orthopedic disorders, and age-related cardiovascular disease."

“Regenerative medicine” refers to an emerging field of therapeutic product development that may allow all human cell and tissue types to be manufactured on an industrial scale. This new technology is made possible by the isolation of human embryonic stem (“hES”) cells, and by the development of “induced pluripotent stem (“iPS”) cells” which are created from regular cells of the human body using technology that allows adult cells to be “reprogrammed” into cells with pluripotency similar to hES-like cells. These pluripotent hES and iPS cells have the unique property of being able to branch out into each and every kind of cell in the human body, including the cell types that make up the brain, the blood, the heart, the lungs, the liver, and other tissues. Unlike adult-derived stem cells that have limited potential to become different cell types, pluripotent stem cells may have vast potential to supply an array of new regenerative therapeutic products, especially those targeting the large and growing markets associated with age-related degenerative disease. Unlike pharmaceuticals that require a molecular target, therapeutic strategies in regenerative medicine are generally aimed at regenerating affected cells and tissues, and therefore may have broader applicability. Regenerative medicine represents a revolution in the field of biotechnology with the promise of providing therapies for diseases previously considered incurable.

The field of regenerative medicine includes a broad range of disciplines, including tissue banking, cellular therapy, gene therapy, and tissue engineering. Our commercial efforts in regenerative medicine include the development and sale of products designed for research applications in the near term as well as products designed for diagnostic and therapeutic applications in the medium and long term. Through our ESI BIO division, we offer advanced human stem cell products and technologies that can be used by researchers at universities and at companies in the bioscience and biopharmaceutical industries. We have developed research and clinical grade hES cell lines that we market for both basic research and therapeutic product development. Our subsidiary, ES Cell International Pte Ltd (“ESI”), has

developed six hES cell lines that are among the best characterized and documented cell lines available today. Developed in compliance with the principles of current Good Manufacturing Practices ("cGMP") that facilitate transition into the clinic, these hES cell lines are extensively characterized and five of the six cell lines currently have documented and publicly-available genomic sequences. The ESI hES cell lines are now included in the Stem Cell Registry of the National Institutes of Health ("NIH"), making them eligible for use in federally funded research, and all are available for purchase through our ESI BIO division at http://esibio.com/products/. We are working with several collaborators to enable the use of these lines for production of cell therapy products for investigational new drug enabling studies. ESI BIO also markets human embryonic progenitor cells ("hEPCs"), which are called PureStem® progenitors and were developed using PureStem® (previously designated ACTCellerate)™ technology. These hEPCs are purified lineages of cells that are intermediate in the developmental process between embryonic stem cells and fully differentiated cells. We expect that hEPCs will simplify the scalable manufacture of highly purified and identified cell types and will possess the ability to become a wide array of cell types with potential applications in research, drug discovery, and human regenerative stem cell therapies. The PureStem® progenitors are also available for purchase through http://esibio.com/products/.

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Research products can be marketed without regulatory or other governmental approval, and thus offer relatively near-term business opportunities, especially when compared to therapeutic products. Certain research products, such as ESI hES lines and HyStem® hydrogels, have the advantage of being "translatable to the clinic" meaning that these products are available as economical research grade or clinical grade products. Consequently, these products allow researchers more assurance that they will be acceptable for use in future clinical trials. The medical devices and diagnostics that we and our subsidiaries are developing will require regulatory approval for marketing, but the clinical trial and approval process for medical devices is often faster and less expensive than the process for the approval of new drugs and biological therapeutics. Our current and near-term product opportunities, combined with expected long-term revenues that could be derived from cell-based therapeutic products under development at our subsidiaries, provide us with a balanced commercial strategy.

Our HyStem® hydrogel product line is one of the components in our near-term revenue strategy. HyStem® is a patented biomaterial that mimics the human extracellular matrix, which is the network of molecules surrounding cells in organs and tissues that is essential to cellular function. Many tissue engineering and regenerative cell-based therapies will require the delivery of therapeutic cells in a matrix or scaffold to sustain cell survival after transplantation and to maintain proper cellular function. HyStem® is a unique hydrogel that has been shown to support cellular attachment and proliferation in vivo.

Renevia™ is a clinical grade formulation of our HyStem®-C, a biocompatible, implantable hyaluronan and collagen-based matrix for cell delivery in human clinical applications. As an injectable product, Renevia™ may address an immediate need in cosmetic and reconstructive surgeries and other procedures by improving the process of transplanting adipose derived cells, mesenchymal stem cells, or other adult stem cells. We will need to obtain approval by the United States Food and Drug Administration (the "FDA") and comparable regulatory agencies in foreign countries in order to market Renevia™ as a medical device. We recently conducted our first European clinical trial of Renevia™ without cells to determine the safety, tolerability, and acceptance of Renevia™ after subcutaneous injection. Examinations of the subjects after they received Renevia™ injections and through the four-week follow-up period have shown that Renevia™ was well-tolerated by all subjects with no serious adverse events or subject withdrawals. Subsequent clinical studies are planned to document the efficacy of Renevia™ as a delivery matrix for adipose cells to restore normal skin contours in patients where the subcutaneous adipose tissue has been lost to lipoatrophy, beginning with HIV related facial lipoatrophy. Lipoatrophy is a localized loss of fat beneath the skin. Lipoatrophy is often a consequence of the normal aging process where the loss of fat in the cheeks or the back of the hands contributes to an aged appearance, but lipoatrophy can also be associated with trauma, surgery, and diseases, and is frequently suffered by HIV patients being treated with anti-viral drugs.

We have commenced development of two new products based on our HyStem® technology platform. The new products are unique formulations utilizing some of the same cGMP components that we are using in our clinical trials of Renevia.™ The first of these new products is ReGlyde,™ a cross-linked thiol-modified hyaluronan hydrogel for the management and protection of tendon injuries following surgical repair of the digital flexor or extensor tendons of the hand. The product is intended to be applied to the repaired tendon area via a syringe or similar device immediately prior to closing of the surgical area in order to prevent the tendon from attaching to the surrounding tissue. Separation of the tendon from surrounding tissue has been shown to significantly reduce post-surgical adhesions that can lead to complications such as restricted finger mobility and flexibility. The second new product, Premvia,™ is a HyStem® hydrogel formulation of cross-linked thiol-modified hyaluronan and thiol-modified gelatin for the management of wounds by providing a hydrating tissue matrix that permits cell, tissue, and vasculature in-growth.

Our HyStem® hydrogels may have other applications when combined with the diverse and scalable cell types our scientists have isolated from hES cells. HyStem® products are also currently being used by researchers at a number of leading medical schools in pre-clinical studies of stem cell therapies, including research that we are funding at UCLA for the treatment of ischemic stroke. Other researchers are conducting work with HyStem® in research to facilitate wound healing, to treat brain cancer, vocal fold scarring, and for myocardial infarct repair. Recent publications have

highlighted the combined use of HyStem® hydrogels with PureStem® progenitors resulting in a combined product that produces cartilage-producing cell masses known as chondrocytes. We call this experimental product HyStem®-4D. In collaboration with William Marsh Rice University, we are also using HyStem® technology to develop 3D cell culture platforms for improved methods of screening new anti-cancer drug candidates.

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Our subsidiary OncoCyte is developing novel products for the diagnosis and treatment of cancer in order to improve the quality and length of life of cancer patients. Based on large unmet need, market size, and data generated thus far from patient sample screening, OncoCyte is presently focusing its efforts on developing PanC-Dx™ diagnostic products for use in detecting breast, bladder, and lung cancers. Clinical studies designed to test the performance of PanC-Dx™ markers in these three cancers are currently underway, and completion of the studies is expected by the end of 2014. The performance of the marker panels in determining the presence or the progression of disease in various categories of patients in these clinical studies will determine the specific nature of the test to be developed and the approval pathway that OncoCyte will pursue.

Our subsidiary, LifeMap Sciences, Inc. ("LifeMap Sciences") markets, sells and distributes GeneCards®, the leading human gene database, as part of an integrated database suite that includes LifeMap Discovery®, the database of embryonic development, stem cell research and regenerative medicine; and MalaCards, the human disease database.

Our majority owned subsidiary Cell Cure Neurosciences is developing cell therapies for retinal and neural degenerative diseases. Cell Cure Neurosciences' lead product is OpRegen®, a proprietary formulation of embryonic stem cell-derived retinal pigmented epithelial cells developed to address the high, unmet medical needs of people suffering from age-related macular degeneration.

On October 1, 2013, our subsidiary Asterias acquired the stem cell assets of Geron Corporation ("Geron"), including patents and other intellectual property, biological materials, reagents and equipment for the development of new therapeutic products for regenerative medicine. The product candidates under development from various cell types that Asterias acquired from Geron are summarized in the following table:

Product Candidate Description	Target Market	Estimated Number of Potential Patients [1]	Status
OPC1 – Glial Cells	Spinal Cord Injury	12,000 new cases per year in U.S.	Phase I Trial initiated in U.S. 5 Patients treated – no serious adverse events related to the OPC1 drug product to date.
	Multiple Sclerosis ("MS")	180,000 new cases per year in U.S.	Proof of principle achieved in animal models.
	Canavan's Disease[2]	Rare	Proof of principle achieved in animal models.
	Stroke	800,000 new cases per year in U.S.	Pre-clinical research.
VAC1 – Autologous Monocyte – Derived Dendritic Cells (infused cells derived from the treated patient)	Cancer	Prostate: 240,000 new cases per year in U.S.	Phase I study in metastatic prostate cancer completed (Journal of Immunology, 2005, 174: 3798-3807).
VAC2 – Dendritic Cells	Lung Cancer	Acute myelogenous leukemia: more than 12,000 new cases per year in U.S. 226,000 new cases per year in U.S.	Phase I/II study in acute myelogenous leukemia completed. Manuscript in preparation. Cells derived and characterization studies performed (parameters analyzed

		showed normal cell functions in vitro[3]).
Multiple Myeloma	22,000 new cases per year in U.S.	Scalable manufacturing methods under development
Prostate Cancer	240,000 new cases per year in U.S	Proof of concept established in multiple human in vitro[3] systems.

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Product Candidate Description	Target Market	Estimated Number of Potential Patients	Status
CHND1 – Chondrocytes	Osteoarthritis	25 million total patients in U.S.	Cells derived and partly characterized. Early non-clinical studies have been performed in animal models of osteoarthritis.
	Degenerative Disk Disease	400,000 new spinal fusion cases per year in U.S.	Pre-clinical research.
CM1 – Cardiomyocytes	Heart Failure	6 million total patients in U.S.	Cells derived and characterization studies performed (parameters analyzed showed normal cell functions in vitro[3]).
	Myocardial Infarction	900,000 new cases per year in U.S.	Proof of concept in three animal models of disease. Scalable manufacturing established. First in man clinical trial designed.
IC1 – Islet Cells	Type 1 and some Type 2 Diabetes	5 million total insulin dependent patients in U.S.	Cells derived and partly characterized (most, not all normal cell functions verified in vitro[3]). Proof of concept in rodent diabetes model. Scalable manufacturing methods under development.

(1) The estimates of the numbers of potential patients shown in the table are based on data for the United States only and do not include potential patients in other countries.

(2) Canavan's Disease is a congenital neurological degenerative disease in which the growth of the myelin sheath surrounding nerves is inhibited resulting in mental retardation, loss of motor function, abnormal muscle tone, poor head control and enlarged head. Death usually occurs before age 4.

(3) In vitro means in tissue culture dishes.

Asterias may also use the acquired assets, along with technology that it may develop itself or that it may acquire from third parties, to pursue the development of other products. Asterias' product development efforts may be conducted by Asterias alone or in collaboration with others if suitable co-development arrangements can be made.

Plasma Volume Expander Products

We have developed and licensed manufacturing and marketing rights to Hextend®, a physiologically balanced blood plasma volume expander used for the treatment of hypovolemia in surgery, emergency trauma treatment, and other applications. Hypovolemia is a condition caused by low blood volume, often from blood loss during surgery or from injury. Hextend® maintains circulatory system fluid volume and blood pressure and helps sustain vital organs during surgery or when a patient has sustained substantial blood loss due to an injury. Hextend® is the only blood plasma volume expander that contains lactate, multiple electrolytes, glucose, and a medically approved form of starch called

hetastarch. Hextend® is sterile, so its use avoids the risk of infection. Health insurance reimbursements and HMO coverage now include the cost of Hextend® used in surgical procedures.

Hextend® is manufactured and distributed in the United States by Hospira, Inc., and in South Korea by CJ Cheil Jedang Corp. ("CJ"), under license from us.

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Key Accomplishments in 2013

- Our subsidiary, Asterias completed its acquisition of Geron's stem cell assets, including patents and other intellectual property, biological materials, reagents and equipment for the development of new therapeutic products for regenerative medicine. The contributed assets include four cell lines, each with animal proof of concept, from which multiple therapeutic product candidates may be selected by Asterias for development in the fields of neurology, oncology, orthopedics, and cardiology.

- We conducted a clinical safety study of Renevia™ at The Stem Center in Palma de Mallorca, Spain, a patient therapy center, laboratory, and research facility located within the hospital Clinica USP Palmaplanas in Palma. Examinations of the subjects after they received Renevia™ injections have shown that Renevia™ was well tolerated by all subjects with no serious adverse events or subject withdrawals.

- Our subsidiary OncoCyte Corporation entered into a Sponsored Research Agreement and a Material Transfer Agreement with The Wistar Institute to collaboratively develop lung cancer diagnostic products. OncoCyte scientists will analyze blood samples obtained from patients in a Wistar clinical study to determine levels of tumor-associated proteins found in the blood samples. The data obtained from the samples received from Wistar's ongoing multi-center study may allow OncoCyte to more rapidly develop a diagnostic test for lung cancer to be marketed in the U.S. and other countries.

- Our subsidiary, Asterias entered into a Non-Exclusive License Agreement with the Wisconsin Alumni Research Foundation ("WARF") under which Asterias was granted a worldwide non-exclusive license to use certain WARF patents and WARF-owned embryonic stem cell lines in the development and commercialization of therapeutic, diagnostic and research products.

- We commenced the development of two new products based on our HyStem® technology platform. The new products are unique formulations utilizing some of the same cGMP components used in Renevia.™ The first of these new products is ReGlyde,™ a cross-linked thiol-modified hyaluronan hydrogel for the management and protection of tendon injuries following surgical repair of the digital flexor or extensor tendons of the hand. The second new product, Premvia,™ is a HyStem® hydrogel formulation of cross-linked thiol-modified hyaluronan and thiol-modified gelatin for the management of wounds by providing a hydrating tissue matrix that permits cell, tissue, and vasculature in-growth.

- We consolidated our research products business into a new ESI BIO division and a new ESI BIO branding program. The ESI BIO brand and US-based operating division will now be our primary developer, manufacturer and distributor of our growing portfolio of stem cell based research products. This new division includes our Singapore subsidiary ES Cell International Pte Ltd. , that will serve as an Asian manufacturer and research product distribution point. This consolidation will allow for a more focused approach on the branding, development, manufacture and marketing of our research products portfolio.

Additional Information

HyStem®, Hextend®, ESpy®, *PureStem*®, and PentaLyte® are registered trademarks of BioTime, Inc., and Renevia,™ Premvia,™ ReGlyde,™ and ESpan™ are trademarks of BioTime, Inc. ACTCellerate™ is a trademark licensed to us by Advanced Cell Technology, Inc. ReCyte™ is a trademark of ReCyte Therapeutics. PanC-Dx™ is a trademark of OncoCyte. LifeMap Discovery® is a registered trademark of LifeMap Sciences. OpRegen® is a registered trademark of Cell Cure Neurosciences. GeneCards® is a registered trademark of Yeda Research and Development Co. Ltd.

We were incorporated in 1990 in the state of California. Our principal executive offices are located at 1301 Harbor Bay Parkway, Alameda, California 94502. Our telephone number is (510) 521-3390nd dispose of such shares as

follows: (i) with respect to the 16,504 shares held in trusts created under the Will of Mary E. Dalrymple, with his co-trustee, David J. Dalrymple; (ii) with respect to the 59,416 shares held by Dalrymple Holding Corporation, with the other officers and shareholders of said corporation, David J. Dalrymple and Edward C. Dalrymple, Jr.; and (iv) with respect to the 30,230 shares held by Susquehanna Supply Company, with the other officers and shareholders of Susquehanna Supply Company. Robert H. Dalrymple does not have the power to vote or direct the voting of or dispose or direct the disposition of the shares owned by Elizabeth T. Dalrymple.

Joanne F. Dalrymple

Joanne F. Dalrymple shares the power to vote and dispose of the 307,720 shares held by the Dalrymple Family Limited Partnership with David J. Dalrymple. Joanne F. Dalrymple does not have the power to vote or direct the voting of or dispose or direct the disposition of the shares owned by her husband.

Dalrymple Family Limited Partnership

Through its two general partners, David J. Dalrymple and Joanne F. Dalrymple, Dalrymple Family Limited Partnership has voting and dispositive power over 307,720 shares."

Item 5 is further amended by deleting part (c) in its entirety and inserting the following in the place thereof:

"(c)

David J. Dalrymple

On January 9, 2012, David J. Dalrymple acquired 846 shares by grant from the Issuer.

Robert H. Dalrymple

On January 9, 2012, David J. Dalrymple acquired 692 shares by grant from the Issuer.

Joanne F. Dalrymple

Joanne F. Dalrymple has effected no transactions in the Issuer's common stock during the past sixty (60) days.

Dalrymple Family Limited Partnership

Dalrymple Family Limited Partnership has effected no transactions in the Issuer's common stock during the past sixty (60) days."

Item 6. Contracts, Arrangements, Understandings or Relationships With Respect to Securities of the Issuer.

Item 7. Material to be Filed as Exhibits.

Signature:

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

Dated: February 24, 2012

Signature: /s/David J. Dalrymple
David J. Dalrymple

Signature:

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

Dated: February 24, 2012

Signature: /s/Robert H. Dalrymple
Robert H. Dalrymple

Signature:

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

Dated: February 24, 2012

Signature: /s/Joanne F. Dalrymple
Joanne F. Dalrymple

Signature:

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

Dated: February 24, 2012

Signature: /s/David J. Dalrymple
Dalrymple Family Limited Partnership
By: David J. Dalrymple, general partner