

BIOTIME INC  
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SCHEDULE 14A

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INFORMATION REQUIRED IN PROXY STATEMENT

SCHEDULE 14A INFORMATION

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Dear Fellow Shareholders,

Every year we have the opportunity to write this letter accompanying the Annual Meeting of Shareholders of BioTime, Inc. As in years past, it is our pleasure to summarize some of the successful milestones from the past year, and to communicate our vision of where we plan to take the Company in the future. This past year, we've seen significant progress in validating the core technologies of the Company and transferring lab-bench science to a development track that may yield first-in-class therapies for unmet needs in medicine. To evaluate BioTime from the management perspective, let's begin by examining the opportunity before us in light of the current state of the regenerative medicine industry.

***Regenerative medicine: a revolutionary means of treating disease***

The field of regenerative medicine began with the search for a means to rebuild tissues afflicted with chronic degenerative disease. Currently some 75% of health care costs are associated with chronic diseases, and those costs are expected to grow significantly in the coming years as a result of the approaching tsunami of aging baby boomers. Unlike mechanics who can repair a machine by replacing broken components, medical science never had an effective means of producing replacement tissues from the multitude of cell types in the human body, until now. Cells and tissues available from organ donation are often not suitable for use due to potential transplant rejection.

Given the large unmet need for cell and tissue replacement therapies to treat degenerative diseases, an effort was organized in 1995 to build a new class of medical therapies based on pluripotent stem cells capable of proliferating without limit. The discovery of these stem cells brought into focus the possibility of developing industrial-scale means of producing various cell types of the human body that could be used to replace tissues lost as a result of the onset of degenerative diseases. In the late 1990s, it also became clear that it was going to become possible to make such cells genetically identical to those of a patient on an affordable basis through what are called reprogramming technologies. These new technologies provide the opportunities of manufacturing all of the cell types of the human body on an industrial scale and matching those cells, when necessary, to the patient to eliminate transplant rejection. This new approach has the potential to provide therapies for some of the most significant unsolved problems in medicine, such as heart failure, in which the loss of heart muscle cells leads to a weakened heart. Many other age-related chronic degenerative diseases could potentially be treated with these novel technologies, including Parkinson's disease, osteoarthritis, osteoporosis, age-related macular degeneration, and atherosclerosis, to name a few.

The stem cells that have caused this excitement are of two types: human embryonic stem (hES) cells and induced pluripotent stem (iPS) cells. hES cells are cultures of continuously proliferating cells (cell lines), and were originally derived from clusters of cells resulting from surplus fertilized

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egg cells produced through *in vitro* fertilization procedures and that were designated by the donors to be discarded. iPS cells are cells produced from a donated cell of the body, such as skin cells, and then coaxed back to an hES-like state by means of genetic modification. While hES cells are seen as an "off-the-shelf" approach to making all the cells of the body, iPS cells are seen as a means of making all of these cells genetically matched to a patient in cases in which transplant rejection would otherwise be a problem.

As revolutionary as hES and iPS cells are, it became clear during recent years that the promise of these cells is intimately linked to a significant hurdle. Put quite simply, these cells really do make *all* of the cells of the body, and they tend to display this immense power even when it is undesirable, such as when scientists are trying to generate only *one* cell type for therapeutic use. As a result, many different cell types that form a human being were arising in laboratory dishes, even when only one cell type was desired, and scientists had no effective means of sorting these cells in order to manufacture a medical-grade product of a single cell type. While scientists quickly published hundreds of scientific reports describing methods of making the many diverse cell types of the body as you may have read the biotechnology industry faced the tall hurdle of making cells in a purified and fully identified state, under Good Manufacturing Practices (GMP) standards, while simultaneously scaling cell production up to a volume sufficient to treat millions of patients. As the biotechnology industry and large pharmaceutical companies struggled with these issues, BioTime scientists were inventing entirely novel manufacturing technologies that we believe will redefine the industry. Let's discuss some of those in turn.

#### ***Four foundational cornerstones in this emerging industry***

##### **1. Clinical-grade master cell banks of stem cells**

For certain clinical applications, replacement cells will likely be manufactured for all people from a single line of hES cells, without risking transplant rejection. These are highly coveted "off-the-shelf" product opportunities and are therefore widely considered low-hanging fruit in the industry. These cells are the focus of most of our development efforts. For procedures that involve transplanting new healthy cells into the retina of the eye, into the brain, or into the joints, or in cases in which specially designed cells are used to target tumors to destroy them, the cells will ideally be manufactured from a source of hES cells produced under GMP standards, including a complete sequence of their DNA to insure the manufacture of reliable and safe products. BioTime maintains a bank of six GMP hES cell lines acquired with our purchase of the Singapore-based company ES Cell International Pte. Ltd. (ESI). ESI previously developed the cell bank with approximately \$30 million of funding, provided in part by the Government of Singapore. We have signed agreements with the California Institute for Regenerative Medicine (CIRM) and the University of California system to distribute five of those research-grade and GMP-compliant hES cell lines to numerous California-based researchers. Should the research using BioTime's cell lines result in successful products, BioTime will enjoy a royalty on sales without additional expenditures on our part. To make our GMP cell lines more attractive to researchers, we obtained approval from the National Institutes of Health for the use of our cell lines in federal funded research, and we have published the first complete DNA sequencing of these cell lines, demonstrating their normality and likely suitability for the manufacture of a wide array of new medical products.

**2. Purity and identity: the *sine qua non***

Beginning in 2005, several of the scientists who are now at BioTime began to develop an entirely novel approach for the manufacture of products from hES and iPS cells. Called *ACTCellerate*, this technique allows scientists to expand the lineages of cell types downstream of hES and iPS cells from a single cell already committed to making a specific cell type. These new proliferating lines of cells are no longer hES or iPS cells, but instead are all monoclonal embryonic progenitor cells committed to producing distinct and identified cell types. Since millions of these cells can be propagated in the laboratory, they are very scalable to potentially meet the needs of many hundreds of thousands of patients, and because they are all derived from one cell type, we believe we have simultaneously solved the problem of making the cells pure. In addition to clearing the most significant hurdles for the industrial scale-up of over 200 cell types in the human body, this technique has allowed us to capture the gene expression fingerprint of essentially all human genes, and file numerous patent applications on the cell lines, claiming compositions of matter, methods of expansion, and uses in the treatment of a wide array of diseases. Much of the validation of the *ACTCellerate* technology has been undertaken by means of a generous \$4.7 million grant from CIRM.

**3. A robust technology for the manufacture of patient-specific cells through reprogramming**

For those cases in which an off-the-shelf product would likely be rejected by a patient's immune system, BioTime scientists have invented a proprietary reprogramming technology called *ReCyte*, which is designed to reprogram a patient's cells, such as skin cells, back to hES-like stem cells so that all the cell types in the body, identical to the patient, can be produced for a wide array of potential clinical applications. Our *ReCyte* technology is a proprietary method that differs from most other published iPS techniques, and may have distinct advantages over the competing approaches. One such advantage is the addition of a novel mechanism, identified at the prestigious Wistar Institute in Philadelphia, for regulating the reprogramming of cells. Licensed by BioTime, we believe this technology is very important in both the stem cell field and in the development of new cancer therapeutic strategies. We currently have a research program underway at our subsidiary ReCyte Therapeutics, Inc. in collaboration with Wistar Institute scientists to advance this exciting breakthrough.

**4. Focusing on near- and intermediate-term commercialization**

A major challenge of biotechnology in general, and of stem cell companies in particular, is the relatively long timelines to commercial viability of their products, especially when novel therapeutic strategies are involved. Despite a supportive approach from the Food and Drug Administration, those biotech companies in the sector that have focused only on long-term product development programs have often suffered from dwindling market capitalization and difficulties raising the needed capital to bridge the gap between preclinical development and late-stage clinical trials where large pharmaceutical companies may be willing to provide funding for the completion of product development in exchange for marketing rights. To address these issues, we have implemented a commercial model with near-term and intermediate-term commercialization strategies, and we have formed a corporate partnership with large pharma for the leading cell-based therapy of one of our subsidiaries. Near-term revenues are being generated

by our current royalties from the sale of our plasma volume expander product Hextend® in the United States and South Korea, and from the sale of research products, including our current line of *ACTCellerate* cell lines and associated *ESpan* culture media, *HyStem* hydrogels, human embryonic stem cell lines, and revenues being generated by the recent acquisition of worldwide marketing rights to the online database *GeneCards*® by our subsidiary LifeMap Sciences, Inc. Intermediate revenues are anticipated from the planned launch of *Renevia* as a cell delivery device expected in late 2013, and the planned launch of *PanC-Dx* as a novel blood-based cancer screen in 2014.

We believe our choice of *HyStem*® hydrogels like *Renevia*, as an extracellular matrix for the propagation of human stem cells and as a means of cell delivery for human clinical applications, is a strategic choice of a near-term product. While many types of matrices have been developed, there are numerous reasons why few are as likely as our hydrogel technology to be commercialized. Our hydrogels fulfill the necessary biological criteria they are resorbable, biocompatible, and benefit from their ability to be injected with cells into the body through a syringe and then polymerize within the body without the release of inflammatory toxic byproducts. They also have been demonstrated to possess the proper physical and chemical properties for cellular attachment, which is needed for the survival and repopulation of stem cells *in vivo*. We therefore plan to utilize *HyStem*® in a number of our future products in combination with our cell lines, and we also sell *HyStem*® products now in the research product markets through a global distribution network.

### ***Salient milestones from the past year***

In the past year we announced numerous strategic advances in building the foundation of our company, including the following achievements.

#### ***Advanced near- and intermediate-term product development***

- We successfully completed ISO 10993 biocompatibility studies for *Renevia* (previously known as *HyStem*®-Rx). The results of these preclinical studies demonstrated the safety and biocompatibility of *Renevia*. The first clinical application of *Renevia* will be for use with autologous adipose cells to restore subcutaneous tissue lost as a result of injury, oncologic resection, or congenital defects. Our goals for the launch of *Renevia* include obtaining the CE mark necessary for marketing *Renevia* in European Union countries by year-end 2013.
- We made several key advances in the development of *PanC-Dx*, OncoCyte Corporation's novel diagnostic device to detect the presence of various human cancers. We evaluated more than 50 potential cancer biomarkers that we discovered using antibody-based technology on blood samples from a proprietary sample bank derived from over 600 donors, including patients with cancers of the breast, colon, and pancreas, as well as healthy volunteers. We have selected seven of those serum markers for monoclonal antibody production.

- We entered into agreements with USCN Life Science, Inc. of Wuhan, China, granting BioTime an option to license USCN's antibody-producing cell lines and certain related technology for potential use in manufacturing *PanC-Dx* and also a distribution agreement allowing us to market USCN's assay kit products for the research market.

*Progress in building upon our intellectual property base*

- We announced the issuance of United States patent number 7,928,069 covering certain aspects of the composition of *HyStem*<sup>®</sup> hydrogels and patent number 7,981,871, titled "Modified Macromolecules and Associated Methods of Synthesis and Use", covering additional aspects of the composition of *HyStem*<sup>®</sup> hydrogels. The patents and related patent family members, held by the University of Utah, are licensed to BioTime and its subsidiaries for the manufacture of research products and for therapeutic uses when combined with human cells. These patents are of significant strategic value to BioTime and its family of disease-focused subsidiaries.
- In January 2012, we announced that we had obtained an exclusive license from The Wistar Institute in Philadelphia, PA for technology related to a gene designated as *SP100*. Wistar Institute researchers have demonstrated pivotal roles for this gene in both cancer and stem cell biology. Scientists at BioTime's subsidiaries OncoCyte Corporation and ReCyte Therapeutics, Inc. plan to apply the discovery in their product development.
- BioTime entered into an exclusive license agreement with Cornell University for the worldwide development and commercialization of technology developed at Weill Cornell Medical College for the differentiation of human embryonic stem cells into vascular endothelial cells. This technology is being used by our subsidiaries OncoCyte Corporation and ReCyte Therapeutics, Inc.

*Expanded research product offerings*

- In May 2012, LifeMap Sciences, Inc. completed the acquisition of XenneX, Inc. As a result, LifeMap Sciences now holds the exclusive, worldwide licenses from Yeda Research and Development Company Ltd. (Yeda), the technology transfer arm of the Weizmann Institute of Science, to market the online databases *GeneCards*<sup>®</sup> and *PanDaTox*.
- LifeMap Sciences, Inc. also entered into a license agreement with Yeda to market a new database called *MalaCards*, a database of human diseases that is based on the *GeneCards*<sup>®</sup> platform. The *GeneCards*<sup>®</sup> and *MalaCards* databases will be available as part of an integrated database suite with LifeMap Sciences' own *LifeMap* stem cell database.
- We have elected to market progenitors of muscle stem cells bearing hereditary diseases. BioTime will produce the products from five human embryonic stem cell lines acquired from Reproductive Genetics Institute. The muscle cell lines display the genes for Duchenne muscular dystrophy, Emery-Dreifuss muscular dystrophy, spinal muscular atrophy Type I,

facioscapulohumeral muscular dystrophy 1A, and Becker muscular dystrophy. When developed, the progenitor cell lines will be marketed to researchers seeking new treatment modalities for these diseases.

*Advanced R&D collaborations*

- In conjunction with our license agreement with The Wistar Institute, BioTime agreed to fund research at the Institute to advance *SP100* gene-related technology, and will have certain rights to negotiate additional licenses for any technologies invented as a result of the research.
- We similarly entered into a sponsored research agreement with Weill Cornell Medical College for collaborative research on the differentiation of human embryonic stem cells into vascular endothelial cells. The technology may provide an improved means of generating vascular endothelial cells on an industrial scale, and may be utilized by BioTime and its subsidiaries in a diverse array of products, including products under development at ReCyte Therapeutics, Inc. to treat age-related vascular disease, as well as products being developed at OncoCyte Corporation targeting the delivery of toxic payloads to the developing blood vessels of tumors.

*Expanded and strengthened management team and Board of Directors*

- Andrew C. von Eschenbach, M.D. has joined the Boards of Directors of BioTime and OncoCyte Corporation. Dr. von Eschenbach is the President of Samaritan Health Initiatives, Inc., a health care policy consultancy, and is an Adjunct Professor at University of Texas MD Anderson Cancer Center. Dr. von Eschenbach served as Commissioner of the Food and Drug Administration from September 2005 to January 2009, after serving as Director of the National Cancer Institute at the National Institutes of Health.
- In October 2011, we appointed Peter S. Garcia as BioTime's Chief Financial Officer. Mr. Garcia served as Chief Financial Officer of six biotech and high-tech companies over the past 16 years, and was instrumental in leading multiple merger and acquisition transactions for those companies.
- This year, our Board of Directors formed a three-member Science and Technology Committee, chaired by Dr. von Eschenbach, to oversee the development and commercialization of BioTime's technology and products in regenerative medicine and oncology.

*Key research publications and presentations*

- BioTime and its subsidiaries presented updates on their operations, objectives, recent developments, and strategies at a BioTime-sponsored Investor Day in New York City on April 23, 2012. Presentations as well as videos of the event, including presentations by Dr. West and the principals of the Company's subsidiaries, are available for viewing on BioTime's website at [www.biotimeinc.com](http://www.biotimeinc.com).



- We published in the peer-reviewed journal *Stem Cell Research* the complete genome sequence analysis of five clinical-grade human embryonic stem cell lines. Evaluating the genomic and sequence integrity of human ES cell lines: comparison to normal genomes is the first such analysis of the entire genome of human embryonic stem cell lines and further establishes BioTime's lead in developing fully characterized cell lines intended for use in the manufacture of therapeutics.
- We published in the peer-reviewed journal *Regenerative Medicine* a paper detailing a study which characterized a progenitor cell line produced from hES cells using proprietary *ACTCellerate* technology and demonstrated a scalable source of highly purified and identified progenitor cells capable of making definitive (non-hypertrophic) cartilage. The report notes that the cells are capable of regenerating cartilage with long sought-after markers indicating that the cells may be useful in the treatment of osteoarthritis, which currently afflicts over 26 million people in the United States. The study also revealed that these cells can be directly expanded on a scale needed for industrial manufacture, which will be necessary in order to make transplantable cells available in commercial quantities.
- We announced the publication of a scientific paper, Functional performance of human cardiosphere-derived cells delivered in an *in situ* polymerizable hyaluronan-gelatin hydrogel, in which we discuss the demonstrated effectiveness of *HyStem*<sup>®</sup>-C in the transplantation of human heart muscle-derived cells in an animal model of heart disease.
- We made presentations of our products, technologies, and business strategies at the following scientific and investor meetings: *7<sup>th</sup> Annual New York Stem Cell Summit*; *ROTH 24th Annual Growth Stock Conference*; *2012 Maxim Group Growth Conference*; *8th GTC Stem Cell Summit 2012*; *BioCentury Future Leaders in the Biotech Industry Conference*; and the *GTC 2011 5th Advances in Stem Cell Discovery & Development Conference*.

### ***Implementing our business strategy: strength in diversification***

We have grown to become an international organization that includes seven subsidiaries, each focused on a particular field or market area within regenerative medicine. In building these companies, our business strategy has been to utilize a broad technology platform to create the greatest possible value for our shareholders. Four of these companies have already raised outside capital, although BioTime remains the majority owner of all seven. Each company is developing its business in various ways, including activities such as hiring key personnel, conducting preclinical research, developing products, and establishing important customer relationships. These efforts are intended, over time, to lead each subsidiary to become self-sustaining. For BioTime, the result should be substantial value creation through our ownership of equity in each company. Recent videos of presentations from the principals of these subsidiaries are available online at [www.biotimeinc.com](http://www.biotimeinc.com).

***Increasing shareholder value***

In summary, we believe that by accumulating some of the most advanced manufacturing technologies for developing products from hES and iPS cells, combined with strategic near-term revenue-generating products, we have the opportunity to establish BioTime as the leader in the emerging field of regenerative medicine. Our future success will now depend on our skills in executing this strategic plan. Key milestones for the next 12 months include the completion of the *Renevia* clinical trial; the filing by our subsidiary CellCure Neurosciences, Ltd. of an investigational new drug (IND) application for *OpRegen* to treat dry age-related macular degeneration of the retina; and the initiation of OncoCyte Corporation's *PanC-Dx* patient study. We will also be actively seeking to acquire new technologies and expand our corporate partnerships and collaborations. We also anticipate growing revenues from the sales of research products through the LifeMap Sciences integrated database suite.

We would like to thank you and all of our fellow shareholders for your support as we continue our work to turn the vast potential of regenerative medicine into a source of new medical products to improve the length and quality of life of millions of people around the world. We welcome you to join us again in New York City on June 26, 2012 for our Annual Meeting of Shareholders and look forward to meeting all who are able to attend.

Sincerely,

Michael D. West, Ph.D.  
President & CEO

Alfred D. Kingsley  
Chairman of the Board

*May 18, 2012*

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