PLURISTEM THERAPEUTICS INC
Form 10-K
September 12, 2011

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

FORM 10-K

(Mark One)

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

For the fiscal year ended June 30, 2011

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 001-31392

PLURISTEM THERAPEUTICS INC.
(Name of registrant as specified in its charter)

Nevada	98-0351734
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
MATAM Advanced Technology Park, Building No. 20, Haifa, Israel	31905
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number 011-972-74-7107171

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

Title of each class	Name of each exchange on which registered
Common Stock, par value $0.00001	Nasdaq Capital Market

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

None.
(Title of class)

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 during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files).

Yes o 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. x

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer or a non-accelerated filer. See definition of "accelerated filer and large accelerated filer" 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 x

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act).

Yes o No x

State the aggregate market value of the voting and non-voting common equity held by non-affiliates computed by reference to the price at which the common equity was last sold, or the average bid and asked prices of such common equity, as of the last business day of the registrant's most recently completed second fiscal quarter.

$34,558,487

Indicate the number of shares outstanding of each of the registrant's classes of common stock, as of the latest practicable date.

42,924,219 as of September 1, 2011

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Our financial statements are stated in thousands United States Dollars (US$) and are prepared in accordance with United States Generally Accepted Accounting Principles (U.S. GAAP).

In this annual report, unless otherwise specified, all dollar amounts are expressed in United States dollars.

As used in this annual report, the terms "we", "us", "our", "the Company", and "Pluristem" mean Pluristem Therapeutics Inc. and our wholly owned subsidiary, unless otherwise indicated.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

The statements contained in this Annual Report on Form 10-K that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. Such forward-looking statements may be identified by, among other things, the use of forward-looking terminology such as "believes," "intends," "plans" "expects," "may," "will," "should," or "anticipates" or the negative thereof or other variations thereon or comparable terminology, and similar expressions are intended to identify forward-looking statements. We remind readers that forward-looking statements are merely predictions and therefore inherently subject to uncertainties and other factors and involve known and unknown risks that could cause the actual results, performance, levels of activity, or our achievements, or industry results, to be materially different from any future results, performance, levels of activity, or our achievements, or industry results, expressed or implied by such forward-looking statements. Such forward-looking statements appear in Item 1 – "Business" and Item 7 – "Management's Discuss and Analysis of Financial Condition and Results of Operations," as well as elsewhere in this Annual Report and include, among other statements, statements regarding the following: the expected development and potential benefits from our products in treating various medical conditions, the exclusive license agreement we entered into with United Therapeutics Corporation, the prospects of entering into additional license agreements, or other forms of cooperation with other companies, our pre clinical and clinical trials plan, including entering Phase II clinical trials and achieving regulatory approvals, our plan to build a manufacturing facility and expand our manufacturing capacity, developing capabilities for new clinical indications of placenta expanded cells (PLX), the potential market demand for our products, our expectations regarding our short- and long-term capital requirements, our outlook for the coming months and information with respect to any other plans and strategies for our business.

The factors discussed herein, including those risks described in Item 1A. "Risk Factors", and expressed from time to time in our filings with the Securities and Exchange Commission could cause actual results and developments to be materially different from those expressed in or implied by such statements. The forward-looking statements are made only as of the date of this filing, and except as required by law we undertake no obligation to publicly update such forward-looking statements to reflect subsequent events or circumstances.

PART I

Item 1. Business.

Our Current Business

We are a leading bio-therapeutic company developing standardized cell therapy products for the treatment of life threatening diseases. We are developing a pipeline of products, stored ready-to-use, derived from human placenta, a non-controversial, non-embryonic, adult cell source. Placental-derived adherent stromal cells are grown in the Company's proprietary PluriX™ three-dimensional process that allows cells to grow in a more natural environment and enable us to produce large quantities of clinical grade cells. We refer to the cells that are grown in the PluriX™ as our PLacental eXpanded cells, or PLX cells. We are expanding our in-house manufacturing capacity so that we will be able to grow large scale quantities of our cells efficiently and without reliance on outside vendors.

We were incorporated as a Nevada corporation in 2001. We have a wholly owned research and development subsidiary in Israel called Pluristem Ltd.

Our strategy is to develop and manufacture cell therapy products for the treatment of multiple disorders via several routes of administration. We plan to execute this strategy both independently, using our own personnel and via relationships with research and clinical institutions, or in collaboration with other companies, such as United Therapeutics Corporation, or United. We plan to have in-house manufacturing capacity of clinical grade PLX cells in commercial quantities and to control all of our proprietary manufacturing processes in order to assist in executing this strategy.

We believe that intramuscular administration, or IM, which means that the cells are administrated locally to the muscle and not systemically, may be suited for a number of different clinical indications. Such indications include peripheral artery disease, or PAD, critical limb ischemia, or CLI, intermittent claudication, or IC, muscle injuries, thromboangiitis obliterans, or Buerger's disease, neuropathic pain, wound healing and orthopedic injuries. In addition, we have reported pre-clinical studies utilizing successfully our proprietary PLX cells when administered systemically via the intravenous route, or IV, in treating multiple sclerosis, ischemic stroke, inflammatory bowel disease and radiation exposure. Under our exclusive license agreement with United, we plan to participate in the development and commercialization of a PLX cell-based product for the treatment of Pulmonary Arterial Hypertension, or PAH.

Our first product in development, called PLX-PAD, is intended to improve the quality of life of millions of people suffering from PAD.

Recent Developments

In January 2011, we successfully completed a parallel scientific advisory process with the European Medicines Agencies (EMA) and the US Food and Drug Administration (FDA) that will allow us to pursue a comprehensive approach towards the treatment of two major components of PAD, IC and CLI, with our placenta-derived PLX cells. The comprehensive clinical plan includes a multinational Phase II study in IC and a multinational Phase II/III pivotal study in CLI.

In February 2011, we closed a firm commitment underwritten public offering of 11,000,000 units, with each unit consisting of one share of the Company's common stock and one warrant to purchase 0.4 of a share of common stock, at a purchase price of $3.25 per unit. The underwriters exercised in full their over-allotment option to purchase an additional 1,650,000 units. The net proceeds from the offering were approximately $38 million.

On March 1, 2011, together with the Charite University Hospital of Berlin, or Charite, we announced the results of a preclinical study demonstrating significant improvement in the recovery of muscle function, when compared to controls, following the local administration of PLX cells in a muscle injury mice model. This study suggests that our PLX cells have the potential to treat muscle injuries caused by surgery or accident. Subject to regulatory approval, we intend to conduct clinical trials for muscle injury indications.

On April 13, 2011, following completion of three and six month clinical follow-ups using our PLX cells in CLI, the end-stage of PAD, we announced that the data collected from our two open-label, dose-escalation, Phase I clinical trials conducted in the United States and Germany suggests that PLX-PAD is safe, improves quality of life, and is potentially effective in treating patients and reducing amputations.

On June 19, 2011, we entered into an exclusive license agreement, or the License Agreement, with United, for the use of our PLX cells to develop and commercialize a cell-based product for the treatment of PAH. The License Agreement provides that United will receive exclusive worldwide license rights for the development and commercialization of our PLX cell-based product to treat PAH. The License Agreement provides for the following consideration payable to us: (i) $7 million paid to us in August 2011; (ii) up to $37.5 million upon reaching certain regulatory milestones with respect to the development of a product to treat PAH; (iii) reimbursement of up to $10 million of certain of our expenses if we establish a manufacturing facility in North America upon meeting certain milestones; (iv) reimbursement of certain costs in connection with the development of the product; and (v) following commercialization of the product, royalties and the purchase of commercial supplies of the developed product from us at a specified margin over our cost.

On August 22, 2011 the FDA granted our PLX cells orphan status designation for the treatment of Buerger's disease. A concurrent application in Europe at the EMA’s Committee for Orphan Medicinal Products is pending.

Scientific Background

Cell therapy is an emerging and promising field within the regenerative medicine area. The characteristics and properties of cells vary as a function of tissue source and growth conditions. The human placenta provides a unique, renewable, uncontroversial source of non-embryonic, adult cells and represents a new approach in the cell therapy field.

The use of our PLX cells for human therapy does not require tissue matching prior to administration. Thus, it allows for the development of a ready-to-use “off-the-shelf” product.

Our Technology

We develop and intend to commercialize cell therapy production technologies and products. We are expanding non-controversial, placental-derived Adherent Stromal Cells, or ASCs, via a proprietary three dimensional (3D) process, termed PluriX™, into therapeutics for a variety of degenerative, ischemic, inflammatory and autoimmune disorders.

PluriX™ uses a system of stromal cell cultures and substrates to create an artificial three dimensional environment where placental-derived stromal cells (obtained after birth) can grow. Our three-dimensional process enables the large scale production of reproducible, high quality cell products, and is capable of manufacturing large numbers of PLX doses originating from different placentas. Additionally, our manufacturing process has demonstrated batch-to-batch consistency, an important manufacturing component of biological products.

Product Candidates

- PLX-PAD - Intermittent Claudication and Critical Limb Ischemia

We are developing PLX-PAD cells as an allogeneic therapeutic product to treat CLI and IC which results from PAD. PLX-PAD cells are stored “ready to use” and can be shipped to hospitals and clinics for use as IM treatment to the affected limb in clinical trials for patients suffering from CLI and IC. Two Phase I studies were performed to evaluate

the safety of PLX-PAD in patients with CLI. The studies were conducted in parallel in Germany and the U.S. The trial in Germany was performed at the Franziskus-Krankenhaus Institute of Berlin and a total of 15 patients were enrolled in this study. The trial in the US was performed at three sites: Duke University Hospital, Stanford University Hospital and the Center for Therapeutic Angiogenesis (supported by the University of Alabama). A total of 12 adults with the disease were included in this clinical trial in the U.S.

On April 13, 2011, we announced that following completion of three and six month clinical follow-ups, data from our two open-label, dose-escalation, Phase I clinical trials suggests that PLX-PAD is safe, improves quality of life, and is potentially effective in treating patients and reducing amputations in those suffering from CLI, the end-stage of PAD. Among the 27 patients treated with PLX-PAD, only one amputation was recorded at the six month follow-ups representing a 3.7% amputation rate. This represents a 75% reduction in the amputation rate compared to historical data, which varies from 20-25%.

Intermittent Claudication and Critical Limb Ischemia

PAD arises when there is significant narrowing of large arteries supplying blood to all of the extremities but most commonly the legs. Narrowing of these arteries is usually caused by cholesterol build-up in the artery (atherosclerosis) but can occur from an inflammation of the arterial wall (arteritis). Patients afflicted with PAD have symptoms that range from calf pain on exercise (IC) to resting pain, skin ulceration, or gangrene in people with CLI. About 15% of people with IC eventually develop CLI1, particularly if they are afflicted with risk factors associated with the development and worsening of PAD and include cigarette smoking, diabetes, hypertension and obesity.

Analysis of data from the 2009 update on heart disease and stroke statistics2 indicates that approximately eight million people over the age of 40 in the United States are afflicted with PAD. PAD increases significantly with age, rising to as high as approximately 20% of the population of those over the age of 70, which has resulted in a growing market for therapies intended to treat this disorder. According to The Sage Group Report of April 17, 2007 an estimated 2 million people in the U.S. have CLI. Reflecting the ageing population, this number is projected to grow to almost 2.8 million by 20203. However, if the prevalence of diabetes continues to increase, there could be a significant increase of CLI by 2020.

Although medications such as vasodilators and anti-platelet therapies are used for treating PAD, the general consensus among physicians is that there currently exists no adequate medical therapy for PAD. Endovascular therapies such as balloon dilation and revascularization surgery can be quite helpful for selected patients. However, it has been estimated that approximately 25% of CLI patients are not suitable for such procedures4.

- Other product candidates

There have been favorable preclinical results administering PLX cells in several additional indications.

The table below summaries the status of the studies we have performed:

Indication	Status
Diabetic Foot Ulcers	Proof of concept
Adjuvant Hip Replacement Surgery	Pre-clinical
Athletic Injuries	Pre-clinical
Inflammatory Bowel Disease	Proof of concept
Multiple Sclerosis	Proof of concept
Neuropathic Pain	Pre-clinical
Ischemic Stroke	Pre-clinical
Adjuvant for UCB Transplantation	Pre-clinical
Radiation exposure	Proof of concept

1 See Intermittent claudication: a risk profile from the Framingham Heart Study. Circulation 1997;96:44–49.
2 See Circulation. 2009;119:e21-e181. Published online before print December 15, 2008.

3 See The Sage Group: The Sage Group Report of April 17, 2007 (http://thesagegroup.us/pages/news/april17_2007.php).
4 See Histological changes after implantation of autologous bone marrow mononuclear cells for chronic critical limb ischemia. Bone Marrow Transplant. 2007 May; 39(10):647-8.

In addition, we plan to commence the development of a cell-based product for the treatment of PAH using our PLX, as provided for by the Licensing Agreement.

Intellectual Property

We understand that our success will depend, in part, on maintaining our intellectual property and therefore we are committed to protecting our technology and product candidates with patents and other methods described below.

We are the sole owner of 15 issued patents and 76 patent applications in the U.S. and Europe as well as in additional countries worldwide, including in the Far East and South America.

Based on the well established understanding support that the characteristics and therapeutic potential of a cell product are largely determined by the source of the cells and by the methods and conditions used during their manufacturing process, our patent portfolio includes multilayered claims on the various unique aspects of ASCs.
Our patent portfolio includes claims on:

- Our propriety expansion method for 3D Stromal Cells;
- Composition of matter claims on the cells;
- The therapeutic use of PLX cells for the treatment of a large variety of medical conditions; and
- Selection criteria for determination of cells suitable for administration.

Through our experience with ASC-based product development, we have developed expertise and know-how in this field and have established the ability to manufacture clinical grade PLX cells in-house. Certain aspects of our manufacturing process are covered by patents and patent applications. In addition, specific aspects of our technology are kept as know-how and trade secrets, protected by Pluristem's confidentiality agreements with our employees, consultants, contractors, manufacturers and advisors. These agreements generally provide for protection of confidential information, restrictions on the use of materials and assignment of inventions conceived during the course of performance of services for us.

Except with respect to the License Agreement with United, the intellectual property we own is not subject to third party rights. In addition, we have no obligations to pay royalties to any third party, except for royalties, to the OCS which are limited to repayment the grant amount received plus interest (see note 6D in our audited consolidated financial statements for fiscal 2011 included elsewhere in this Form 10-K).

The intellectual property coverage of our technology and biologic drug candidates is multi-layered and relies on the combination of multiple patents. The following table provides a description of our key patents and patent applications and is not intended to represent an assessment of claims, limitations or scope. There is a risk that our patents will be invalidated, and that our pending patent applications will not result in issued patents or that we can be certain that we will not infringe any patents that may be issued to others. See "Risk Factors - We must further protect and develop our technology and products in order to become a profitable company". The expiration dates of these patents, based on filing dates, range from 2019 to 2026. Actual expiration dates will be determined according to extensions received based on the Hatch-Waxman Act. We believe that even upon expiration of certain of our patents we will continue to be in a good competitive position with our competitors due to several layers of patents and trade secrets.

Pluristem's Patent Portfolio

Patent	Jurisdiction	Subject Matter	Related Product(s)
Method And Apparatus For Maintenance And Expansion Of Hemopoietic Stem Cells And/Or Progenitor Cells	United States Japan, Europe, Mexico, Australia, South Africa, Israel, Russia, New Zealand, India, China, Hong Kong, Canada	Process and methods	PLX
Methods for Cell Expansion and Uses of Cells and Conditioned Media Produced Thereby for Therapy	United States Japan, Europe, Mexico, Australia, South Africa, Israel, Russia, New Zealand, India, China, Hong Kong, Canada, Brazil, Korea, Singapore	Process and methods, Composition of matter, Method of treating	PLX
Adherent Cells from Adipose or Placenta Tissues and Use Thereof in Therapy	United States Japan, Europe, Mexico, Australia, South Africa, Israel, Russia, New Zealand, India, China, Hong Kong, Canada, Brazil, Korea, Singapore	Composition of matter, Method of treating	PLX

Research and Development

Our research and development expenses were $8,311,000 and $6,123,000 in fiscal year 2011 and 2010 respectively, before deducting the participation by the Office of the Chief Scientist and grants by other third parties.

Foundational Research. Our initial technology, the PluriX™ Bioreactor system, was developed in the Technion - Israel Institute of Technology's Rappaport Faculty of Medicine, in collaboration with researchers from the Weizmann Institute of Science. This technology was further developed by our research and development teams.

Ongoing Research and Development Plans

In July 2007, we entered into a five year collaborative research agreement with the Center for Regenerative Therapies at Charite. Pluristem and Charite are collaborating on a variety of indications utilizing PLX cells. According to the agreement, we will be the exclusive owner of the technology and any products produced as a result of the collaboration. We are currently conducting several pre-clinical trials in collaboration with Charite.

Over the last year we have also engaged into research and development projects with NYU Medical Center for the study of PLX cells in the treatment of diabetic foot ulcers and with Hadassah University Medical Center in Jerusalem to continue a previously conducted animal study indicating that PLX cells are potentially effective in the treatment of radiation sickness.

On June 19, 2011, we entered into the License Agreement, for the use of our PLX cells to develop and commercialize a cell-based product for the treatment of PAH. The License Agreement provides that United will receive exclusive worldwide license rights for the development and commercialization of our PLX cell-based product to treat PAH. The License Agreement provides for the following consideration payable to us: (i) $7 million paid to us in August 2011; (ii) up to $37.5 million upon reaching certain regulatory milestones with respect to the development of a product to treat PAH; (iii) reimbursement of up to $10 million of certain of our expenses if we establish a manufacturing facility in North America upon meeting certain milestones; (iv) reimbursement of certain costs in connection with the development of the product; and (v) following commercialization of the product, royalties and the purchase of commercial supplies of the developed product from us at a specified margin over our cost.

We plan to continue to collaborate with universities and academic institutions and corporate partners worldwide to fully leverage our expertise and explore the use of our cells in other indications.

Our research and development facilities are in Haifa, Israel.

In-House Clinical Manufacturing Ability

We have the in-house capability to conduct clinical cell manufacturing. The facility has been approved as a Good Manufacturing Practices (GMP) standard site for the purpose of manufacturing PLX cells by an inspector from the EMA. In addition, the FDA approved the design of our clean room.

In July 2011, we entered into an agreement with MTM – Scientific Industries Center Haifa Ltd., for the lease and construction of a new state-of-the-art GMP manufacturing facility. The new facility will be located near our headquarters and existing facilities in MATAM Park, Haifa, Israel. The lease of the new facility is expected to commence in January 2012 for a period of approximately five years with an option to extend the lease for an additional 5 years.

The new facility is expected to be cGMP/GTP compliant for clinical cell manufacturing and designed specifically to meet both EMA and FDA regulatory requirements as well as the standards outlined by the Israeli Ministry of Health. The facility is expected to have the capacity to produce PLX cells to meet our needs for the foreseeable future. As we widen our clinical product candidate portfolio and prepare to launch large-scale clinical trials in the U.S. and Europe, the new facility will enable us to meet increased in-house manufacturing capacity requirements and meet marketing demands upon product approval.

We receive the human placentas used for our research and manufacturing activities from various hospitals in Israel. Any medical waste related to the use of placentas is treated in compliance with local environmental laws and standards.

Government Regulation

The development, manufacturing, and marketing of our cell therapy product candidates are subject to the laws and regulations of governmental authorities in the U.S. and the European Union as well as other countries in which our products will be marketed in the future. Specifically, in the U.S., the FDA and in Europe, the EMA, regulate new product approvals to establish the safety and efficacy of these products among other activities. Furthermore, various governmental statutes and regulations also govern or influence testing, manufacturing, safety, labeling, storage and record keeping related to such products and their marketing. Governments in other countries have similar requirements for testing and marketing.

The process of obtaining these approvals and the subsequent compliance with appropriate statutes and regulations require the expenditure of substantial time and money. This process takes a number of years and the expenditure of significant resources. There can be no assurance that our product candidates will ultimately receive regulatory approval.

Regulatory Process in the United States

Our product candidates are subject to regulation as biological products under the Public Health Service Act and the Food, Drug and Cosmetic Act. The FDA generally requires the following steps for pre-market approval or licensure of a new biological product:

- Pre-clinical laboratory and animal tests conducted in compliance with the Good Laboratory Practice, or GLP, requirements to assess a drug's biological activity and to identify potential safety problems, and to characterize and document the product's chemistry, manufacturing controls, formulation, and stability.

- Submission to the FDA of an Investigational New Drug, or IND application, which must become effective before clinical testing in humans can begin;

- Obtaining approval of Institutional Review Boards, or IRBs, of research institutions or other clinical sites to introduce the biologic drug candidate into humans in clinical trials;

- Conducting adequate and well-controlled human clinical trials to establish the safety and efficacy of the product for its intended indication conducted in compliance with Good Clinical Practice, or GCP, requirements;

- Compliance with current Good Manufacturing Practices, or cGMP regulations and standards;

- Submission to the FDA of a Biologics License Application, or BLA, for marketing that includes adequate results of pre-clinical testing and clinical trials;

- FDA reviews the marketing application in order to determine, among other things, whether the product is safe, effective and potent for its intended uses; and

- Obtaining FDA approval of the BLA, including inspection and approval of the product manufacturing facility as compliant with cGMP requirements, prior to any commercial sale or shipment of the pharmaceutical agent. The FDA may also require post-marketing testing and surveillance of approved products, or place other conditions on the approvals.

Regulatory Process in Europe

The European Union (EU) has approved a regulation specific to cell and tissue products and our PLX-PAD cell therapy product candidate is regulated under this Advanced Therapy Medicinal Product (ATMP) regulation.

For products that are regulated as an ATMP, the EU Directive requires:

- Compliance with current Good Manufacturing Practices, or cGMP regulations and standards, pre-clinical laboratory and animal testing;

- Filing a Clinical Trial Application (CTA) with the various member states or a centralized procedure; Voluntary Harmonisation Procedure (VHP), a procedure which makes it possible to obtain a coordinated assessment of an application for a clinical trial that is to take place in several European countries. Obtaining approval of affiliated Ethic Committees of research institutions or other clinical sites to introduce the biologic drug candidate into humans in clinical trials;

- Adequate and well-controlled clinical trials to establish the safety and efficacy of the product for its intended use; and