PLURISTEM THERAPEUTICS INC
Form 10-K
September 07, 2016

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

FORM 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended June 30, 2016

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.
(Exact 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. 5, Haifa, Israel	31905
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number 011-972-74-7108607

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 No

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 No

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 No

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

Yes No

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.

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 Accelerated filer Non-accelerated filer
Smaller reporting company

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

Yes No

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.

$84,296,685

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

80,723,647 as of August 31, 2016

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

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

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

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

The statements contained in this Annual Report on Form 10-K, or Annual Report, 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 discussion and Analysis of Financial Condition and Results of Operations," (especially in the section titled "Outlook") 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 agreements we entered into with CHA Biotech Co. Ltd., or CHA, and clinical trials to be conducted according to such agreement;
- the prospects of entering into additional license agreements, or other forms of cooperation with other companies and medical institutions;
- the Memorandum of Understanding we entered into with Fukushima Medical University, Fukushima Global Medical Science Center and the potential for the development of our PLX-R18 cells for the treatment of ARS, and for morbidities following radiotherapy in cancer patients;
- our belief that PLX-PAD may be effective in treating critical limb ischemia and femoral neck fracture;
- our belief that PLX R18 may be effective in treating Acute Radiation Syndrome (ARS);our belief that we may obtain orphan drug status for some of our products;
- the potential for the accelerated approvals of some of our products with the European Medicines Agency and Japan’s Pharmaceuticals and Medical Devices Agency;
- the prospects of having in-house production capacity to grow clinical-grade PLX cells in commercial quantities;
- our pre-clinical and clinical trials plans, including timing of conclusion of trials;
- our belief that placenta expanded, or PLX, cells may be effective in supporting bone marrow transplantation and in treating bone marrow suppression from radiation and chemotherapy;

- achieving regulatory approvals, including under accelerated paths;
- our marketing plans, including timing of marketing our first product, PLX-PAD;
- developing capabilities for new clinical indications of PLX and new products;
- our expectation to compete based upon our intellectual property portfolio, our in-house manufacturing efficiencies and the efficacy of our products;
- the potential market demand for our products;
- our expectation that in the upcoming years our research and development expenses, net, will continue to be our major operating expense;
- our expectations regarding our short- and long-term capital requirements;
- our outlook for the coming months and future periods, including but not limited to our expectations regarding future revenue and expenses; 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, or SEC, could cause actual results and developments to be materially different from those expressed in or implied by such statements. In addition, historic results of scientific research, clinical and preclinical trials do not guarantee that the conclusions of future research or trials would not suggest different conclusions. Also, historic results referred to in this Annual Report would be interpreted differently in light of additional research, clinical and preclinical trials results. 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

Pluristem Therapeutics Inc. is a leading developer of placenta-based cell therapy product candidates for the treatment of multiple ischemic, inflammatory and hematologic conditions. Our lead indications are critical limb ischemia, recovery after surgery for femoral neck fracture, and acute radiation syndrome. Pivotal, multinational clinical trials are planned for our PLX-PAD product in critical limb ischemia and femoral neck fracture, and the National Institutes of Health’s, or NIH, National Institute of Allergy and Infectious Diseases, or NIAID, is currently conducting a dose selection trial with PLX-R18 in the hematologic component of acute radiation syndrome. Each of these indications is a severe unmet medical need. Together, these treatments could address a multibillion dollar global market.

PLX cells are derived from a class of placental cells that are harvested from donated placentas at the time of full term delivery of a live baby. PLX cell products require no tissue matching prior to administration. They are produced using our proprietary three-dimensional expansion technology. Our manufacturing facility complies with current Good Manufacturing Practice requirements and has been approved by the U.S. Food and Drug Administration, or FDA, and the European, Japanese and Israeli regulatory authorities for production of PLX-PAD for late stage trials and marketing. We expect to have in-house production capacity to grow clinical-grade PLX cells in commercial quantities.

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We were incorporated in Nevada in 2001, and have a wholly owned subsidiary in Israel called Pluristem Ltd., or the Subsidiary. We operate in one segment and our operations are focused on the research, development, clinical trials and manufacturing of cell therapeutics and related technologies.

Our goal is to make significant progress with our robust clinical pipeline and our anticipated pivotal trials in order to ultimately bring innovative, potent therapies to patients who need new treatment options. We intend to shorten the time to commercialization of our first product, PLX-PAD, by leveraging the unique accelerated regulatory pathways that exist in Europe and Japan to bring innovative products to the market efficiently, in order to address life-threatening diseases. We believe that these accelerated pathways create substantial opportunities for us and for the cell therapy industry as a whole. We are pursuing these accelerated pathways for PLX-PAD in critical limb ischemia and femoral neck fracture. Our second product, PLX R18, is under development in the United States for ARS via the animal rule regulatory pathway, which requires no human efficacy trials for approval. We expect to demonstrate the real-world impact and value of our pipeline, technology platform, and commercial-scale manufacturing capacity.

In May 2015, we announced that the PLX-PAD cell program in CLI had been selected for the Adaptive Pathways pilot project of the European Medicines Agency (EMA). In addition, we reached an agreement with Japan's Pharmaceuticals and Medical Devices Agency (PMDA) on the design of the final trial needed to apply for conditional approval of PLX-PAD cells in the treatment of CLI. The approval of the protocol for the 75-patient trial was part of a larger agreement on the development of PLX-PAD via Japan's new accelerated regulatory pathway for regenerative medicine. In August 2016, we received a positive FDA response to our pivotal Phase III protocol for PLX-PAD in CLI. Our intention is to initiate these CLI studies in early 2017, and obtain initial approval in the coming two to three years.

In July 2016, we announced our intent to conduct a Phase III trial assessing our PLX-PAD cells in recovery following surgery for femoral neck fracture in the United States and Europe. In addition, the EMA confirmed that this indication would also be eligible for the Adaptive Pathways project.

In February 2016, we announced that the NIAID, a part of the NIH, will initiate studies in large animals to select the appropriate doses for PLX-R18 as a medical counter measure in the treatment of the hematologic component of Acute Radiation Syndrome, or ARS. These studies have been initiated. Once the optimal dose is determined in large animals, a pivotal trial could be conducted, the results of which may be used to support a Biologics License Application for PLX-R18 for this indication under the Animal Rule regulatory pathway. The NIAID supports and collaborates on the dosing studies, and Pluristem supplies the PLX-R18 cells. In December 2015, we also signed a Memorandum of Understanding for a collaboration with Fukushima Medical University, Fukushima Global Medical Science Center. The purpose of the collaboration is to develop our PLX-R18 cells for the treatment of ARS, and for morbidities following radiotherapy in cancer patients.

We made progress in our Phase II intermittent claudication (IC) trial, a randomized, double blind, placebo controlled, multinational clinical study. We have enrolled 160 patients to date and have expanded the clinical trial to include a total of 170 patients, with enrollment completion expected in 2016. We currently have active clinical sites in the United States, Israel, Germany, and South Korea.

The FDA cleared our Investigational New Drug application to begin a Phase I trial of PLX-R18 cells to treat incomplete hematopoietic recovery following HCT. We plan to initiate the clinical trial in the United States in calendar 2016.

In December 2015, the FDA granted our PLX-PAD cells Orphan Drug Designation in the treatment of severe preeclampsia. We are currently conducting additional pre-clinical studies in order to advance towards a Phase I trial.

On December 8, 2015, we received a notice from United Therapeutics Corporation, or United, terminating our exclusive license agreement, or the United Agreement. Pursuant to the United Agreement termination clause, we

regained full rights to PLX in the field of Pulmonary Arterial Hypertension, or PAH, as well as all clinical data and regulatory submissions. We may continue the development of this indication subject to interest of potential licensing partners in the U.S. and Japan.

Scientific Background

Cell therapy is an emerging 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 from which our PLX cells are derived provides an uncontroversial source of non-embryonic, adult cells and represents an innovative approach in the cell therapy field. The different factors that PLX cells release suggest that the cells can be used therapeutically for a variety of ischemic, inflammatory, autoimmune and hematological disorders.

PLX cells do not require tissue matching prior to administration. This allows for the development of ready-to-use / "off-the-shelf" allogeneic products.

Our Technology

We develop, and intend to commercialize, cell therapy production technologies and products that are derived from the human placenta. Our PLX cells are adherent stromal cells, or ASCs, that are expanded using a proprietary 3D process. This system utilizes a synthetic scaffold to create an artificial 3D environment where placental-derived stromal cells can grow. Our 3D process enables the large-scale monitored and controlled 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 challenge for biological products.

Product Candidates

Our primary objective is to be the leading provider of allogeneic cell therapy products that are true off-the-shelf products that do not require any matching or additional manipulation prior to administration. From the physician’s and patient’s perspective, our PLX products are comparable to any other product delivered in a vial. Our PLX products are administered using a standard needle and syringe. Our PLX products are in clinical stage development for multiple indications such as cardiovascular, orthopedic, pulmonary, and women’s health diseases.

Our business model for commercialization and revenue generation includes, but is not limited, to the following activities that we may conduct with both pharmaceutical and medical device companies: partnerships, licensing deals, and joint ventures. To date, we have a strategic partnership with CHA Biotech Co. Ltd., or CHA, in South Korea for both IC and CLI for the Korean market only. CHA is currently conducting PLX clinical studies in South Korea, and, following regulatory approval, if received, we contemplate forming a joint venture equally owned by us and CHA to market PLX products in South Korea.

The relationship with CHA is intended to leverage our expertise in manufacturing high quality, placenta-derived cells, using our proprietary, scalable, efficient 3D cell manufacturing platform that supports the cost-effective mass production of PLX cells. Our policy for this partnership is to retain control of the manufacturing of PLX cell products and their associated intellectual property.

We believe that using the placenta as a unique cell source, combined with our innovative research, development and high quality manufacturing capabilities, will be the "engine" that drives this platform technology towards the successful development of many PLX cell therapy products.

Our Clinical Development Product Candidates

Peripheral and Cardiovascular Diseases – We are investigating using PLX-PAD cells for treatments for various stages of peripheral arterial disease, from early stage IC to advanced CLI.

We have completed two Phase I safety/dose-finding clinical trials for CLI, one in the United States and one in Germany. These CLI trials demonstrated that no blood type or human leukocyte antigen matching is required, and that the administration of PLX-PAD cells is safe, even if two doses are administered to a patient from the same placental source on two different occasions. In addition, PLX-PAD cells are potentially effective in reducing the frequency of amputations in CLI patients. Generally, the FDA and the EMA require the primary endpoint for pivotal CLI clinical trials to be Amputation Free Survival, or AFS, at one year. The pooled data from the two studies we conducted suggest an AFS rate at one year of 86% in PLX-treated patients versus an AFS ranging between 48% to 81% in patients from placebo arms in other trials.

Following our promising Phase I trials in CLI, a large, international, Phase II, double-blind, randomized, placebo-controlled, 4-arm trial was initiated in the United States, Germany, Israel and South Korea to assess the safety and efficacy of PLX-PAD in patients suffering from IC. Similar to the Phase I studies in CLI, PLX-PAD cells are administered intramuscularly into the patient's affected leg. The primary efficacy endpoint for the study is the patient's maximal walking distance on a treadmill. The initial sample size was 150 and we expanded the IC trial to enroll an additional 20 patients to be randomized in order to preserve the study's original design to administer two injections to each of 150 patients. Twenty of the 150 patients originally enrolled did not complete the trial with two injections. Previous findings in clinical and preclinical studies of PLX cells demonstrated the superior efficacy of two injections vs. a single injection in certain indications.

In April 2015, Japan's PMDA approved the proposed quality and large-scale manufacturing methods for PLX-PAD cells for use in clinical trials. This approval is an important milestone for initiation of a Phase I/II study in CLI, and we plan to submit an application for conditional, time-limited approval for marketing of PLX-PAD cells for treatment of CLI through Japan's Accelerated Pathway for Regenerative Medicine. The new regulatory pathway could potentially significantly reduce time to market for cell therapies such as PLX-PAD cells. Two additional consultation meetings were held at the end of July 2015 to discuss with the PMDA the safety of PLX-PAD and the design of a proposed study in CLI patients to be conducted in Japan. In August 2015, the PMDA granted safety clearance to PLX-PAD cells for use in clinical trials. We received clearance for the clinical study and agreed with the PMDA on the terms for conditional marketing approval in December 2015. The next step consists of submitting a clinical trial notification to the PMDA to enable us to potentially start a Phase II study of PLX-PAD in CLI in late 2016.

Additionally, in May 2015, the PLX-PAD clinical development program was selected for the EMA's Adaptive Pathways pilot project and one of only 6 companies that successfully passed through the different stages of the project. The goal of the project is to improve timely access for patients to new medicines. It allows for early marketing authorization of a therapy in a restricted patient population, followed by additional assessments and the possibility of later approval for use in broader patient populations. Our first indication to be developed through this new regulatory approach is CLI. It is estimated that there are 500 to 1,000 new cases of CLI per a one million population per year in the United States and Europe, and the prevalence is expected to increase significantly in the coming decades due to an expected increase in diabetic patients and aging population. CLI therefore represents a major commercial opportunity. Acceptance of our cells for the treatment of CLI into the Adaptive Pathways could significantly curtail the time and investment needed to bring this product to market. Pluristem has conducted a parallel scientific advice with EMA and European health technology assessment bodies in March 2016, under the Adaptive Pathways project, in order to discuss the clinical development plan in CLI. In addition we have had a pre-IND interaction with FDA on the same protocol in July 2016. As an outcome of these interactions, we plan to conduct a Phase III study in CLI in 2017 in the United States and EU, subject to the clearance of our applications.

Orthopedic Diseases – A Phase I/II, randomized, double-blind, placebo controlled study to assess the safety and efficacy of intramuscular injections of allogeneic PLX PAD cells for the regeneration of injured gluteal musculature after total hip replacement has been conducted in Germany under the approval of the Paul Ehrlich Institute, or PEI. In this study, PLX-PAD cells or a placebo were injected into the traumatized gluteal muscle during total hip replacement surgery. In July 2013, we announced that enrollment for this clinical trial was completed. In January 2014, we announced that the study met its primary efficacy endpoint, namely the change in maximal voluntary isometric contraction force of the gluteal muscle at six months after total hip replacement. Patients treated with PLX-PAD had a significantly greater improvement of maximal voluntary muscle contraction force than the placebo group (p=0.0067). The one-year safety follow-up of all the patients was completed at the beginning of July 2014. The study was concluded with two year safety follow up in July 2015. At two years of follow-up no case of new cancer was reported.

In July 2016, we announced our intention to conduct a Phase III trial assessing our PLX-PAD cells in recovery following surgery for femoral neck fracture in the United States and Europe. In addition, the EMA confirmed that this indication would be eligible for the Adaptive Pathway regulatory approval. We are currently in discussions with respect to the FDA submission of the Phase III protocol. In addition, we submitted this protocol to the EMA following consultation with the Adaptive Pathways Project Group.

Recovery following Hematopoietic cell transplantation ("HCT") – Following positive data from the use of PLX-R18 cells in animals in stimulating hematopoiesis in injured bone marrow and following bone marrow transplantation, we intend to pursue the development of PLX-R18 in the treatment of recovery following HCT.

In March 2015, we reported positive data from three independent preclinical studies of PLX-R18. Results from these trials, as well as those from nineteen prior studies conducted by the NIAID , Case Western University, Cleveland, Ohio, and Hadassah Medical Center, Jerusalem, Israel, collectively suggest that PLX-R18 is safe and may significantly improve outcomes after bone marrow failure and/or support hematopoietic cell transplantation. Data collected on the mechanism of action show that PLX-R18 acts by enhancing production of platelets and white and red blood cells in cases of severely damaged bone marrow, and may also accelerate engraftment of transplanted hematopoietic cells. With these capabilities, PLX-R18 could potentially treat a broad range of indications related to bone marrow function which, taken together, constitute a substantial global market.

We met with FDA representatives to discuss the initiation of a Phase I first-in-human clinical study of PLX-R18 for the treatment of incomplete hematopoietic recovery following HCT. We received IND approval in January 2016. We anticipate initiating the Phase I trial in the United States in late 2016.

ARS – We have conducted several in-vivo studies for the evaluation of PLX-R18 for the treatment of ARS, in cooperation with the NIAID.

NIH continues to support us and a pilot study in large animals has been initiated to determine the most appropriate dose of PLX-R18 for recovery of patients with hematopoietic syndrome of ARS.

Regulatory and Clinical Affairs Strategy

Our cell therapy development strategy is to hold open and frequent discussions with regulators at all stages of development from preclinical trials to more advanced regulatory stages. We utilize this strategy in working with the FDA, the EMA, Japan’s PMDA, Germany’s PEI and the Israeli Minister of Health, or MOH, and we are also working with the Ministry of Food and Drug Safety, or MFDS, of South Korea authority via our collaborator CHA.

The Adaptive Pathways pilot project is part of the EMA’s efforts to improve timely access for patients to new therapies. It targets treatments with the potential to heal serious conditions with an unmet medical need, and may reduce the time to a medicine's approval or to its reimbursement for targeted patient groups. The pilot is open to clinical programs in early stages of development only. After a therapy is selected for the program, the Adaptive

Pathways Discussion Group provides detailed guidance to the applicant regarding the formal regulatory processes that precede a trial targeting early approval and further expansion of the indications.

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 76 issued patents and 135 patent applications in the United States, Europe, China and Japan, as well as in additional countries worldwide, including Israel, countries in the Far East and South America (in calculating the number of issued patents, each European patent validated in multiple jurisdictions was counted as a single patent). In April 2016, the Subsidiary entered into a licensing agreement with TES Holdings Co., Ltd., a venture company derived from the University of Tokyo, to obtain a key patent in Japan to cover the treatment of ischemic diseases with placental cell therapy. This license is subject to future single low-digit royalties from sales of our product for treatment in the field of ischemic diseases in Japan, until expiry of the patent in 2023. This license follows the grant of two key patents to us by the Japanese Patent Office, which address three dimensional methods for expanding placental and adipose cells, and specified cell therapies produced from placental tissue using these methods.

Based on the well-established understanding 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 culturing, our patent portfolio includes different types of claims that protect the various unique aspects of our technology.

Our multi-national portfolio of patent and patent applications includes the following claims:

·Our proprietary expansion methods for 3D stromal cells;
·Composition of matter claims covering the cells;
·The therapeutic use of PLX cells for the treatment of a variety of medical conditions; and
·Cell-culture, harvest, and thawing devices.

Through our experience with ASC-based product development, we have developed expertise and know-how in this field and have established procedures for manufacturing clinical-grade PLX cells in our facilities. Certain aspects of our manufacturing process are covered by patents and patent applications. In addition, specific aspects of our technology are retained as know-how and trade secrets that are protected by our 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 an obligation to assign to us inventions conceived during the course of performing services for us.

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. In some cases, a jurisdiction is listed as both pending and granted for a single patent family. This is due to pending continuation or divisional applications of the granted case.

There is a risk that our patents will be invalidated, and that our pending patent applications will not result in issued patents. We also cannot be certain that we will not infringe on 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 2020 to 2035. Actual expiration dates will be determined according to extensions received based on the Drug Price Competition and Patent Term Restoration Act of 1984 (P.L. 98-417), commonly known as the "Hatch-Waxman" Act, that permits extensions of pharmaceutical patents to reflect regulatory delays encountered in obtaining FDA market approval. The Hatch-Waxman Act is based on a U.S. federal law and therefore only relevant to U.S. patents.

Our Patent Portfolio

Patent Name/ Int. App. No.	Pending Jurisdictions	Granted Jurisdictions	Expiry Date
METHOD AND APPARATUS FOR MAINTENANCE AND EXPANSION OF HAEMATOPOIETIC STEM CELLS AND/OR PROGENITOR CELLS PCT/US2000/02688	United States, Europe	United States, Japan, Europe, Mexico, Australia, South Africa, Israel, Russia, New Zealand, India, China, Hong Kong, Canada	February 4, 2020
METHODS FOR CELL EXPANSION AND USES OF CELLS AND CONDITIONED MEDIA PRODUCED THEREBY FOR THERAPY PCT/IL2007/000380	United States, Europe, Israel, China, Hong Kong, Canada, Brazil, Korea	Japan, Europe, Israel, Singapore, Russia, South Africa, Australia, India, Korea, Mexico, Hong Kong, China	March 23, 2027
ADHERENT CELLS FROM PLACENTA TISSUE AND USE THEREOF IN THERAPY PCT/IL2008/001185	United States, Europe, Korea, Israel, China, Hong Kong, Canada, Brazil, Russia, Japan	United States, Europe, Singapore, Australia, Hong Kong, South Africa India, Mexico, Japan	September 2, 2028
METHODS OF TREATING INFLAMMATORY COLON DISEASES PCT/IL2009/000527	United States, Brazil, Canada, China, Europe, Hong Kong, Israel	Russia, South Africa	May 26, 2029
METHODS OF SELECTION OF CELLS FOR TRANSPLANTATION PCT/IL2009/000844	United States, Europe, Israel, Hong Kong		September 1, 2029
ADHERENT CELLS FROM PLACENTA TISSUE AND USE THEREOF IN THERAPY PCT/IL2009/000846	United States, Europe, Israel, India, Singapore, Hong Kong, Canada, China, Brazil	United States, Russia, Australia, South Africa, Mexico, Europe	September 1, 2029
ADHERENT CELLS FROM PLACENTA TISSUE AND USE THEREOF IN THERAPY PCT/IL2009/000845	Israel	United States, Europe	September 1, 2029
ADHERENT STROMAL CELLS DERIVED FROM PLANCENTAS OF MULTIPLE DONORS AND USES THEREOF PCT/IB2011/001413	United States, Israel, Hong Kong	Europe	April 21, 2031
ADHERENT CELLS FROM PLACENTA AND USE OF SAME IN DISEASE TREATMENT PCT/IB2010/003219	United States, Canada, China, Europe, Hong Kong, Israel, India	United States, Europe,China, Australia, New Zealand, South Africa, Hong-Kong, Mexico	November 29, 2030

METHODS AND SYSTEMS FOR HARVESTING ADHERENT STROMAL CELLS PCT/IB2012/000933	United States, Australia, Canada, China, Europe, Hong Kong, Israel, India, Korea, Mexico, Singapore	South Africa	April 15, 2032
METHODS FOR TREATING RADIATION OR CHEMICAL INJURY PCT/IB2012/000664	United States, Europe, Hong Kong, Israel, Korea, Japan		March 22, 2032
SKELETAL MUSCLE REGENERATION USING MESENCHYMAL STEM CELLS PCT/EP2011/058730	United States, Israel, Hong Kong	Europe	May 27, 2031
GENE AND PROTEIN EXPRESSION PROPERTIES OF ADHERENT STROMAL CELLS CULTURED IN 3D PCT/IB2014/059114	United States, Israel		February 20, 2034
DEVICES AND METHODS FOR CULTURE OF CELLS PCT/IB2013/058184	United States, Europe, China, Korea, Brazil, Hong Kong, India, Mexico, Russia	Europe, Canada, China, Europe, Israel, Japan, Singapore	August 31, 2033
METHODS FOR PREVENTION AND TREATMENT OF PREECLAMPSIA PCT/IB2013/058186	United States, Europe, China, Japan, Korea, Canada, Israel, Singapore, Australia, Hong Kong	South Africa	August 31, 2033
METHOD AND DEVICE FOR THAWING BIOLOGICAL MATERIAL PCT/IB2013/059808	United States, Europe, China, Japan, Korea, Canada, Brazil, Israel, India, Russia, Singapore, Australia, Hong Kong		October 31, 2033
SYSTEMS AND METHODS FOR GROWING AND HARVESTING CELLS PCT/IB2015/051559	International (PCT) Application Taiwan		March 3, 2035
DRUG CONTAINING HUMAN PLACENTA-ORIGIN MESENCHYMAL CELLS AND PROCESS FOR PRODUCING VEGF USING THE CELLS		Japan	March 28, 2023

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Research and Development

Our research and development expenses were $22,856,000, $23,416,000 and $24,938,000 in fiscal years 2016, 2015 and 2014, respectively, before deducting the participation by the Israel Innovation Authority, or IIA (previously the Office of the Chief Scientist, or IIA), and grants by third parties.

Foundational Research

Our initial technology, the PluriX™ Bioreactor system, was invented at the Technion - Israel Institute of Technology's Rappaport Faculty of Medicine, in collaboration with researchers from the Weizmann Institute of Science. This technology has been further significantly developed by our research and development teams over the ensuing years.

Ongoing Research and Development Plans

In July 2007, we entered into a five-year collaborative research agreement with the Berlin-Brandenburg Center for Regenerative Therapies at Charité - University Medicine Berlin, or Charité. In August 2012, we extended our collaborative research agreement with Charité for a period of five years through 2017. We and Charité 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. Charité will receive between 1% to 2% royalties from new developments that have been achieved during the joint development.

In recent years we have also engaged in research and development projects with other leading research institutions such as Hadassah University Medical Center, or Hadassah, in Jerusalem, Israel, and the Texas A&M Health Science Center (Texas A&M) in Round Rock, Texas. In addition, we also signed a memorandum of understanding (MOU) for a collaboration with Fukushima Medical University.

We used the services of Texas A&M for conducting a pre-clinical trial with PLX cells in a mice model of pre-eclampsia. We have no current or ongoing obligations to Texas A&M.

We have used the services of Hadassah to conduct pre-clinical trials from 2011 through 2013, mainly in the field of radiation-induced hematopoietic failure. We are currently performing additional studies with Hadassah furthering our understanding of the mechanism of action of the PLX-R18 product. We have no current or ongoing obligations to Hadassah.

We are performing proof of concept studies in conjunction with the Israeli Duchenne Association, or ADI, to assess the utility of PLX-PAD in alleviating symptoms of Duchenne muscular dystrophy.

We signed an MOU with for a collaboration with Fukushima Medical University, Fukushima Global Medical Science Center. The purpose of the collaboration is to develop Pluristem's PLX-R18 cells for the treatment of ARS, and for morbidities following radiotherapy in cancer patients. The collaboration will proceed alongside research supported by the NIH, which is studying PLX-R18 as a potential treatment for the hematologic component of ARS.

On June 26, 2013, we entered into an exclusive out-licensing and commercialization agreement, or the CHA Agreement, with CHA, for conducting clinical trials and commercialization of our PLX-PAD product in South Korea in connection with two indications: the treatment of CLI and IC. We will continue to retain rights to our proprietary manufacturing technology and cell-related intellectual property.

The first clinical study to be performed as part of the CHA Agreement is a Phase II trial in IC. This study is part of our multination phase II study. The Korean arm study was approved in November 2013 by South Korea’s MFDS.