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

TABLE OF CONTENTS

		Page
PART I		2
Item 1.	Business.	2
Item 1A.	Risk Factors.	14
Item 1B.	Unresolved Staff Comments.	28
Item 2.	Properties.	29
Item 3.	Legal Proceedings.	29
Item 4.	Mine Safety Disclosures.	29
PART II		29
Item 5.	Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.	29
Item 6.	Selected financial data.	30
Item 7.	Management's Discussion and Analysis of Financial Condition and Results of Operations.	31
Item 7A.	Quantitative and Qualitative Disclosures About Market Risk.	40
Item 8.	Financial Statements and Supplementary Data.	41
Item 9.	Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.	42
Item 9A.	Controls and Procedures.	42
Item 9B.	Other Information.	43
PART III		44
Item 10.	Directors, Executive Officers and Corporate Governance.	44
Item 11.	Executive Compensation.	49
Item 12.	Security Ownership of Certain Beneficial Owners and Management and Related Stockholders Matters.	57
Item 13.	Certain Relationships and Related Transactions and Director Independence.	59
Item 14.	Principal Accounting Fees and Services.	59
PART IV		61
Item 15.	Exhibits.	61

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.

2

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

9

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.

Upon the first regulatory approval for a PLX product in South Korea, if granted, for the specified indications, we and CHA will establish an equally owned joint venture. The purpose of the joint venture will be to commercialize PLX cell products in South Korea. Additionally, we will be able to use the data generated by CHA to pursue the development of PLX product candidates outside of South Korea.

In addition, and as contemplated by the CHA Agreement, in December 2013, we and CHA executed a mutual investment pursuant to which we issued 2,500,000 shares of our common stock in consideration for 1,011,504 shares of CHA, which reflects total consideration to each of us and CHA of approximately $10,414,000.

The term of the CHA Agreement extends from June 24, 2013 until the later of the expiration, lapse, cancellation, abandonment or invalidation of the last valid patent claim covering the development of the product indications. The CHA Agreement contains customary termination provisions, including in the event that the parties do not reach an agreement upon a development plan for conducting the clinical trials.

Upon termination of the CHA Agreement, the license granted thereunder will terminate, and all rights included therein will revert to us, whereupon we will be free to enter into agreements with any other third parties for the granting of a license in or outside South Korea or to deal in any other manner with such rights as it shall see fit in our sole discretion.

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.

In-House Clinical Manufacturing

We have the in-house capability to perform clinical cell manufacturing. Our state-of-the-art GMP grade manufacturing facility in Haifa has been in use since February 2013 for the main purpose of clinical grade, large-scale manufacturing. The facility's new automated manufacturing process and products were approved for production of PLX-PAD for clinical use by the FDA, PEI, Korean MFDS, PMDA and the Israeli MOH. Our second product, PLX R18, was cleared by the FDA and the Israeli Ministry of Health for clinical use. Furthermore, the site was inspected and approved by an EU qualified person (European accreditation body), approving that the site and production processes meet the current GMP for the purpose of manufacturing clinical grade products. Following the clinical approval of the facility, we are moving forward with our planned clinical trials based on cells manufactured in the new, efficient and improved manufacturing processes.

We obtain the human placentas used for our research and manufacturing activities from various hospitals in Israel after receiving a written informed consent by the mother and pathogen clearance. 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 United States and the European Union as well as other countries in which our products will be marketed in the future like Japan, Israel and South Korea. Specifically, the FDA in the United States and the EMA in Europe must approve the product for marketing. 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, resources and money. There can be no assurance that our product candidates will ultimately receive marketing approval, or, if approved, will be reimbursed by public and private health insurance.

There are several stages every drug has to go through during its development process. Among these are:

- Performance of nonclinical laboratory and animal studies 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. In accordance with regulatory requirements, nonclinical safety and toxicity studies are conducted under Good Laboratory Practice requirements to ensure their quality and reliability;

11

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

- The manufacture of the product according to GMP regulations and standards; and

- Potential post-marketing clinical testing and surveillance of the product after marketing approval, which can result in additional conditions on the approvals or suspension of clinical use.

Approval of a drug for clinical studies in humans and approval of marketing are sovereign decisions of states, made by national, or, in case of the European Union, international regulatory competent authorities.

The Regulatory Process in the United States

In the United States, our product candidates are subject to regulation as a biological product under the Public Health Service Act and the Federal Food, Drug and Cosmetic Act. The FDA, regulating the approval of clinical trials and marketing applications in the United States, generally requires the following steps prior to approving a new biological product either for clinical studies or for commercial sale:

- Submission of an Investigational New Drug 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 drug candidate into humans in clinical trials;

- Submission to the FDA of a Biologics License Application, or BLA, for marketing authorization of the product, which must include adequate results of pre-clinical testing and clinical trials;

- FDA review of the BLA in order to determine, among other things, whether the product is safe and effective for its intended uses; and

- FDA inspection and approval of the product manufacturing facility at which the product will be manufactured.

The Regulatory Process in Europe

In the European Union, our investigational cellular products are regulated under the Advanced Therapy Medicinal Product regulation, a regulation specific to cell and tissue products.This European Union regulation requires:

- Filing a Clinical Trial Application with the various member states or via a centralized procedure (Voluntary Harmonisation 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 ethics committees of clinical sites to test the investigational product into humans in clinical trials;

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

- Since our investigational cellular products are regulated under the Advanced Therapy Medicinal Product regulation, the application for marketing authorization to the EMA is mandatory within the 28 member states of the EU. The EMA is expected to review and approve the Marketing Authorization Application.

12

In April 2015, the EMA designated PLX-PAD as a somatic cell therapy medicinal product and as a tissue-engineered product.

In April 2015, the Pediatric Committee of the EMA granted PLX-PAD a waiver for the requirement to submit a pediatric investigational plan for all indications falling under "treatment of peripheral atherosclerosis", including IC and CLI.

In May 2015, we were selected by EMA for development of PLX-PAD cells via the Adaptive Pathways approach, with the potential to reach the market several years faster than the traditional regulatory approval pathway.

Other Regulations

In Japan, we have completed the required regulatory interactions with the PMDA, prior to the submission of clinical trial notification, in the framework of the new regulations for regenerative therapy effective in November 2014, which promote expedited approval for regenerative therapies that are being developed for seriously debilitating/life-threatening indications. We intend to develop PLX-PAD for CLI using this regulatory approach, with the potential to reach the market via conditional approval after a Phase I/II study.

In general, the approval procedure varies among countries, and may involve additional preclinical testing and clinical trials. The requirements and time required may differ from those required for FDA or EMA approval. Each country may impose certain procedures and requirements of its own. Most countries other than the United States, the European Union and Japan are willing to consider requests for marketing approval only after the product had been approved for marketing by either the FDA, the EMA or the PMDA. The decision regarding marketing approval is made following the submission of a dossier that is thoroughly assessed and critically addressed.

Clinical trials

Typically, in the United States, the European Union as well as in Japan, clinical testing involves a three-phase process, although the phases may overlap. In Phase I, clinical trials are conducted with a small number of healthy volunteers, or patients in cases of ethical issues with using healthy volunteers, and are designed to provide information about product safety and to evaluate the pattern of drug distribution and metabolism within the body. In Phase II, clinical trials are conducted with a homogenous group of patients afflicted with the specific target disease, in order to determine preliminary efficacy, optimal dosages and expanded evidence of safety. In some cases, an initial trial is conducted in diseased patients to assess both preliminary efficacy and preliminary safety and patterns of drug metabolism and distribution, in which case it is referred to as a Phase I/II trial. Phase III clinical trials are generally large-scale, multi-center, controlled trials conducted with a heterogeneous group of patients afflicted with the target disease, in order to provide statistically valid proof of efficacy, as well as safety and potency. The Phase III trials represent the trials that are considered for confirmation of efficacy and safety and are the most important ones for the approval. In some circumstances, a regulatory agency may require Phase IV, or post-marketing, trials if it feels that additional information needs to be collected about the drug after it is on the market.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data and clinical trial investigators to minimize risks. The sponsor of a clinical trial is required to submit an annual safety report to the relevant regulatory agencies, in which serious adverse events must be reported, and also to submit in an expedited manner any individual serious adverse events that are suspected to be related to the tested drug,. An agency may, at its discretion, re-evaluate, alter, suspend, or terminate the clinical study based upon the data that have been accumulated to that point and its assessment of the risk/benefit ratio to the patient.

Employees

We presently employ a total of 169 full-time employees and 8 part-time employees, of whom 154 full-time employees and 8 part-time employees are engaged in research, manufacturing and clinical trials.

Competition

The regenerative medicine field is characterized by intense competition, as global pharma players are becoming more engaged in the cell therapy field based on the advancements made in clinical trials and due to the new favorable regenerative medicine legislation in certain regions. We face competition from both allogeneic and autologous cell therapy companies, academic, commercial and research institutions, pharmaceutical companies, biopharmaceutical companies, and governmental agencies. Some of the clinical indications we currently have under development are also being investigated in preclinical and clinical programs by others.

There are multiple participants in the cell therapy field based in the United States, Europe, Japan, Korea, and Australia such as Athersys, Inc., Capricor Therapeutics, Inc., Celgene Corporation, ReNeuron Group plc, Tigenix NV, SanBio Inc., Healios K.K., Cytori Therapeutics, Green Cross Cell Corp. and Mesoblast LTD. Among other things, we expect to compete based upon our intellectual property portfolio, our in-house manufacturing efficiencies, and the efficacy of our products. Our ability to compete successfully will depend on our continued ability to attract and retain experienced and skilled executive, scientific and clinical development personnel to identify and develop viable cellular therapeutic candidates and exploit these products commercially. Given the magnitude of the potential opportunity for stem cell therapy, we expect competition in this area to intensify.

Available Information

Additional information about us is contained on our Internet website at www.pluristem.com. Information on our website is not incorporated by reference into this report. Under the "SEC Filings" and “Financial Information” sections, under the "Investors & Media" section of our website, we make available free of charge our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) of the Securities Exchange Act of 1934, as amended (Exchange Act), as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Our reports filed with the SEC are also made available to read and copy at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. You may obtain information about the Public Reference Room by calling the SEC at 1-800-SEC-0330. Reports filed with the SEC are also made available on its website at www.sec.gov. The following Corporate Governance documents are also posted on our website: Code of Business Conduct and Ethics, and the Charters for each of the Committees of our Board of Directors.

Item 1A. Risk Factors.

The following risk factors, among others, could affect our actual results of operations and could cause our actual results to differ materially from those expressed in forward-looking statements made by us. These forward-looking statements are based on current expectations and except as required by law we assume no obligation to update this information. You should carefully consider the risks described below and elsewhere in this Annual Report before making an investment decision. Our business, financial condition or results of operations could be materially adversely affected by any of these risks. Our common stock is considered speculative and the trading price of our common stock could decline due to any of these risks, and you may lose all or part of your investment. The following risk factors are not the only risk factors facing our Company. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our business.

Our likelihood of profitability depends on our ability to license and/or develop and commercialize products based on our cell production technology, which is currently in the development stage. If we are unable to complete the

development and commercialization of our cell therapy products successfully, our likelihood of profitability will be limited severely.

We are engaged in the business of developing cell therapy products. We have not realized a profit from our operations to date and there is little likelihood that we will realize any profits in the short or medium term. Any profitability in the future from our business will be dependent upon successful commercialization of our potential cell therapy products and/or licensing of our products, which will require significant additional research and development as well as substantial clinical trials.

If we are not able to successfully license and/or develop and commercialize our cell therapy product candidates and obtain the necessary regulatory approvals, we may not generate sufficient revenues to continue our business operations.

So far, the products we are developing have completed only one Phase I/II clinical trial of Gluteal Musculature rehabilitation after total hip arthroplasty (efficacy, ongoing for safety) and two Phase I clinical trials for CLI. Our early stage cell therapy product candidates may fail to perform as we expect. Moreover, even if our cell therapy product candidates successfully perform as expected, in later stages of development they may fail to show the desired safety and efficacy traits despite having progressed successfully through pre-clinical or initial clinical testing. We will need to devote significant additional research and development, financial resources and personnel to develop commercially viable products and obtain the necessary regulatory approvals.

If our cell therapy product candidates do not prove to be safe and effective in clinical trials, we will not obtain the required regulatory approvals. If we fail to obtain such approvals, we may not generate sufficient revenues to continue our business operations.

Even if we obtain regulatory approval of a product, that approval may be subject to limitations on the indicated uses for which it may be marketed. Even after granting regulatory approval, the FDA, the EMA, the PMDA and regulatory agencies in other countries continue to regulate marketed products, manufacturers and manufacturing facilities, which may create additional regulatory barriers and burdens. Later discovery of previously unknown problems with a product, manufacturer or facility, may result in restrictions on the product or manufacturer, including a withdrawal of the product from the market. Further, regulatory agencies may establish additional regulations that could prevent or delay regulatory approval of our products.

We cannot market and sell our cell therapy product candidates in the United States, Europe, Japan, or in other countries if we fail to obtain the necessary regulatory approvals or licensure.

We cannot sell our cell therapy product candidates until regulatory agencies grant marketing approval, or licensure. The process of obtaining regulatory approval is lengthy, expensive and uncertain. It is likely to take at least several years to obtain the required regulatory approvals for our cell therapy product candidates, or we may never gain the necessary approvals. Any difficulties that we encounter in obtaining regulatory approval may have a substantial adverse impact on our operations and cause our stock price to decline significantly.

To obtain marketing approvals in the United States and Europe for cell therapy product candidates we must, among other requirements, complete carefully controlled and well-designed clinical trials sufficient to demonstrate to the FDA ,the EMA and the PMDA that the cell therapy product candidates is safe and effective for each disease for which we seek approval. So far, we have successfully conducted Phase I/II and Phase I clinical trials for our PLX-PAD product. Several factors could prevent completion or cause significant delay of these trials, including an inability to enroll the required number of patients or failure to demonstrate adequately that cell therapy product candidates are safe and effective for use in humans. Negative or inconclusive results from or adverse medical events during a clinical trial could cause the clinical trial to be repeated or a program to be terminated, even if other studies or trials relating to the program are successful. The FDA, the EMA or the PMDA can place a clinical trial on hold if, among other reasons, it finds that patients enrolled in the trial are or would be exposed to an unreasonable and significant risk of illness or injury. If safety concerns develop, we, the FDA, the EMA or the PMDA could stop our trials before completion.

15

If we are not able to conduct our clinical trials properly and on schedule, marketing approval by FDA, EMA, PMDA and other regulatory authorities may be delayed or denied.

The completion of our clinical trials may be delayed or terminated for many reasons, such as:

- The FDA, the EMA or the PMDA does not grant permission to proceed or places additional trials on clinical hold;
- Subjects do not enroll in our trials at the rate we expect;
- The regulators may ask to increase subject's population in the clinical trials;
- Subjects experience an unacceptable rate or severity of adverse side effects;
- Third-party clinical investigators do not perform our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, GCP and regulatory requirements, or other third parties do not perform data collection and analysis in a timely or accurate manner;
- Inspections of clinical trial sites by the FDA, EMA, PMDA or MFDS and other regulatory authorities find regulatory violations that require us to undertake corrective action, suspend or terminate one or more sites, or prohibit us from using some or all of the data in support of our marketing applications; or
- One or more IRBs suspends or terminates the trial at an investigational site, precludes enrollment of additional subjects, or withdraws its approval of the trial.

Our development costs will increase if we have material delays in our clinical trials, or if we are required to modify, suspend, terminate or repeat a clinical trial. If we are unable to conduct our clinical trials properly and on schedule, marketing approval may be delayed or denied by the FDA, EMA, PMDA and other regulatory authorities.

We may need to raise additional financing to support the research, development and manufacturing of our cell therapy products and our products in the future but we cannot be sure we will be able to obtain additional financing on terms favorable to us when needed. If we are unable to obtain additional financing to meet our needs, our operations may be adversely affected or terminated.

It is highly likely that we will need to raise significant additional capital in the future. Although we were successful in raising capital in the past, our current financial resources are limited and may not be sufficient to finance our operations until we become profitable, if that ever happens. It is likely that we will need to raise additional funds in the near future in order to satisfy our working capital and capital expenditure requirements. Therefore, we are dependent on our ability to sell our common stock for funds, receive grants or to otherwise raise capital. There can be no assurance that we will be able to obtain financing. Any sale of our common stock in the future will result in dilution to existing stockholders and could adversely affect the market price of our common stock. Also, we may not be able to borrow or raise additional capital in the future to meet our needs or to otherwise provide the capital necessary to conduct the development and commercialization of our potential cell therapy products, which could result in the loss of some or all of one's investment in our common stock.

Favorable results from compassionate use treatment or initial interim results from a clinical trial do not ensure that later clinical trials will be successful and success in early stage clinical trials does not ensure success in later-stage clinical trials.

PLX cells have been administered as part of compassionate use treatments, which permit the administration of the PLX cells outside of clinical trials. No assurance can be given that any positive results are attributable to the PLX cells, or that administration of PLX cells to other patients will have positive results. Compassionate use is a term that is used to refer to the use of an investigational drug outside of a clinical trial to treat a patient with a serious or immediately life-threatening disease or condition who has no comparable or satisfactory alternative treatment options. Regulators often allow compassionate use on a case-by-case basis for an individual patient or for defined groups of patients with similar treatment needs.

There is no assurance that we will obtain regulatory approval for PLX cells. We will only obtain regulatory approval to commercialize a product candidate if we can demonstrate to the satisfaction of the FDA, the EMA, the PMDA or other applicable regulatory authorities, in well-designed and conducted clinical trials, that the product candidate is safe and effective and that the product candidate, including the cell production methodology, otherwise meets the appropriate standards required for approval. Clinical trials can be lengthy, complex and extremely expensive processes with uncertain results. A failure of one or more clinical trials may occur at any stage of testing.

Success in early clinical trials does not ensure that later clinical trials will be successful, and initial results from a clinical trial do not necessarily predict final results. While results from treating patients through compassionate use have in certain cases been successful, we cannot be assured that further trials will ultimately be successful. Results of further clinical trials may be disappointing.

Even if early stage clinical trials are successful, we may need to conduct additional clinical trials for product candidates with patients receiving the drug for longer periods before we are able to seek approvals to market and sell these product candidates from the FDA and regulatory authorities outside the United States. Even if we are able to obtain approval for our product candidates through an accelerated approval review program, we may still be required to conduct clinical trials after such an approval. If we are not successful in commercializing any of our lead product candidates, or are significantly delayed in doing so, our business will be materially harmed.

We may not successfully maintain our existing exclusive out-licensing agreement with CHA, or establish new collaborative and licensing arrangements, which could adversely affect our ability to develop and commercialize our product candidates.

One of the elements of our business strategy is to license our technology to other companies. Our business strategy includes establishing collaborations and licensing agreements with one or more pharmaceutical or biotechnology companies. To date, we have a strategic partnership with CHA for both the IC and CLI indications in Korea. CHA will conduct PLX clinical studies in South Korea, and, following approval, a joint venture equally owned by both parties will be established to market PLX products in South Korea. Our PLX cells are also being used in South Korean sites participating to our International IC study through our partnership with CHA. Notwithstanding, we may not be able to further establish or maintain such licensing and collaboration arrangements necessary to develop and commercialize our product candidates. Even if we are able to maintain or establish licensing or collaboration arrangements, these arrangements may not be on favorable terms and may contain provisions that will restrict our ability to develop, test and market our product candidates. Any failure to maintain or establish licensing or collaboration arrangements on favorable terms could adversely affect our business prospects, financial condition or ability to develop and commercialize our product candidates.

Our agreements with our collaborators and licensees may have provisions that give rise to disputes regarding the rights and obligations of the parties. These and other possible disagreements could lead to termination of the agreement or delays in collaborative research, development, supply, or commercialization of certain product

candidates, or could require or result in litigation or arbitration. Moreover, disagreements could arise with our collaborators over rights to intellectual property or our rights to share in any of the future revenues of products developed by our collaborators. These kinds of disagreements could result in costly and time-consuming litigation. Any such conflicts with our collaborators could reduce our ability to obtain future collaboration agreements and could have a negative impact on our relationship with existing collaborators.

We may not be able to secure and maintain research institutions to conduct our clinical trials.

We rely on research institutions to conduct our clinical trials. Specifically, the limited number of centers experienced with cell therapy product candidates heightens our dependence on such research institutions. Our reliance upon research institutions, including hospitals and clinics, provides us with less control over the timing and cost of clinical trials and the ability to recruit subjects. If we are unable to reach agreements with suitable research institutions on acceptable terms, or if any resulting agreement is terminated, we may be unable to quickly replace the research institution with another qualified institution on acceptable terms. We may not be able to secure and maintain suitable research institutions to conduct our clinical trials.

We have limited experience in conducting and managing large human trials. If we fail in the conduct of such trials, our business will be materially harmed.

Even though we conducted Phase I/II and Phase I trials for our PLX-PAD product and have recruited employees who are experienced in managing and conducting clinical trials, we have limited experience in this area. We will need to expand our experience and rely on consultants in order to obtain regulatory approvals for our therapeutic product candidates. The failure to successfully conduct clinical trials could materially harm our business.

Our product development programs are based on novel technologies and are inherently risky.

We are subject to the risks of failure inherent in the development of products based on new technologies. The novel nature of our therapeutics creates significant challenges in regards to product development and optimization, manufacturing, government regulation, third-party reimbursement and market acceptance. For example, the FDA, the EMA, the PMDA and other countries' regulatory authorities have relatively limited experience with cell therapies. Very few cell therapy products have been approved by regulatory authorities to date for commercial sale, and the pathway to regulatory approval for our cell therapy product candidates may accordingly be more complex and lengthy. As a result, the development and commercialization pathway for our therapies may be subject to increased uncertainty, as compared to the pathway for new conventional drugs.

There are very few drugs and limited therapies that the FDA or EMA and other regulatory authorities have approved as treatments for some of the disease indications we are pursuing. This could complicate and delay FDA, EMA or other countries' regulatory authorities approval of our biologic drug candidates.

There are very few drugs and limited therapies currently approved for treatment of CLI, IC, ARS or HCT. As a result, the clinical efficacy endpoints, or the criteria to measure the intended results of treatment may be difficult to determine. Despite our eligibility for certain accelerated pathways, this could increase the difficulty of our obtaining FDA, EMA or other countries' regulatory authorities approval to market our products.

Our cell therapy drug candidates represent new classes of therapy that the marketplace may not understand or accept.

Even if we successfully develop and obtain regulatory approval for our cell therapy candidates, the market may not understand or accept them. We are developing cell therapy product candidates that represent novel treatments and will compete with a number of more conventional products and therapies manufactured and marketed by others, including major pharmaceutical companies. The degree of market acceptance of any of our developed and potential products will depend on a number of factors, including:

- the clinical safety and effectiveness of our cell therapy drug candidates and their perceived advantage over alternative treatment methods, if any;

- adverse events involving our cell therapy product candidates or the products or product candidates of others that are cell-based; and

- the cost of our products and the reimbursement policies of government and private third-party payers.

If the health care community does not accept our potential products for any of the foregoing reasons, or for any other reason, it could affect our sales, having a material adverse effect on our business, financial condition and results of operations.

If our processing and storage facility or our clinical manufacturing facilities are damaged or destroyed, our business and prospects would be adversely affected.

If our processing and storage facility, our clinical manufacturing facilities or the equipment in such facilities were to be damaged or destroyed, the loss of some or all of the stored units of our cell therapy drug candidates would force us to delay or halt our clinical trial processes. We have two clinical manufacturing facilities located in Haifa, Israel. If these facilities or the equipment in them are significantly damaged or destroyed, we may not be able to quickly or inexpensively replace our manufacturing capacity.

The clinical manufacturing process for cell therapy products is complex and requires meeting high regulatory standards; we have limited manufacturing experience and know-how. Any delay or problem in the clinical manufacturing of PLX may result in a material adverse effect on our business.

Our facility and its commercial scale manufacturing process for PLX-PAD have received approval from the FDA, EMA, Germany's PEI, the Korean MFDS and the PMDA. However, the clinical manufacturing process is complex and we have no experience in manufacturing our product candidates at a commercial level. There can be no guarantee that we will be able to successfully develop and manufacture our product candidates in a manner that is cost-effective or commercially viable, or that our development and manufacturing capabilities might not take much longer than currently anticipated to be ready for the market. In addition, if we fail to maintain regulatory approvals for our manufacturing facilities, we may suffer delays in our ability to manufacture our product candidates. This may result in a material adverse effect on our business.

We are dependent upon third-party suppliers for raw materials needed to manufacture PLX; if any of these third parties fails or is unable to perform in a timely manner, our ability to manufacture and deliver will be compromised.

In addition to the placenta used in the clinical manufacturing process of PLX we require certain raw materials. These items must be manufactured and supplied to us in sufficient quantities and in compliance with current GMP. To meet these requirements, we have entered into supply agreements with firms that manufacture these raw materials to current GMP standards. Our requirements for these items are expected to increase if and when we transition to the manufacture of commercial quantities of our cell-based drug candidates.

In addition, as we proceed with our clinical trial efforts, we must be able to continuously demonstrate to the FDA, EMA, and other regulatory authorities that we can manufacture our cell therapy product candidates with consistent characteristics. Accordingly, we are materially dependent on these suppliers for supply of current GMP-grade materials of consistent quality. Our ability to complete ongoing clinical trials may be negatively affected in the event that we are forced to seek and validate a replacement source for any of these critical materials.

We may not be able to take advantage of the new regulatory pathways in Europe and Japan to shorten our time to market our products.

Recent regulatory pathways in Europe and Japan may allow for early commercialization of our products and reducing the time to market our products. The purpose of Europe's Adaptive Pathways is to shorten the time it takes for innovative medicines to reach patients with serious conditions that lack adequate treatment options. After a therapy is selected for the program, the Adaptive Pathways group conducts high level discussions and provides guidance to the applicant regarding the formal regulatory processes that precede a trial targeting early approval and further expansion of the indications. In Japan, a new law regarding regenerative therapies, including cell therapies, came into effect. The new law allows for conditional, time-limited approval of products for marketing after limited proof of efficacy.

In May 2015, the EMA selected our PLX cell program in CLI for its Adaptive Pathway project. In addition, the PMDA approved the proposed quality and large-scale manufacturing methods for PLX-PAD and has cleared our PLX-PAD cells for use in clinical trials in Japan. However, since these new regulatory pathways are relatively new, we may not be able to meet the regulatory requirements and as a result would not benefit from early access to the market.

If we encounter problems or delays in the research and development of our potential cell therapy products, we may not be able to raise sufficient capital to finance our operations during the period required to resolve such problems or delays.

Our cell therapy products are currently in the development stage and we anticipate that we will continue to incur substantial operating expenses and incur net losses until we have successfully completed all necessary research and clinical trials. We, and any of our potential collaborators, may encounter problems and delays relating to research and development, regulatory approval and intellectual property rights of our technology. Our research and development programs may not be successful, and our cell culture technology may not facilitate the production of cells outside the human body with the expected result. Our cell therapy products may not prove to be safe and efficacious in clinical trials. If any of these events occur, we may not have adequate resources to continue operations for the period required to resolve the issue delaying commercialization and we may not be able to raise capital to finance our continued operation during the period required for resolution of that issue. Accordingly, we may be forced to discontinue or suspend our operations.

Existing government programs and tax benefits may be terminated.

We have received certain Israeli government approvals under certain programs and may in the future utilize certain tax benefits in Israel by virtue of these programs. To remain eligible for such tax benefits, we must continue to meet certain conditions. If we fail to comply with these conditions in the future, the benefits we receive could be canceled and have to pay additional taxes. We cannot guarantee that these programs and tax benefits will be continued in the future, at their current levels or at all. If these programs and tax benefits are ended, our business, financial condition and results of operations could be materially adversely affected.

Because we received grants from the Israel Innovation Authority, or IIA, we are subject to on-going restrictions.

We have received royalty-bearing grants from the IIA, for research and development programs that meet specified criteria. The terms of the IIA's grants limit our ability to transfer know-how developed under an approved research and development program outside of Israel, regardless of whether the royalties are fully paid. Any non-Israeli citizen, resident or entity that, among other things, becomes a holder of 5% or more of our share capital or voting rights, is entitled to appoint one or more of our directors or our Chief Executive Officer, or CEO, serves as a director of our Company or as our CEO is generally required to notify the same to the IIA and to undertake to observe the law governing the grant programs of the IIA, the principal restrictions of which are the transferability limits described above. For more information, see "Item 7. Management's Discussion and Analysis of Financial Condition and Results

of Operations - Liquidity and Capital Resources".

We have limited operating history, which raises doubts with respect to our ability to generate revenues in the future.

We have a limited operating history in our business of developing and commercializing cell production technology. Until we entered into the United Agreement, which was terminated in December 2015, we did not generate any revenues. It is not clear when we will generate additional revenues or whether we will experience further delays in recognizing revenues such as resulted from a clinical hold. Our primary source of funds has been the sale of our common stock and government grants. We cannot give assurances that we will be able to generate any significant revenues or income in the future. There is no assurance that we will ever be profitable.

If we do not keep pace with our competitors and with technological and market changes, our technology and products may become obsolete and our business may suffer.

The cellular therapeutics industry, of which we are a part, is very competitive and is subject to technological changes that can be rapid and intense. We have faced, and will continue to face, intense competition from biotechnology, pharmaceutical and biopharmaceutical companies, academic and research institutions and governmental agencies engaged in cellular therapeutic and drug discovery activities or funding, both in the United States and internationally. Some of these competitors are pursuing the development of cellular therapeutics, drugs and other therapies that target the same diseases and conditions that we target in our clinical and pre-clinical programs.

Many of our competitors have greater resources, more product candidates and have developed product candidates and processes that directly compete with our products. Our competitors may have developed, or could develop in the future, new products that compete with our products or even render our products obsolete.

If we fail to obtain or maintain orphan drug exclusivity for our products, our competitors may sell products to treat the same conditions and our revenue will be reduced.

Our business strategy focuses on the development of drugs that are eligible for FDA and European Union orphan drug designation. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, defined as a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the European Union, the EMA’s Committee for Orphan Medicinal Products, or COMP, grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union Community. Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of a life threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biological product.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer is unable to assure sufficient product quantity. In the European Union, orphan drug designation also entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity is granted following drug or biological product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties can be approved for the same condition. Even with orphan drug exclusivity, if a third party were to prepare or market a product which infringes upon our intellectual property, we may need to initiate litigation, which may be costly, to enforce our rights against such party. After an orphan drug is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is safer, more effective, or makes a major contribution to patient care. Orphan drug designation on its own neither shortens the development time or regulatory review time for a drug.

While orphan drug products are typically sold at a high price relative to other medications, the market may not be receptive to high pricing of our products.

We develop our product candidates to treat rare and ultra-rare diseases, a space where medications are usually sold at high prices compared with other medications. Accordingly, even if regulatory authorities approve our product candidates, the market may not be receptive to, and it may be difficult for us to achieve, a per-patient per-year price high enough to allow us to realize a return on our investment.

We depend to a significant extent on certain key personnel, the loss of any of whom may materially and adversely affect our Company.

Our success depends to a significant extent on the continued services of certain highly qualified scientific and management personnel, in particular, Zami Aberman, our CEO and Chairman, and Yaky Yanay, our Chief Operating Officer, or COO, President and Chief Financial Officer, or CFO. We face competition for qualified personnel from numerous industry sources, and there can be no assurance that we will be able to attract and retain qualified personnel on acceptable terms. The loss of service of any of our key personnel could have a material adverse effect on our operations or financial condition. In the event of the loss of services of such personnel, no assurance can be given that we will be able to obtain the services of adequate replacement personnel. We do not maintain key person insurance on the lives of any of our officers or employees.

The patent approval process is complex and we cannot be sure that our pending patent applications or future patent applications will be approved.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our and any future licensors' patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or products or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. The laws of foreign countries may not protect our rights to the same extent as the laws of the United States and we may not be able to obtain meaningful patent protection for any of our commercial products either in or outside the United States.

No assurance can be given that the scope of any patent protection granted will exclude competitors or provide us with competitive advantages, that any of the patents that have been or may be issued to us will be held valid if subsequently challenged, or that other parties will not claim rights to or ownership of our patents or other proprietary rights that we hold. Furthermore, there can be no assurance that others have not developed or will not develop similar products, duplicate any of our technology or products or design around any patents that have been or may be issued to us or any future licensors. Since patent applications in the United States and in Europe are not publicly disclosed until patents are issued, there can be no assurance that others did not first file applications for products covered by our pending patent applications, nor can we be certain that we will not infringe any patents that may be issued to others.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. We have yet to conduct comprehensive freedom-to-operate searches to determine whether our proposed business activities or use of certain of the patent rights owned by us would infringe patents issued to third parties. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference proceedings before the U.S. Patent and Trademark Office. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. For example, we are aware of issued third party patents directed to placental stem cells and their use for therapy and in treating various diseases. We may need to seek a license for one or more of these patents. No assurances can be given that such a license will be available on commercially reasonable terms, if at all. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors are able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

The market for our products will be heavily dependent on third party reimbursement policies.

Our ability to successfully commercialize our product candidates will depend on the extent to which government healthcare programs, as well as private health insurers, health maintenance organizations and other third party payers will pay for our products and related treatments.

Reimbursement by third party payers depends on a number of factors, including the payer’s determination that use of the product is safe and effective, not experimental or investigational, medically necessary, appropriate for the specific patient and cost-effective. Reimbursement in the United States or foreign countries may not be available or maintained for any of our product candidates. If we do not obtain approvals for adequate third party reimbursements, we may not be able to establish or maintain price levels sufficient to realize an appropriate return on our investment in product development. Any limits on reimbursement from third party payers may reduce the demand for, or negatively affect the price of, our products. The lack of reimbursement for these procedures by insurance payers has negatively affected the market for our products in this indication in the past.

Managing and reducing health care costs has been a general concern of federal and state governments in the United States and of foreign governments. In addition, third party payers are increasingly challenging the price and cost-effectiveness of medical products and services, and many limit reimbursement for newly approved health care products. In particular, third party payers may limit the indications for which they will reimburse patients who use any products that we may develop. Cost control initiatives could decrease the price for products that we may develop, which would result in lower product revenues to us.

Our success depends in large part on our ability to develop and protect our technology and our cell therapy products. If our patents and proprietary rights agreements do not provide sufficient protection for our technology and our cell therapy products, our business and competitive position will suffer.

Our success will also depend in part on our ability to develop our technology and commercialize cell therapy products without infringing the proprietary rights of others. We have not conducted full freedom of use patent searches and no assurance can be given that patents do not exist or could not be filed which would have an adverse affect on our ability to develop our technology or maintain our competitive position with respect to our potential cell therapy products. If our technology components, devices, designs, products, processes or other subject matter are claimed under other existing United States or foreign patents or are otherwise protected by third party proprietary rights, we may be subject to infringement actions. In such event, we may challenge the validity of such patents or other proprietary rights or we may be required to obtain licenses from such companies in order to develop, manufacture or market our technology or products. There can be no assurances that we would be able to obtain such licenses or that such licenses, if available, could be obtained on commercially reasonable terms. Furthermore, the failure to either develop a commercially viable alternative or obtain such licenses could result in delays in marketing our proposed products or the inability to proceed with the development, manufacture or sale of products requiring such licenses, which could have a material adverse effect on our business, financial condition and results of operations. If we are required to defend ourselves against charges of patent infringement or to protect our proprietary rights against third parties, substantial costs will be incurred regardless of whether we are successful. Such proceedings are typically protracted with no certainty of success. An adverse outcome could subject us to significant liabilities to third parties and force us to curtail or cease our development of our technology and the commercialization our potential cell therapy products.

We have built the ability to manufacture clinical grade ASCs in-house. Through our experience with ASC-based product development, we have developed expertise and know-how in this field. To protect these expertise and know-how, our policies require 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 for us. These agreements might not effectively prevent disclosure of our confidential information.

We must further protect and develop our technology and products in order to become a profitable company.

If we do not complete the development of our technology and products in development by the time our patents expire, create additional sufficient layers of patents or other intellectual property rights, other companies may use the technology to develop competing products. If this happens, we may lose our competitive position and our business would likely suffer.

Furthermore, the scope of our patents may not be sufficiently broad to offer meaningful protection. In addition, our patents could be successfully challenged, invalidated or circumvented so that our patent rights would not create an effective competitive barrier. We also intend to seek patent protection for any of our potential cell therapy products once we have completed their development.

We also rely on trade secrets and unpatentable know-how that we seek to protect, in part, by confidentiality agreements with our employees, consultants, suppliers and licensees. These agreements may be breached, and we might not have adequate remedies for any breach. If this were to occur, our business and competitive position would suffer.

The price of our common stock may fluctuate significantly.

The market for our shares of common stock may fluctuate significantly. A number of events and factors may have an adverse impact on the market price of our common stock, such as:

- results of our clinical trials or adverse events associated with our products;
- the amount of our cash resources and our ability to obtain additional funding;
- changes in our revenues, expense levels or operating results;
- entering into or terminating strategic relationships;
- announcements of technical or product developments by us or our competitors;
- market conditions for pharmaceutical and biotechnology stocks in particular;
- changes in laws and governmental regulations, including changes in tax, healthcare, competition and patent laws;
- disputes concerning patents or proprietary rights;
- new accounting pronouncements or regulatory rulings;
- public announcements regarding medical advances in the treatment of the disease states that we are targeting;
- patent or proprietary rights developments;
- regulatory actions that may impact our products;
- disruptions in our manufacturing processes; and
- competition.

In addition, a market downturn in general and/or in the biopharmaceutical sector in particular, may adversely affect the market price of our securities, which may not necessarily reflect the actual or perceived value of our Company.

Future sales of our shares may cause the prevailing market price of our shares to decrease.

Future sales of our common stock, or the perception that such sales may occur, could cause immediate dilution and adversely affect the market price of our common stock.

We are exposed to fluctuations in currency exchange rates.

A significant portion of our business is conducted outside the United States. Therefore, we are exposed to currency exchange fluctuations in other currencies such as the New Israeli Shekel, or NIS, and the Euro, because a portion of our expenses in Israel and Europe are paid in NIS and Euros, respectively, which subjects us to the risks of foreign currency fluctuations. Our primary expenses paid in NIS are employee salaries, fees for consultants and subcontractors and lease payments on our Israeli facilities. During 2016, we entered into forward contracts and other derivative instruments to hedge against some of the risk of changes in future cash flows from payments of payroll and related expenses and costs of operations denominated in NIS.

25

The dollar cost of our operations in Israel will increase to the extent increases in the rate of inflation in Israel are not offset by a devaluation of the NIS in relation to the dollar, which would harm our results of operations.

Since a considerable portion of our expenses such as employees' salaries are linked to an extent to the rate of inflation in Israel, the dollar cost of our operations is influenced by the extent to which any increase in the rate of inflation in Israel is or is not offset by the devaluation of the NIS in relation to the dollar. As a result, we are exposed to the risk that the NIS, after adjustment for inflation in Israel, will appreciate in relation to the dollar. In that event, the dollar cost of our operations in Israel will increase and our dollar-measured results of operations will be adversely affected. We cannot predict whether the NIS will appreciate against the dollar or vice versa in the future. Any increase in the rate of inflation in Israel, unless the increase is offset on a timely basis by a devaluation of the NIS in relation to the dollar, will increase labor and other costs, which will increase the dollar cost of our operations in Israel and harm our results of operations.

Potential product liability claims could adversely affect our future earnings and financial condition.

We face an inherent business risk of exposure to product liability claims in the event that the use of our products results in adverse effects. We may not be able to maintain adequate levels of insurance for these liabilities at reasonable cost and/or reasonable terms. Excessive insurance costs or uninsured claims would add to our future operating expenses and adversely affect our financial condition.

Our principal research and development and manufacturing facilities are located in Israel and the unstable military and political conditions of Israel may cause interruption or suspension of our business operations without warning.

Our principal research and development and manufacturing facilities are located in Israel. As a result, we are directly influenced by the political, economic and military conditions affecting Israel. Since the establishment of the State of Israel in 1948, a number of armed conflicts have taken place between Israel and its Arab neighbors. During July and August 2014 and November 2012, Israel was engaged in an armed conflict with a militia group and political party which controls the Gaza Strip, and during the summer of 2006, Israel was engaged in an armed conflict with Hezbollah, a Lebanese Islamist Shiite militia group and political party. These conflicts involved missile strikes against civilian targets in various parts of Israel, including areas in which our employees and some of our consultants are located, and negatively affected business conditions in Israel.

In addition, Israeli-based companies and companies doing business with Israel, have been the subject of an economic boycott by members of the Arab League and certain other predominantly Muslim countries since Israel's establishment. Although Israel has entered into various agreements with certain Arab countries and the Palestinian Authority, and various declarations have been signed in connection with efforts to resolve some of the economic and political problems in the Middle East, we cannot predict whether or in what manner these problems will be resolved. Wars and acts of terrorism have resulted in significant damage to the Israeli economy, including reducing the level of foreign and local investment.

Furthermore, certain of our officers and employees may be obligated to perform annual reserve duty in the Israel Defense Forces and are subject to being called up for active military duty at any time. All Israeli male citizens who have served in the army are subject to an obligation to perform reserve duty until they are between 40 and 49 years old, depending upon the nature of their military service.

Our cash may be subject to a risk of loss and we may be exposed to fluctuations in the market values of our portfolio investments and in interest rates.

Our assets include a significant component of cash. We adhere to an investment policy set by our investment committee which aims to preserve our financial assets, maintain adequate liquidity and maximize returns. We believe that our cash is held in institutions whose credit risk is minimal and that the value and liquidity of our deposits are

accurately reflected in our consolidated financial statements as of June 30, 2016. Currently, we hold part of our current assets in bank deposits and part is invested in bonds, government bonds and a combination of corporate bonds and relatively low risk stocks. However, nearly all of our cash and bank deposits are not insured by the Federal Deposit Insurance Corporation, or the FDIC, or similar governmental deposit insurance outside the United States. Therefore, our cash and any bank deposits that we now hold or may acquire in the future may be subject to risks, including the risk of loss or of reduced value or liquidity, particularly in light of the increased volatility and worldwide pressures in the financial and banking sectors. In the future, should we determine that there is a decline in value of any of our portfolio securities which is not temporary in nature, this would result in a loss being recognized in our consolidated statements of operations.

The trend towards consolidation in the pharmaceutical and biotechnology industries may adversely affect us.

There is a trend towards consolidation in the pharmaceutical and biotechnology industries. This consolidation trend may result in the remaining companies having greater financial resources and technical discovery capabilities, thus intensifying competition in these industries. This trend may also result in fewer potential collaborators or licensees for our therapeutic product candidates. Also, if a consolidating company is already doing business with our competitors, we may lose existing licensees or collaborators as a result of such consolidation.

This trend may adversely affect our ability to enter into license agreements or agreements for the development and commercialization of our product candidates, and as a result may materially harm our business.

Our marketable securities include our investment in CHA shares as part of the license agreement signed with CHA in June 2013; we may be exposed to fluctuations in the market values of the shares, as well as to fluctuations in the KRW exchange rate to U.S. dollar.

As part of the CHA Agreement, in June 2013 the parties invested in each other’s equity. As of June 30, 2016, we held 400,368 CHA shares valued at $5.4 million. The shares are listed on the KOSDAQ and the shares' price is denominated in KRW. We are exposed to changes in the market price of CHA shares, as well as to exchange rates fluctuations in the KRW currency compared to the U.S. dollar.

Although our internal control over financial reporting was considered effective as of June 30, 2016, there is no assurance that our internal control over financial reporting will continue to be effective in the future, which could result in our financial statements being unreliable, government investigations or loss of investor confidence in our financial reports.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, we are required to furnish an annual report by our management assessing the effectiveness of our internal control over financial reporting. This assessment must include disclosure of any material weaknesses in our internal control over financial reporting identified by management. In addition, our independent registered public accounting firm must annually provide an opinion on the effectiveness of our internal control over financial reporting. Management's report as of the end of fiscal 2016 concluded that our internal control over financial reporting was effective. In addition, our registered independent public accounting firm provided an opinion that our internal control over financial reporting was effective as of the end of fiscal 2016. There is, however, no assurance that we will be able to maintain such effective internal control over financial reporting in the future. Ineffective internal control over financial reporting can result in errors or other problems in our financial statements. In the future, if we or our registered independent public accounting firm are unable to assert that our internal controls are effective, our investors could lose confidence in the accuracy and completeness of our financial reports, which in turn could cause our stock price to decline. Failure to maintain effective internal control over financial reporting could also result in investigation or sanctions by regulatory authorities.

Because substantially all of our officers and directors are located in non-U.S. jurisdictions, you may have no effective recourse against the management for misconduct and may not be able to enforce judgment and civil liabilities against our officers, directors, experts and agents.

Substantially all of our directors and officers are nationals and/or residents of countries other than the United States, and all or a substantial portion of their assets are located outside the United States. As a result, it may be difficult to enforce within the United States any judgments obtained against our officers or directors, including judgments predicated upon the civil liability provisions of the securities laws of the United States or any U.S. state.