



## **Pluristem Issues Letter to Shareholders**

**HAIFA, ISRAEL, January 12, 2015** - [Pluristem Therapeutics Inc.](http://www.pluristem.com) (NasdaqCM, TASE: PSTI), a leading developer of placenta-based cell therapy products, today issued a Letter to Shareholders from its chairmen and CEO, Zami Aberman.

**Dear fellow stockholders,**

Pluristem had a dynamic and exciting 2014. We reported outstanding results in a Phase 2 trial in muscle injury, continued recruitment for two ongoing clinical studies in intermittent claudication and pulmonary arterial hypertension, and laid the groundwork for additional potential clinical studies in several strategically chosen indications. In 2014 we introduced our second Placental eXpanded cell therapy product called PLX-R18 (formerly PLX-RAD); this was a direct outcome of Pluristem's unique ability to use a single cell source, the placenta, to develop multiple products. We obtained FDA, E.U., South Korean Ministry of Food and Drug Safety and Israeli Ministry of Health approvals of our high-capacity manufacturing process in our new facility, and initiated coordinated efforts to establish additional business collaborations with pharmaceutical companies currently looking for technologies and partnerships in the cell therapy arena.

Our focus for 2015 is to make significant progress in our clinical pipeline and shorten the time to market for our first product. We are intent on leveraging the new regulatory environments in the E.U. and Japan that now offer unique opportunities for accelerated paths to bring new products to market. These new pathways create substantial opportunities for Pluristem and for the cell therapy industry as a whole. We will explore these accelerated pathways for several of our current clinical indications, such as critical limb ischemia (CLI), as well as for carefully selected hematologic indications which represent substantial unmet needs that we hope to address with our second product. We will continue developing placenta-derived cell therapy products that we anticipate will lead to significant improvement in the lives of patients, and expect to demonstrate the real-world impact and value of our pipeline, technology platform and commercial-scale manufacturing capacity. In order to achieve these goals, we will continue to pursue a well-defined strategy in order to: (1) methodically advance our two products, PLX-PAD and PLX-R18, by running well-designed trials for carefully selected indications; (2) target opportunities for accelerated paths to market (3) differentiate ourselves with our advanced

manufacturing capacity and the unique technology that enables development of additional product candidates; (4) pursue advantageous partnering deals and collaborations for our technology and therapeutic products.

### **Clinical Pipeline – Continued Momentum**

In 2014 we made clear progress in advancing our pipeline. Our pipeline is focused on serious illnesses in areas of high unmet medical need. In January of 2014 we announced significant results in a muscle injury trial conducted in Germany. The injury was due to a muscle incision made intentionally in the context of standard hip replacement surgery. This study demonstrated the advantages of the PLX platform by showing that those patients treated with PLX-PAD cells achieved 6 months after surgery, a 500% improvement from baseline in the change of muscle force that could be generated by the muscle purposefully cut during surgery, as compared to placebo ( $p=0.0067$ ). This improvement in the change of muscle force was correlated with muscle volume increase. The findings strongly suggest that PLX-PAD cells could be used to improve soft tissue regeneration. We made progress in our Phase 2 intermittent claudication trial, a randomized, double blind, placebo controlled, multinational study. We added sites in South Korea to this trial, which was already underway in Israel, U.S. and Germany. As of today we have 23 active clinical sites, and expect to complete recruitment of this Phase 2 trial in 2015. We also anticipate that our partner, United Therapeutics, will complete an ongoing Phase 1 trial of PLX-PAD cells in pulmonary arterial hypertension, which will potentially lay the groundwork for a Phase 2 study.

We plan to take advantage of the new regulatory pathways in Europe and Japan to initiate advanced trials in CLI. In addition, we will progress with a Phase 2/3 trial in an orthopedic indication, which would build on our findings in muscle injury. In Europe, Adaptive Licensing now allows for limited commercialization after a successful Phase 2 trial for indications that meet defined criteria. We expect that this new legislation could attract potential strategic partners as it may feasibly shorten the time to market for our PLX product candidates. On November 25<sup>th</sup>, 2014 a new law regarding regenerative therapies, including cell therapies, came into effect in Japan. The new law allows conditional approval after limited proof of efficacy. We have been working with a Japanese consulting firm to help us with our business development initiative in that country in order to potentially partner and benefit from the new regulatory environment. We are enjoying strong interest from several pharmaceutical companies to proceed with indications in both these markets and will continue to work to foster this interest and potentially close a licensing deal.

We expect to continue to progress towards submission of an IND in 2015 for a Phase 1 trial of our PLX-PAD cells in severe preeclampsia. We believe that this study will provide important data about the safety of our cell therapy for the treatment of severe preeclampsia. In 2014, we completed positive preclinical and safety studies in both healthy pregnant animals and animal models of preeclampsia, and applied to the FDA for permission to conduct an initial clinical trial. The FDA requested additional animal studies and had some observations about the inclusion

criteria of the proposed clinical study. We will continue to actively communicate with the FDA to address their questions and to start the clinical study upon approval. In parallel, we will continue to seek orphan designation for our cells in the treatment of all preeclampsia (both moderate and severe preeclampsia). We submitted an application in 2014. The FDA has requested additional information from us before determining whether to grant orphan status. Preeclampsia is a potentially lethal complication of pregnancy with no cure for the mother except delivery of her baby; when delivery occurs remote from term there are often serious negative consequences for the baby. We are committed to the program and the potential promise it holds to address a serious, unmet medical need faced by pregnant women every year.

In 2015, as noted above, we plan to evaluate the potential of our second cell therapy product, PLX-R18, in several indications in the hematologic space. These conditions represent substantial unmet needs.

### **Passion for Innovation**

Our R&D group and Clinical and Medical Department have targeted several hematologic indications, each of which represents a significant unmet medical need. We are pleased with the substantial interest we see in our second cell therapy product, PLX-R18, and have established vibrant academic collaborations with Case Western Reserve University and Hadassah Medical Center to study it. Professors at these academic centers will conduct preclinical research to determine if PLX-R18 enhances engraftment of hematopoietic stem cells to treat deficient bone marrow. We hope to receive data from these collaborations in the coming months. The NIAID, a part of the National Institutes of Health, is also conducting preclinical trials of PLX-R18. They are studying whether the cells are an effective treatment for acute radiation syndrome (ARS), a potentially lethal condition that develops after exposure to high levels of radiation, as can occur after a nuclear disaster. Current NIAID studies focus on understanding the mechanisms by which the cells reduce mortality and enhance hematological recovery; these were examined in our previously conducted studies in a murine model of ARS.

### **Transforming Cell Therapy Manufacturing**

Building on the 2014 FDA, E.U., South Korean, and Israeli approvals of the manufacturing process in our new facility, in 2015 we will continue to assert and demonstrate that **“the process is the product”**. It has been and will continue to be central to our company strategy to carefully control every aspect of cell therapy production in order to ensure the consistent, reliable manufacture of homogeneous batches of cells. We have shown that variations in the environment in which mesenchymal-like adherent stromal cells are expanded can modify their characteristics. For example, the range and type of therapeutic proteins that our cells secrete vary according to the micro-environment in which they grow. It is this very micro-environment that we change in order to produce distinct products to target different indications. The precisely controlled and efficient development process is made possible by our first-in-class,

three dimensional cell expansion technology platform, which is protected by our patent portfolio; the portfolio includes 34 granted patents and over 120 pending applications worldwide.

Due to strong interest from outside companies, in 2015 we will seek to out-license the device we have developed to thaw cells. The device was designed to ensure the quality and consistency of the thawing process, which is needed to maintain the consistent quality and potency of any cell therapy products. Using our process, we expect that the cell products used in each of our trials, and potentially in commercialization, will be consistent in their relevant characteristics and therapeutic efficacy.

### **Program for Long-Term Growth in 2015**

We expect to continue our clinical trials in the U.S., Germany, Australia, Israel and South Korea for intermittent claudication and pulmonary arterial hypertension, and pursue opportunities presented by the new Adaptive Licensing pathway in the E.U. and the Regenerative Medicine Law in Japan. We are developing two distinct products simultaneously and are optimistic of achieving game-changing cell therapies for some of the indications that they target. We continue to develop additional discrete products using our unique technology platform. As we work to execute our business plan and achieve our clinical and business development goals, we will engage in transparent and clear communication to better showcase our potential value and achievements in 2015.

We see great opportunities to continue building our company in 2015. These opportunities are based on a foundation of great science and technology, a focus on advancing the development of effective cell therapy products that may enable a better quality of life for patients, and an organization wholly committed to working towards its goals and to effectively responding to evolving regulatory and economic prospects for success.

I am very excited about what the future holds and am confident that Pluristem will attain its goals for 2015. Our strategy is sound and our organization is aligned around our mission to enable us to develop cell therapy products for patients in need, while continuing to build our business and be a leader in our industry. Thank you for your commitment to Pluristem.

Sincerely,

Zami Aberman  
Chairman and Chief Executive Officer

## **About Pluristem Therapeutics**

*Pluristem Therapeutics Inc. is a leading developer of placenta-based cell therapies. The Company's patented PLX (PLacental eXpanded) cells are a drug delivery platform that releases a cocktail of therapeutic proteins in response to a host of local and systemic inflammatory and ischemic diseases. PLX cells are grown using the Company's proprietary 3D micro-environmental technology and are an "off-the-shelf" product that requires no tissue matching prior to administration.*

*Pluristem has a strong intellectual property position, Company-owned GMP certified manufacturing and research facilities, strategic relationships with major research institutions and a seasoned management team. For more information visit [www.pluristem.com](http://www.pluristem.com), the content of which is not part of this press release.*

## **Safe Harbor Statement**

*This press release contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995 and federal securities laws. For example, we are using forward-looking statements when we discuss our goals and plans for 2015, our plans to continue to progress our clinical trials and advance our product candidates ; our anticipation that our product candidates will lead to significant improvement in the lives of patients, our communication with the FDA; our plan to seek to out-license the device we developed to thaw cells; our plan to pursue opportunities presented by the new Adaptive Licensing pathway in the E.U. and the Regenerative Medicine Law in Japan and our expectation to attract potential strategic partners. These forward-looking statements and their implications are based on the current expectations of the management of Pluristem only, and are subject to a number of factors and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. The following factors, among others, could cause actual results to differ materially from those described in the forward-looking statements: changes in technology and market requirements; we may encounter delays or obstacles in launching and/or successfully completing our clinical trials; our products may not be approved by regulatory agencies, our technology may not be validated as we progress further and our methods may not be accepted by the scientific community; we may be unable to retain or attract key employees whose knowledge is essential to the development of our products; unforeseen scientific difficulties may develop with our process; our products may wind up being more expensive than we anticipate; results in the laboratory may not translate to equally good results in real surgical settings; results of preclinical studies may not correlate with the results of human clinical trials; our patents may not be sufficient; our products may harm recipients; changes in legislation; inability to timely develop and introduce new technologies, products and applications; loss of market share and pressure on pricing resulting from competition, which could cause the actual results or performance of Pluristem to differ materially from those contemplated in such forward-looking statements. Except as otherwise required by law, Pluristem undertakes no obligation to publicly release any revisions to these forward-looking statements to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events. For a more detailed description of the risks and uncertainties affecting Pluristem, reference is made to Pluristem's reports filed from time to time with the Securities and Exchange Commission.*

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