



New Data Show Pluristem's PLX Cells Regulate the Immune System

Study results published in peer-reviewed scientific journal

HAIFA, ISRAEL, July 27, 2015 -- [Pluristem Therapeutics Inc.](http://www.pluristem.com) (NasdaqCM: PSTI , TASE: PLTR), a leading developer of placenta-based cell therapy products, today announced the publication of a [scientific study](#) regarding PLacental eXpanded (PLX) cells in the prominent peer-reviewed journal *Stem Cells*. The paper, titled "Mesenchymal stromal cells prevent allostimulation *in vivo* and control checkpoints of Th1 priming: migration of human DC to lymph nodes and NK cell activation", describes the findings of a recent mechanism of action study conducted by independent scientists at the Berlin-Brandenburg Center for Regenerative Therapy at Charité - University Medicine Berlin. The paper was co-authored by scientists from the Charité and Pluristem.

The study demonstrated mechanisms by which PLX cells and other mesenchymal stromal cells (MSC) influence the immune system in order to modulate immune reactions and to prevent immune reactions against the cells when they are administered as an off-the-shelf product (unmatched). It was demonstrated *in vitro* that MSC, and in particular PLX cells, control the induction of an immune response at several points. The main target for MSC and PLX cells in this process are dendritic cells, which are the key player in inducing a T-cell immune response. Moreover, *in vivo* data from patients suffering from critical limb ischemia who were treated with PLX cells in a phase I/II study confirmed that HLA-unmatched PLX cells did not provoke an immune response in immunocompetent patients. These findings confirm the feasibility of using PLX cells in an off-the-shelf manner, and explain the mechanisms that make this possible.

"Our findings in this study provide novel evidence for the regulation of several checkpoints of T-cell priming by PLX cells and other MSC, via modulation of the crosstalk between myeloid dendritic cells and natural killer cells. While the complete mechanism of immunomodulation by PLX cells requires further investigation, this study demonstrates how PLX cells might inhibit the immune responses of Type 1 T helper cell," stated the study's Principal Investigator, Dr. Hans-Dieter Volk, Director of the Berlin-Brandenburg Center for Regenerative Therapy and head of the Institute of Medical Immunology at the Charité.

"The investigation of the interaction between unmatched PLX cells and patient immune systems is central to Pluristem's clinical research. This research may lead to a new understanding of how PLX cells influence, and potentially heal, the immune system, thereby possibly expanding the use of PLX cells for new indications," stated Pluristem CEO Zami Aberman. "By modulating a patient's immune response, PLX cells could potentially help treat severe diseases of the immune

system such as aplastic anemia, which has been designated as an orphan indication, autoimmune diseases such as multiple sclerosis and lupus, as well as graft versus host disease (GVHD),” Aberman added.

Additional Findings from the Study

PLX cells, and other MSC, affected complex pathways in order to prevent the priming of Type 1 T helper cell (Th1) responses towards major histocompatibility complex mismatches. The study utilized both *in vitro* and *ex vivo* data from PLX cells and other MSC. *In vivo* evidence came from patients in a study of PLX cells for critical limb ischemia. Peripheral blood mononuclear cells (PBMC), collected from the patients at different time points after PLX injection, were re-stimulated with the corresponding PLX-PAD cells or unrelated third party donor PBMC. The *in vivo* induced memory Th1 response was measured by using the IFN- γ Elispot test. There was no, or only very marginal, Th1 priming specific for the MHC-mismatch even after application of high-dose allogeneic PLX cells. Collectively, the study data indicated that MSC, and in particular PLX cells, inhibit the priming of Th1-driven immune responses via modulation of myeloid dendritic cell (mDC). The maturation, migration to stimulatory chemokines, and the release of NK and T-cell stimulating cytokines of mDC are inhibited by PLX cells and some other MSC. For example, mDC exposed to PLX/MSC secreted reduced levels of IL-12p70 and IL-1 β and increased levels of IL-10 and IL-1Ra, representing a cytokine profile typical for tolerogenic dendritic cells (ToDC), which are required for the development and maintenance of immunological tolerance.

About the Berlin-Brandenburg Center for Regenerative Therapy

The [Berlin-Brandenburg Center for Regenerative Therapy](#) was established as an interdisciplinary translational center with the aim of enhancing endogenous regeneration by cells, biomaterials, and factors which can be used to develop and implement innovative therapies and products. The primary focus of the Center is on diseases of the immune system, the musculoskeletal system and the cardiovascular system for which only insufficient treatment options are available.

About Pluristem Therapeutics

[Pluristem Therapeutics Inc.](#) is a leading developer of placenta-based cell therapy products. The Company has reported robust clinical trial data in multiple indications for its patented PLX (PLacental eXpanded) cells. The cells release a cocktail of therapeutic proteins in response to inflammation, ischemia, hematological disorders, and radiation damage. PLX cell products are grown using the Company's proprietary three-dimensional expansion technology. They are off-the-shelf, requiring 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.

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 the findings of the scientific study and the evidence they provide, that the research may lead to a new understanding of how PLX cells influence and potentially heal the immune system through paracrine and endocrine effects, and opens the window for the use of PLX cells for new indications, or that the data from the study suggest the potential for PLX cells to treat a range of severe conditions related to immune function, or that PLX cells could potentially help treat diseases of the immune system such as aplastic anemia, and autoimmune diseases such as multiple sclerosis, lupus and graft versus host disease (GVHD). 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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