ASX Release

FDA Allows PTX IND for Leukemia Phase Ib & II Trials

- PTX now has four FDA approved INDs demonstrating the strength of its cancer treatment assets
- Follows Phase I study that demonstrated 17 out of 32 patients achieved disease stabilization. These were patients with advanced leukemia with few remaining treatment options

Melbourne, Australia 8 January 2016: Clinical stage oncology company Prescient Therapeutics Ltd (PTX) has secured US Food and Drug Administration (FDA) approval for its Investigational New Drug (IND) application for the forthcoming Phase Ib and Phase II clinical trial and program in acute myeloid leukemia (AML).

The study will combine PTX's lead drug candidate, the novel Akt inhibitor PTX-200, together with the chemotherapeutic agent cytarabine, in refractory or relapsed patients with AML.

The Phase Ib and Phase II studies will be led by hematologist Professor Jeffrey Lancet at the Moffitt Cancer Center and Research Institute (Moffitt) in Tampa, FL USA .

Professor Lancet was a Principal Investigator on single agent PTX-200's earlier Phase I AML clinical trial conducted at the Moffitt and MD Anderson Cancer Center in patients with advanced hematologic malignancies. The study showed that 17 out of 32 patients treated with PTX-200 exhibited stable disease, and three patients with AML had significant responses, with bone marrow blast reductions of over 50%.

These results were all the more encouraging when considering their advanced disease stage, the normally rapid progression of these diseases and the absence of therapeutic options.

These promising results demonstrate that PTX-200 may have significant efficacy in AML, especially in patients with aberrantly hyper-activated Akt.

PTX Chief Scientific Officer Professor Said Sebti, said, "This is another validation of PTX assets and further cements the close relationship between Moffitt and PTX. We are fortunate to have Professor Lancet as the Principal Investigator on the trial given his vast experience with leukemia and his detailed working knowledge of our drug."

PTX Chairman Mr Steve Engle, said, "For most US investors and pharmaceutical companies an FDA IND is the "gold standard" pathway for developing a drug. This is an important milestone for PTX that sets key development parameters agreed with the world's most important regulatory agency."

"Remarkably, PTX now has four open INDs with the FDA, which represents a particularly valuable pipeline with increasingly promising commercial potential especially compared with other ASX biotech companies."

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Clinical Study Details

The new study has two parts, a Phase Ib study part and a Phase II study.

The Phase Ib study will enroll 15-18 patients and is an open-label, dose escalation study, using a standard design for dose escalation and for determining the safe dose to be used in combination with cytarabine in the Phase II part of the study. Four dose levels will be evaluated, with the initial dose level of 25 mg/m^2 PTX-200. Each dose level will be increased by 10 mg/m^2. Doses will be administered for a maximum of four 21-day cycles. Safety and clinical activity will be evaluated at the end of each cycle.

The Phase II study is open-label with administration of the recommended phase dose of PTX-200 for two 21-day cycles.

PTX-200 will be co-administered with cytarabine in both the Phase I and Phase II parts of the study. In determining the maximum tolerated dose (MTD), this study may also enroll patients with other forms of acute leukemia, including Acute Lymphoblastic Leukemia (ALL) and blast phase Chronic Myeloid Leukemia (CML).

The primary objectives are to:

- Determine the safety and MTD of PTX-200 given in combination with cytarabine in relapsed or refractory acute leukemia or relapsed or refractory blast phase CML (Phase I); and
- Determine clinical activity of PTX-200 + cytarabine in first relapsed AML (Phase II).

The secondary objectives are:

- To assess the effect of PTX-200 on phospho-Akt (p-Akt) signaling, proliferation and apoptosis within leukemia cells;
- Correlative studies to determine baseline p-Akt expression and signaling within leukemic blasts and the ability of PTX-200 to downregulate p-Akt signaling, to inhibit proliferation and induce apoptosis; and
- To evaluate the pharmacokinetics of PTX-200.

About AML

AML is a form of cancer that affects the blood and bone marrow, resulting in the overproduction of immature white blood cells, preventing the sufferer from producing normal blood cells and therefore rendering them unable to fight infections, to prevent bleeding and may become anemic. AML remains a largely incurable illness, with 5 year survival rates of less than 30%.[1]

AML is the most common acute leukemia in adults, with an estimated 20,830 new cases diagnosed and an estimated 10,460 deaths in the US alone in 2015.[2] The projected number of new cases for 2015 increased by 7,000 (i.e. over 50%) from that in 2013.[2,3]

For relapsed AML, in general, remission rates are low (especially if the initial complete response (CR) duration is less than 1 year), remission duration is short (generally on the order of 3-6 months), and overall survival is less than 1 year.[4] Older individuals (>60 years) experience both inferior CR and survival rates following initial therapy.[5,6] Hence, newer, effective therapies are greatly needed for both older patients as well as those with relapsed or refractory disease. This is precisely the area that PTX-200 is targeting.

About PTX-200

PTX-200 is a novel and selective Akt activation inhibitor. It is both anti-proliferative and pro-apoptotic.

Most Akt inhibitors seek to work by mimicking ATP, a molecule used by all kinases in the cells, and therefore off target effects are likely to result in toxicities.

By contrast, the mechanism by which PTX-200 inactivates Akt is not by inhibiting its kinase, but rather by binding to the PH domain of Akt and preventing its binding to the plasma membrane where it must be localized to be phosphorylated and activated.[7] Therefore, by preventing Akt binding to the plasma membrane, PTX-200 inhibits Akt, but without the off target toxic effects of kinase inhibitors.

Hyperactive Akt is a prominent feature of many human cancers and is correlated with resistance to chemotherapy. Please refer to Appendix 1 at the end of this announcement for a more detailed rationale for combining PTX-200 with cytarabine in AML.

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APPENDIX 1

Rationale for Combined Therapy with PTX-200 and Cytarabine in AML

Signal transduction pathways play an important role in the homeostasis, growth, and survival of cells. One such signal transduction pathway, comprises the lipid kinase, phosphatidylinositol 3-kinase (PI3K), and the protein serine/threonine kinase, Akt. Persistent hyper-activation of the PI3K/Akt axis occurs frequently in human cancers, causing uncontrolled cell growth, survival, invasion and metastasis, and serving as an important mode of neoplastic propagation and resistance to cytotoxic therapies. As such, this pathway is an attractive target for the development of novel therapeutic strategies in many different malignancies.

In the setting of hematologic malignancies, particularly AML, the PI3K/Akt signaling pathway appears to be critical for cell survival. Several investigators have demonstrated that this pathway is hyper-activated in AML from cell lines and fresh biopsies.[8-10] In addition, the persistent activation status of this pathway positively affects leukemic cell survival and inhibition of this pathway including the use of PI3K inhibitors induces apoptosis.[8,11] The hyper activation of this pathway (high phosphor-Akt levels at baseline) is associated with poor overall survival of AML patients.[10]

Another intriguing aspect of the PI3K/Akt pathway is its potential role as a mediator of resistance to cytotoxic chemotherapy in many cancers, including AML. In primary patient AML cells and cell lines, it has been demonstrated that Akt activation is protective against chemotherapeutic agents, including cytarabine and etoposide.[8] When added to chemotherapeutic compounds, pharmacologic inhibitors of the PI3K/Akt pathway have been shown to synergize with chemotherapy in eliciting apoptosis within leukemic cells, suggesting the importance of this pathway in mediating chemotherapy resistance in AML.[8,12,13] Mechanistically, the importance of the PI3K/Akt pathway in chemotherapy resistance is becoming better understood. In AML, the cytoprotective effect induced by leukemic adherence appears to be mediated by PI3K/Akt activation, such that by pharmacologically inhibiting PI3K, the protective effect from adherence is abrogated.[14] Other recent evidence has also highlighted the importance of PI3K/Akt for the upregulation of multidrug resistance-associated protein 1, an important multidrug resistance modulator.[15] Taken together, these findings suggest a potential role for combining cytotoxic chemotherapy with pharmacologic inhibitors of PI3K/Akt in AML.

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About Prescient Therapeutics Limited (PTX)

PTX is a clinical stage oncology company developing novel compounds that show promise as potential new therapies to treat a range of cancers that have become resistant to front line chemotherapy.

Lead drug candidate PTX-200 inhibits an important tumor survival pathway known as AKT, which plays a key role in the development of many cancers, including breast and ovarian cancer, as well as leukemia. This highly promising compound is now the focus of two current clinical trials. The first is a Phase Ib/II study examining PTX-200 in breast cancer patients at the prestigious Montefiore Cancer Center in New York and the H. Lee Moffitt Cancer Center in Tampa, Florida. A Phase Ib/II trial of the compound in combination with current standard of care is also underway in patients with recurrent or persistent platinum resistant ovarian cancer at the Moffitt Cancer Center. These trials are funded in part by grants from the U.S. National Cancer Institute. In addition, PTX is planning the above-described Phase Ib/II trial evaluating PTX-200 as a new therapy for Acute Myeloid Leukemia.

PTX's second novel drug candidate, PTX-100, is a first in class compound with the ability to block an important cancer growth enzyme known as geranylgeranyl transferase (GGT). It also blocks the Ral and Rho circuits in cancer cells which act as key oncogenic survival pathways, leading to apoptosis (death) of cancer cells. PTX-100 was well tolerated and achieved stable disease in a Phase I trial in advanced solid tumors.

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