



ASX Release

Prestigious *Nature* Publication Highlights Novel PTEN Cancer Approach with Prescient's PTX-100

- PTX-100 effective in inhibiting newly-identified cancer causing pathway
- The combination of PTX-100 and photodynamic therapy is highly effective in cancers with defective PTEN
- Potential to also combine PTX-100 with PTX-200 in PTEN defective cancers

Melbourne, Australia (19 June 2017): Clinical-stage oncology company Prescient Therapeutics Ltd (ASX: PTX; Prescient) announced that a pre-clinical study published in the scientific journal *Nature* this week indicates that Prescient's geranylgeranyl transferase inhibitor GGTI-2418, known as PTX-100, plays a key role in mitigating a new cancer pathway discovered by Professor Michele Pagano at New York University's Langone Medical Center, in New York. *Nature* is regarded as one of the world's most cited and prestigious scientific publications.

In the study, Professor Pagano's group in collaboration with Prescient's Chief Scientific Officer Professor Said Sebti, demonstrated new details about the tumor suppressor gene, PTEN, which is defective in 30-60% of certain breast, brain and uterine cancers.

"When defective, PTEN cannot control a protein known as FBXL2, which is thought to be responsible for cancer growth in many patients." said Professor Pagano.

Professor Pagano's study also showed in mouse models that when administered with Prescient's drug candidate PTX-100, plus photodynamic therapy, FBXL2 is "switched-off" allowing abnormal cells to self-destruct. Therefore, patients whose tumors harbor defective PTEN may also be more likely to respond to a combination of PTEN and photodynamic therapy.

Professor Said Sebti said "These findings have important translational implications for Prescient as patients whose tumors harbor defective PTEN may be more likely to respond to a combination of PTX-100 and photodynamic therapy."

"Furthermore, given that PTEN is known to also suppress the Akt tumor survival pathway, patients with PTEN defective tumors could respond to a combination of PTX-100 and an Akt inhibitor like PTX-200."

Prescient's CEO and Managing Director, Steven Yatomi-Clarke said "This discovery of a new cancer-causing pathway targeted by PTX-100 is an exciting development for Prescient. Our precision medicine strategy uses targeted therapies to address specific cancer mutations. Therefore, this discovery opens up a new frontier of clinical possibilities for PTX-100."



PTEN has been the subject of cancer research for many years, but this new study is very exciting in showing a novel way in which defective PTEN adds to cancer risk, and more importantly, demonstrates that it can be inhibited with PTX-100.”

PTX-100 was developed by Professor Sebti, Chair of the Department of Drug Discovery at H. Lee Moffitt Cancer Center, and Chief Scientific Officer at Prescient Therapeutics, and NYU President Andrew Hamilton while he was at Yale University. PTX-100 has already been tested as a single agent in patients with advanced solid tumors in a Phase 1 trial and will be the focus of studies in rare hematological malignancies.

The *Nature* publication can be previewed at www.nature.com.

ENDS

FBLX2

FBXL2 is a cancer-causing protein in tumors where PTEN is defective prompting the researchers to look for ways to block FBXL2 in these cancers. To this end, they took advantage of the fact that FBXL2 requires a piece of lipid called geranylgeranyl to localize in the ER membrane near IP3R3, and disabled FBXL2 with GGTI-2418, a drug that blocks the attachment of geranylgeranyl to proteins.

GGTI-2418 was developed by Said Sebti, Chair of the Department of Drug Discovery at Moffitt Cancer Center, and Chief Scientific Officer at Prescient Therapeutics, and NYU President Andrew Hamilton while he was at Yale University. Currently being clinically developed by Prescient Therapeutics, GGTI-2418 (PTX-100) has already been tested as a single agent in patients in a Phase 1 trial, and will enter clinical trials in combination with other drugs.

Photodynamic Therapy

Photodynamic therapy (PDT) is a treatment that uses special drugs, called photosensitizing agents, along with light to kill cancer cells. The drugs only work after they have been activated or “turned on” by certain kinds of light.

Experiments showed that PDT significantly reduced tumor weight and cancer growth rate in mice where PTX-100 made sure that IP3R3 was there to trigger cell death. PDT had little effect on cancer cells with depleted supplies of PTEN or IP3R3. Pagano says his team in collaboration with Sebti’s team is set to study next the effect of combining GGTI-2418 with PDT in patients with low PTEN, as well as the combination of GGTI-2418, PDT and P13K/AKT inhibitors.

Also of note, the research team found that blocking the ability of FBXL2 to target IP3R3 with GGTI-2418 made tumors in mice more vulnerable to photodynamic therapy or PDT. PDT, which is based on the ability of photosensitizer drugs to cause cytotoxicity after irradiation with visible light, has been applied in the clinic with encouraging results to treat non-small cell lung cancer, dermatological cancers, and premalignant lesions of the upper digestive tract, and is currently in clinical trials for treatment of a large variety of other malignancies, including prostate, brain, and breast cancers.

About Prescient Therapeutics Limited (Prescient)

Prescient 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.



Prescient's 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. Unlike other drug candidates that target Akt inhibition which are non-specific kinase inhibitors that have toxicity problems, PTX-200 has a novel mechanism of action that specifically inhibits Akt whilst being comparatively safer. This highly promising compound is now the focus of three current clinical trials, currently on clinical hold. The first is a Phase 1b/2 trial evaluating PTX-200 as a new therapy for relapse and refractory Acute Myeloid Leukemia, being conducted at Florida's H. Lee Moffitt Cancer Center (Moffitt); Yale Cancer Center in New Haven, Connecticut (Yale) and Kansas University Medical Center (KUMC) under the leadership of Professor Jeffrey Lancet, MD.

Prescient is also conducting a Phase 1b/2 study examining PTX-200 in breast cancer patients at the prestigious Montefiore Cancer Center in New York and the Moffitt. The third trial is a Phase 1b/2 trial of PTX-200 in combination with current standard of care is also underway in patients with recurrent or persistent platinum resistant ovarian cancer at the Moffitt.

Prescient'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 1 trial in advanced solid tumors and will be the focus of studies in rare hematological malignancies.

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