US FDA Allowance of IND for PTX-100 Phase 2 Trial

MELBOURNE Australia, 23 December 2024: Prescient Therapeutics Limited (ASX: PTX), a clinical-stage oncology company developing innovative therapies to combat cancer, is pleased to announce that the U.S. Food and Drug Administration (FDA) has cleared the Investigational New Drug (IND) application for the Phase 2 clinical trial of PTX-100, the company's first-in-class Ras pathway inhibitor. The trial will focus on relapsed and refractory cutaneous T-cell lymphomas (r/r CTCL). The IND allowance paves the way for the commencement of the Phase 2 study, and marks a significant milestone for Prescient. PTX-100 has Orphan Drug Designation from the US FDA for all T-cell lymphomas.

The Phase 2 trial builds on compelling Phase 1b data demonstrating PTX-100's potential to address key unmet medical needs in T-cell lymphomas (TCL), including r/r CTCL. The Phase 1b study has enrolled 19 TCL patients and reported an excellent safety profile of PTX-100 at 500, 1,000 and 2,000 mg/m^2. To date, there has been a 42% overall response rate amongst all evaluable TCL patients. 5 out of 7 evaluable CTCL patients received clinical benefit. Responders had a median progression-free survival (PFS) of 12.2 months, surpassing the typical median PFS of approximately 3.1 months associated with standard care treatment vorinostat. The Phase 1b trial remains open, with one patient (a complete responder) still remaining on treatment.

Phase 2 protocol summary

Target patient population: r/r CTCL patients with advanced disease. Patients must have received and failed at least two prior lines of systemic therapy.

Study Sites: 15 sites globally, including Australia, US and eventually Europe. The trial will be led out of Melbourne under the Principal Investigator, global TCL expert professor H. Miles Prince, AM.

The trial will be in two parts: dose optimisation (optimal biologically effective dose) and efficacy. Prescient remains hopeful that the FDA will consider the Ph2b data as a registrational study.

Phase 2a: Dose optimisation of up to 40 patients, with two groups of up to 20 patients randomised either 500 or 1,000 mg/m^2 of PTX-100 A safety review committee (SRC) will meet to determine the optimum dose for Phase 2b. An interim analysis may be undertaken.

Phase 2b: Efficacy and safety determination in approximately 75 r/r CTCL patients.

Primary endpoint: Objective response rate (i.e. proportion of patients with complete or partial responses).

Secondary endpoints: Skin responses, progression free survival; duration of response; time to response; complete response rate; overall survival; time to next treatment; safety; pharmacokinetics and quality of life.

Key risks: Drug development involves many inherent risks. Key risks and mitigations include:

Risk	Mitigation strategy
Enrolment rates may be slower than expected, which may impact timelines	Work with CRO for optimal site selection; close monitoring of site enrolment; identification of back-up sites; regular KOL engagement
Safety issues may arise	Closely monitor patients for adverse events; undertaking additional drug-drug interaction studies in parallel to Phase 2a; exclusion criteria to minimise enrolment of potentially vulnerable patients
PTX-100 may not perform as well as expected or required	This study is evaluating PTX-100 as a monotherapy. Future studies should evaluate beneficial combinations with other TCL therapies.

Prescient CEO and Managing Director, Steven Yatomi-Clarke, commented: "The FDA's clearance of our IND for PTX-100 is a transformative milestone for Prescient. This achievement is the culmination of tireless work from the Prescient team this year, and builds upon years of rigorous preclinical and clinical development, positioning us to unlock the therapeutic and commercial potential of PTX-100. Prescient thanks the clinical and industry experts who have provided valuable feedback into the study design, which adds to the confidence we have of this program. We look forward to commencing the study with world leaders in CTCL, and hope to bring a safe and effective therapy to this area of unmet patient need."

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About Prescient Therapeutics Limited (Prescient)

Prescient Therapeutics (ASX: PTX) is a clinical stage oncology company developing personalised medicine approaches to cancer, including targeted and cellular therapies.

Targeted Therapy

PTX-100 is a first in class compound with the ability to block an important cancer growth enzyme known as geranylgeranyl transferase-1 (GGT-1). It disrupts oncogenic Ras pathways by inhibiting the activation of Rho, Rac and Ral circuits in cancer cells, leading to apoptosis (death) of cancer cells. PTX- 100 is believed to be the only GGT-1 inhibitor in the world in clinical development. PTX-100 demonstrated safety and early clinical activity in a previous Phase 1 study and recent PK/PD basket study of hematological and solid malignancies. PTX-100 is now in a Phase 1b expansion cohort study in T cell lymphomas, where it is showing encouraging efficacy and safety. The US FDA has granted PTX-100 Orphan Drug Designation for all T-cell Lymphomas. A Phase 2 study focussing on cutaneous T-cell lymphomas is underway.

Cell Therapy Platforms

CellPryme-M: Prescient's novel, ready-for-the-clinic, CellPryme-M technology enhances adoptive cell therapy performance by shifting T towards a central memory phenotype, improving persistence, and increasing the ability to find and penetrate tumours. CellPryme-M is a 24-hour, non-disruptive process during cell manufacturing. Cell therapies that could benefit from additional productivity in manufacturing or increased potency and durability in-vivo, would be good candidates for CellPryme-M.

CellPryme-A: CellPryme-A is an adjuvant therapy designed to be administered to patients alongside cellular immunotherapy to help them overcome a suppressive tumour microenvironment. CellPryme-A significantly decreases suppressive regulatory T cells; increases expansion of CAR-T cells in vivo; increases tumour penetration of CAR-T cells. CellPryme-A improves tumour killing and host survival of CAR-T cell therapies, and these benefits are even greater when used in conjunction with CellPryme-M pre-treated CAR-T cells.

OmniCAR: is a universal immune receptor platform enabling controllable T-cell activity and multi- antigen targeting with a single cell product. OmniCAR's modular CAR system decouples antigen recognition from the T-cell signalling domain. It is the first universal immune receptor allowing post- translational covalent loading of binders to T-cells. OmniCAR is based on technology licensed from Penn; the SpyTag/SpyCatcher binding system licensed from Oxford University; and other assets. OmniCAR is in pre-clinical development.

The targeting ligand can be administered separately to CAR-T cells, creating on-demand T-cell activity post infusion and enables the CAR-T to be directed to an array of different tumour antigens. OmniCAR provides a method for single-vector, single cell product targeting of multiple antigens simultaneous or sequentially, whilst allowing continual re-arming to generate, regulate and diversify a sustained T-cell response over time.

Find out more at www.ptxtherapeutics.com or connect with us via X @PTX_AUS and LinkedIn.

The Board of Prescient Therapeutics Limited has approved the release of this announcement.

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Supplemental COVID-19 Risk Factors

Please see our website: Supplemental COVID-19 Risk Factors