# PTX-100 Phase 1b study demonstrates excellent safety and promising efficacy in T-cell lymphoma patients

## Key points

- **Phase 1 recruitment of 25 patients completed, including 19 r/r TCL patients**
- **Study endpoints (safety; PK; PD) successfully met**
- **Excellent safety profile, with no drug-related SAEs**
- **Preliminary efficacy observed in r/r TCL patients exceeding that expected from standard of care (SoC)**
    - **Clinical responses in 4/9 assessable patients (44%)**
    - **Clinical benefit rate of 6/9 (66%)**
    - **Impressive durability, with median progression-free survival (PFS) of 12.2 months**
- **Planning to initiate Phase 2 trial in 2024**

**MELBOURNE Australia, 11 December 2023:** Prescient Therapeutics (ASX: PTX), a clinical stage oncology company developing personalised therapies for cancer, is pleased to announce results from its Phase 1b study of PTX-100 in patients with advanced malignancies, with a focus on patients with relapsed and refractory T-cell lymphomas (r/r TCL). The results were presented at the prestigious American Society of Hematology (ASH) Annual Meeting in San Diego, California.

In summary, the study successfully achieved its primary objectives of demonstrating safety and determining pharmacokinetics (PK) and pharmacodynamics (PD), and also successfully demonstrated preliminary efficacy in r/r TCL patients exceeding that expected from standard of care. Phase 1b recruitment is completed, although several patients remain on study. Prescient is currently working diligently towards a Phase 2 trial in r/r TCL, due to start around mid-2024, which will be a major catalyst for the company.

## Aims

The aim of this Phase 1 study was to evaluate the safety, PD and PK and preliminary efficacy of PTX-100 administered in increasing doses in patients with advanced malignancies. Given that efficacy was observed early in patients with r/r TCL, this patient population became the focus of an expansion cohort.

## Trial design

This Phase 1b consists of a 3+3 dose escalation at doses of 500, 1000 and 2000 mg/m$^2$ PTX-100. PTX-100 is administered by intravenous infusion over 60 minutes on days 1 to 5 of a 14 day cycle for 4 cycles. Disease response is assessed via CT, MRI or PET-CT or per standard of care after 4 cycles. Patients with a complete response (CR), partial response (PR) or stable disease (SD) may be eligible for continued treatment with PTX 100, dosed in 21 day cycles with response assessment every 3 months.

Recruitment took place at Epworth under the leadership of Principal Investigator, Professor H. Miles Prince, AM. Solid tumour patients for the early dose-escalation component of the study were also recruited at PASO Medical in Victoria. Recruitment has concluded, but four patients currently remain on study.

## Results

**Patient demographics**
25 patients with advanced malignancies were recruited to the study, comprising 19 patients with r/rTCL, of whom 11 had peripheral TCL (PTCL) and 8 had cutaneous TCL (CTCL). R/r TCL patients had failed a median of 3 prior lines of therapy, and maximum of 6 prior lines of therapy.

Six non-TCL patients were recruited to the dose escalation component of the study to assess safety (three pancreatic cancer patients; two colorectal cancer patients; and one myeloma patient). Overall, the age range of patients was 44-81 years, with a median age of 69 years. Seven patients were female and 18 patients were male.

**Safety**
PTX-100 was extremely well tolerated at all doses. There were no serious adverse events that were related to PTX-100.

Overall, PTX-100 has exhibited an excellent safety profile, especially in light of the fragile patient population and the relatively high toxicities of many incumbent therapies for r/r TCL.

**Efficacy**
Efficacy was determined by follow-up scans at the end of cycle 4 of treatment (C4). Nine patients were determined to be eligible for efficacy assessment so far. No efficacy was observed in the non-TCL patients.

Two r/r PTCL patients and two r/r CTCL patients experienced clinical responses, including two r/r PTCL patients with CRs (complete eradication of disease), for an overall response rate (ORR) of 4/9, or 44%. Additionally, two CTCL patients had durable SD greater than 6 months, for a clinical benefit rate of 6/9, or 66%.

Prescient and its investigators consider an ORR over 30% and a CBR over 45% to be promising for a drug in r/r TCL.

**Table 1: Response Rates & Clinical Benefit Rates**

| Evaluable for Response | Overall Response Rate<br>CR + PR | Clinical Benefit Rate<br>CR + PR + SD>6months |
|---|---|---|
| r/r PTCL (n=4) | 50% (2/4) | 50% (2/4) |
| r/r CTCL (n=5) | 40% (2/5) | 80% (4/5) |
| r/r TCL (n=9) | 44% (4/9) | 66% (6/9) |

Durations of responses were impressive, with median PFS of 12.2 months for all assessable r/r TCL patients; 13.6 month for r/r CTCL and 7.4 months for r/r PTCL.

For context, several key opinion leaders consider that a benchmark median PFS for a registration study in r/r TCL is 5-6 months[1].

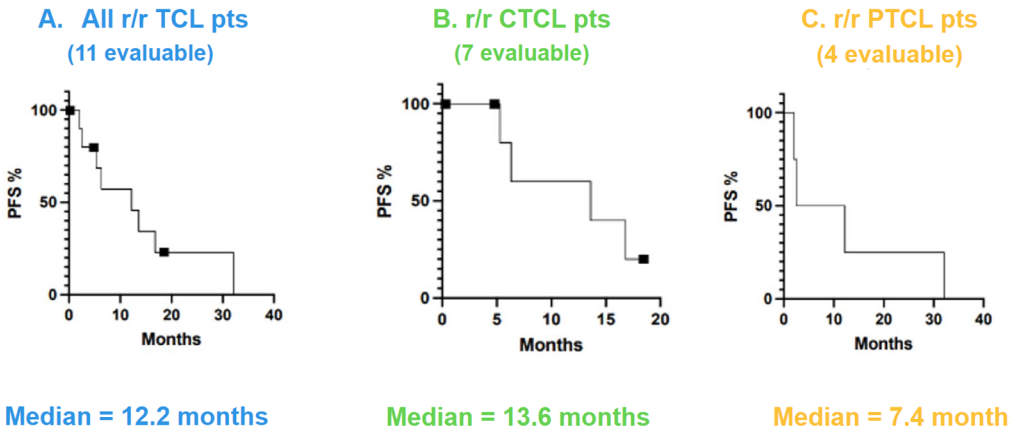


**Figure 1: median time to progression.** Patients with follow up assessment at end of cycle 4 plus two ongoing patients not yet at cycle 4, were included. **A.** all evaluable r/rTCL patients; **B.** all available r/r CTCL patients; **C.** all available r/r PTCL patients. Black squares represent patients still on study.

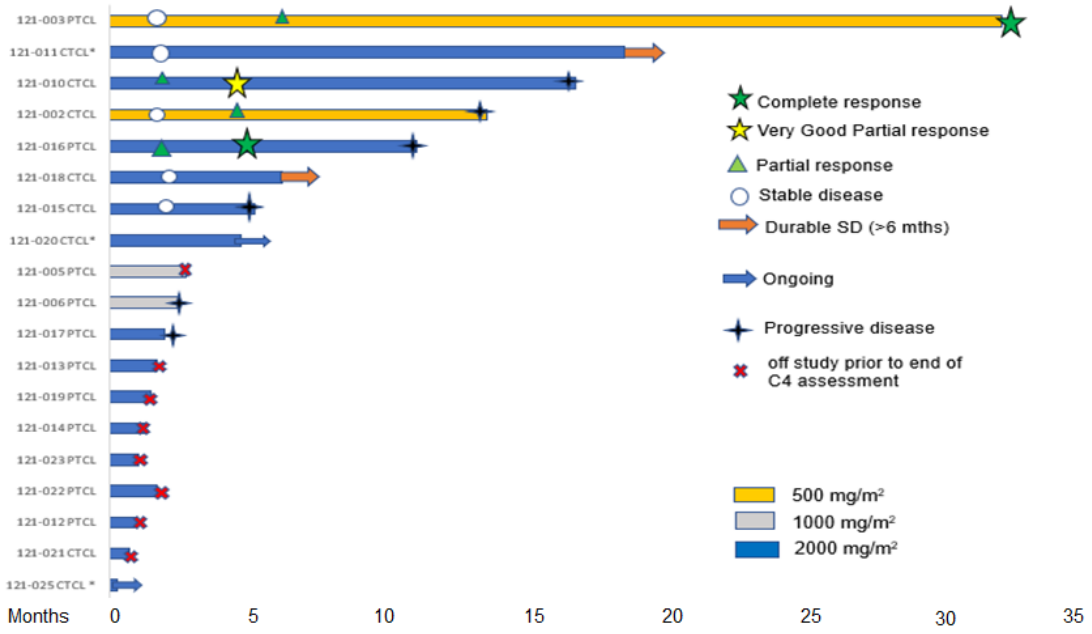


**Figure 2. Months on study swimmer plot for r/r TCL patients.** The two TCL patients in the 500 mg/m$^2$ dose remained on study for 14 (CTCL) and 32 (PTCL) months. Patients marked with a red cross withdrew before the end of cycle 4. Patient 003 is off study and assessed as CR.

[1] S.M. Horowitz *et al*; Blood Dec 2021

## Conclusion

This Phase 1b trial has successfully met its objectives. PTX-100 indicates promising safety profile and well-tolerated up to 2,000 mg/m$^2$ in this difficult to treat patient population.

PD studies demonstrated that PTX-100's target, GGT-1, was engaged at all 3 doses with sustained inhibition demonstrated over 72 hours after the day 5 dose.

Although efficacy was not the focus of this Phase 1b study, clinical activity is demonstrated in evaluable r/rTCL patients with an ORR of 44% (4/9), and a median PFS of 12.2 months, which compares very favourably with responses expected using standard of care therapies in this patient population, which is generally expected to be an ORR of around 30% and median PFS of 4 months.

## Next steps

Following the success of the Phase 1 study, Prescient is now planning a Phase 2 study in r/r TCL. As recently disclosed, Prescient is currently designing the study with input from key opinion leaders and regulatory consultants ahead of an FDA meeting Q1/Q2 2024; with the aim of opening the study around mid 2024. A manufacturing campaign is also underway to supply this study.

## Commentary

Principal Investigator of the study, and globally renowned haematologist, Professor H. Miles Prince A.M, said, "These Phase 1b results highlight the excellent tolerability of PTX 100 among TCL patients. Beyond monotherapy, PTX's excellent safety profile make it a viable option for exploring combination therapies in the future."

"In addition to PTX-100's safety, early indications suggest promising efficacy in both systemic and cutaneous T cell lymphomas, as evidenced by several patients exhibiting clinical responses and others demonstrating durable stable disease. Notably, the median PFS of 12.2 months surpasses the usual expectations associated with standard care treatments, which typically yield a median PFS of around 4 months."

"This compelling outcome fuels my enthusiasm to advance into a Phase 2 study. I am hopeful that expanding this research will provide a beacon of hope for patients facing limited treatment options and poor anticipated outcomes."

Prescient CEO and Managing Director, Steven Yatomi-Clarke, said, "Prescient is very pleased with the data from this Phase 1b study in patients with relapsed and refractory TCL. The data has surpassed our expectations, from both safety and early efficacy perspectives, especially in this difficult to treat patient population. The team is working judiciously with its advisors in planning and working towards the Phase 2 study, which Prescient believes will be a watershed moment for the company."

- Ends -

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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 Therapies*

**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.

**PTX-200** is a novel PH domain inhibitor that inhibits an important tumour 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, PTX-200 has a novel mechanism of action that specifically inhibits Akt without non-specific kinase inhibition effects. PTX-200 is currently in a Phase 1b/2 trial in relapsed and refractory AML, where it has resulted in 4 complete remissions so far. PTX-200 previously generated encouraging Phase 2a data in HER2-negative breast cancer and Phase 1b in recurrent or persistent platinum resistant ovarian cancer.

### *Cell Therapies*

**CellPryme-M:** Prescient's novel, ready-for-the-clinic, CellPryme-M technology enhances adoptive cell therapy performance by shifting T and NK cells 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 Twitter @PTX_AUS and LinkedIn.

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

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