

ASX Release

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REDUCTION OF A FURTHER CANCER MARKER (p-4E-BP1) CONFIRMS PPL-1 ACTIVE IN HUMAN CANCER TRIAL

PharmAust Limited ("PharmAust") (ASX: PAA & PAAO) is pleased to report that analysis of a further cancer marker, 4E Binding Protein 1 (p-4E-BP1), in the white blood cells from patients that have received PPL-1 at the Royal Adelaide Hospital (RAH) has shown a meaningful reduction. Four out of five patients treated with PPL-1 showed a reduction in this cancer marker. Malignancy is often characterised by changes to various cancer markers. Tumour markers are used to help detect, diagnose, and manage various types of cancer. A decrease in the level of a tumour marker may indicate that the cancer is responding to treatment, whereas no change or an increase may indicate that the cancer is not responding.

Research published in peer review journals^{1,2,3} has shown that phosphorylated 4E-BP1 (p-4E-BP1) expression in breast, ovarian, and prostate tumours is associated with malignant progression and an adverse prognosis for the patient. This marker has been claimed to be a highly relevant molecular marker of malignant potential. Our recently reported marker p70S6K and p-4E-BP1 are frequently up-regulated in cancer and have been assumed to be driving forces in tumour genesis. p-4E-BP1 expression has also been correlated with later tumour staging and is a prognostic factor of survival time after surgery.

Professor David Morris, inventor of the use of PPL-1 in cancer therapy and surgeon at the St George Hospital said "This observation provides further confirmation of the biological activity of PPL-1 in man by inhibiting a key cancer growth marker p-4E-BP1. This finding supports our studies on p70S6K in cancer cells and in animal models".

The primary objective of PharmAust's "First in Man" trial is to demonstrate safety in a rising dose format. Evaluation of white blood cells of patients who have received PPL-1 for either three or seven consecutive days has shown that the levels of p-4E-BP1 are reduced as compared to its levels at Day 0 before treatment started. In some patients marked reductions of p-4E-BP1 were observed (greater than 90%).

PharmAust's Executive Chairman, Dr Roger Aston said "This new data continues to provide support for PPL-1 as a new class of anticancer drug. Screening of these key cancer markers in patients at the higher doses of PPL-1, about to start at the Royal Adelaide Hospital, will potentially provide exciting new results for PPL-1."

PPL-1 is an approved veterinary drug launched in recent years by one of the leading global animal health corporations for the treatment of parasitic diseases in sheep. PharmAust, through its wholly owned subsidiary, Pitney Pharmaceuticals Pty Limited, owns patents on the use of PPL-1 in cancer and malignant disease. The drug will be potentially administered to patients suffering from diverse cancers. Recruitment will include selection of patients suffering from lung, pancreas, oesophageal, gastric, colorectal, ovarian, breast, prostate, liver, sarcoma, lymphoma, and melanoma.

The cancer chemotherapy market (estimated at \$42 billion/annum)⁴ is currently the fastest growing sector within the pharma industry, mainly driven by the identification of new potential therapeutic targets. This growth is further fuelled by the magnitude of the disease worldwide, currently estimated at more than 25 million people suffering from cancer globally, and an estimated 5 million people dying each year from the disease.

1. Armengol, G. et al. 4E-binding protein 1: a key molecular "funnel factor" in human cancer with clinical implications, *Cancer Res*, 2007;67(16): 7551-5
2. The mTOR effectors 4EBP1 and S6K2 are frequently coexpressed, and associated with a poor prognosis and endocrine resistance in breast cancer: a retrospective study including patients from the randomised Stockholm tamoxifen trials. Karlsson et al. *Breast Cancer Research* 2013, 15:R96
3. 4E-Binding Protein 1: A Key Molecular "Funnel Factor" in Human Cancer with Clinical Implications Gemma Armengol,1 Federico Rojo,1 Josep Castellvi,1 Carmela Iglesias,1 Miriam Cuatrecasas, Berta Pons,1 Jose' Baselga, and Santiago Ramo'n y Cajal. *Cancer Res* 2007; 67: (16). August 15, 2007
4. Reference: Research and Markets.com accessed 14th February 2014:
http://www.researchandmarkets.com/reports/335548/chemotherapy_market_insights_20062016_a

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