

**Preliminary PI-88 Phase 2 Prostate Cancer Results  
to be Presented at the American Society for Clinical Oncology (ASCO)  
2008 Genitourinary Cancer Symposium**

**Brisbane, Australia. 13 February 2008:** Progen Pharmaceuticals Limited (ASX: PGL; NASDAQ: PGLA) today announced positive preliminary efficacy results from a phase 2 investigator-initiated trial of PI-88 in combination with the chemotherapeutic agent Taxotere<sup>®</sup> (docetaxel) administered to patients with prostate cancer. Dr Gavin Marx, Royal North Shore Hospital, Sydney Haematology and Oncology Clinics, the principal investigator conducting the trial, will present the preliminary results of the study today at the American Society for Clinical Oncology (ASCO) 2008 Genitourinary Cancer Symposium in San Francisco.

The investigator-initiated study was a randomized two-arm open-label study design that assessed efficacy and safety of two dose schedules (4 days/week and 7 days/week) of subcutaneous PI-88 in combination with three-weekly Taxotere<sup>®</sup> (75 mg/m<sup>2</sup>, IV on day 1). The study comprised a lead-in phase 1 safety component to establish the maximum tolerated dose (MTD) of PI-88 at each of the two dosing schedules, followed by a randomized phase 2 component expanding the two dose schedule.

70% of the 55 patients recruited to the trial had a decrease in serum Prostate Specific Antigen (PSA) of greater than 50% for three weeks or longer. These efficacy results compare favourably with the pivotal TAX327 Taxotere<sup>®</sup> registration trial, where 45% of patients had at least a 50% decrease in serum PSA level<sup>1</sup>. PSA is a substance produced in the prostate gland, a high level of which may indicate the presence of cancer. In patients with advanced prostate cancer, many clinicians use increasing levels of PSA as an indicator of disease progression.

The trial concluded enrollment early due to a higher-than-expected rate of febrile neutropaenia, a side effect involving a decrease in white blood cells with associated fever. This is a known side effect of Taxotere<sup>®</sup>, but was seen in this trial at a substantially greater rate than is generally considered typical for that drug.

Two patients are continuing with PI-88 treatment after successfully completing the combination treatment. Specifically, one patient has remained on the study after 74 weeks while the other remains after 40 weeks.

Dr James Garner, Progen's Vice President of Clinical and Medical Affairs commented "We are encouraged by the efficacy trends demonstrated in this patient population. Prostate cancer is an indication with continuing high unmet medical need and there is a clear demand for new therapies here. The febrile neutropaenia rates seen in this study are difficult to interpret, given that this small investigator-led study lacks a control group. We have not seen evidence of febrile neutropaenia in our previous clinical experience combining PI-88 with Taxotere<sup>®</sup>, and there is no biological reason to suspect that the combination might result in increased toxicity. We will discuss this unexpected finding with our clinical and scientific advisors to determine the appropriate next steps in terms of development."

Justus Homburg, Progen's Chief Executive Officer continued, "Prostate cancer continues to be an indication we are interested to explore more, therefore, we will continue to analyze the results and do additional work to establish how best to combine PI-88 with existing therapies in this indication. In the interim, our phase 3 study in the adjuvant hepatocellular carcinoma setting is expected to begin recruitment shortly. We do not anticipate any concern regarding febrile neutropaenia in this phase 3 study, as it is a monotherapy study in a patient population with which we already have substantial clinical data."

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<sup>1</sup> Tannock et al, 2004, N. Engl J Med, 351, 1502-12

**About Progen:** Progen Pharmaceuticals Limited is an Australian-based globally focused biotechnology company committed to the discovery, development and commercialization of small molecule therapeutics primarily for the treatment of cancer.

**About PI-88:** PI-88 is one of a new class of multi-targeted cytostatic cancer therapeutics. It is a novel anti-cancer compound with a first-in-class mechanism as a heparan sulfate mimetic. Its anti-tumor activity is based on inhibition of two biological processes – angiogenesis (the growth of new blood vessels) and metastasis (the spread of cancer to other sites) – critical to the growth and progression of cancer.

**About Prostate Cancer:** Prostate cancer is the most common type of cancer in men in the United States, apart from skin cancer, and the third leading cause of cancer death in men. An estimated 219,000 new cases will occur in the United States in 2007, and about 27,000 men will die of the disease, according to the American Cancer Society. Worldwide, more than 670,000 men are diagnosed with prostate cancer every year, accounting for one in nine of all new cancers in males.

The most effective treatment for disseminated prostate cancer is androgen deprivation depletion from surgical or pharmacological means. Prostate tumors that have stopped responding to or are growing despite the use of active hormone treatment strategies are characterized as androgen-independent prostate cancer. At that point, other options, such as chemotherapy, are often considered. Taxotere<sup>®</sup>, in combination with prednisone, was approved by the FDA in 2004 for the treatment of patients with metastatic AIPC. The majority (more than 80 percent) of newly diagnosed stage IV patients who fail hormone therapy are currently treated with Taxotere<sup>®</sup> either alone or in combination. Other options include mitoxantrone, estramustine or prednisone monotherapy as second-line treatment.

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This press release contains forward-looking statements that are based on current management expectations. These statements may differ materially from actual future events or results due to certain risks and uncertainties, including without limitation, risks associated with drug development and manufacture, risks inherent in the extensive regulatory approval process mandated by the United States Food and Drug Administration and the Australian Therapeutic Goods Administration, delays in obtaining the necessary approvals for clinical testing, patient recruitment, delays in the conduct of clinical trials, market acceptance of PI-88, PI-166 and other drugs, future capital needs, general economic conditions, and other risks and uncertainties detailed from time to time in the Company's filings with the Australian Securities Exchange and the United States Securities and Exchange Commission. Moreover, there can be no assurance that others will not independently develop similar products or processes or design around patents owned or licensed by the Company, or that patents owned or licensed by the Company will provide meaningful protection or competitive advantages.

# Clinical Appendix

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The following additional information is provided in accordance with the Code of Best Practice for ASX Reporting by Life Science Companies.

**Trial Title:** A randomized phase 2 study of two dose schedules of PI-88 in combination with Taxotere® in patients with androgen-independent prostate cancer.

## Investigators and Clinical Sites:

This trial was an investigator-initiated trial. The investigators designed the protocol, managed the trial and will be reporting the results at the American Society for Clinical Oncology (ASCO) 2008 Genitourinary Cancer Symposium in San Francisco, United States. To support the trial, Sanofi-Aventis provided Taxotere® and Progen supplied PI-88

Due to an unexpected high incidence of febrile neutropenia, the trial's investigators decided to conclude enrolment early and proceed to analysis. Final data analysis and results are expected in Q2 2008.

### *Principle Investigator:*

Dr Gavin Marx – Royal North Shore Hospital, Sydney Haematology and Oncology Clinics

### *Co-ordinating Investigators:*

Dr Nick Pavlakis, Royal North Shore Hospital  
Dr Craig Underhill - Border Medical Oncology  
Dr Stephen Begbie, Port Macquarie Base Hospital  
Dr Adam Boyce, Lismore Base Hospital  
Dr Paul de Souza, St George Hospital  
Dr Francis Parnis, Adelaide Cancer Center

## Trial Objectives:

### **The Primary Objective:**

The primary objective of the trial was to determine the Prostate Specific Antigen (PSA) response (proportion of patients achieving a decline in PSA of greater than 50%, sustained for a period of at least three weeks) in patients with Androgen-Independent Prostate Cancer (AIPC) treated with Taxotere® and prednisone in combination with PI-88 administered four days per week versus Taxotere® and prednisone in combination with PI-88 administered seven days per week.

### **Secondary Objectives:**

- ▶ Radiologic Response Rate (RR) in patients with measurable disease
- ▶ PSA progression-free survival
- ▶ Overall survival
- ▶ Safety and tolerability
- ▶ Quality of Life Functional Assessment of Cancer Therapy – Prostate questionnaire (FACT-P)
- ▶ Exploratory predictive value of biologic parameters C-reactive protein (CRP), vascular endothelial growth factor (VEGF), interleukin-6 (IL6), D-dimer

## Methods:

Patients with histologically or cytologically proven prostate adenocarcinoma that were unresponsive or refractory to hormone therapy were recruited into the trial. The study was a randomised 2-arm open-label study which assessed efficacy and safety of two dose schedules (4 days/week and 7 days/week) of subcutaneous PI-88 in combination with 3-weekly Taxotere® (75 mg/m<sup>2</sup>, IV on day 1). The study comprised a lead-in phase 1 safety component to establish the maximum tolerated dose (MTD) of PI-88 at each of the 2 dosing schedules, followed by a randomised phase 2 component expanding the 2 dose schedule.

Twenty-one patients were enrolled in the lead-in component and two PI-88 dose schedules were recommended: 130mg day 1-7 or 250mg day 1-4. A further 35 patients were randomised to further evaluate the two schedules in the Phase 2 component. Up to a maximum of 10 three-week treatment cycles of Taxotere<sup>®</sup> were permitted and patients were allowed to continue PI-88 treatment until either toxicity or disease progression occurred.

The trial began in August 2005 and was conducted at 7 sites around Australia.

## Results:

Fifty patients are evaluable for response and fifty-five evaluable for toxicity.

- ▶ Median age was 70 (range 53 - 84).
- ▶ Median PSA was 151 (0.2 - 2000)
- ▶ Median Gleason score was 8 (range 6 - 10)

Metastases were present in bone, lymph nodes and liver in 80%, 26% and 7%, respectively.

### Primary Objective – PSA response rate:

Serum PSA was measured every three weeks and a response was defined as a reduction from baseline of at least 50% that was maintained for at least three weeks. The overall rate of PSA response in the trial was 70%. Due to the smaller sample size than originally planned, no statistical analyses have been completed on this patient population. These efficacy results compare favourably with the pivotal registration TAX327 Taxotere<sup>®</sup> trial where 45% of patients had at least a 50% decrease in serum PSA levels for 3 weeks or longer<sup>2</sup>.

### Secondary Objectives:

The median survival for the patients enrolled in the study was 16.25 months with 1 year survival rate of 72%. Additional efficacy assessments including biologic response markers such as VEGF, CRP, IL-6 evaluations are currently being evaluated.

### Safety Analysis:

The most common grade 1 – 2 toxicities were fatigue, alopecia and nausea. Grade 1 - 2 peripheral neuropathy occurred in 24% of patients. The table below details the incidence of Grade 3 - 4 toxicities.

#### Grade 3/4 toxicities

Toxicity	Percentage (%)
Diarrhoea	6
Dehydration	11
Fatigue	16
Nausea	16
Thrombocytopenia	22
Febrile Neutropenia	27

### Febrile neutropenia

Recruitment to the study was closed early due to a higher-than-expected incidence of febrile neutropaenia of 27%. There were no treatment related deaths. The mechanism of this result is to be further examined. Febrile neutropaenia is a known side effect of Taxotere<sup>®</sup> treatment, but has not previously been reported in monotherapy or combination therapy trials of PI-88, including other trials in conjunction with Taxotere<sup>®</sup> or other cytotoxic agents.

<sup>2</sup> Tannock et al, 2004, N. Engl J Med, 351, 1502-12