ASX Announcement | 15 February 2021
Noxopharm Limited (ASX:NOX)

15 February 2021 **Sydney, Australia**

Cancer Conference Presentation Confirms Potential Breakthrough For Stage 4 Prostate Cancer Patients

- **Drug combination NOX66 (Veyonda®) and ^{177}lutetium-PSMA-617 delivers high response rates in heavily pre-treated men with end-stage prostate cancer**
- **Median Overall Survival of 19.7 months a potential breakthrough in the treatment of end-stage prostate cancer**

Sydney 15 February 2021: Australian clinical-stage drug development company Noxopharm Limited (ASX:NOX) is pleased to provide a more detailed summary of the data from the LuPIN study that was formally presented to the American Society of Clinical Oncology (ASCO) Genitourinary Cancers Symposium on 13 February 2021.

Noxopharm CEO, Dr Graham Kelly, said, "The top level comment is that the LuPIN drug combination of Veyonda® and the Novartis radiopharmaceutical drug, ^{177}lutetium-PSMA-617, has delivered a high anti-cancer response, resulting in a major survival outcome in men who have exhausted effective treatment options. Importantly, it has done so in a well-tolerated way.

We also note that **46%** of men were able to complete the full 6 cycles of treatment. This is important from a commercial point of view because the ability to administer up to 6 cycles of the Novartis radiopharmaceutical over a treatment course of about 7-8 months is dependent on PSA levels continuing to indicate a response to treatment. Getting almost half of the men to receive a full 6 cycle treatment course carries important clinical and commercial implications.

The exact degree of survival benefit the drug combination is providing will require a placebo-controlled study. Nevertheless, given that men with Stage 4 prostate cancer who have exhausted all standard treatment options have very limited survival prospects, having half of the men in the LuPIN study survive at least 19.7 months, with 19 of the 56 still alive, is a remarkable outcome pointing to a major anti-cancer effect.

The way that Veyonda is joining with the Novartis drug to produce this potent anti-cancer effect is the subject of ongoing studies. As a selective inhibitor of sphingosine kinase and STING signaling, Veyonda is associated with multiple anti-cancer functions, falling mainly into oncotoxic and immunotherapy functions. Our working hypothesis, based on pre-clinical data, is that the LuPIN effect of Veyonda is an oncotoxic effect via two mechanisms. First, by blocking cell division, it is holding cancer cells at a point in

their cycle where their DNA is most susceptible to the damaging effects of the ^{177}lutetium radiation. Second, by blocking the repair of the damaged DNA, the damaged cell then self-destructs.

Statistical analysis will be conducted at the conclusion of the study to determine if there is a dose-response effect of Veyonda, although the 1200 mg dose looks to be our therapeutic dose.

All in all, we see this result as heralding a new era in the treatment of Stage 4 prostate cancer," Kelly said.
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Data details

1. Patient population

56 men were enrolled who had progressive, metastatic disease that was heavily pre-treated with taxanes (docetaxel, cabazitaxel) and an androgen signalling inhibitor (ASI) (enzalutamide or abiraterone).

- **53/56** had received both taxanes and an ACI**; 3** patients 1 taxane and an ASI
- Median baseline PSA (prostate specific antigen) level (normal range 1-4) was **115 ug/L** (range 46-476)
- 19 patients had < 20 metastases; 37 > 20 metastases.

2. PSA response

PSA level in blood is a marker of prostate cancer cell activity.

- **86%** (48/56) had any PSA reduction
- **61%** (34/56) had a PSA reduction >50%
- A reduction >50% is termed a *'PSA response'* and is accepted generally as indicating a meaningful anti-cancer response.

3. PSA progression free survival (PSA PFS)

PSA PFS is the time to disease progression based on PSA levels.

- The median PSA PFS was **7.5 months** *with a confidence interval of 5.9-9.0 months*
- **5/56** men have not progressed.

4. Overall survival

Median Overall Survival (OS) is that time when 50% of men have died and 50% remain alive.

- Median OS was **19.7 months** *with a confidence interval of 9.5-30.0 months*
- **34% (19/56) men remain alive**.

5. Safety

Toxicities, in descending order of frequency, were anaemia, xerostomia (dry mouth), anal irritation, nausea, thrombocytopaenia, constipation, pneumonia, neutropaenia. Most were Grade 1 (requiring no intervention), with anaemia and fatigue the only Grade 3 toxicities.

Graham Kelly, CEO and Managing Director of Noxopharm, has approved the release of this document to the market on behalf of the Board of Directors.

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About LuPIN

LuPIN is an Investigator-Initiated Phase Ib/2a, single-arm, open label study which enrolled 56 men with mCRPC who were PSMA-positive and who had been heavily pre-treated with docetaxel, cabazitaxel and either abiraterone and/or enzalutamide, but whose disease nevertheless was progressing. The study was divided into 4 cohorts of 400 mg (8 patients), 800 mg (8 patients), 800 mg (16 patients) and 1200 mg (24 patients) Veyonda (NOX66) in combination with ^{177}Lu-PSMA-617.

The Phase 1 part of the study was intended to establish the safety of the combination treatment. The Phase 2 expansion part was intended to determine preliminary efficacy signals of Veyonda in combination treatment.

Imaging inclusion criteria include a PSMA PET/CT with uptake intensity in metastases more than twice the normal liver uptake and no discordant disease on FDG PET/CT. All men received up to 6 doses of ^{177}Lu-PSMA-617 at 6-weekly intervals and Veyonda every cycle on days 1-10.

About Noxopharm

Noxopharm Limited (ASX:NOX) is an Australian clinical-stage drug development company focused on the treatment of cancer and cytokine release syndrome/septic shock.

Veyonda is the Company's first pipe-line drug candidate currently in Phase 2 clinical trialing. Veyonda has three main drug actions – highly selective inhibition of sphingosine kinase, STING signaling and autophagy. Sphingosine kinase inhibition contributes to its dual-acting oncotoxic and immuno-oncology functions designed to enhance the effectiveness and safety of standard oncology treatments, i.e., chemotherapies and immune checkpoint inhibitors; STING signaling inhibition provides an anti-inflammatory effect, contributing to an anti-cancer action, but also potentially blocking sepsis; autophagy inhibition is believed to augment the immunotherapy effect of radiotherapy, in particular the triggering of an abscopal response.

Noxopharm also is the major shareholder of US biotechnology company Nyrada Inc (ASX:NYR), and wholly owns Pharmorage, a private drug development company focused on drug development in the areas of sepsis and autoimmunity.

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