ASX Announcement | 5 August 2021
Noxopharm Limited (ASX:NOX)

Survival Advantage of Adding Veyonda® to LuPSMA Therapy Confirmed by Pre-Clinical Study

Highlights

- **Important animal study shows that adding Veyonda to ^{177}lutetium-PSMA-617 results in regression of prostate cancer**
- **Explains the contributory role of Veyonda in the impressive median overall survival outcome of 19.7 months achieved in the phase I/II LuPIN study in combination with the Novartis drug**
- **Full clinical details of the LuPIN study published this week in a highly respected medical journal**
- **Both developments further support the Company's belief in a key role for Veyonda in the emerging multi-billion dollar radioligand therapy market.**

Sydney 5 August 2021: Australian clinical-stage drug development company Noxopharm Limited (ASX:NOX) announces two developments relating to the use of Veyonda® to enhance the survival benefit of ^{177}lutetium-PSMA-617 (LuPSMA) treatment in men with metastatic castrate-resistant prostate cancer.

Pre-clinical study

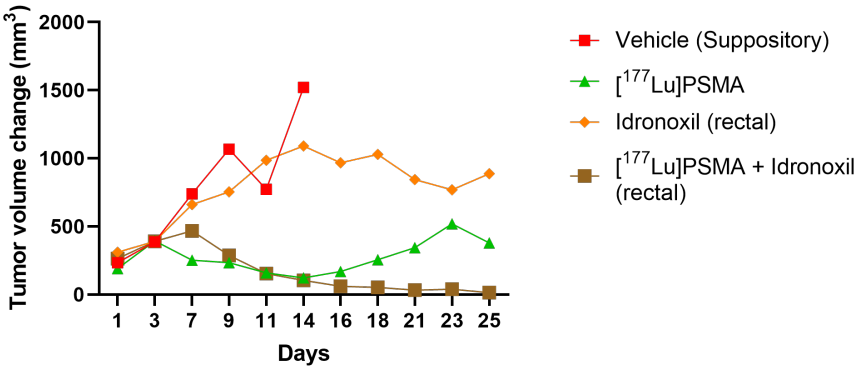
The first of these developments is important pre-clinical evidence confirming the ability of Veyonda to enhance the cancer-killing effect of LuPSMA treatment. The study was conducted by a research group led by Professor Kristofer Thurecht at The University of Queensland and had the aim of separating a combination effect (Veyonda + LuPSMA) from that of either drug alone.

Professor Kristofer Thurecht, University of Queensland, said, *"The combination of Veyonda with LuPSMA exhibited an impressive synergistic therapeutic response, with sustained and almost complete regression of the tumour and minimally-observed systemic toxicity. This combined response was not observed in any of the animals treated with monotherapy."*

The study involved mice bearing tumours of human PSMA-positive prostate cancer (PC3-PIP) cells. LuPSMA was dosed on a single occasion with the equivalent of a human dose; idronoxil was dosed (rectally) twice daily for 10 days. Tumour size was recorded and mice were euthanised when tumours reached a pre-determined size, leading to a calculation of median overall survival (time when 50% of animals had died).

LuPSMA alone had a clear anti-cancer effect in this model, slowing down tumour growth and extending survival substantially. However, the addition of Veyonda had an even more profound anti-cancer effect, going beyond blocking tumour growth into full regression of most of the tumours, to the extent that median overall survival could not be determined.

Figure showing change in tumour volume (from starting 200-300 mm^3) in mice treated with (i) suppository base alone (control group), (ii) idronoxil alone, (iii) ^{177}Lu-PSMA-617 alone, or (iv) idronoxil + ^{177}Lu-PSMA-617.



The median overall survivals results are shown below:

	Median Overall Survival (days)
Control	11.5
Veyonda alone	13.5
LuPSMA alone	40
LuPSMA + Veyonda	**>50. Not determined due to tumour regression.**

LuPIN trial

The second development is the publication of the LuPIN phase I/II clinical trial data in the highly respected The Journal of Nuclear Medicine. The abstract is available at the following link.

https://jnm.snmjournals.org/content/early/2021/07/29/jnumed.121.262552

The data is the more detailed version of a presentation in February 2021 to the American Society of Clinical Oncology (ASCO) GU meeting and reported to the ASX on 15 February 2021. The final tumour response data for this phase I/II study in 56 men is: 86% had a reduction in PSA levels; 61% had a PSA reduction >50%; median PSA progression-free survival was 7.5 months; **median overall survival was 19.7 months**.

Noxopharm CEO , Graham Kelly, said, "Men with prostate cancer that has spread and stopped responding to all available therapies have very limited survival prospects, generally in the order of 5-8 months. Which is why a median overall survival outcome of 19.7 months in the LuPIN trial was so impressive.

Based on the published survival experience of LuPSMA therapy alone, we were in little doubt that Veyonda had played a major role in that outcome. However, for some, the question of a combination effect versus a LuPSMA therapy alone effect remained, a question we are confident now has gone a long way to being answered by the animal study. In that study, LuPSMA on its own had an impressive anti-cancer effect, but nothing like the effect when Veyonda was added and the tumours mostly disappeared.

We see Veyonda having a major commercial future in the rapidly growing field of radioligand therapy, not just in prostate cancer, but across the broad cancer spectrum. With a wide and growing number of companies developing novel radioligand drugs, this is a commercial opportunity that the Company is able to carve out as a separate market segment while it undertakes the other 3 programs, IONIC, DARRT and CEP, in its 4-pillars strategy."

Glossary

Radioligand: A radioligand combines a radioactive isotope to a carrier, typically an antibody that carries

^{177}lutetium-PSMA-617: Lutetium isotope attached to an antibody fragment (617) against the prostate surface membrane antigen (PSMA)

PC3-PIP cells: The PC3 cell line was established from a bone metastases of Grade 4 prostate cancer and subsequently engineered to express high levels of PSMA.

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.

-ENDS-

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 177Lu-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 177Lu-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 trialling. Veyonda® has two main drug actions – a moderating effect on the ceramide/sphingosine-1-phosphate balance and inhibition of STING signalling. Activity against the former target contributes to its dual-acting oncotoxic and immunomodulatory functions designed to enhance the effectiveness and safety of standard oncology treatments, i.e., chemotherapies, radiation therapies and immune checkpoint inhibitors. Activity against the latter target provides an anti-inflammatory effect, as well as contributing to an anti-cancer action, but also potentially blocking septic shock.

Noxopharm is running comprehensive drug discovery programs in both oncology and inflammation, and is the major shareholder of US biotechnology company, Nyrada Inc (ASX:NYR), active in the areas of drug development for cardiovascular and neurological diseases.

To learn more, please visit: noxopharm.com

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Forward Looking Statements

This announcement may contain forward-looking statements. You can identify these statements by the fact they use words such as “aim”, “anticipate”, “assume”, “believe”, “continue”, “could”, “estimate”, “expect”, “intend”, “may”, “plan”, “predict”, “project”, “plan”, “should”, “target”, “will” or “would” or the negative of such terms or other similar expressions. Forward-looking statements are based on estimates, projections and assumptions made by Noxopharm about circumstances and events that have not yet taken place. Although Noxopharm believes the forward-looking statements to be reasonable, they are not certain. Forward-looking statements involve known and unknown risks, uncertainties and other factors that are in some cases beyond the Company’s control (including but not limited to the COVID-19 pandemic) that could cause the actual results, performance or achievements to differ materially from those expressed or implied by the forward-looking statement.