ASX Announcement | 19 March 2021
Noxopharm Limited (ASX:NOX)

Noxopharm IONIC Immuno-Oncology Trial Commences

Highlights:

- **Ethics Approval received for IONIC-1 clinical trial, with trial to commence immediately in Australian hospitals**
- **IONIC-1 to test combination of Veyonda® with blockbuster Bristol Myers Squibb drug, Opdivo® (nivolumab)**
- **Aim is to use Veyonda to overcome resistance to drugs such as Opdivo**
- **Success should expand multi-billion dollar drug sector considerably and deliver major NOX shareholder value**

Sydney 19 March 2021: Australian clinical-stage drug development company Noxopharm Limited (ASX:NOX) is pleased to announce that the IONIC-1 trial supported by Noxopharm and Bristol Myers Squibb (BMS) received final ethics approval to start recruiting patients.

The IONIC-1 trial (*previously announced on 9 November 2020*) is a Phase 1b trial in approximately 30 cancer patients, combining Veyonda® with the BMS immune checkpoint inhibitor, Opdivo® (nivolumab), for the treatment of a range of tumour types.

Immune checkpoint inhibitors (ICI) such as nivolumab have had spectacular results in some patients with a small number of cancer types, but remain inactive in most forms of cancer. The IONIC-1 study will explore whether adding Veyonda to ICI therapy will overcome tumor resistance to nivolumab, making more cancer types responsive to nivolumab.

The ICI market is a multi-billion-dollar market predicted by market analysts to generate sales of up to US$45 billion by 2025 through strong year-on-year growth. Increasing the number of cancer types that respond to ICI therapy would expand the market even more, leaving any company with the technology to help achieve that goal in a highly valuable position. The ICI market currently is dominated by two major global pharmaceutical companies, one of which is Bristol Myers Squibb.

Medical Oncologist Professor de Souza BScMed MB BS MPH PhD FRACP, Principal Investigator of this trial, said in Sydney today, 'We're now ready to begin recruiting patients into IONIC-1. The potential of this trial to bring effective checkpoint inhibitor treatment to a broader range of patients is an exciting prospect. If we're able to enhance the effect of BMS's nivolumab with Veyonda, this will bring some truly life-changing treatment to cancer patients' lives and will change the way that cancer is treated worldwide.'

The IONIC-1 trial will commence immediately. There will be two cohorts of patients, one cohort comprising patients who have not had previous nivolumab treatment because they have cancers

considered unsuitable for ICI use, and the other cohort will be patients whose cancers have displayed resistance to nivolumab treatment.

Trial endpoints are (i) safety and tolerability of the drug combination, (ii) efficacy (based on regular scans), and (iii) effect on various blood biomarkers. The trial is open-label, with the Company anticipating being able to report on progress at intervals.

The Company regards a successful outcome as the combination treatment achieving stable disease or better

- in patients with cancer types regarded as inherently resistant to ICI drugs, and/or
- in patients whose cancer has progressed on nivolumab treatment, and
- to have done so without creating additional safety issues compared to nivolumab on its own.

Immune checkpoint inhibitors and Veyonda

Immune checkpoints are one of the key ways cancer cells avoid destruction by the immune system, allowing the cancer to survive and spread throughout the body. Immune checkpoints are proteins expressed on the surface of cancer cells, forming a protective shield that blocks immune cells (T-cells) from attacking them. Drugs such as nivolumab remove this shield, facilitating immune cell killing of the cancer cell. Resistance to this class of drug is thought to be associated with a lack of immune cells within individual tumours, with loss of the protective shield devalued by the absence of immune cells to take advantage of the situation. Veyonda is a first-in-class, selective inhibitor of sphingosine-1-phosphate (S1P), reversing the S1P gradient that expels immune cells from tumours, thereby allowing repopulation of tumours with active immune cells.

The IONIC-1 trial is predicated on the basis that this so-called COLD to HOT conversion of tumours will prove to be the essential co-factor with nivolumab for effective immune control of cancer.

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 IONIC-1

IONIC-1 is a pilot-study exploring the safety and efficacy signals of Veyonda in combination with Opdivo for patients with solid tumours. There will be two cohorts: one cohort of patients that has progressed on Opdivo and one cohort with patients who are treatment naïve to Opdivo. Both cohorts will be enrolled in parallel. Approximately 30 patients will participate in the study. The first part of the study will be a dose-escalation design with Veyonda doses ranging from 1200 mg to 2400 mg. The second part will be a dose expansion of the highest dose that is safe and well tolerated. The Opdivo dose will be 240 mg intravenously once every 14 days for both cohorts.

About Noxopharm

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

Veyonda® is the Company's first pipe-line drug candidate currently in Phase 2 clinical trialling. Veyonda® has two main drug actions – inhibition of sphingosine kinase and inhibition of STING signalling. Activity against the former target contributes to its dual-acting oncotoxic and immuno-oncology functions designed to enhance the effectiveness and safety of standard oncology treatments, i.e. chemotherapy, radiotherapy and immune checkpoint inhibitors. Activity against the latter target provides an anti-inflammatory effect, also contributing to an anti-cancer action, but also potentially blocking sepsis.

Noxopharm also is the major shareholder of US biotechnology company Nyrada Inc (ASX:NYR).

To learn more, please visit: noxopharm.com

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