First DARRT-2 Cohort Fully Enrolled. Australian Site Joins Prestigious US Sites

Highlights

- **Momentum of patient and site recruitment gathering pace with first dose group fully enrolled in DARRT-2 Phase 2 trial**
- **First Australian trial site added to two prestigious US sites**
- **DARRT-2 trial marks the first time Veyonda has been used to treat patients in the U.S.**
- **Noxopharm sees DARRT cancer immunotherapy treatment as potentially addressing the challenges seen with other immunotherapy treatments.**

Sydney 14 December 2021: Australian clinical-stage drug development company Noxopharm Limited (ASX:NOX) announces completion of enrolment of the first dose cohort of patients in its DARRT-2 Phase 2 clinical trial.

DARRT (Direct and Abscopal Response to Radiotherapy) is an experimental immunotherapy cancer treatment based on the combination of Veyonda® and a well-tolerated low dose of external beam radiotherapy.

The aim of DARRT treatment is to trigger an immune response in a single tumour, resulting in tumours in the rest of the body resolving despite not receiving any radiation. This form of immune response is known as an abscopal response and is the subject of considerable clinical interest worldwide because of its potential to offer significant benefits over other forms of immunotherapies. Those potential benefits include a broader range of responding cancer types, fewer side-effects, greater access to treatment, fewer logistical challenges, and greater cost-effectiveness.

As previously announced (*ASX: 10 Jun 2021, 1 Jul 2021, 4 Nov 2021*), DARRT-2 is being undertaken across multiple sites in North America, Europe, and Australia involving approximately 100 patients with metastatic cancers (prostate, breast, lung) who are eligible for low-dose radiotherapy.

The DARRT-2 trial marks the first time that Veyonda has been made available to patients in the United States, with patients enrolled at both the prestigious Beverly Hills Cancer Center in Los Angeles and the renowned MD Anderson Cancer Center in Houston, one of the largest cancer treatment centres in the world and consistently rated one of the best cancer treatment centres in the U.S. The first Australian site is also open for enrolment.

Interest in the trial is strong and growing, with the first dosage group quickly enrolled following study opening.

Noxopharm CMO, Dr Gisela Mautner, said, “This Phase 2 study builds on our Phase 1 trial where we saw promising signals that it may be possible to achieve cancer reduction through the abscopal

response. A combination of Veyonda and low-dose radiation therapy would be a very important new treatment option for cancer patients worldwide as many of the current immuno-therapy treatments have considerable limitations."

DARRT-2 builds on the early promise seen in the Phase 1 DARRT-1 study by increasing the intensity of Veyonda treatment.

The initial cohort of 3 patients are receiving a daily dose of 1200 mg Veyonda, the same dose used in DARRT-1. The clinical response of these patients will be reviewed by the Safety Steering Committee after the first cycle before enrolling patients in the 1600 mg dose, with 2400 mg the final dose.

Patients will be scanned on a regular basis to measure their response to treatment, and interim safety updates will be provided over the course of 2022.

More sites in Australia, USA and Europe will come online progressively over the next few months.

-ENDS-

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.

About DARRT
DARRT stands for Direct and Abscopal Response to Radiotherapy. It involves the application of low-dose (up to 25 Gy) external beam radiotherapy in 1-5 fractionated doses to a single tumour in a single treatment cycle. Veyonda is administered daily for up to 14 days in conjunction with the single radiotherapy cycle, and then in repeated monthly cycles without radiotherapy.

DARRT-2 builds on the encouraging safety and efficacy data from DARRT-1 but expanding into higher dosages of Veyonda (potentially up to 2400 mg daily), repeat cycles of Veyonda, and three different cancer types (prostate, breast, lung). Endpoints will be safety and tolerability, as well as clinical measures of efficacy such as tumour size changes, time until disease progression, health-related quality of life measurements, and overall survival.

The aim of DARRT is to use idronoxil, the active ingredient in Veyonda, to provide a unique combination of events: (i) to augment radiation-induced damage of both nuclear and mitochondrial DNA damage, (ii) to prevent repair of that damaged DNA both enzymatically and by autophagy, thereby augmenting an interferon-led local immune response that becomes systemic, and (iii) through blocking sphingosine-1-phosphate, to facilitate entry of activated T-cells into tumours.

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/TBK1 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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