



ASX Announcement | 13 November 2020
Noxopharm Limited (ASX:NOX)

Independent Discovery Validates DARRT Cancer Therapy

Highlights:

- **NOX DARRT treatment being developed as breakthrough, cost-effective, accessible immunotherapy treatment for patients with metastatic cancer**
- **DARRT aiming to transform whole-of-body abscopal response from rare to commonplace**
- **DARRT rationale now validated by a key independent discovery from a major U.S. university**
- **Major boost to Company's plan as it moves to open DARRT-2 Phase 2 trial**

Sydney 13 November 2020: Australian clinical-stage drug development company Noxopharm Limited (ASX:NOX) is pleased to note that a recent discovery by a major U.S. university group significantly validates the Company's novel DARRT treatment program comprising Veyonda® and radiotherapy.

The discovery relates to how Veyonda combines with radiotherapy to produce a striking whole-of-body anti-cancer response known as an 'abscopal response' in patients with metastatic cancer.

A complete abscopal response is regarded as the ultimate form of treatment for metastatic cancer. In a patient with multiple tumours it involves delivering a well-tolerated low dose of radiation to a single tumour, triggering an immune response in that single tumour that results in other tumours throughout the body literally 'melting' away in a matter of weeks. Patients with a complete abscopal response generally remain in remission for life.

Up to now the abscopal response has remained an extraordinarily rare and elusive phenomenon with the mechanisms behind it remaining a mystery. Now a study conducted by the Weill Cornell Medical College, New York, and recently published in the prestigious scientific journal, *Nature Immunology*, sheds light on the mechanism, finally offering a path to making it more commonplace¹.

This mechanism happens to be one of the ways that Veyonda works as an anti-cancer agent, putting Veyonda and the DARRT treatment regimen in the box seat to make abscopal responses commonplace and potentially putting Noxopharm in the world spotlight.

This discovery provides a rational explanation for why the Company has seen Veyonda deliver clear evidence of abscopal responses:

- the first two patients ever treated with DARRT treatment (on a compassionate use basis) delivered notable abscopal responses – one complete (late-stage prostate cancer) and one partial (leiomyosarcoma)



- in the DARRT-1 Phase 1b study (involving men with late-stage prostate cancer, meaningful tumour responses including abscopal responses were observed in a significant number of men, marking the first time that abscopal responses were reported in prostate cancer in more than extremely isolated cases. It is even more notable that this encouraging outcome in DARRT-1 was achieved using what the Company now regards as a sub-optimal course of Veyonda treatment.

Recent U.S. discovery: The Weill Cornell group have been at the forefront of clinical efforts to induce abscopal responses using radiation in a range of cancers, but with limited success. Their breakthrough discovery is that the ability of radiotherapy to trigger an abscopal response is dependent on blocking a type of cell repair process known as autophagy.¹ Radiation damages the cancer cells, with those cells then using autophagy to repair the damage. Where autophagy is blocked and the damage remains unrepaired, then an anti-cancer immune response is triggered that can spread body-wide.

The relevance of this to Noxopharm is that blocking autophagy is one of the recognised anti-cancer mechanisms used by idronoxil, the active ingredient in Veyonda.²

Graham Kelly, Noxopharm CEO and Managing Director, said, “For the overwhelming majority of patients, once a cancer spreads from its point of origin and becomes metastatic, the best that current treatments offer is to delay the inevitable. Which is why the concept of using a short course of radiotherapy, free of all the downsides of chemotherapy, to trigger an immune response that in a matter of weeks causes most or all other tumours to disappear, appears such an unrealistic dream.”

“But our experience shows that this is no dream. The clinical data shows that Veyonda very clearly is boosting the chances of triggering an abscopal response. The Weill Cornell discovery, combined with what we learnt from the DARRT-1 study about Veyonda dosing, means we go into the upcoming DARRT-2 study with a high degree of confidence that we are on the edge of a major breakthrough in cancer therapy.”

DARRT-2: Noxopharm now will test the ability of Veyonda to induce abscopal effects in a Phase 2 study involving about 200 patients. DARRT-2 is a Phase 2 multinational study, currently being planned for a start in early-2021 that will further test the DARRT treatment regimen in late-stage cancers such as prostate cancer where immunotherapies generally have proven ineffective to date. Compared to DARRT-1, Veyonda will be dosed in what the Company believes is a more therapeutic way including repeat monthly cycles and higher dosages (up to 2400 mg daily). Endpoints will be safety, Veyonda dose-response effect, DCR, ORR, PFS, QoL and OS.

References

1. Yamazaki T et al. Mitochondrial DNA drives abscopal responses to radiation that are inhibited by autophagy (2020). *Nature Immunol* 21, 1160-1171. <https://doi.org/10.1038/s41590-020-0751-0>
2. Miyamoto M et al (2018). Phenoxodiol increases cisplatin sensitivity in ovarian clear cancer cells through XIAP down-regulation and autophagy inhibition. *Anticanc Res* 38, 301-306. doi.10.21873/anticancer.12222

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 DARRT**

DARRT stands for Direct and Abscopal Response to Radiotherapy. It involves the application of low-dose (~25 Gy) external beam radiotherapy in ~5 fractionated doses to a single secondary tumour. Veyonda is administered daily for up to 14 days per cycle in repeat monthly cycles.

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 immunotherapy functions designed to enhance the effectiveness and safety of standard oncology treatments, i.e., chemotherapies, 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

Investor & Corporate enquiries:

Prue Kelly
M: 0459 022 445
E: info@noxopharm.com

Company Secretary:

David Franks
T: +61 2 8072 1400
E: David.Franks@automicgroup.com.au

Media Enquiries

Julia Maguire
The Capital Network
E: julia@thecapitalnetwork.com.au
T: + 61 2 8999 3699

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