DARRT-2 Study Update and Clarification

- **Clarification that the upcoming DARRT-2 trial is a Phase 2 trial**
- **In light of higher dosages of Veyonda now in use, a small Phase 1 dose-escalation arm has been added to confirm safety, but the bulk of patients will be enrolled in the Phase 2 part**
- **Also, the original focus on late-stage prostate cancer has been expanded to include late-stage breast and lung cancer patients**
- **Multi-national trial on track to be conducted in sites in Australia, U.S., France and Hungary.**

Sydney 10 June 2021: Australian clinical-stage drug development company Noxopharm Limited (ASX:NOX) is pleased to update the market on progress with its DARRT-2 trial and to correct a typographical error in the Company's latest Newsletter in which the trial was noted as being Phase 1.

DARRT-2 is a Phase 2 trial seeking to generate the phenomenon of the *abscopal response* in cancer patients. This response is a phenomenon where an immune/inflammatory response within a single lesion following low-dose radiotherapy, in turn triggers a whole of body immune response that results in shrinkage of non-irradiated lesions elsewhere in the body.

DARRT-2 will involve approximately 100 patients with progressive, metastatic prostate, breast or lung cancers that have failed standard treatment options and are eligible for low-dose, palliative external beam radiotherapy (RT) to a single lesion.

The multi-national trial will be conducted in Australia, U.S., France and Hungary in approximately 15 sites. The international contract research organisation, Parexel, is overseeing the study, with final trial logistics being put in place.

Dr Gisela Mautner, Noxopharm Chief Medical Officer, said, "The DARRT-2 study is an important study for us as it builds on the successful results of DARRT-1. The difference between the two studies is that DARRT-2 will be a much bigger study and will explore a more intensive treatment with Veyonda. To increase the value of the study, we have added a

second trial arm to include a small number of breast and lung cancer patients. This will ensure that, apart from the main focus of the study in prostate cancer, we also will generate results in two additional cancer types."

Dr Graham Kelly, Noxopharm CEO and Managing Director, said, "The abscopal response is a highly attractive cancer treatment goal because it provides the opportunity for a major anti-cancer outcome from a generally safe and minimally invasive treatment. The challenge is that it is a very rare phenomenon that to date has proven difficult to reproduce on a consistent basis.

Recent research has pointed to a reason for this being the need to block a certain type of repair process called autophagy of mitochondrial DNA damaged by the radiation.[1] Other research points to idronoxil, the active ingredient in Veyonda, blocking autophagy.[2] It is the combination of that effect and the drug's known immuno-stimulatory effects, together with the earlier DARRT-1 trial data, that provides the confidence that we might have the ability to achieve consistently higher response rates to make DARRT a practical treatment option."

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. https://vtps://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 downregulation and autophagy inhibition. Anticanc Res 38, 301-306. doi.10.21873/anticanres.12222

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 – 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 oncolytic and immunostimulatory 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 septic shock.

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

To learn more, please visit: noxopharm.com

END

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.

Investor, Corporate & Media enquiries:
Prue Kelly
M: 0459 022 445

Company Secretary:
David Franks
T: +61 2 8072 1400

E: info@noxopharm.com E: David.Franks@automicgroup.com.au

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.