ASX Announcement **19 May 2020**

FDA allows Veyonda® Pre-IND Submission for COVID-19

- **FDA allows pre-IND submission for use of Veyonda® in COVID-19 patients**
- **Intention to use Veyonda® to prevent a cytokine storm and resulting septic shock**
- **Aim is to reduce need for intensive care and to lower mortality rates**
- **Potential for conversion to fully expedited IND**

SYDNEY, May 19, 2020: Noxopharm (ASX:NOX) today announces that on advice from the U.S. Food and Drug Administration (FDA), the Company has lodged a pre-Investigational New Drug (pre-IND) submission for a clinical trial of Veyonda® in patients with SARS-CoV-2 (COVID-19) infection. The submission is based on a response to a package submitted to the FDA summarising the rationale for conducting a clinical trial with an inhibitor of cGAS-STING signalling.

The urgency of the situation means that if the pre-IND is evaluated positively by the FDA, it can be converted into a fully expedited IND approval. The conversion of a pre-IND into a full IND is a new option offered to high priority COVID-submissions and reduces the time and complexity of the FDA review process significantly.

Veyonda® has a mechanism of action that Noxopharm believes marks it as a prospective treatment of septic shock in COVID-19 patients, a condition associated with inflammatory and clotting problems and believed to be contributing to multi-organ failure and death in COVID-19 patients.[1,2]

Pre-clinical research conducted by the Hudson Institute of Medical Research has shown that one of the anti-cancer mechanisms of action of idronoxil (the active ingredient in Veyonda®) is potent inhibition of the cGAS-STING signalling pathway.

The cGAS-STING signalling pathway is responsible for alerting the body's immune system to the presence of an invading virus by triggering the production of cytokines. This pathway is critically important to generating an immune response that contributes to the great majority of COVID-19 patients recovering uneventfully. However, in a small proportion of patients who develop breathing problems leading to low oxygen levels, tissue damage in major organs triggers a second and excessive wave of cGAS-STING signalling, resulting in a so-called 'cytokine storm', amplifying existing tissue damage and inducing blood clotting problems.[3,4]

A number of COVID-19 clinical trials are being conducted with drugs inhibiting individual components of the 'cytokine storm' such as IL-6 and TNF -alpha. The basis of the Noxopharm submission to the FDA is that by inhibiting the cGAS-STING signalling pathway, Veyonda® offers a special opportunity to block a broader range of cytokines at their source, potentially reducing the severity of septic shock and the number of patients dying from it, or potentially even preventing it altogether.

The proposed study involves three steps – (i) dose-response, (ii) dose confirmation, and (iii) dose expansion. The dose expansion study will compare Veyonda® with current standard of care treatment.

Given the pandemic status, the Company anticipates receiving a decision by the FDA shortly.

References:
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2. Zhou et al. (2020). Clinical course and risk factors for mortality of patients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet, 395(10229):1054–1062. https://doi.org/10.1016/ S0140-6736(20)30566-3. https://www.ncbi.nlm.nih.gov/pubmed/32171076
3. Benmerzoug et al (2019). Self-DNA sensing in lung inflammatory diseases. Trends in Immunology, 40 (8). https://doi.org/10.1016/j.it.2019.06.001. https://www.ncbi.nlm.nih.gov/pubmed/31262653
4. Zhang et al (2020). TMEM173 Drives Lethal Coagulation in Sepsis. Cell host and Microbe, 27(4): 556-570. https://doi.org/10.1016/j.chom.2020.02.004. https://www.ncbi.nlm.nih.gov/pubmed/32142632

About Veyonda®

Veyonda® (NOX66) is a suppository dosage formulation of the experimental anti-cancer drug, idronoxil. Idronoxil is a first-in-class dual inhibitor of production of the key secondary pro-survival messenger, sphingosine-1-phosphate, and of the cGAS-STING signaling pathway. Over-expression of both sphingosine-1-phosphate and cGAS-STING are incriminated in cancer.

About IND

An IND (investigational New Drug) grant is an authorization by the FDA to administer an investigational drug to humans. An IND is granted after extensive review of pre-clinical data (animal pharmacology and toxicology), manufacturing information (quality control and quality assurance factors) and a well-designed clinical protocol. A primary criterion for approval is that patients will not be subjected to unreasonable risks.

About Noxopharm

Noxopharm is a clinical-stage Australian drug development company with offices in Sydney and New York. The Company has a primary focus on the development of Veyonda® and is the major shareholder in Nyrada Inc, a spin-off company developing a pipeline of non-oncology drugs.

www.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:
Catherine Strong
Citadel-MAGNUS
T: 02 8234 0111
E: cstrong@citadelmagnus.com

Graham Kelly, CEO and Chairman of Noxopharm, has approved the release of this document to the market.

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 that could cause the actual results, performance or achievements to differ materially from those expressed or implied by the forward-looking statement.