ASX Announcement **19 June 2020**

COVID-19 Trial Program to Commence in Europe

- **NOX proceeding with its COVID-19 clinical program in Europe while discussions with FDA continue**
- **Phase 1 trial aiming to confirm proof-of-principle and safety of Veyonda® in a timely and cost-effective way before committing to a considerably larger study**
- **End-points include safety, tolerability, clinical responses and biomarker (cytokine) data**
- **Targeting patients with moderate respiratory distress to prevent progression into virally-induced septic shock**
- **Based on anti-inflammatory effects of Veyonda as first-in-class inhibitor of the STING pathway**

SYDNEY, June 19, 2020: NOX announces commencement of its NOXCOVID clinical program with a planned Phase 1 trial in Europe. This action is designed to provide important safety data and proof-of-principle of Veyonda as a potential treatment of septic shock before committing the Company to a major study.

Noxopharm is progressing its NOXCOVID program in two parallel paths :-

1. Initiation of a Phase 1 study (NOXCOVID-1) in COVID-19 patients in Europe to provide key safety and clinical evidence of proof-of-principle cost-effectively;
2. Continuing discussions with FDA towards gaining Investigational New Drug (IND) approval for an expanded clinical trial in USA.

Dr Graham Kelly, Noxopharm CEO**,** said, "Septic shock is a lethal condition that occurs when the body experiences severe tissue damage associated with viral and bacterial infections and trauma. Instead of the body repairing the damage, the repair process goes into overdrive and creates even more damage. Apart from COVID-19 patients, septic shock is thought to be responsible for about ten million deaths worldwide every year, or one in five deaths. COVID-19 simply has brought to the fore the lack of an effective treatment for this very common but severe problem."

"We previously, on April 21 this year, announced that Veyonda works in the laboratory in a way that indicates the potential to block the formation of the so-called cytokine storm leading to septic shock. We need to confirm this in a clinical setting as quickly and as cost-effectively as we can. The implications for the Company in having a positively acting drug are very substantial and that is the main reason why we have chosen to run a Phase 1 study in Europe."

NOXCOVID-1

NOXCOVID-1 is a Phase 1 dose-escalation and dose-expansion study focusing on safety and proof-of-principle endpoints (biomarker and clinical responses). It will be in up to approximately 40 patients who have been admitted to hospital for respiratory insufficiency (not requiring artificial ventilation) associated with the SARS-CoV-2 virus. UK-based contract research organisation, Clinical Accelerator, has been appointed to oversee the trial, and Australian company, Datapharm, will process the data. A clinical protocol has been designed acting on the advice of Australian, U.S. and European clinicians, and incorporating FDA guidance.

Veyonda is intended for patients with early-stage respiratory disease who are at risk of developing a cytokine storm and septic shock. The aim is to prevent the onset of the cytokine storm that inflicts tissue damage in the lungs and other major organs. Veyonda is not intended to replace other potential treatments like dexamethasone that may provide a clinical benefit in patients with mode advanced disease already experiencing a cytokine storm.

Subject to regulatory approvals, NOXCOVID-1 will be conducted in Ukraine and Moldova, where there is a rising number of COVID-19 cases and deaths as the pandemic moves eastward across Europe. Three hospitals in Ukraine and three in Moldova have been identified and their respective intensive care specialists have indicated strong interest in participating.

The process of obtaining regulatory approval for the trial from central regulatory authorities and local hospital ethics committees is underway. Ukraine has an expedited COVID-19 clinical trial approval process.

Dr Gisela Mautner, Noxopharm CMO, said, “Intensive care doctors in Ukraine and Moldova have responded enthusiastically to the opportunity to use Veyonda given the case-loads they currently are experiencing. The key aim of this Phase 1 study is to confirm the safety of Veyonda in patients at risk of septic shock, and to confirm that Veyonda has the ability to block or considerably reduce the development of the cytokine storm contributing to the death of COVID-19 patients.”

FDA Pre-IND Submission Update

As previously advised, Noxopharm has lodged a pre-IND submission with the U.S. FDA for a trial in COVID-19 patients. The Company has received a prompt and extensive response from the FDA, with the Company agreeing to certain recommended design changes in the clinical protocol.

However, the opportunity to conduct a study in Eastern Europe has led to the decision to carve out the dose-escalation and dose-expansion arms of the proposed U.S. study in order to generate the all-important safety and early proof-of-principle efficacy data (based on biomarkers and clinical signals) in what the Company believes will be a far more timely and cost-effective manner than would have been possible in the U.S. The Company anticipates that it should be possible to commence a trial in Eastern Europe an estimated 4-5 months earlier than in the U.S.; per patient costs in the U.S. are estimated at 4-5 times that in Eastern Europe.

The Company sees the future of the program resting on the demonstration of safety and proof-of-principle in the NOXCOVID-1 study, providing the Company with the information needed to make key strategic decisions before committing to the funding of a larger trial.

Kelly said, "While Veyonda is first and foremost an anti-cancer drug, and we are pressing on with our DARRT and LuPIN programs as primary opportunities, a successful treatment of septic shock represents both an enormous commercial opportunity and a pressing humanitarian need that we cannot ignore."

Figure 1 depicts the biological rationale for the use of Veyonda (as a STING pathway inhibitor) in COVID-19 patients with poor lung function, including patients with acute respiratory distress syndrome (ARDS) who are at risk of developing a cytokine storm.

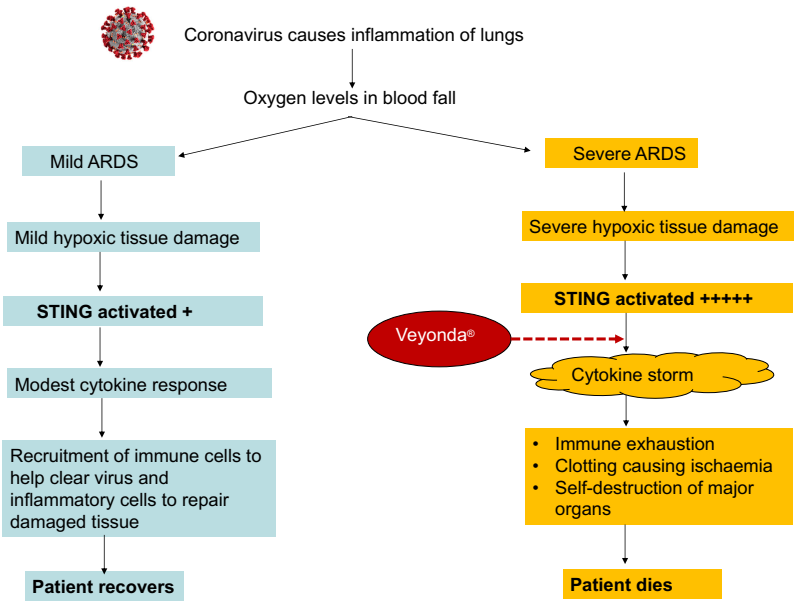

Figure 1. COVID-19 patient scenarios and Veyonda

The NOXCOVID program builds on the recent finding that idronoxil, the active ingredient in Veyonda, blocks the STING signalling pathway, believed to be a key trigger of septic shock.[1] Septic shock is a lethal condition associated with severe tissue damage associated with viral and bacterial infections, extensive surgery, trauma etc.[2] Septic shock is responsible for an estimated 10 million deaths globally each year, accounting for about 20% of all deaths.[3]

Currently there is no effective treatment for septic shock beyond supportive intensive care, including artificial ventilation.[4]

About COVID-19, Septic Shock, STING

The great majority of cases of COVID-19 are mild, but up to 20 percent of infected individuals require hospitalisation for serious or severe symptoms generally associated with hypoxia (low levels of oxygen) stemming from poor lung function.[5] In about 5% of these cases, oxygen levels becomes so critically low that patients can rapidly progress into ARDS, septic shock and multiple organ failure requiring critical care measures including mechanical ventilation and dialysis.[6]

ARDS, septic shock and ensuing failure of multiple organs (lungs, heart, kidneys, intestines, brain) in COVID-19 patients is being recognised as an abnormally excessive inflammatory response to widespread tissue damage generated by severe hypoxia.[7, 8] Rather than a normal inflammatory response being triggered that repairs the tissue damage in a controlled way, the response becomes over-active and uncontrolled, inflicting even more damage by causing clotting of blood in arteries supplying major organs.[9]

The intracellular protein STING (*Stimulator of Interferon Genes*) is now being increasingly pointed at as a potential key player in this hyperinflammatory response.[10, 11] One of the roles of STING is to detect tissue damage and to trigger the repair response. It does this *via* the release of compounds known as pro-inflammatory cytokines whose role it is to drive tissue repair. The abnormally excessive inflammatory response in some COVID-19 patients is the result of excessively high levels of cytokines in what is referred to as a *cytokine storm*. [12]

Blocking the cytokine storm has been identified as a valid approach to the treatment of COVID-19 patients suffering ARDS and at high risk of septic shock. [13]

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 STING signaling pathway.[14] Over-expression of both sphingosine-1-phosphate and cGAS-STING are incriminated in cancer. [15-20]

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.

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The Board of Noxopharm has approved the release of this document to the market.

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