ASX Announcement | 23 August 2021
Noxopharm Limited (ASX:NOX)

NOXCOVID Clinical Program to Expand Following Positive Phase 1 Clinical Results

Highlights

- **NOXCOVID Phase 1 clinical trial of Veyonda ® (idronoxil) preliminary topline data released**
- **Veyonda being positioned as an anti-inflammatory drug in COVID-19 patients with moderate disease intended to stop progression to severe disease**
- **Aim is to suppress a self-harming inflammatory response to damaged lung tissue without compromising a protective immune response to the coronavirus**
- **37/38 patients hospitalised with moderate respiratory disease and elevated pro-inflammatory markers were able to complete their treatment course and be discharged**
- **Only 1/38 required mechanical ventilation and this patient was the only death in the full analysis group**
- **Company to pursue use of Veyonda in both in-hospital and outpatient management**
- **Preliminary discussions underway for participation in funded clinical trial platforms.**

Sydney 23 August 2021: Australian clinical-stage drug development company Noxopharm Limited (ASX:NOX) releases preliminary top line data of its NOXCOVID phase 1 clinical trial.

The Company cautions that the preliminary data released today is top-line only and has been released for the purpose of allowing the Company to speak openly with health authorities. The full data continues to be analysed and is expected to be released in several weeks.

The role being proposed for Veyonda® is an anti-inflammatory drug that does not compromise the ability of the body to fight coronavirus infection.

Over 90% of individuals infected with the SARS-CoV-2 virus recover from the infection with non-critical symptoms. Those patients who do go on to develop critical symptoms, in many cases do so because of an excessive inflammatory response to viral-induced damage in the lungs and other organs.[1,2] This hyper-inflammation can go on to trigger widespread inflammation of the lining of blood vessels, disseminated coagulation, septic shock and multi-organ failure.[3,4]

This has led to standard anti-inflammatory drugs such as prednisone and dexamethasone becoming standard of care in the management of hospitalised COVID-19 patients.[5] However, the appropriateness of these drugs in less severe cases remains a point of concern given their immune-suppressing effects, potentially slowing the clearance of the virus from the lungs and increasing the risk of secondary infections from bacteria and other viruses.[6]

The unique mechanism of action of idronoxil (*ASX: to be announced 23 August 2021*) points to an anti-inflammatory action while still preserving the body's ability to fight the virus, potentially making it a suitable anti-inflammatory in patients with early or moderate COVID-19 disease.

On the basis of the data, Noxopharm, in partnership with Hudson Institute of Medical Research ('Hudson Institute'), now will seek to have Veyonda join one or more of the platform programs being conducted globally looking to identify a basket of treatments for COVID-19 disease.

These global clinical studies are being undertaken as a matter of urgency in the expectation that new variants may challenge the protection offered by current vaccines, potentially returning the world to an emergency situation where hospital services are under stress. Noxopharm is unaware of any drugs with a similar purpose to that of Veyonda being tested in those studies.

Following this phase 1 study, it will be important to test the effects of Veyonda in a larger randomised controlled study.

The lack of any safety concerns with Veyonda in COVID-19 patients, plus its self-administration, leads Noxopharm to see Veyonda holding promise in at least 2 clinical scenarios: (i) treating patients with moderate disease who are admitted to hospital, and (ii) treating patients with milder disease on an out-patient basis to avoid hospitalization.

Clinician-scientist Marcel Nold, Professor of Paediatric Immunology at Monash University and Hudson Institute, and paediatrician at Monash Children's Hospital, a world-renowned researcher in the field of cytokine biology and interventional immunology, said, "In Veyonda, Noxopharm has an exciting opportunity at hand. Based on what is known today, its properties give it the potential to address a gap in our armoury of COVID therapeutics: patients can self-administer, allowing its use at home; its mechanism of action may enable treatment of moderately-ill COVID patients; and, importantly, it could also be effective against other viruses."

Noxopharm CEO and Managing Director, Graham Kelly PhD, said, "Our target patients are those with a moderate degree of pneumonia experiencing breathing difficulties. Behind this pneumonia is an inappropriately excessive inflammatory response to the presence of the virus in the lungs. The objective is to use Veyonda to dampen that inflammatory response before it escalates to the point of triggering an even greater inflammatory response that can go on to cause even more widespread tissue damage. The challenge is to dampen down the inflammatory response without compromising the ability of the body to fight the virus.

No major safety issues were identified in the trial, and the recovery of 37 of 38 patients rated as having moderate disease requiring hospitalization and supplementary oxygen for the majority of patients, can be described as highly encouraging.

Critically, only 1 of the 38 patients who received the full course of Veyonda treatment progressed to severe COVID-19 symptoms requiring mechanical ventilation, and that patient eventually died.

With the support of Hudson Institute, a key partner in determining this potential anti-inflammatory benefit of Veyonda, Noxopharm is now in the process of reaching out to a number of local and global initiatives involved in preparing for ongoing challenges from this pandemic. We are targeting in particular

those trials involving hospitalised patients with moderate disease as well as those focusing on out-patient treatment strategies.

The world is entering unchartered waters with health authorities world-wide seeking a basket of treatments capable of filling cracks that may come from new variants of the virus. We see a well-tolerated anti-inflammatory as a key part of that armoury", Kelly said.

The study was conducted at three sites in the Republic of Moldova. The study was managed by a UK-based contract research company, and blood cytokine/biomarker assays and clinical data analysis including statistical analysis conducted in Australia.

Noxopharm is indebted to the medical staff and patients involved in this study given the challenging conditions experienced in Europe in late-2020 and early-2021 with consecutive waves of infection.

Key data

(i) Key patient metrics

- 16/22 (M/F), mean age 55.5 years (range: 37-78)
- Mean baseline NEWS2 Score: 4.8
- Veyonda treatment daily for 14 days
- 41 patients received at least 1 dose of Veyonda, but needed to have had at least 12 days of Veyonda treatment to be included in the full analysis geoup, with 38 patients achieving this
- Concomitant therapy: 28/38 (74%) received combined dexamethasone/prednisone for a mean of 6.6 days

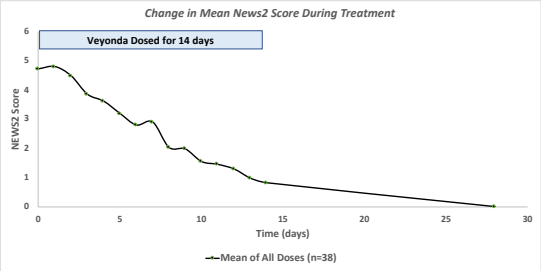
(ii) Clinical Responses

- 27/38 (71%) required supplementary oxygen
- 1 patient (3%) progressed to requiring mechanical ventilation and that patient eventually died
- 37/38 patients recovered and were discharged
- The Safety Steering Committee declared each dose cohort as safe including the highest dose of 1800 mg

(iii) NEWS2 Score. Figure 1 shows the change in mean NEWS2 Score over the course of Veyonda treatment. This includes all 38 patients: 37/38 patients returned to a healthy (<1) level by the end of the 14 days of Veyonda treatment.

The NEWS2 (National Early Warning Score) score is an early warning score developed for monitoring hospitalised patients and is an aggregate score of 7 clinical parameters: respiration rate, oxygen saturation, any supplemental oxygen, temperature, systolic blood pressure, heart rate, and level of consciousness.[7] An aggregate score between 5-6 is regarded as the threshold for urgent response. The baseline NEWS2 Score range in the NOXCOVID patients was between 4-6.

Figure 1. NEWS2 Score over time.
All Veyonda doses combined.



(iv) Cytokine/biomarker levels

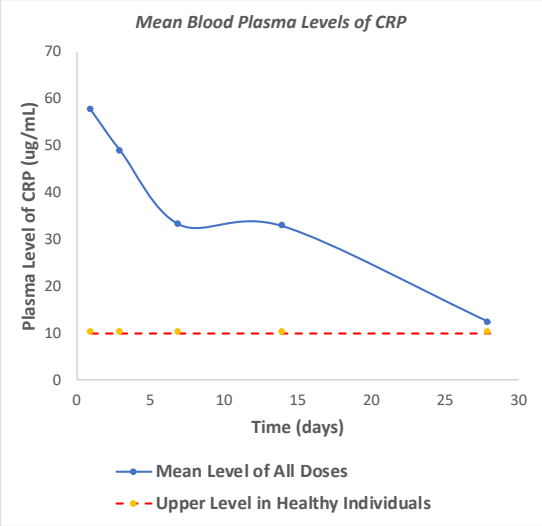
The Company previously announced (*ASX: 22 April 2021*) that an interim analysis of the first 18 patients showed that key cytokines/biomarkers (IL-1b, IL-4, IL-6, IL-10, TNF-a, CRP and D-dimer) had not risen as would have been expected with worsening of the disease.

A total of 53 cytokines and biomarkers were assayed over the 28 days of review:

- IL-1β, IL-4, IL-6, IL-10, TNF-α were low or within normal range at baseline, and remained stable over the course of the study
- Five cytokines or biomarkers showed elevated levels on admission to hospital: CRP, IFN-g, IL-IRA, β2M and D-dimer, each regarded as markers of COVID-19 disease progression.[8]
- CRP, IFN-g and IL-1RA returned to normal or near-normal levels over the course of the study; β2M and D-dimer levels trended slightly down.

Figure 2 shows the average course of CRP levels in the 38 patients, with mean levels halving by end of 14 days of Veyonda treatment, returning to normal levels by Day 28. CRP is a protein of liver origin whose levels rise in response to inflammation. CRP is considered a predictive marker of the seriousness of COVID-19 disease.[9-11]

Figure 2. Blood levels of C-reactive protein over time.
All Veyonda doses combined.



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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 Hudson Institute of Medical Research

A global bioscience medical research leader, Hudson Institute's sole focus is on powering breakthrough scientific discoveries into improved health care that will transform lives. We strive to improve human health through groundbreaking, collaborative, medical research discoveries and the translation of these to real world impact.

Hudson Institute scientists research five areas of medical need:

- Inflammation
- Reproductive health and pregnancy
- Infant and child health
- Cancer
- Hormones and health

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 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

Investor, Corporate & Media 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

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