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ASX Announcement | 8 March 2021
Noxopharm Limited (ASX:NOX)

NOXCOVID Trial Advances to Final Stage

- **Positive review of hospitalized COVID-19 patients triggers approval to move from Part 1 to Part 2 of the trial**
- **Top dose of 1800 mg Veyonda® daily to be used in final patient cohort**
- **Tests on blood cytokine levels in Part 1 patients underway**

Sydney 8 March 2021: Australian clinical-stage drug development company Noxopharm Limited (ASX:NOX) announces that Veyonda® has been approved to move into its second and final stage of the NOXCOVID-1 clinical trial on the advice of the clinicians treating the NOXCOVID-1 patients.

Part 1 of the NOXCOVID-1 trial involved 26 patients and was a dose-escalation arm testing the safety of increasing (400, 600, 800, 1200, 1800 mg) daily Veyonda dosages. The 1800 mg dose was deemed by the clinicians to be sufficiently well tolerated in patients with moderate COVID-19 disease to become the preferred dose. The high tolerance of the drug by patients with very poor lung function provides further evidence of the safety of Veyonda in patients with acute illness.

NOXCOVID-1 Trial Recap
Veyonda is being tested for its ability to block the phenomenon known as cytokine release syndrome (CRS), or *cytokine storm*, and thereby reduce long-term disabilities and death in COVID-19 patients.

This '*storm*' leads on to a life-threatening condition known as septic shock, associated with a broad range of long-term disabilities in both young and older patients, and death in severe cases. It is not specific to the current pandemic, although the death rate from the pandemic currently stands at over 2.5M, many of which are believed to involve CRS and septic shock. To put this in context, pre-pandemic, septic shock was believed responsible for an estimated 10 million death p.a., putting it in the top 5 major causes of human death globally from disease.[1]

It is a so-called *'storm'* because of a sudden and entirely inappropriate surge in the blood of dozens of pro-inflammatory chemicals known as cytokines, resulting in damaging levels of inflammation in blood vessels and major organs. In the case of infection with the COVID-19 virus or other viruses such as the influenza virus, the trigger for CRS is virally-induced lung damage.

Veyonda is being tested for its ability to block the development of CRS in COVID-19 patients with moderate lung damage that is placing them at high risk of developing CRS and septic shock. The aim is to prevent their progression on to needing mechanical ventilation and ICU care, the development of a range of long-term disabilities identified as being associated with COVID-19 disease, and death.

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COMMENT

Noxopharm CEO, Dr Graham Kelly, said, "The high potency of Veyonda in blocking cytokine release from damaged tissue in the laboratory meant we were obliged to adopt a very cautious and methodical approach when being used for the first time in patients with poor lung function. We can now be confident that Veyonda, despite its potency, is well tolerated at a dosage we believe will be therapeutic.

What marks Veyonda as a highly promising drug prospect, where many other drugs have failed in this quest, is its ability to block the release of a wide range of these cytokines. Many of these other drugs block individual cytokines. In the face of surging levels of large numbers of cytokines, it is rational to think that the more cytokines a treatment can block, the better the outcome is likely to be in CRS.

Moving onto Part 2 of the trial represents an important step towards our goal of seeing Veyonda become an effective and safe treatment of septic shock, not just in COVID-19 patients, but as one of the most common causes of human death from infections and severe trauma."

NEXT STEPS

Part 2 of the NOXCOVID-1 trial now is starting to recruit a minimum of 10 and up to 15 patients with moderate to severe lung dysfunction. Patients will be treated for up to 14 days with an 1800 mg Veyonda dose each day.

Part 1 patient blood (Cohorts 1-4) currently is being analysed for 60 pro-inflammatory (cytokines, chemokines) factors in what the Company believes will be one of the most comprehensive analyses of its kind in COVID-19 disease.

COMMITMENT

Noxopharm is committed to pursuing its NOXCOVID program for two main reasons:

1. Despite the advent of COVID-19 vaccines, emerging news of new mutant strains of the virus points to a likely ongoing long-term need for effective treatments for COVID-19 patients who go on to develop lung damage and are at high risk of septic shock
2. The current pandemic represents a small proportion of patients who die each year from septic shock. Even once the pandemic abates, the need for an effective and safe ongoing treatment for septic shock will remain.

1. Rudd KE et al (2020). Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study. Lancet 395:200-211

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.

-ENDS-

About NOXCOVID-1

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NOXCOVID-1 is a Phase Ib study aiming to demonstrate that in COVID-19 patients who are at risk of developing a cytokine storm and septic shock, that Veyonda is (i) well tolerated, and (ii) can halt disease progression into the cytokine release syndrome (CRS) and septic shock.
NOXCOVID-1 is a two-part study comprising dose-escalation followed by dose-expansion. The dose-escalation phase comprises 5 patient cohorts (400, 600, 800, 1200 and 1800 mg Veyonda daily dosages). The dose-expansion phase will use the dose determined to be the optimal.
The study is focusing on safety and proof-of-principle endpoints (biomarker and clinical responses). Approximately 40 patients will be recruited who have been admitted to hospital for respiratory insufficiency (not requiring artificial ventilation) associated with the SARS-CoV-2 virus. Patients will be treated for between 14-28 days depending on their clinical response. The pharmacological rationale is that the first-in-class anti-inflammatory action of Veyonda via the STING signaling pathway will block the release of a broad range of cytokines including a number of interleukins regarded as pivotal to CRS.
The aim is to use Veyonda to prevent the cytokine onslaught from occurring in the first place, rather than other anti-inflammatory treatments such as dexamethasone that provide a partial clinical benefit in patients already experiencing a cytokine storm.

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 trialing. Noxopharm also is the major shareholder of US biotechnology company Nyrada Inc (ASX:NYR), and wholly owns Pharmorage, a private drug development company focused on drug development in the areas of sepsis and autoimmunity.

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