ASX Announcement | 22 April 2021
Noxopharm Limited (ASX:NOX)

Interim NOXCOVID Data Shows Veyonda® Potentially Preventing Cytokine Storm

Highlights

- **Blood samples of first 18 NOXCOVID trial patients analysed for a large suite of inflammatory biomarkers**
- **None of the biomarkers linked to severe COVID-19 disease increased after initiation of Veyonda® treatment**
- **Data indicative of a putative protective effect of Veyonda against hyper-inflammation ('*cytokine storm*') in patients with moderate COVID-19 disease**
- **Key step in the potential development of Veyonda as a treatment for septic shock responsible for an estimated 10 million deaths p.a.**
- **Data supports international patent application lodged 30th March 2021. That provisional patent now becomes a potentially very valuable commercial asset**

Sydney 22 April 2021: Australian clinical-stage drug development company Noxopharm Limited (ASX:NOX) is pleased to provide interim data from its NOXCOVID trial. The purpose of the interim analysis was to help prepare the Company for its next steps in the event of positive data given the current status of the pandemic.

The interim data points to Veyonda® in a cohort of 18 patients with moderately severe COVID-19 disease, providing protection against progression of severe inflammation associated with a worsening of the disease.

The major challenge for hospital services during the current pandemic is the high level of care required for those patients experiencing rapid deterioration of lung function, leading to acute respiratory distress syndrome, septic shock and major disabilities or death. A key factor associated with disease worsening is the excessive production of inflammatory factors normally invoked to facilitate tissue repair and combat infection in a process known as the *cytokine storm*.[1-3] A number of these inflammatory factors have been described as biomarkers of the severity of COVID-19 disease based on increased levels in COVID-19 patients at the start of the infection and further increases occurring with a worsening of their disease.[4]

The current analyses involved a large panel of biomarkers associated with inflammation, coagulation and sepsis, in particular including those biomarkers linked to a worsening of COVID-

19. The analyses were conducted in the first 18 COVID patients enrolled in the study on blood samples collected on Days 1, 3, 7, 14 and 28 of treatment.

That analysis shows that those biomarkers associated with worsening COVID-19 disease[1,2], notably **IL-1β, IL-4, IL-6, IL-10, TNF-α, CRP and D-dimer,** did not rise in any of the 18 patients, including falling in a number of patients.

While correlation of these responses with clinical data will soon be underway, these interim findings point to a protective effect of Veyonda against disease progression and the development of a cytokine storm.

Noxopharm in collaboration with Hudson Institute of Medical Research has discovered that Veyonda has potent anti-inflammatory properties through inhibition of STING signalling, a signalling pathway thought to fuel toxic inflammation and tissue damage in patients with low oxygen level.[5] While further studies are ongoing to implicate this pathway, the observation that none of the key biomarkers identified as being associated with increasing severity of COVID-19 disease[1,2] were increased after initiation of Veyonda treatment, is consistent with the anti-inflammatory effects of Veyonda.

The use of a drug that blocks STING signalling in COVID-19 is of major scientific interest because of the putative key role of STING in triggering a cytokine storm.[5,6] Veyonda is the first drug to reach the clinic that blocks the STING signalling pathway, marking the NOXCOVID trial as an important test of this theory. Noxopharm is pleased to note that today's interim analysis is consistent with a role for STING signalling in COVID-19 disease and thereby a potential important role for Veyonda in the ongoing management of the pandemic.

Comments

Associate Professor Michael Gantier of Hudson Institute of Medical Research, said, "While further correlations with clinical data are essential to gain a full picture, the fact that none of the inflammatory biomarkers progressed in these cohorts of moderately sick COVID-19 patients is aligned with a putative protective effect of Veyonda."

Graham Kelly, Noxopharm CEO, said, "The world is facing an enormous challenge in vaccinating enough people to achieve global herd-immunity in the face of waves of emerging mutant strains of the virus. Until we successfully meet that challenge, millions of people are likely to continue to suffer severe COVID-19 disease involving major disabilities and death. That is where we see Veyonda playing a key role, with its STING blocking action stopping the inflammatory process in patients with moderate COVID-19 disease moving from having a positive effect, to being seriously self-destructive. The interim data released today points to Veyonda delivering on this promise.

Treatments that stop patients progressing into needing high-level health care such as mechanical ventilation and occupying ICU beds is a major industry goal. Our confidence is growing that

Veyonda will form part of meeting that goal, and in so doing, potentially save many lives and deliver shareholders a potentially highly valuable and much sought after asset."

Next steps

The biomarker data from the top Veyonda (1800 mg) dose cohort is expected within the next few weeks. That will be followed by a review of the final clinical data on completion of treatment of the final patient. Clinical status (WHO COVID-19 grade, co-morbidities) and other therapies will need to be taken into account. After reviewing all data, the Company will consult with its medical and business development advisors along with government bodies including drug regulators.

Patent Application

The Company announced last week (6th April 2021) that it had lodged an international patent application on the use of Veyonda to prevent the cytokine storm and septic shock in virally-induced diseases. The provisional patent claims were based on pre-clinical data. Today's interim human data, in the Company's view, confirms the pre-clinical data and substantiates the provisional claims. The patent application provides the Company with a potentially highly valuable asset that Noxopharm expects with confirmatory clinical data to be keenly sought after within the industry.

References

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2. Kox M et al (2020) Cytokine Levels in Critically Ill Patients With COVID-19 and Other Conditions. JAMA 324, 1565 (2020).
3. Dorward DA et al. (2021) Tissue-specific immunopathology in severe COVID-10. Am J Respir Crit Care Med 203, 192-201
4. Samprathi M, Jayashree M (2021) Biomarkers in COVID-19: an up-to-date review. Front Pediatr 30 March https://doi.org/10.3389/fped.2020.607647
5. Bertholet J-M et al (2020) Lymphocyte Changes in Severe COVID-19: Delayed Over-Activation of STING? Front Immunol 11:607069. doi: 10.3389/fimmu.2020.607069
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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.

-ENDS-

About NOXCOVID

NOXCOVID-1 is a Phase I study being conducted in Eastern European hospitals aiming to demonstrate that in COVID-19 patients who are at risk of developing a cytokine storm and septic shock, that Veyonda:

- is well tolerated, and
- can halt disease progression into the cytokine release syndrome and septic shock.

NOXCOVID-1 is a two-part study comprising dose-escalation followed by dose-expansion. The dose-escalation phase comprised 5 patient cohorts (400, 600, 800, 1200 and 1800 mg Veyonda daily dosages). The dose-expansion phase (20 patients) used 1800 mg dose. 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. The aim is to prevent a cytokine onslaught that aggravates lung damage leading to patients requiring mechanical ventilation plus inflicts damage to blood vessels that lead to clotting and major organ failure.
Veyonda is not intended to replace other potential anti-inflammatory treatments like dexamethasone that may provide a clinical benefit in patients with more advanced disease already experiencing a cytokine storm.

About STING
STING (Stimulator of Interferon Genes) plays a key role in innate immunity, detecting the presence of invading organisms (eg., viruses) and cancer and responding by triggering the production of interferon. In the case of viral infections, STING signalling is responsible for antiviral responses, innate immune responses and pro-inflammatory cytokine release.

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 oncotoxic and immuno-oncology 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 Limited (ASX:NOX) is an Australian clinical-stage drug development company focused on the Noxopharm also is the major shareholder of US biotechnology company Nyrada Inc (ASX:NYR).

To learn more, please visit: noxopharm.com

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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.