



**ASX Announcement | 6 April 2021
Noxopharm Limited (ASX:NOX)**

Compelling New Data Moves Noxopharm to Protect Major Veyonda® Opportunity in Septic Shock Treatment

Highlights:

- **Noxopharm responds to compelling COVID-19 pre-clinical data by lodging an International PCT patent application**
- **Patent intended to protect extended use of Veyonda beyond cancer into septic shock applications**
- **Lack of effective treatments means that septic shock is responsible for an estimated 10 million deaths per annum, plus at least another 3 million deaths from COVID-19**
- **Pre-clinical data confirms actions of Veyonda widely considered fundamental to blocking the cytokine storm that leads to septic shock**
- **Data produced by Australian academic collaborators independent of the Company**
- **Analysis of NOXCOVID trial patient blood samples underway.**

Sydney 6 April 2021: Australian clinical-stage drug development company Noxopharm Limited (ASX:NOX) is pleased to announce lodgement of an international patent application aimed at protecting the use of Veyonda® (idronoxil) in blocking the development of septic shock associated with infections such as COVID-19 and influenza viruses.

Veyonda is being developed as an anti-cancer drug that enhances the effectiveness of standard anti-cancer treatments. One of its anti-cancer actions is the blocking of a signalling pathway called STING that serves as trigger for an immune response and repair of damaged tissue. In some individuals, the STING response is inappropriately excessive, pushing the individual over into septic shock.

Veyonda appears to be the first drug that blocks STING in the clinic. With an estimated 1 person dying globally every 3 seconds from cancer and 1 every 3 seconds from septic shock, the commercial opportunity for Veyonda has just doubled, underlining the commercial importance of the recent patent lodgement.

Urgent need and major opportunity

Septic shock occurs in response to viral and bacterial infections from viruses (eg., COVID-19 and influenza viruses) and a wide range of bacterial infections and parasites (eg., malaria) when an inappropriate, dramatic and self-destructive inflammatory response occurs. Large numbers of pro-inflammatory chemicals known as cytokines are released into the blood, creating a range of problems such as clotting that lead to multiple organ damage and death. The chemical response is known as a cytokine release syndrome (CRS) and the entire process is known as septic shock.¹⁻⁵



Septic shock is believed responsible for an estimated 10 million deaths globally per annum,⁶ with an estimated extra 3 million additional deaths from the current pandemic⁷ to be added to that figure and which also includes hundreds of thousands of deaths each year from influenza epidemics.⁸

So-called 'long COVID' symptoms (eg., long-lasting fatigue, breathing problems, headaches), along with severe organ damage (eg., limb amputation, diabetes, kidney and heart failure) and death, all are outcomes associated with septic shock.

Septic shock currently is managed with supportive treatments including drugs and fluids to restore blood pressure, anti-inflammatories such as dexamethasone, and antibiotics/antivirals. However, the key need, that of providing a reduction in cytokine levels in a safe and comprehensive manner remains largely unmet.

The aim of Veyonda is to block the cytokine cascade stemming from an inappropriately high STING response. The objective is to use Veyonda in patient with poor lung function, and by stopping them from tipping over into CRS, thereby reduce the incidence of long-term disability and death and relieve the strain on high-care medical services.

Highly encouraging pre-clinical data

The pre-clinical data is the result of collaborations with eminent Australian scientists at Hudson Institute of Medical Research and the John Curtin School of Medical Research, Australian National University.

The key message from the pre-clinical data is the ability of idronoxil (active ingredient in Veyonda), via STING blocking, to block the production of a suite of cytokines, including ones thought to be involved in septic shock, and in particular, the cytokines associated with excessive clotting. CRS and septic shock are associated with spikes in blood levels of multiple cytokines.⁹ General consensus is that blocking CRS will require reducing levels of a number, if not all, implicated cytokines. Trials to date in COVID-19 patients with drugs that block individual cytokines either have failed for that reason or have proven only moderately effective at best.

The ability of Veyonda to block the generation of multiple cytokines is distinctive and is what marks it as an exciting treatment prospect for septic shock.

The main elements of the pre-clinical data are:

- the capacity of idronoxil to potently block the STING signalling pathway, a key pathway in the CRS response, in a wide range of cells including immune cells
- the identification of a novel molecular target believed involved in the STING signalling pathway, providing an important new drug target not previously identified
- the ability of idronoxil to inhibit the release of IL-6 and TNF- α from human cells and confirmed in mice models (Figure 1). IL-6 and TNF- α are two key cytokines that rise in COVID-19 patients
- early data indicating the capacity of idronoxil to lower the levels of cytokines in the lung fluid of mice infected with Type A influenza virus.

Taken together, these pre-clinical data confirm the strong effect of idronoxil on the cytokine-driven biological mechanisms believed to underly septic shock.

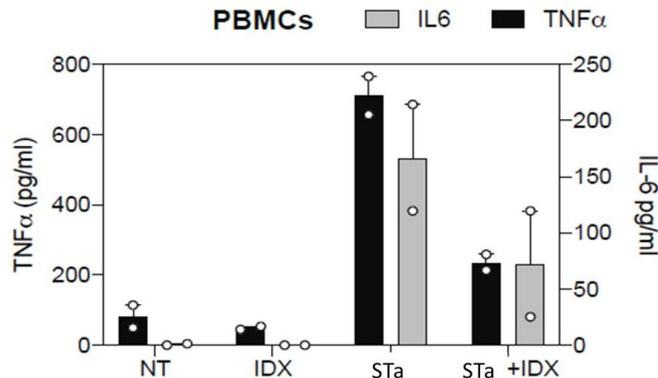


Figure 1: Human peripheral blood mononuclear cells (PBMCs) from two different human blood donors were stimulated with a STING agonist (activator) leading to increased IL-6 and TNF α production. The production of both key cytokines was reduced significantly by idronoxil.

In a comprehensive analysis, Noxopharm currently is testing the blood samples from its NOXCOVID trial patients for an extensive range of cytokines and looks forward to reporting on this in a matter of weeks.

Patent details

The application is entitled ‘*Methods for the treatment of inflammation associated with infection*’ (PCT/AU2021/050282) with a filing date of 30 March 2021.

GLOSSARY

<i>Cytokine</i>	Signalling molecules that regulate immune and inflammatory responses
<i>IL-6</i>	Interleukin-6. A major cytokine mediating immunity and inflammation. One of the cytokines that show a major increase in the blood in COVID-19 patients
<i>TNF-α</i>	Tumour necrosis factor-alpha. Another major pro-inflammatory cytokine
<i>STING</i>	Stimulator of Interferon Genes. Detects the presence of foreign infective organisms and triggers immune and inflammatory responses through the release of Type 1 interferon. Thought to be a primary signalling pathway underlying the triggering of septic shock
<i>Septic shock</i>	A critical drop in blood pressure or blood flow leading to multiple organ failure and potentially death.

References

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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 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 also is the major shareholder of US biotechnology company Nyrada Inc (ASX:NYR).

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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