NOXOPHARM

FOCUS

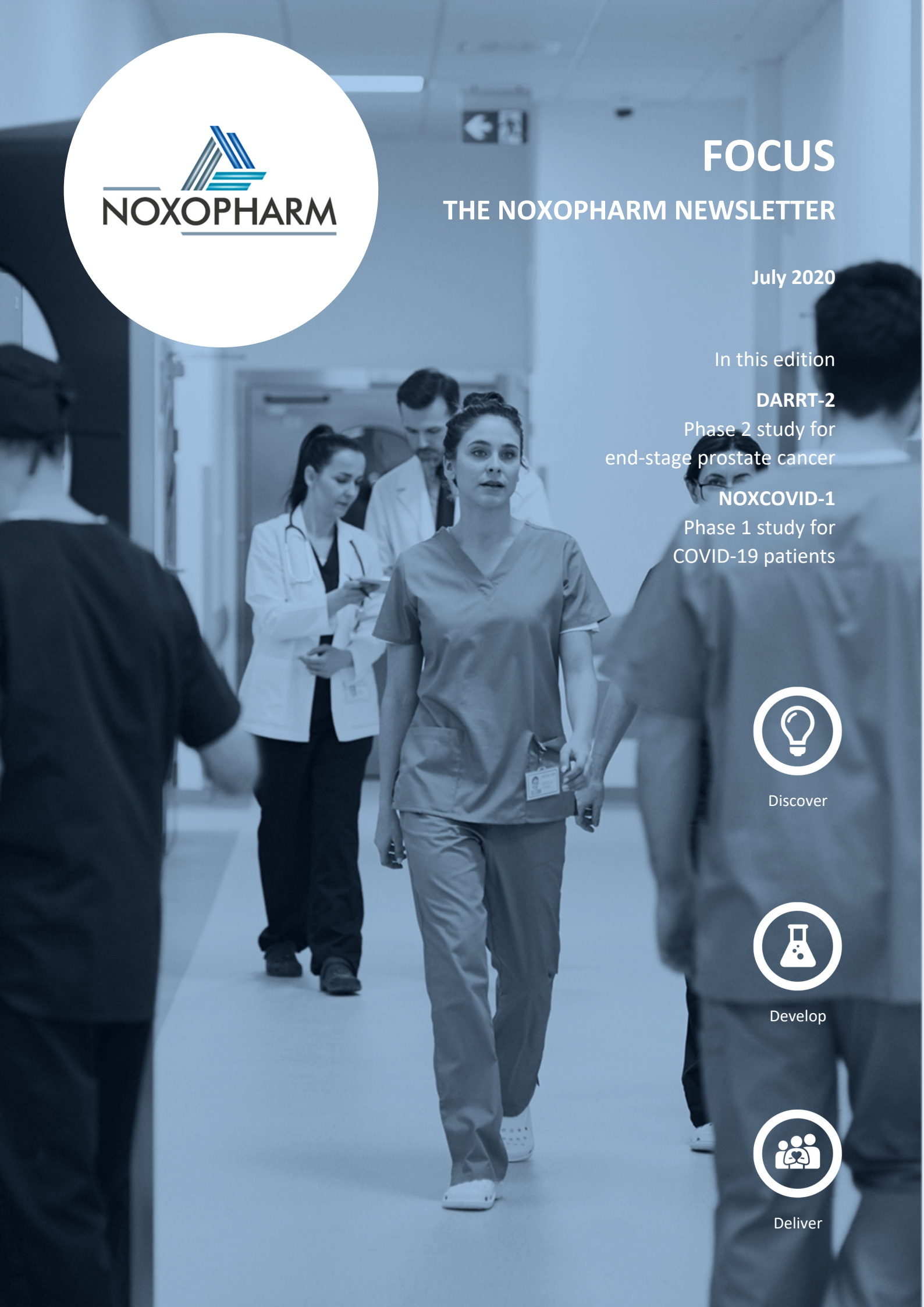
THE NOXOPHARM NEWSLETTER

July 2020

In this edition

DARRT-2
Phase 2 study for
end-stage prostate cancer

NOXCOVID-1
Phase 1 study for
COVID-19 patients



Discover

Develop

Deliver

DARRT-2 coming

With the DARRT-1 study now wrapped up, the Company is busy moving its flagship DARRT program into a Phase 2 study.

DARRT Program in a nutshell

DARRT - a potential new dawn in cancer therapy. An immunotherapy treatment designed to offer patients with end-stage cancer a meaningful last-line treatment when all else has failed

DARRT – aiming to provide pain relief, a better quality of life and a halt to tumour progression when the alternative is short-term palliative care

DARRT-2 trial in a nutshell

DARRT-2 – a Phase 2, proof-of-principle study of the DARRT treatment regimen in end-stage prostate cancer

DARRT-2 - intended as a catalyst for an industry deal based on showing a meaningful anti-cancer response in patients whose cancer has progressed on last-line treatment including progression on treatment with a drug acquired by a major pharma company in 2016 in a **US$14 billion** deal

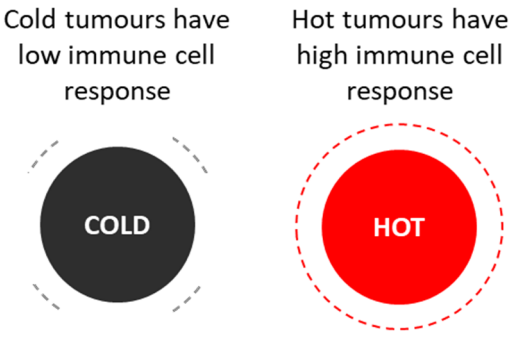
What is DARRT?

Simple. It's an immunotherapy regimen comprising Veyonda® and radiotherapy that aims to convert 'COLD' tumours (lacking immune activity) into 'HOT' tumours (high immune activity). DARRT stands for Direct and Abscopal Response to Radiotherapy and we envisage it becoming a widely-used and standard last-line therapy for many forms of cancer.

Cancers are able to flourish because the body's immune system is failing to do its job. Immunotherapy is designed to restore the competency of the immune system to attack cancer cells. There are many forms of immunotherapy under development, and while some are proving their worth in some forms of cancer, it has yet to deliver on its promise for a larger number of cancer patients. We see DARRT having the potential to deliver on that promise.

The problem appears to lie in most human tumours being 'COLD'. The aim of DARRT is to convert tumours to a 'HOT' state by waking up the body's dormant immune system. DARRT involves a combination of low-dose radiotherapy and Veyonda®. Radiotherapy is good at activating immune cells within the tumours it hits, but with radiotherapy being limited to hitting isolated tumours, the challenge is how to spread the awoken immune response in a few irradiated tumours to the dozens or even hundreds of other non-irradiated tumours scattered throughout the body. That is where Veyonda® comes in. Veyonda® breaks down the barrier that tumours erect to keep immune cells out. Without that barrier, activated immune cells can access the tumours, making them 'HOT' and susceptible to immune attack.

The ultimate goal of DARRT is an anti-cancer response somewhere between stopping the cancer from growing, through to its eradication.



Apply **DARRT (Radiotherapy + VEYONDA®)** to convert COLD tumours to HOT tumours to promote immune response

Why are we committing to DARRT-2?

Because the data from our Phase 1b (DARRT-1) study strongly points to DARRT being an exciting new anti-cancer treatment potentially worth a lot of money.

Safety and tolerability are the key initial hurdles in the drug development pathway and our first DARRT study passed those hurdles with flying colours.

In addition, we saw a number of promising efficacy signals in respect to pain and PSA (prostate specific antigen) and tumour responses. Importantly, these responses were durable, i.e., many of them were maintained until the last study visit at 6 months. The DARRT-1 data was published and presented a few months ago at ASCO (American Society of Clinical Oncology), the premier international oncology conference representing physicians of all oncology sub-specialties and other healthcare professionals who care for people with cancer.

If we can repeat the DARRT-1 outcome in a much larger study, as we are confident of doing, then we believe that shareholders will have a major and potentially very valuable asset on their hands.

How large is the market opportunity?

Not every man who develops prostate cancer dies of it, in fact only about 1 in 10 men diagnosed with prostate cancer go on to die from it. However, that still leaves a lot of men succumbing to this disease, with prostate cancer killing about 3,300 men each year in Australia[1], 33,300 in the U.S.[2] and 77,000 in the EU.[3] Globally, the number is believed to be about 300,000 p.a.[4]

As large as the need and opportunity is in prostate cancer, the Company's real target is end-stage disease of almost any type of solid cancer (not leukaemias) because DARRT has not been designed to be specific just to prostate cancer. We cannot be sure that DARRT will work in every form of cancer, but we are confident that it will work in enough common cancer forms to lead to arguably the largest market sector in the oncology world. We see prostate cancer simply as a starting point and a pointer to what should be possible on a larger scale.

What will DARRT-2 look like?

It will be a multi-national study involving about 200 men across several continents. Patients will be men with progressive, metastatic, castration-resistant prostate cancer who have failed all forms of standard therapy. Patients will be randomised either to the DARRT regimen or to palliative standard of care. The key endpoints will be around establishing whether the DARRT treatment regimen provides a meaningful anti-cancer response compared to standard of care.

Who is running DARRT-2?

Dr Gisela Mautner (CMO), Jeanette Bell (COO) and Sujith Nayar (Senior Clinical Program Manager) is the in-house clinical team overseeing the trial. They will work hand-in-hand with a contract research organisation with multi-national clinical trial experience that will provide the day-to-day management of the study.

When will DARRT-2 start?

DARRT-2 has already started, in the sense that the planning process is well underway. The NOX team is working very hard to fulfill all administrative and clinical study requirements to be able to start enrolling the first patient as soon as possible. We have set a target of recruiting the first patient early in the New Year.

What will it mean to me as a shareholder if DARRT-2 is successful?

- It will mean that Veyonda® becomes a realistic commercial prospect in the search for a new last-line therapy for end-stage prostate cancer, a market the Company assesses as being a multi-billion dollar one
- It will mean the Company (and the market) being able to ascribe a dollar value to Veyonda® based on Phase 2 data
- It will mean having the clinical data to enter into discussions with potential industry partners.

References.

1. Cancer Australia. https://prostate-cancer.canceraustralia.gov.au/statistics
2. American Cancer Society. www.cancer.org
3. Carioli G et al (2020) European cancer mortality predictions for the year 2020 with a focus on prostate cancer. Annals of Oncology https://doi.org/10.1016/j.annonc.2020.02.009
4. Rawla P (2019) Epidemiology of prostate cancer. World Journal of Oncology 10:63-89

NOXCOVID-1 coming

An opportunity that the Company is embracing cautiously but with a firm degree of optimism.

NOXCOVID program in a nutshell

Using Veyonda® to block the hyper-inflammatory response in COVID-19 patients known to be causing a high proportion of COVID-19 deaths and long-term disabilities in recovered patients

NOXCOVID-1 trial in a nutshell

A Phase 1 pilot study of Veyonda® in moderately ill COVID-19 patients who are at high risk of developing severe lung disease or septic shock

Aim 1 = to assess the safety of Veyonda in this patient group

Aim 2 = to test the theory that blocking the STING signalling pathway will prevent or reduce the development of a cytokine storm that puts COVID-19 patients at risk of septic shock and death

Why do we think that Veyonda® is worth trying in COVID-19 patients?

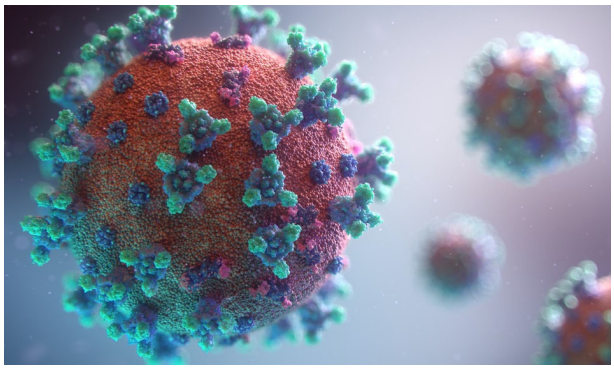
It boils down to one of the unique ways that Veyonda® works as an anti-cancer drug, and that happens to be a way (called blocking STING signalling) that many scientists believe could help avoid many COVID-19 deaths. Based on what we already know about COVID-19, it is a compelling theory, but the problem for doctors up to now has been an inability to test that theory. No drug already in the clinic is known to work in that way. **The good news for Noxopharm is that Veyonda® is such a drug. Veyonda® blocks STING signalling and is clinic-ready.**

What sort of patients may respond to Veyonda®?

Veyonda® is intended only for those COVID-19 patients who have developed lung problems and are considered to be at high risk of deteriorating and dying from the infection. The aim is to use Veyonda® to stop the disease progressing to the point where patients need mechanical ventilation and intensive care.

For most people who contract COVID-19, the disease is little different to any other mild viral infection (eg. colds, influenza). The presence of the virus triggers two responses - an immune response that brings immune cells into the respiratory system to eradicate the virus and an inflammatory response that repairs the damage in the respiratory system caused by the virus. These are neatly coordinated in mild to moderate responses and see most people recover within a matter of 10 days or so. Veyonda® is not intended for these people.

SARS-COV-2 virus

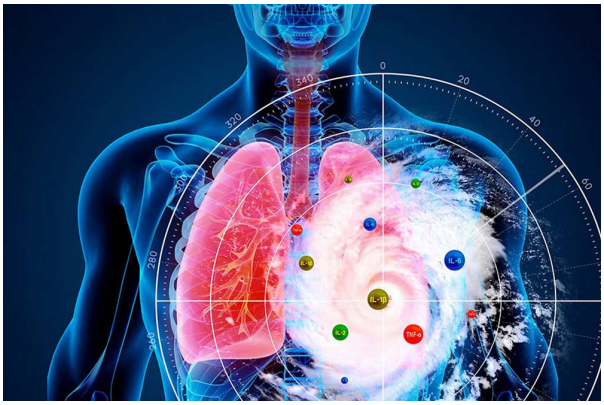


Neither are we planning on using Veyonda® in patients at the other end of the disease spectrum where they have severe disease from COVID-19 and require mechanical ventilation. These patients have a very high risk of dying. The drugs, dexamethasone and remdesivir, have shown some benefit in these patients.

Veyonda® is intended for the middle of these two ends of the spectrum with the aim of stopping patients progressing from the moderate end of the disease spectrum to the severe end. The patients who will be enrolled in the study are the COVID-19 patients who are at high risk of developing more than mild lung damage. That damage reduces the patient's ability to absorb oxygen, resulting in even further tissue damage that tips the patient over into severe illness known as septic shock. Septic shock comes from a completely over-the-top inflammatory response to the virus and the damage it is causing to the lungs. This hyper-inflammatory response triggers the production of proteins known as cytokines to such a high level that it is referred to as a 'cytokine storm'.

These high cytokine levels then cause clotting problems that shut off blood to major organs, triggering septic shock. Septic shock has a very high mortality rate.

Cytokine storm



The aim is to use Veyonda® to stop patients reaching the tipping point that takes them down the road of a cytokine storm and septic shock. The justification for using Veyonda® in this way comes from laboratory data showing it to be a potent blocker of the cytokine storm in tissues damaged by low levels of oxygen.

Why have you decided to run the initial study in Europe?

The simple answer is timing and cost. We want to reach the point of knowing whether Veyonda® is likely to be successful in the quickest and least expensive way.

The U.S. is the most expensive country in the world in which to run clinical trials. COVID-19 patients in the U.S. requiring ICU care for about 3 weeks will cost about US$150,000-200,000 per patient. Multiply that by 200 patients and then add all the other clinical trial costs and you suddenly are looking at a considerable amount of money.

Noxopharm anticipates that when it receives an IND, government or partner funding will be available to run a study. In the meantime, we considered it prudent to conduct a small pilot study in up to about 40 patients in countries where the costs would not be so prohibitive, but to do so by following standard procedures and using hospitals where the data will be acceptable to both U.S. and EC regulatory authorities.

COVID-19 patients in the U.S. require 3 weeks of ICU care at a cost of **US$150,000 to US$200,000 per person**

What are your plans with the FDA?

As time was (and still is) of the essence, we have run two processes in parallel over the last few months. One work stream was to work with Australian and European clinicians to design a pilot-study and one was to engage with the FDA in the US.

We took the first step in the IND process by filing what is known as a pre-IND submission. The FDA responded positively to that submission with guidance on the design of the proposed clinical study.

However, at this point, the European process has been much faster and will be much more cost-effective than the U.S. approach.

The dialogue with the FDA is continuing, and depending on the results of the European trial, we will modify our IND submission accordingly.

What will it mean to shareholders if the European study is successful?

'Success' in our terms means two things:

(i) that the Veyonda® treatment has been well tolerated, and

(ii) that we are seeing positive efficacy signals.

If we achieve both of these outcomes, then:

1. We will have the proof-of-concept data we need to conduct a larger trial in the U.S. and/or EU
2. We will have the data needed to attract the funding for such a trial
3. We will know that we have a potentially major clinical indication in the offing, not just in COVID-19 patients, but in the broader market opportunity of septic shock
4. It creates another reason for a re-rating of the Company
5. It creates another reason for the Company becoming an attractive M&A target

Isn't running a NOXCOVID trial going to affect the DARRT program?

We wouldn't be committing to the NOXCOVID program if we thought so, because starting and completing DARRT-2 in a timely manner remains our priority. NOXCOVID-1 has been fully costed and budgeted for without slowing down in any way the DARRT-2 timetable. In fact, we expect some of the clinical data we will be gathering in NOXCOVID-1 to be useful in the DARRT program. The Company will continue to review its capacity to run both DARRT and NOXCOVID programs and to take any action to prioritise resources to DARRT if and as required.

What do you see as the ultimate benefit of the NOXCOVID program to the Company?

Three years ago we realised that our isoflavonoid technology platform offered drug discovery opportunities well beyond the cancer field. Instead of ignoring that, we created Nyrada Inc as a self-funded vehicle to exploit non-cancer opportunities. Nyrada now is independent and NOX shareholders hold a valuable indirect interest in those non-oncology opportunities.

NOXCOVID is another such non-oncology opportunity. We have firm laboratory evidence that the same isoflavonoid chemistry platform that spawned Nyrada is offering significant potential in the field of septic shock, and with septic shock being a major community problem well beyond COVID-19, Noxopharm sees a significant commercial opportunity and the potential for another Nyrada situation.

We will have more information to share with you on our website that we will add to as we progress. Please visit the website to find more about our story, our science, and our plans for the future.

www.noxopharm.com

Noxopharm Limited
ABN 50 608 966 123

Level 4, 828 Pacific Highway
Gordon 2072 NSW AUSTRALIA

Graham Kelly, CEO and Chairman of Noxopharm, has approved the release of this document to the market.

Email: info@noxopharm.com
Phone:(+61) 2 9144 2223

Address: PO Box 292,
Gordon 2072 NSW AUSTRALIA

Forward Looking Statements: This Newsletter may contain forward-looking statements. You can identify these statements by the fact they use words such as “aim”, “anticipate”, “assume”, “believe”, “continue”, “could”, “estimate”, “expect”, “intend”, “may”, “plan”, “predict”, “project”, “plan”, “should”, “target”, “will” or “would” or the negative of such terms or other similar expressions. Forward-looking statements are based on estimates, projections and assumptions made by Noxopharm about circumstances and events that have not yet taken place. Although Noxopharm believes the 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. No representation, warranty or assurance (express or implied) is given or made by Noxopharm that the forward-looking statements contained in this press release are accurate and undue reliance should not be placed upon such statements.