ASX ANNOUNCEMENT **6 January 2021**

Noxopharm Shareholder Update 2021

- **Veyonda® emerging as major new immunotherapy drug with potential $multi-billion value based on first-in-class ability to boost effectiveness of all three major forms of cancer treatment – immuno-oncology therapy, radiotherapy, chemotherapy**
  - **IONIC study to test ability of Veyonda to boost response to major immuno-oncology drug, Opdivo® (Bristol Myers Squibb), a sector with p.a. sales of US$20 billion**
  - **LuPIN study testing ability of Veyonda to boost response to US$6 billion radiopharmaceutical, ^{177}LuPSMA-617 (Novartis). Important survival data being released mid-February 2021**
  - **DARRT-2 study testing ability of Veyonda to be first drug to achieve high rates of abscopal effect in patients with prostate, breast or lung cancers**
- **NOXCOVID trial progressing as planned with the aim of blocking cytokine release syndrome and preventing deaths and long-term disability. Trial likely to expand as the pandemic death rates rise across Europe**
- **Strong cash position following recent capital raise of A$23M.**

6 January 2021 Sydney, Australia: Australian clinical stage drug development company, Noxopharm Limited (ASX:NOX), provides this shareholder update as a summary of R&D progress in 2020 and a guide to what 2021 is expected to hold for the Company.

SUMMARY

Noxopharm is confident that its lead drug candidate, Veyonda®, can boost the response rates to most forms of cancer therapies in a way that promises to revolutionise the treatment of cancer and position Noxopharm as a major commercial target.

Last year showed what was possible scientifically and clinically, resulting in growing industry interest; the Company sees 2021 as the year where that interest begins to be converted into transactional/partnering discussions.

(i) Strategic Objectives

Restoring immune function inside tumours is arguably the current major prize in oncology. All because an active immune system is now known to be essential if all forms of cancer therapy are

to reach their full potential, including not just the new wave of immuno-oncology therapies, but also the standard chemotherapies and radiotherapies that continue to be the backbone of cancer treatment. The result is that major Pharmaceutical companies currently are actively engaging with Biotechnology companies holding novel immunotherapy technologies, with a range of high value transactional deals on offer in the multi-billion dollar range.

Noxopharm believes through Veyonda that it has achieved a leading position in the race to develop an immunotherapy drug capable of restoring immune function to tumours, the so-called COLD to HOT effect, and is confident that this leading position will translate shortly into commercial discussions. To that end, the Company is in the process of assembling an experienced Business Development capability in-house to work with external advisors to meet this opportunity head-on.

Noxopharm is well underway with preparing the fundamental requirements of any commercial deal (clinical data, intellectual property protection, mechanism of action). This opportunity, along with our short and long-term strategies and robust 2021/2022 R&D plan, is designed with those transactional/partnering requirements in mind and will position Noxopharm well for successful commercial discussions.

(ii) Portfolio Overview

Noxopharm is acting strategically in developing an innovative and diverse portfolio of clinical research to establish the credentials of Veyonda as the leading and most broadly-acting immunotherapy drug.

Veyonda has the potential to extend a range of treatment options for those living with cancer, whether this be, by way of example:

- a patient with a solid cancer such as breast cancer or a sarcoma being treated with chemotherapy drugs like carboplatin and doxorubicin, or
- a patient with prostate, breast or lung cancer receiving externally delivered radiotherapy, or
- a patient with prostate cancer receiving an intravenous radiopharmaceutical, or
- a patient with ovarian or bowel cancer or melanoma receiving immuno-oncology treatment.

Noxopharm foresees Veyonda boosting the responses rates to all these therapies in a way that promises to revolutionise the treatment of cancer.

What really distinguishes Veyonda and marks it as a potentially highly valuable drug is not just an ability to deliver this much sought-after immunotherapy function, but the strong indication that it possesses a range of additional key anti-cancer functions including anti-inflammatory and anti-autophagy effects. It is the sum of these various functions that differentiates Veyonda as unique and the first potential companion treatment for most forms of cancer treatment - a feat not achieved to date and creating a market valuation position not previously explored.

(iii) Overall Perspective

Noxopharm believes that it is a case of being in the right place at the right time with Veyonda and its mechanisms of action that dove-tail perfectly into the unmet needs of some highly valued markets. There is no more highly prized sector in the field of oncology than a demonstrated ability to overcome the high level of resistance to checkpoint inhibiting drugs such as Opdivo. With checkpoint inhibitors (Opdivo®, Yervoy®, Keytruda®) enjoying annual sales collectively of US$20 billion, overcoming resistance to them carries the potential reward of generating sales many analysts predict will be in excess of US$100 billion. This opportunity overshadows almost every other sector of the pharmaceutical market, and success, even modest success, has the capacity to bring very substantial rewards. Should Veyonda achieve this, and Noxopharm believes it can, then the Company looks forward to a re-rating that reflects the value of the contribution being made by Veyonda to that potential sales lift.

But there are many other prizes that the Company can achieve with its other programs. The DARRT and LuPIN opportunities are both potentially huge, as the majority of large and medium size pharma companies are eager to acquire new drugs to increase their market share in oncology. Both programs have delivered sufficient clinical data to date to be confident of their ultimate success. This means that the Company has three active programs that together or separately have a big chance of being attractive to several potential partners, which will make future negotiations very interesting.

The DARRT and LuPIN opportunities we have been reporting on continue to drive the value proposition of Veyonda and sit squarely within the Company's overall commercial strategy and focus.

The NOXCOVID program is an altruistic, opportunistic situation that will be carefully managed within the context of the Company's commercial strategy. With valid questions remaining about the ability of the pandemic to be fully controlled by vaccination, humanitarian reasons alone dictate the need to come up with companion therapies to assist patients who succumb to serious lung dysfunction. For that reason, Noxopharm will press forward with what it regards as a unique opportunity to deliver an effective block to cytokine release syndrome and septic shock.

(iv) Resources

Noxopharm made remarkable progress in 2020 with a core team of just 17 dedicated individuals. That team will need to grow modestly in 2021 to meet a significant uptick in clinical and preclinical activities as the Company takes steps to package itself as a highly desirable partnering opportunity with a rich portfolio of research on offer.

The Company starts the year with a solid cash position of approximately A$23 million, with the anticipated Australian Government's 2020 R&D Rebate yet to be banked. This puts the Company in a strong position to execute its R&D plans.

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DETAILS

(a) IONIC-1 Study

IONIC-1 is a pilot Phase I/II study, with Noxopharm and US$140 billion Bristol Myers Squibb (NYSE:BMY) co-operating to see if Veyonda can overcome resistance to nivolumab (Opdivo®) found in most cancers. Success could pave the way for an Opdivo/Veyonda combination becoming standard of care for most forms of solid cancer.

The Opdivo/Veyonda combination will be administered to two types of patients:

a) those with cancers known to be capable of responding to Opdivo (eg. melanoma, lung and bladder cancers) showing mild progression after having failed to respond to Opdivo
b) those with cancer types (almost all other forms of cancer) shown by experience to be unlikely to respond to Opdivo and therefore not exposed to Opdivo, and which are showing mild progression on chemotherapy or targeted therapy.

Under the supervision of Professor Paul de Souza, this study is due to start in three Sydney cancer clinics in early-Q12021.

Treatment will be given in 2-weekly cycles; Opdivo is to be administered on Day 1 and Veyonda on Days 1-7 of each cycle. Veyonda will be tested at three escalating dosages – 1200, 1800, 2400 mg daily.

Patients will be scanned at 2, 4, 6, 12, 18 and 24 months to determine response to treatment. Given that none of the cancers are expected to respond in any meaningful way to the Opdivo treatment on its own, any benefit of the combination treatment can be attributed to a large extent to Veyonda and should become evident relatively early in the trial. The early scans (2 and 4 months) are designed to detect response to treatment, and the later scans (6-24 months) the durability of any response.

Efforts to make the new wave of immuno-oncology therapies (checkpoint inhibitors) work in more patients and deliver longer-lasting benefit, currently dominate the global pharma industry. All driven by the opportunity to lift current sales of these drugs (US$20 billion) to levels well in excess of that. Noxopharm is confident that it is in a unique and key position in this race via a number of key factors:

- pre-clinical evidence showing idronoxil achieving the essential breaking down of the barrier responsible for excluding immune cells from tumours (COLD to HOT conversion)
- idronoxil works across most cancer types, offering the prospect of Veyonda boosting the effectiveness of drugs like nivolumab across the full cancer spectrum
- Veyonda is not reliant on a single mechanism of action, possessing a unique combination of multiple anti-cancer functions that add up to a powerful anti-cancer effect.

(b) DARRT-2 Study

DARRT-2 is a Phase II study testing the ability of the combination of Veyonda and low-dose external beam radiotherapy to induce an anti-cancer immunological response known as an abscopal response. Noxopharm is one of just a handful of companies known to be pursuing this response as a form of cancer therapy and is confident that it has the leading position.

An abscopal response is a highly desirable anti-cancer response, offering the prospect of a durable and partial or complete response from a relatively non-invasive, relatively inexpensive and very well-tolerated course of treatment. The challenge up to now has been elevating an extremely rare phenomenon into a clinically relevant level of response to match that of the other new wave of immuno-oncology treatments such as nivolumab. A recent study by Weill-Cornell University in the U.S. has shed ground-breaking light on this problem and why an abscopal response can be so difficult to generate. They showed that triggering an abscopal response is highly dependent on blocking the cancer cell's ability to repair the damage caused by the radiation; retaining that damage helps trigger the immune response behind the abscopal response. That damage is repaired by a process known as autophagy, and idronoxil, the active ingredient in Veyonda, is a potent inhibitor of autophagy.

Noxopharm sees pursuit of its DARRT program in parallel with the IONIC program in 2021 as an important strategic play for the following reasons:

- despite a high level of resistance to Opdivo, it still enjoys annual sales of US$8 billion. If Veyonda is successful in boosting the response rate to nivolumab even by a modest amount, the commercial value of that effect by Veyonda would likely trump all other R&D activities. However, until we see that success, abundant caution dictates that we spread the risk
- it is not a matter of wondering if the Veyonda/radiotherapy combination can produce an abscopal response - the Phase I DARRT-1 study showed that it can. DARRT-2 builds on that by using a more intensive Veyonda dosage regimen that the Company believes is likely to be considerably more effective, as well as broadening the application of DARRT into breast and lung cancer.

DARRT-2 is a multi-national study in approximately 100-150 patients with prostate, breast and lung cancers that have progressed. Escalating dosages of Veyonda (1200, 1600, 2400 mg) are being tested in combination with a fixed dose (low-dose) of radiotherapy.

This study is being prepared for sites in North America, Europe, and Australia. First patient is expected to be enrolled in Q2 2021. With some 30 sites expected to be involved, the aim is to see enrolment well advanced by the end of 2021.

Patients will be scanned at 3, 6, 12 and 24 months, marking Q1 2022 as likely providing guidance on the success or otherwise of this novel approach to cancer therapy.

(c) LuPIN study

This Phase 2 study in 56 men with end-stage prostate cancer has completed the treatment phase and currently is in the follow-up phase of measuring 12-month overall survival. Q3 2021 is the 12-month end-point.

The key question being asked in this study is whether Veyonda can elevate the modest response rates to the Novartis radiopharmaceutical, ^{177}lutetium-PSMA-617 acquired in 2018 through a US$6 billion series of acquisitions. Deeper responses leading to longer patient survival, more so than more men responding, is the main objective.

An earlier Australian-wide study of the Novartis drug alone in men with advanced prostate cancer showed a median overall survival (OS) of **13.5 months**, a meaningful improvement on historical survival data for men at this stage of disease. However, the duration of the response is modest in most men, leading St Vincent's Hospital Sydney, one of the major sponsors in the world of this form of experimental therapy, to ask whether the addition of Veyonda could improve survival outcomes even more.

In Feb 2020, the LuPIN investigators reported to an international cancer conference that the median OS for the first 32 patients at that time was **17.1 months**, a noteworthy increase on **13.5 months**. This coming February (11-13 Feb 2021), the study investigators led by Associate Professor Louise Emmett are reporting on the progressive median OS of all 56 men to the same conference – the *American Society of Clinical Oncology (ASCO) Genitourinary Cancers Symposium* in San Francisco. If the median OS continues to be as good or hopefully improved beyond the previously reported 17.1 months, then Noxopharm believes it will have a significant medical and commercial opportunity on its hands.

(d) NOXCOVID-1 study

Noxopharm is committed to concluding NOXCOVID-1 as quickly as possible in early-2021 and, providing it has a successful outcome, will look to expand into a Phase 2/3 NOXCOVID-2 study involving European and U.S. sites.

Noxopharm is committed to its NOXCOVID Program on the back of compelling data from independent research. That research involved a laboratory model designed to mimic the tissue damage that follows catastrophically low oxygen levels, such as occur in COVID-19 patients with severely impaired lung function. That data showed that idronoxil successfully blocked the release of chemicals known as inflammatory cytokines producing the cytokine release syndrome (CRS) (or so-called 'cytokine storm') responsible for the cataclysmic clotting abnormalities behind most COVID-19 deaths.

The target patient group is individuals with moderate Acute Respiratory Distress Syndrome (ARDS) whose lungs are sufficiently impaired to require supplemental oxygen. The aim of Veyonda is to stop the approximately 30-40% of such patients who suddenly progress into CRS, aggravating the lung dysfunction to the point of requiring intensive care management and

mechanical ventilation and putting the patient at risk of death or recovery with major complications including limb amputation, diabetes, kidney failure etc.

The Company has taken a deliberately cautious approach for two main reasons. First, because we did not want to risk the Veyonda portfolio if we encountered unexpected complications including deaths in a population at such high risk of sudden death or long-term complications. Second, because despite some hundreds of clinical trials, no treatment yet has proven to be effective in preventing this acute progression from general medical care into ICU care, the basis of medical facilities becoming overwhelmed in any pandemic. The unique nature of how Veyonda is working, including potent inhibition of the cellular pathways responsible for CRS, gives the Company confidence that it could succeed where so many others have not.

NOXCOVID-1 has a dose-escalation phase involving 5 dosage cohorts - 400, 600, 800, 1200, 1800 mg Veyonda - followed by a dose-expansion phase at the best tolerated and safest dose. We closed 2020 having completed treatment of the first 4 dose cohorts. We reported on the safety of the treatment in Cohorts 1 and 2, and we expect to report on Cohorts 3 and 4 imminently. In preparation for an eventual successful progression into the expansion arm and potentially beyond, the Company currently is actively exploring expansion of the study into other countries.

(e) Pipeline

Work towards building a robust drug pipeline will continue at an accelerated pace in 2021. The current two programs concern first-in-class treatments for (i) pancreatic carcinoma and cholangiocarcinoma, based on potent, highly selective cytotoxicity, and (ii) brain cancers, based on inhibition of metabotropic glutamate receptor activity. Both programs build on the technology platform that delivered Veyonda and promise through their novelty and meeting unmet need to be high-profile programs.

The anticipated timetable is by mid-2021 to have identified lead drug candidates and to be underway with standard pre-clinical testing programs.

(f) Pharmorage

On November 5 2020, Noxopharm announced the establishment of a new subsidiary, Pharmorage Pty Ltd. The purpose of this new entity is to build on the discovery that idronoxil has anti-inflammatory actions potentially useful in the treatment of cytokine release syndrome and septic shock. Pharmorage has the charter of building a drug development business based around the discovery of drugs to treat septic shock and a range of autoimmune diseases.

In conjunction with a number of eminent Australian researchers, Pharmorage has initiated a number of drug discovery programs that already are starting to bear fruit and which will be reported on progressively in 2021.

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 cytokine release syndrome/septic shock.

Veyonda® is the Company's first pipe-line drug candidate currently in Phase 2 clinical trialing. Veyonda® has two main drug actions – inhibition of sphingosine kinase and inhibition of STING signaling. 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 sepsis.

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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