September 2021 Quarterly Activities Report and Appendix 4C

- **DARRT-2 and IONIC studies reach patient recruitment stage with patients currently being screened**
- **Company builds on positive LuPIN-1 data with moves to develop Veyonda as a first-in-class enhancer of radioligand treatment more broadly**
- **Expert advice recommends development of Veyonda as a COVID-19 treatment; NOXCOVID Consortium established to steer development strategy**
- **Veyonda manufacturing and distribution logistics strengthened ahead of anticipated growth in use**
- **Oncology drug pipeline makes important progress towards identifying three new first-in-class drugs**
- **Pharmorage strengthens its inflammatory drug pipeline and consolidates its relationship with Hudson Institute**
- **Potential commercial value of Veyonda increases as patent claims for therapeutic uses with chemotherapy and radiotherapy granted**
- **Financial position strong at $23.6M ahead of anticipated 2020-2021 R&D Rebate.**

Sydney 14 October 2021: Australian clinical-stage drug development company Noxopharm Limited (ASX:NOX) provides this Quarterly Activities Report and Appendix 4C for the period ending 30 September 2021.

The Company's activities revolve around four core business programs.

Veyonda

Cancer treatment enhancement

Cancer Research Pipeline

Cancer growth factor inhibitors

Veyonda

Septic shock

pharmorage

Chronic inflammatory diseases/autoimmune diseases

Veyonda - Cancer

(i) DARRT, IONIC and CEP Clinical Programs

These three active programs involve executing clinical trials across three continents and engaging with dozens of hospitals. The logistics in coordinating this level of clinical activity is considerable and this quarter saw solid progress in the delivery of hospital contracts, obtaining ethics approvals, conducting site initiations, and the shipment of drug across multiple regions.

The COVID-19 pandemic has had a significant drag this quarter on the Sydney-centric IONIC study with its implementation coinciding with the outbreak of the Delta variant. Travel restrictions, community lockdowns and pressure on hospital resources and staff have had the effect worldwide of reducing the attention of clinicians and hospital administrators to clinical trials, through to delays in patient recruitment, challenges that now happily appear to be largely over in the territories where the Company is conducting its trial programs.

IONIC Program

This quarter:

- The first site qualification was completed, with patient screening getting underway at the end of the quarter
- Pre-enrolment activities also progressed with a number of additional Sydney sites, including major Sydney teaching hospitals, expected to start screening patients very shortly
- A support laboratory also was established at the Ingham Institute of Applied Medical Research in Sydney. This laboratory will conduct a wide range of assays intended to provide insights into how Veyonda is expected to overcome resistance to immune checkpoint inhibitors.

The IONIC trial is an Investigator Initiated Trial, meaning that the logistics of the study are not under the control of the co-sponsors, Noxopharm and Bristol Myer Squibb. Both companies and the trial investigators look forward to getting into the treatment phase of this important trial.

DARRT Program

This quarter:

- All DARRT-2 trial sites across four countries were confirmed, including two highly prestigious U.S. trial sites
- Start-up activities were completed in several sites
- Patient screening has commenced in the U.S.

CEP Program

This quarter:

- seven major U.S. sites confirmed their participation in the study, with patient recruitment targeted to commence before the end of 2021.

(ii) LuPIN Program

This quarter:

- The LuPIN phase 2 trial results were published in the *Journal of Nuclear Medicine*, confirming the median Overall Survival outcome of 19.7 months with the Veyonda/Lu-PSMA-617 combination (*ASX: 5 August 2021*). This is a meaningful anti-cancer response in such late-stage cancer and compares very favourably with Lu-PSMA-617 therapy on its own. Additional findings for this study were: 86% had a reduction in PSA levels; 61% had a PSA reduction >50% and median PSA progression-free survival was 7.5 months

- This effect also was confirmed in a recent animal study where the combination of Veyonda with LuPSMA showed a synergistic effect with sustained and almost complete regression of tumours (*ASX: 5 August 2021*), a response not found in animals treated with LuPSMA or Veyonda alone. The combination therapy went beyond the blocking of tumour growth to the full regression of most of the tumours, to the extent that median overall survival could not be determined

- Both announcements have led to industry and clinician enquiry. A number of those enquiries have been the subject of ongoing discussions this quarter, all with the intention of acting on what the Company believes is a major opportunity for Veyonda to become a standard way of boosting the effectiveness of a range of radioligand products, including ^{177}lutetium-PSMA. The Company will report on those discussions as soon as commercially possible.

(iii) Compassionate Use Program

Noxopharm makes Veyonda available under a compassionate use program. One of the main users of that program is the theranostics division of GenesisCare, a major global radiology provider providing ^{177}lutetium-PSMA treatment for men with late-stage prostate cancer. Over one hundred men now have been treated by GenesisCare in that program, including men with cancers refractory to ^{177}lutetium-PSMA. This quarter the Company commenced working with GenesisCare to collate what is a considerable amount of data which the Company is optimistic will further support the ability of Veyonda to overcome resistance to radioligand therapy.

(iv) Drug supply

As the Company expands its clinical study sites in the US and Europe and responds to requests for access to Veyonda, it has focused on scaling up its manufacturing pipeline to supply this surge in demand. Helping this situation, the Company also was able to generate the supporting data required to increase the shelf-life of Veyonda to a minimum of 18 months. Pack-and-label/distribution centres also were established in Melbourne, San Diego and Berlin that will warehouse and supply drug. Pleasingly, the pandemic has had little or no negative impact upon drug manufacture and supply.

Veyonda – Septic Shock

In this quarter:

- The headline findings of the NOXCOVID-1 trial were released (*ASX: 23 August 2021*), with the final data currently being assembled for publication and conference presentation
- The headline findings were viewed by the Company as highly encouraging in terms of (i) the safety of the drug in patients hospitalized with COVID-19 disease, and (ii) the low rate of disease progression measured by clinical status and levels of blood biomarkers (cytokines) indicative of disease severity.

However, with the dynamics of the pandemic in such a state of flux, the Company wanted expert advice on the merits of continuing with the NOXCOVID program and to this end assembled a panel of local medical and scientific experts.

NOXCOVID Medical Advisory Panel

- **Professor Philip Bardin**, respiratory physician. *Head of the Respiratory and Lung Research Group, Professor of Respiratory Medicine, Faculty of Medicine, Monash University; Research Group Head, Hudson Institute of Medical Research*
- **Professor Robert Booy**, infectious diseases paediatrician. *Senior Professorial Fellow University of Sydney Children's Hospital Westmead Clinical School*
- **Professor Marcel Nold**, respiratory physician/scientist. *Professor of Paediatric Immunology, Monash University; Research Group Head, Hudson Institute of Medical Research*
- **Associate Professor Michael Gantier**, scientist. *Research Group Head, Centre for Innate Immunity and Infectious Disease, Hudson Institute of Medical Research*

The Panel's brief was to form an opinion on whether the NOXCOVID data showed that Veyonda had the potential to provide a meaningful anti-inflammatory effect in patients with moderate COVID-19 disease, and, if so, whether there was a need for such a treatment.

The Panel's advice was in the affirmative to both questions.

With much of the morbidity and mortality in COVID-19 disease believed to be associated with an excessive inflammatory response to the presence of the virus, anti-inflammatory treatment is part of standard treatment of patients with moderate or severe COVID-19 disease. The gap identified by the Panel lies between new anti-viral drugs such as molnupiravir and off-the-shelf anti-inflammatory drugs such as dexamethasone and monoclonal cytokine inhibitors:

- antiviral drugs have promising potential when taken early enough to curb viral replication, but apart from not having any anti-inflammatory action themselves, symptoms of inflammation requiring treatment can persist long after the virus is cleared[1];
- dexamethasone has proven to be of limited benefit in patients with non-severe pneumonia, with side-effects potentially outweighing benefits[2];
- monoclonal antibodies against cytokines such as IL-6 and TNF, while providing some small benefit,[3] are too restrictive in the face of a COVID-19 inflammatory response ('cytokine storm') involving a battery of pro-inflammatory cytokines whose collective actions lead to damage of the lining of blood vessels with resulting blood clotting and catastrophic major organ failure.[4]

The potential of Veyonda as a COVID-19 treatment lies in its unique anti-inflammatory mechanism of action announced this quarter (*ASX: 23 August 2021*). The self-destructive hyper-inflammatory response that occurs in up to an estimated 30% of COVID-19 patients[5] has its roots in two sources.

The first is the presence of the virus itself in lung cells and the second is the lung damage caused by the virus. Both sources trigger separate responses that are funnelled through a common protein switch-point known as TANK-binding kinase 1 (TBK1). **Idronoxil, the active ingredient in Veyonda, is a potent inhibitor of TBK1, offering the opportunity as the only known TBK1 inhibitor in the clinic to block both sources of inflammation in COVID-19 patients.**

With the decision to proceed with the NOXCOVID program, the three parties involved came together to form the NOXCOVID Consortium to serve as a steering committee under the chairmanship of Noxopharm CMO, Dr Gisela Mautner.

NOXCOVID Consortium

- **NOXCOVID Advisory Panel**
- **Hudson Institute of Medical Research**
- **Noxopharm Limited**

The Consortium has begun the process of applying to join one of the fully funded multi-national adaptive trials currently running globally. These trials involve large numbers of patients and include a control arm. They typically involve a number of different drugs, with new drugs being added on a rolling basis to replace others deemed ineffective or unsafe. While inflammation is a major aspect of COVID-19 disease, there appears to be few new anti-inflammatories under test, an opportunity that the Consortium believes makes for a strong case for Veyonda. That case is based on a mechanism of anti-inflammatory action believed highly relevant to the form of hyper-inflammation associated with COVID-19, along with a summary of the NOXCOVID-1 Phase 1 clinical data embracing clinical responses, blood cytokine levels, and safety.

References

1. Janik E et al. *Existing drugs considered as promising in COVID-19 therapy*. Int J Mol Sci (2021) 22:5434. https://doi.org/10.3390/ijms22115434
2. *Dexamethasone in hospitalised patients with Covid-19.* The RECOVERY Collaborative Group. N Engl J Med (2021) 384:693-704 doi: 10.1056/NEJMoa2021436
3. Heimfarth L et al. *Drug repurposing and cytokine management in response to COVID-19: a review*. Int Immunopharmacol (2020) 88: 106947 doi: 10.1016/j.intimp.2020.106947
4. Cron, RQ et al. *Calming the cytokine storm in COVID-19. Nat Med* (2021) https://doi.org/10.1038/s41591-021-01500-9
5. Yong SJ. *Long COVID or post-COVID-19 syndrome: putative pathophysiology, risk factors, and treatments*. Infect Dis (Lond) (2021) 53:737-754 doi: 10.1080/23744235.2021.1924397.

Pipeline – Cancer

In this quarter:

- Noxopharm continued to work on finalizing its data package supporting the capacity of idronoxil to lower tumour resistance to immune cell infiltration, with the aim of submitting the first set of results to an international peer-reviewed journal by the end of Q4 2021
- Conducted studies designed to acquire in depth understanding of the role of idronoxil to act as a direct cell death agent in cancer cells, to block autophagy, and to lower resistance toward immune cell infiltration with existing collaborators in Australia, Germany and Hong Kong. A new and important academic collaboration also was established in the U.S.
- A number of key collaborations were established with renowned academic collaborators both in Australia and the U.S. around the concept of blocking 'helper' growth signals sent by

neighbouring stromal cells making major contributions to the aggressive growth of cancers such as brain and pancreatic cancers. In this quarter the Company identified lead molecules for both pancreatic and brain cancer programs and is planning to lodge a provisional patent around these compounds by the end of Q4 2021. An additional important goal of this program is the development of high through-put drug screening assays that will allow for the identification of additional drug candidates in the future, providing Noxopharm with a cutting-edge technology to support its mission of becoming a major drug discovery company.

Pharmorage

A program of integrated studies is part of an ongoing collaboration with Hudson Institute of Medical Research, Monash Health, the Australian National University, and the Centenary UTS Centre for Inflammation. This quarter, those studies confirmed the ability of idronoxil to:

- Block expression of STING induced inflammation genes
- Block cytokine release syndrome triggered by influenza virus in mice
- Decrease influenza viral loads in lungs of infected mice
- Decrease SARS-Co-V2 infection in a strain of mouse genetically modified to mimic human COVID-19 disease.

While the data from these studies serves to provide the scientific rationale for the development of Veyonda in the treatment of COVID-19 disease and sepsis, they also serve as a platform for the development of a new generation of idronoxil-like drugs as specific treatments for chronic inflammation including septic shock and autoimmune diseases.

Patent portfolio

The following key patent developments occurred this quarter in relation to protecting the use of idronoxil (i) in a suppository dosage form, (ii) in combination with chemotherapy, and (iii) in combination with radiation therapy (both externally and internally delivered):

1. **Isoflavonoid composition with improved pharmacokinetics**
   - European application allowed (EP 17778482.4)

2. **Method of treating cancer using a combination treatment entitled "Combination chemotherapy"**
   - Japanese application allowed (JP 2018-555499)

3. **Method of treating cancer by inducing an abscopal response entitled "Radiotherapy improvements"**
   - US application allowed (US 16/091706)

Financial

The Company remains in a strong financial position, with expenditure in line with forecasts. In light of a rapidly expanding clinical program, the Company remains confident of meeting anticipated business expenses over the 2021-22 FY.

- As at 30 September 2021, Noxopharm had $23.6m in cash
- Net cash used for operating activities during the quarter amounted to ($4.4m), compared to ($4.4m) in the quarter to June 2021. The company made payments for research and development of $2.9m during the quarter, compared to $2.9m in the June 2021 quarter
- The company received $1.2m from the exercise of options during the quarter.

** In accordance with Listing Rule 4.7C, payments made to related parties and their associates included in items 6.1 of the Appendix 4C includes Director fees and salary (including superannuation) for executive directors and related parties.

-ENDS-

Dr 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.

About the NOXCOVID Consortium

The Consortium was confirmed on 1st October 2021 and has the purpose of maintaining a watching brief that includes reviewing pre-clinical data and overseeing the NOXCOVID clinical development program. It has no formal structure and participants are free to participate to the extent they can and leave when they wish. Members of the Medical Advisory Panel are entitled to an honorarium based on an hourly rate in accordance with the rules of their respective institutions.

About Hudson Institute of Medical Research

A global bioscience medical research leader, Hudson Institute's sole focus is on powering breakthrough scientific discoveries into improved health care that will transform lives. We strive to improve human health through ground-breaking, collaborative, medical research discoveries and the translation of these to real world impact.

Hudson Institute scientists research five areas of medical need:

- Inflammation
- Reproductive health and pregnancy
- Infant and child health
- Cancer
- Hormones and health

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 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 immunomodulatory functions designed to enhance the effectiveness and safety of standard oncology treatments, i.e., chemotherapies, radiation therapies and immune checkpoint inhibitors. Activity against the latter target provides an anti-inflammatory effect, as well as contributing to an anti-cancer action, but also potentially blocking septic shock.

Noxopharm is running comprehensive drug discovery programs in both oncology and inflammation, and is the major shareholder of US biotechnology company, Nyrada Inc (ASX:NYR), active in the areas of drug development for cardiovascular and neurological diseases.

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

Forward Looking Statements

This announcement 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 (including but not limited to the COVID-19 pandemic) that could cause the actual results, performance or achievements to differ materially from those expressed or implied by the forward-looking statement.

Appendix 4C

Quarterly cash flow report for entities subject to Listing Rule 4.7B

Name of entity

NOXOPHARM LIMITED

ABN	**Quarter ended ("current quarter")**
50 608 966 123	30 September 2021

Consolidated statement of cash flows		**Current quarter $A'000**	**Year to date (3 months) $A'000**
1.	**Cash flows from operating activities**		
1.1	Receipts from customers	12	12
1.2	Payments for		
	(a) research and development	(2,851)	(2,851)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	(42)	(42)
	(d) leased assets	-	-
	(e) staff costs	(930)	(930)
	(f) administration and corporate costs	(615)	(615)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	18	18
1.5	Interest and other costs of finance paid	(8)	(8)
1.6	Income taxes paid	-	-
1.7	Government grants and tax incentives	-	-
1.8	Other (provide details if material)		
1.9	**Net cash from / (used in) operating activities**	**(4,416)**	**(4,416)**

2.	**Cash flows from investing activities**		
2.1	Payments to acquire or for:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	-	-
	(d) investments	-	-
	(e) intellectual property	-	-
	(f) other non-current assets	-	-

Consolidated statement of cash flows		Current quarter $A'000	Year to date (3 months) $A'000
2.2	Proceeds from disposal of:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	-	-
	(d) investments	-	-
	(e) intellectual property	-	-
	(f) other non-current assets	-	-
2.3	Cash flows from loans to other entities	-	-
2.4	Dividends received (see note 3)	-	-
2.5	Other (provide details if material)	-	-
2.6	**Net cash from / (used in) investing activities**	**-**	**-**

3.	**Cash flows from financing activities**		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)	-	-
3.2	Proceeds from issue of convertible debt securities	-	-
3.3	Proceeds from exercise of options	1,205	1,205
3.4	Transaction costs related to issues of equity securities or convertible debt securities	-	-
3.5	Proceeds from borrowings	-	-
3.6	Repayment of borrowings	-	-
3.7	Transaction costs related to loans and borrowings	-	-
3.8	Dividends paid	-	-
3.9	Other (provide details if material)	-	-
3.10	**Net cash from / (used in) financing activities**	**1,205**	**1,205**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	26,796	26,796
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(4,416)	(4,416)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	-	-

Consolidated statement of cash flows		Current quarter $A'000	Year to date (3 months) $A'000
4.4	Net cash from / (used in) financing activities (item 3.10 above)	1,205	1,205
4.5	Effect of movement in exchange rates on cash held	(14)	(14)
4.6	**Cash and cash equivalents at end of period**	**23,571**	**23,571**

5.	Reconciliation of cash and cash equivalents at the end of the quarter (as shown in the consolidated statement of cash flows) to the related items in the accounts	Current quarter $A'000	Previous quarter $A'000
5.1	Bank balances	8,552	7,753
5.2	Call deposits	15,000	19,000
5.3	Bank overdrafts	-	-
5.4	Other (business debit cards)	43	43
5.5	**Cash and cash equivalents at end of quarter (should equal item 4.6 above)**	**23,571**	**26,796**

6.	Payments to related parties of the entity and their associates	Current quarter $A'000
6.1	Aggregate amount of payments to related parties and their associates included in item 1	167
6.2	Aggregate amount of payments to related parties and their associates included in item 2	-

Note: if any amounts are shown in items 6.1 or 6.2, your quarterly activity report must include a description of, and an explanation for, such payments.

7.	**Financing facilities** *Note: the term "facility' includes all forms of financing arrangements available to the entity.* *Add notes as necessary for an understanding of the sources of finance available to the entity.*	**Total facility amount at quarter end $A'000**	**Amount drawn at quarter end $A'000**
7.1	Loan facilities	-	-
7.2	Credit standby arrangements	-	-
7.3	Other (please specify)	-	-
7.4	**Total financing facilities**	-	-

7.5	**Unused financing facilities available at quarter end**	-

7.6 Include in the box below a description of each facility above, including the lender, interest rate, maturity date and whether it is secured or unsecured. If any additional financing facilities have been entered into or are proposed to be entered into after quarter end, include a note providing details of those facilities as well.

8.	**Estimated cash available for future operating activities**	**$A'000**
8.1	Net cash from / (used in) operating activities (item 1.9)	(4,416)
8.2	Cash and cash equivalents at quarter end (item 4.6)	23,571
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	23,571
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	5.3

Note: if the entity has reported positive net operating cash flows in item 1.9, answer item 8.5 as "N/A". Otherwise, a figure for the estimated quarters of funding available must be included in item 8.5.

8.6 If item 8.5 is less than 2 quarters, please provide answers to the following questions:

8.6.1 Does the entity expect that it will continue to have the current level of net operating cash flows for the time being and, if not, why not?

Answer: Yes

8.6.2 Has the entity taken any steps, or does it propose to take any steps, to raise further cash to fund its operations and, if so, what are those steps and how likely does it believe that they will be successful?

Answer: The 2021 ATO Research and Development rebate of approximately $5.8M is expected to be received during the December quarter of 2021.

8.6.3 Does the entity expect to be able to continue its operations and to meet its business objectives and, if so, on what basis?

Answer:

Note: where item 8.5 is less than 2 quarters, all of questions 8.6.1, 8.6.2 and 8.6.3 above must be answered.

Compliance statement

1 This statement has been prepared in accordance with accounting standards and policies which comply with Listing Rule 19.11A.

2 This statement gives a true and fair view of the matters disclosed.

Date: 14 October 2021

Authorised by: By the Board
(Name of body or officer authorising release – see note 4)

Notes

1. This quarterly cash flow report and the accompanying activity report provide a basis for informing the market about the entity's activities for the past quarter, how they have been financed and the effect this has had on its cash position. An entity that wishes to disclose additional information over and above the minimum required under the Listing Rules is encouraged to do so.

2. If this quarterly cash flow report has been prepared in accordance with Australian Accounting Standards, the definitions in, and provisions of, *AASB 107: Statement of Cash Flows* apply to this report. If this quarterly cash flow report has been prepared in accordance with other accounting standards agreed by ASX pursuant to Listing Rule 19.11A, the corresponding equivalent standard applies to this report.

3. Dividends received may be classified either as cash flows from operating activities or cash flows from investing activities, depending on the accounting policy of the entity.

4. If this report has been authorised for release to the market by your board of directors, you can insert here: "By the board". If it has been authorised for release to the market by a committee of your board of directors, you can insert here: "By the [*name of board committee – eg Audit and Risk Committee*]". If it has been authorised for release to the market by a disclosure committee, you can insert here: "By the Disclosure Committee".

5. If this report has been authorised for release to the market by your board of directors and you wish to hold yourself out as complying with recommendation 4.2 of the ASX Corporate Governance Council's *Corporate Governance Principles and Recommendations*, the board should have received a declaration from its CEO and CFO that, in their opinion, the financial records of the entity have been properly maintained, that this report complies with the appropriate accounting standards and gives a true and fair view of the cash flows of the entity, and that their opinion has been formed on the basis of a sound system of risk management and internal control which is operating effectively.