December 2021 Quarterly Activities Report and Appendix 4C

- **Significant advances made across the Company's three main activities – Veyonda®, cancer drug R&D pipeline, and Pharmorage:**
  - ***Veyonda*: treatment underway in the IONIC and DARRT programs with DARRT-2 first dose cohort fully enrolled; first CEP site opens in the U.S. for enrolment**
  - ***Cancer drug pipeline*: Company profile as innovative oncology drug company grows with new first-in-class anti-cancer drugs identified including potential ground-breaking treatments for pancreatic and brain cancers**
  - ***Pharmorage*: Pharmorage makes important discovery of new drug candidates for the treatment of autoimmune diseases and septic shock. Major opportunity added in RNA drug discovery and mRNA vaccine technology through a technology in-licence**
- **Company finishes quarter in strong financial position (A$22.6M), made up by $16.7M supplemented by A$5.9M Federal Govt R&D Rebate received in early-January 2022.**

Sydney 27 January 2022: Australian clinical-stage drug development company Noxopharm Limited (ASX:NOX) provides this Quarterly Activities Report and Appendix 4C for the period ending 31 December 2021.

Veyonda® - Cancer

The Noxopharm cancer clinical trial program made solid progress this quarter with patients under treatment in the IONIC and DARRT trials, and the CEP trial ready to begin patient recruitment.

The program involves prestigious cancer centres in the U.S., Europe and Australia and will see more sites progressively coming online over Q1 2022.

Lockdowns and the emergence of the Omicron variant have had a significant impact on hospital workforces worldwide, inevitably impacting the availability of hospital resources to conduct clinical trials. Nevertheless, Noxopharm is confident that it will meet its budgeted timelines for full patient recruitment across all 3 trials.

(i) IONIC Program

Phase 1 trial in approximately 30 patients with a range of tumour types across a number of Australian sites. Treatment combines Veyonda with the Bristol Myers Squibb checkpoint inhibitor, nivolumab (Opdivo®).

This quarter:

- The first site was opened, with patients enrolled and treated
- Preparations put in place for more sites to open in Q1 2022.

(ii) **DARRT Program**

Phase 2 clinical trial in approximately 100 patients across multiple sites in the U.S., Europe and Australia combining Veyonda with low-dose radiotherapy for the treatment of prostate, breast and lung cancer.

This quarter:

- Two leading U.S. cancer centres - MD Anderson Cancer Center and the Beverly Hills Cancer Center – began recruitment
- The first dose cohort has completed the first treatment cycle
- First Australian site (Macquarie Private Hospital) opened for patient recruitment, with further sites expected to be online soon.

(iii) **CEP Program**

Phase 1 study in approximately 30 patients with soft tissue sarcoma with combination treatment of Veyonda and the chemotherapy drug, doxorubicin.

This quarter:

- The first of several major U.S. sites – Los Angeles's City of Hope Cancer Center - opens for enrolment
- Additional sites in the U.S. are set to be activated shortly.

(iv) LuPIN Program

This program involves the use of Veyonda to enhance the responsiveness of men with late-stage prostate cancer to PSMA radioligand (theranostic) therapy.

This quarter:

- A compassionate use program in Australia now involving over 100 Australian and overseas patients continued as part of an effort under real-world conditions to determine the optimal patient cohort to benefit from the use of Veyonda in combination with ^{177}LuPSMA
- The Company has been approached by a European clinical group for access to Veyonda for further clinical investigations; the negotiations are ongoing.

Veyonda® – Septic Shock

This quarter:

- Major shifts in the nature of the pandemic, combined with an internal ground-breaking scientific discovery, led the Company to a strategic rethink that the Company believes will bring greater long-term commercial benefits

- Those pandemic changes are (i) the effectiveness of vaccines, along with high rates of vaccine uptake, and (ii) the emergence of the Omicron variant with its tendency to upper respiratory tract infection, effectively lowering the risk of lung-associated septic shock
- The effect of those changes has been to shift the short-term need first seen in 2020 around the treatment of catastrophically high rates of septic shock and death, to what the Company sees as a more long-term need for effective treatments of inflammation/autoimmune-based long-COVID symptoms
- The Company remains prepared to re-activate its NOXCOVID should the short-term need re-surface with the emergence of a new, more virulent variant. However, for the moment, the Company will restore the pre-pandemic focus of Veyonda as a highly promising anti-cancer drug candidate
- In its place, Noxopharm intends to build on the discovery announced in 2021 that the prime value of Veyonda as a treatment for cytokine storm and septic shock in COVID-19 lies in the ability of idronoxil (IDX) to block the inflammatory marker, Tank-binding kinase 1 (TBK1), already marked as a key player in the development of autoimmune disease, and now recently identified as a key moderator of the cytokine storm and septic shock in COVID-19 patients
- Noxopharm will pursue this strategy via the Pharmorage TBK1 inhibiting drug program, an opportunity already recognised by a Techvoucher grant of $50,000 from the NSW Department of Health.

Pipeline – Cancer

This quarter:

- Ongoing pre-clinical studies confirmed the exciting potential and novelty of its three pipeline programs – pancreatic cancer drug, brain cancer drug, 2nd generation IDX
- This effort was strengthened (i) by new appointments to the scientific team, (ii) the establishment of new collaborations with prominent research groups within Australia and the U.S., and (iii) the establishment of a Scientific Advisory Panel involving eminent scientists in the cancer field based in Australia, Germany, Hong Kong and the U.S.
- Major milestones were achieved in all three programs with a provisional patent being prepared for lodgement in Q1 2022 to protect newly discovered families of new chemical entities
- The pancreatic cancer program made the most noteworthy progress this quarter as described below:

(i) <u>Pancreatic cancer program</u>

- Noxopharm regards this program, being conducted in collaboration with an Australian university, as potentially ground-breaking, with the strong prospect of a breakthrough in the treatment of pancreatic cancer which for most patients is a highly aggressive cancer, poorly responsive to chemotherapy and therefore with poor survival outcomes
- The aim is a drug that eliminates the cause of aggressive growth, converting pancreatic adenocarcinoma into a slow-growing tumour better able to be managed on a long-term basis by chemotherapy
- International research has now identified the culprit as the connective tissue (stromal cells) in the cancer. At one level, these stromal cells produce chemical signals that drive the aggressive growth of the cancer cells. At another level, these stromal cells also cause scar tissue to build up around the cancer, serving as a shield that blocks access to the cancer by chemotherapy drugs

- The first breakthrough has come with the partnering Australian university's discovery of how to grow human pancreatic cancer biopsies in the laboratory in a way that preserves all components of the cancer tissue, including the all-important stromal cells. This world-first development, currently attracting global attention, provides scientists for the first time with the ability to measure the effect of drugs on the all-important stromal cells
- The second breakthrough has been the design by Noxopharm scientists of drugs with what is believed to be a first-in-class ability to block those roles of cancer-associated stromal cells
- This quarter saw this program take a major step with Noxopharm drugs being added to cultured biopsies of pancreatic cancer collected during surgery and evaluated for their ability to both block the growth of cancer cells and to reduce the scarring effect
- Further details about this potentially ground-breaking program are expected to be released in Q1 2022.

Pharmorage

During this quarter, Pharmorage emerged as a major part of the Company's business consolidated based around its two technology platforms, Pharm-ISO and Pharm-RNA.

(i) Pharm-ISO platform

- Based on the Noxopharm isoflavonoid drug platform, but with a focus on inflammation
- The Company earlier *(ASX: 23 Aug 2021)* announced that its collaboration with Hudson Institute of Medical Research had identified the anti-inflammatory mechanism of action believed behind the ability of idronoxil (IDX) to block the cytokine storm and septic shock associated with COVID-19
- IDX blocks cGAS-STING signalling in response to the presence of the virus in a cell by inhibiting the key downstream signaling protein, Tank-binding kinase 1 (TBK1)
- With recent independent research confirming the key role of the cGAS-STING/TBK1 signalling pathway in COVID-related septic shock, Noxopharm and Hudson saw this as a major drug discovery opportunity in the field of septic shock, augmented by the emerging industry interest in TBK1 as an important new drug target for autoimmune disease
- A provisional patent application was filed on the TBK1 target discovery at the end of December 2021 aimed at protecting novel compounds blocking TBK1 activity. The Company believes that these compounds hold enormous potential to treat various autoimmune disorders as well as septic shock, and a publication describing these findings has been prepared for submission in a highly ranked scientific journal.

(ii) Pharm-RNA platform

- In November, Noxopharm announced the in-licence of a new RNA drug technology platform developed by Hudson. The result of over 15 years of work, the technology is designed to block inflammation at its source by blocking the sensors in a cell that trigger inflammation, offering an entirely novel approach to the treatment of acute and chronic inflammation

- This licensed technology is already well advanced, with drug candidates ready to undergo *in vivo* preclinical studies. Pharmorage currently is focusing on these drug candidates as treatments for autoimmune disorders such as lupus or psoriasis

- The Company also strongly believes that these novel molecules hold the key to making mRNA vaccines safer, more effective and cheaper to produce, placing Pharmorage at the forefront of the fast- growing market of RNA drugs and vaccines.

Patent Portfolio Update

The following key patent developments occurred this quarter:

Further patent applications were allowed that relate to protecting the use of a suppository dosage form of idronoxil in combination with chemotherapy:

Method of treating cancer using a combination treatment entitled "Combination chemotherapy"
European application allowed (EP 17785173.0)
Australian application allowed (AU 2017254774)

An Australian divisional patent application was filed (AU 2021266308) to pursue additional subject matter.

A provisional application directed to new compounds blocking TBK1 activity was filed:

New compounds blocking TBK1 activity entitled "Inhibitors of TBK1 and/or IKKε"
Australian provisional application filed 21 December 2021 (AU 2021904173)

National phase applications were filed in 16 jurisdictions relating to protecting the use of idronoxil in combination with immuno-oncology therapy:

Method of improving immuno-oncology therapy using idronoxil entitled "Immuno-oncology therapy using isoflavone compounds"

A European divisional application was filed to pursue additional subject matter relating to the use of a suppository dosage form of idronoxil to provide a steady state plasma concentration of idronoxil:

Method of providing a steady state plasma concentration of idronoxil entitled "Isoflavonoid composition with improved pharmacokinetics"
European divisional application filed (EP 21214664.1)

A US continuation application was filed to pursue additional subject matter relating to the use of idronoxil in combination with radiotherapy to provide an abscopal effect:

Method of treating cancer using radiotherapy entitled "Radiotherapy improvements"
US continuation application filed (US 17/644,211)

A provisional application directed to an improved suppository dosage form of idronoxil was filed:

Improved suppository dosage form of idronoxil entitled "Improved isoflavone formulation"
Australian provisional application filed 6 October 2021 (AU 2021903191)

Financial Update

- As at 31 December 2021, Noxopharm had A$16.7m in cash
- *The 2021 ATO Research and Development Rebate for A$5.9M was received on 7 January 2022*
- The post-Rebate cash position of: ~A$22.6M meets the Company's forecast funding needs for the next 12 months
- Net cash used for operating activities during the quarter amounted to A$6.9m, compared with A$4.4m in the quarter to September 2021. The company made payments for research and development of A$5.5m during the quarter, compared to A$2.9m in the September 2021 quarter. This increase in R&D expenditure was due to some significant milestones being met in the current clinical trials.

** 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 Noxopharm

Noxopharm Limited (ASX:NOX) is an Australian clinical-stage drug development company focused on the treatment of cancer. The wholly owned subsidiary, Pharmorage Pty Ltd, houses drug development for autoimmune diseases, sepsis (cytokine release syndrome) and RNA drug and vaccine manufacture.

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	31 December 2021

Consolidated statement of cash flows		**Current quarter $A'000**	**Year to date (6 months) $A'000**
1.	**Cash flows from operating activities**		
1.1	Receipts from customers	3	15
1.2	Payments for		
	(a) research and development	(5,472)	(8,323)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	(20)	(62)
	(d) leased assets	-	-
	(e) staff costs	(997)	(1,926)
	(f) administration and corporate costs	(398)	(1,013)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	32	50
1.5	Interest and other costs of finance paid	(9)	(17)
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**	**(6,861)**	**(11,276)**

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 (6 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
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**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	23,571	26,796
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(6,861)	(11,276)
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 (6 months) $A'000
4.4	Net cash from / (used in) financing activities (item 3.10 above)	-	1,205
4.5	Effect of movement in exchange rates on cash held	(19)	(34)
4.6	**Cash and cash equivalents at end of period**	**16,691**	**16,691**

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	3,649	8,552
5.2	Call deposits	13,000	15,000
5.3	Bank overdrafts	-	-
5.4	Other (business debit cards)	42	19
5.5	**Cash and cash equivalents at end of quarter (should equal item 4.6 above)**	**16,691**	**23,571**

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)	(6,861)
8.2	Cash and cash equivalents at quarter end (item 4.6)	16,691
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	16,691
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	2.4

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: The operating cash flows were higher in the December 2021 quarter due to a number of significant milestones being met across the clinical research programs. The forecast operating cash flows are forecast to be lower in the March 2022 quarter.

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 $5.86M was received on 7 January 2022. The Company has put in place an R&D program that it believes represents appropriate use of shareholder funds and appropriate exploitation of the Company's opportunities. However, to sustain the anticipated growth in R&D activities, additional funding will be required within the next 12 months, and the timing, method and quantum of the next capital raise is the subject of ongoing discussions between the Board and potential funders.

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: The Company believes it has sufficient working capital to meet its obligations and proposed business plans for the foreseeable future. Nevertheless, the Company will remain diligent in its oversight of its cash position and will take the necessary steps to ensure that it remains a viable business.

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.

27 January 2022

Date: .....

By order of the Board

Authorised by: .....
(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.