



Date: 29 July 2019

Sydney, Australia

ASX Limited
20 Bridge Street
SYDNEY NSW 2000

APPENDIX 4C – JUNE 2019 QUARTER

- Positive results from two prostate cancer trials
 - Phase 2 trial design gaining momentum
 - Investigational New Drug Application to be submitted to FDA in Q3 2019
 - Pipeline developing based on drug discovery program
 - Board changes underpinning growth
 - **Successful fundraising completed in July intended to fund Company through to a proposed US Listing**
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Sydney, 29 July 2019: Noxopharm Limited (ASX: NOX) ('**Noxopharm**' or the '**Company**') today releases its Appendix 4C for the quarter ended 30 June 2019, as well as providing guidance for the next 12 months. This report is for the Noxopharm Group covering both Noxopharm Limited and its majority-owned subsidiary, Nyrada Inc.

Much of the Company's efforts and resources have been and will continue to be directed to the clinical development of our first clinical-stage asset, Veyonda[®]. Veyonda[®] has a range of lethal effects within cancer cells and in the surrounding cancer microenvironment that include immune-stimulating effects. The breadth of these effects means that Veyonda[®] may add-to or enhance the efficacy of a number of different types of anti-cancer treatments. Together with the good tolerability profile observed to-date in clinical studies combining Veyonda[®] with various forms of radiotherapy or chemotherapy, the Company is confident Veyonda[®] has the potential to be an extremely versatile cancer treatment.

1. Veyonda[®] Clinical Strategy

This versatility means that the Company is, in many ways, spoilt for choice. A challenge that is preferable to having too few options, but one that still needs to be managed. Our approach to this has been to focus the clinical development program as much as possible, whilst ensuring we maintain enough diversity in our program to manage technological and commercial risk. In always following the valid leads that our scientific work discovers, the thinking behind our clinical strategy can be summarized under three key action statements:

- Focus on one cancer where the unmet-need burden for the community is huge e.g. prostate cancer
- Focus on one cancer where the challenge due to too few treatment options is huge e.g. sarcoma
- In focusing on prostate cancer and sarcoma, follow the technological mega-trends e.g. immunology and advancement in radiotherapeutics



This thinking has led us to two key strategic priorities:

1. Establish Veyonda[®] as an essential adjunct to radiotherapy¹ in the treatment of prostate cancer²
2. Broaden the clinical value of Veyonda[®] by improving outcomes in sarcoma³ and increasing response-rates with immuno-oncology agents

2. Veyonda[®] Clinical Program

In progressing towards our two strategic priorities, the Company currently is conducting, supporting or in late stages of planning for four clinical trials:

1. With radiotherapy: the DARRT-1 trial, the LuPIN trial and the DARRT-2 trial
2. With chemotherapy: the CEP-2 trial

2.1. **DARRT-1**

The **D**irect and **A**bscopal **R**esponse to **R**adio**T**herapy -1 trial combines low dose, external beam radiotherapy delivered over 5-8 days with Veyonda[®] administered twice daily for 13-16 days to treat men with late-stage metastatic castration-resistant prostate cancer (mCRPC). During the June quarter we announced that this treatment combination led to lasting disease control, with 57% of the 14 patients in the first phase of the trial remaining progression free over six months. Pain responses also were encouraging with two patients being completely free of pain at 6 months. We also announced that enrolment of the second cohort of 12 patients was completed in May, meaning that we anticipate topline 12-week and 24-week follow-up results for this cohort to be announced in August and November of this year respectively. We look forward to full disclosure of the trial results at an international scientific congress in H1 2020.

2.2. **LuPIN**

The **Lu-PSMA** and **IdroNoxil** trial is investigating the combination of ¹⁷⁷Lu-PSMA-617 and Veyonda[®] in the treatment of patients with late-stage mCRPC. Treatment includes up to six, 42-day treatment cycles consisting of an intravenous injection of ¹⁷⁷Lu-PSMA on day 1 of the cycle and daily administration of Veyonda[®] on days 1-10. Initially 16 patients were recruited to the trial (8 patients treated with 400 mg daily and 400 mg twice daily of Veyonda, respectively). This was subsequently expanded to include another 16 patients (400 mg twice daily) and in the June quarter the company announced that the trial is being expanded again by recruiting a further 24 patients who will be treated with 600 mg twice daily. This decision was driven by our desire to study the 1200 mg dose (target dose for our phase 2, DARRT regimen trial) and by the encouraging data pertaining to the first 16 patients in the trial. Prostate-specific antigen (PSA) response-rates in these patients were high, with 69% of patients achieving a response. Overall survival trends in the study also are encouraging, with 81% of the first 16 patients still alive following a median follow-up of 12 months. This compares favourably with background epidemiological data suggesting that patients with extensively treated, end-stage mCRPC currently have a median life-expectancy of 12-months or shorter⁴.



2.3. **DARRT-2**

Planning is well underway for a phase 2, randomized, controlled trial of the DARRT regimen (low dose radiotherapy plus Veyonda[®]) in mCRPC. A range of potential designs will be discussed with world renowned radiation oncologists, medical oncologists and nuclear medicine physicians in the U.S. and in Australia at upcoming advisory boards planned for Q3 2019. This trial is intended to address questions that will lay the foundation for a range of potential phase 2/3 trial designs in prostate cancer, enabling the company to carefully select and sequence indications to target for regulatory approval.

2.4. **CEP-2**

The Chemotherapy Enhancement Program – 2 trial will combine Veyonda[®] with doxorubicin to treat adult patients with metastatic soft tissue sarcomas (mSTS). mSTS is a rare but devastating group of over 70 different subtypes of cancers that has seen few advances in pharmaceutical treatment in the last 50 years. The company has worked with internationally acclaimed clinical experts in the U.S. to develop the protocol for this trial which will be conducted in the U.S. Currently the Company is in dialogue with the Food and Drug Administration (FDA) with the goal of achieving Investigational New Drug (IND) status in the U.S before the end of the year. The Company also is in preparation to apply to the FDA for Orphan Drug Designation in H2 2019. If successful, this will open access to a range of regulatory and financial benefits that will greatly assist the Company to develop Veyonda[®] for sarcoma.⁵

3. **Non-Clinical Programs**

3.1. **Preclinical research**

The Company's preclinical research program is currently focused on complementing the Veyonda[®] clinical development program. This includes research to support regulatory requirements such as characterizing its pharmacological properties (e.g. pre-clinical safety) and research to inform therapeutic indications. The research informing therapeutic indications is focused on three main areas:

3.1.1. *Mechanisms of radio-sensitisation and abscopal effects*

Encouraging results from studies exploring the abscopal effect accrued in the June quarter and the Company anticipates disclosing and publishing these findings as soon as remaining confirmatory studies conclude. We expect these studies to conclude in Q4 2019.

3.1.2. *Immuno-oncology effects*

During the June quarter the Company disclosed its discovery that the active ingredient in Veyonda[®], idronoxil, promotes both the innate and the adaptive immune systems, activating natural killer (NK) cells and increasing numbers of CD4 and CD8 lymphocytes. The Company believes that these effects are associated with idronoxil activating the STING (Stimulating Interferon Genes) pathway, a self-defence pathway that alerts the innate immune system to cells with damaged DNA e.g. virally infected cells or cancer cells. There currently is considerable interest in the pharmaceutical industry in drugs that trigger STING (known as STING agonists) as a means of boosting the overall low response rates to immuno-oncology drugs. Current STING agonists under development on the whole have been limited to being injected directly into individual tumours. This is because of serious safety concerns related to their mechanism of action that precludes dosing them in a way that exposes the



whole body to their pro-STING effect. Veyonda[®] does not have this limitation, a fact that has been borne out by its high level of tolerability in clinical trials to date. The Company regards this as a major development, with Veyonda[®] representing the first known means of delivering a well-tolerated STING agonist able to reach all cancer cells throughout the body. More work is underway to better characterize the nature and extent of the molecule's STING effects, with the goal of informing designs for combination immuno-oncology trials.

3.1.3. Sarcoma

With over 70 subtypes of soft tissue sarcoma, our work has focused on exploring how consistently Veyonda[®] can be expected to work across these subtypes and how well Veyonda[®] can be expected to work in combination with various chemotherapeutic agents. We remain encouraged by the results we have obtained and continue confidently with planning for CEP-2.

3.2. Manufacturing and dosage form

The maturation of Veyonda[®] as a clinical candidate is being matched by increases in data generation pertaining to the drug substance (e.g. strength, quality, purity) and the drug product (e.g. detailed description of manufacturing processes). Progress also has been made on our 600 mg dosage form and on development of our placebo suppositories which will be identical in appearance to Veyonda[®] itself to ensure adequate blinding in our phase 2 and phase 3 trials.

3.3. Drug Discovery

With the Veyonda[®] program now well-advanced, the Company is accelerating and expanding its drug discovery efforts in its goal to evolve into a biopharmaceutical company with a robust pipeline of anti-cancer drug candidates developed in-house and fully owned by the Company. Several leads have been identified, all with the objective of leveraging the science and know-how that led to the discovery of Veyonda[®] to bring more medicines to the growing number of people living with cancer.

Board

The Board saw a number of changes around the end of the June quarter, reflecting preparation for the Company's anticipated growth over the next 12 months.

The first change was the appointment of CEO and Founder, Dr Graham Kelly, to Chairman, with the appointment of Dr Greg van Wyk as CEO. The purpose of this was to free up Dr Kelly to oversee the proposed dual listing of Noxopharm on a U.S. securities exchange and to deliver the independence of Nyrada Inc from the parent company whilst leveraging Dr van Wyk's strategic and operational expertise to lead the Company into the next stage of its lifecycle – one in which the company will take Veyonda[®] into late stage clinical testing while seeking to grow into a leader in the development of small molecule oncology drugs.

The second change was the resignation of Non-Executive Director, Mr John Moore, in order for him to take up the position of Chairman of Nyrada Inc, thereby creating the third change which was the appointment of Dr Beata Niechoda MD, PhD, MBA as a replacement for Mr Moore. Dr Niechoda had been appointed Special Advisor to the Board earlier this year, providing the Board with an expert and



independent view of the Company's clinical and commercial strategies. The Board is pleased now to have on a formal basis the considerable international pharmaceutical industry experience of Dr Niechoda.

Funding

The Company remains aware of its cash position and constantly strives to balance financial security with the cost (and attendant dilutionary effect) of capital raised on-market. The Company last raised capital some 15 months ago (April 2018), which together with the Australian Government's R&D Rebate Scheme and prudent spending, has allowed it to run and even grow its business over that period.

The latter half of 2018 proved to be a challenging time for raising capital in the biotech sector, a situation which according to the Company's advisors has only started to improve in recent months, leading the Company to look to raise new capital in June/July. With an eye on a proposed dual listing of Noxopharm on a U.S. securities exchange, the Company believed that it was appropriate to seek to raise that new capital in the U.S. as a necessary introduction of the Company to the U.S. capital markets.

The Company has worked with U.S. and UK investment bank, Laidlaw and Company, on capital raising strategies, reviewing a range of options offered to the Company towards the end of the Financial Year. As the market was informed, the Company entered into a funding package that it believed best suited its strategy of using a form of short-term financing that provided the flexibility of utilizing funds when required. Importantly, this will allow the Company to take advantage of any positive market responses to the anticipated news flow up to the time of the proposed U.S. listing and IPO, following which this financing will no longer be used.

The facility provides an immediate injection of AU\$4 million, plus the ability to place up to AU\$2 million worth of ordinary shares each month for a further 12 months, should this be required. While the facility has a nominal maximum AU\$26 million value, (and which could increase with agreement of all parties) the Company does not anticipate utilising anywhere near this amount. The Company intends to work closely with the two U.S. funds who provided this facility to seek to capitalise on what the Company believes will be an upcoming period of strong news flow.

The Company also is anticipating reimbursement of a minimum of \$3M in Q3, 2019 through the Federal Government's R&D Rebate scheme.

Nyrada Inc

This last quarter saw important progress in this Company's development.

A number of steps were taken in preparation for its independence from parent, Noxopharm. Starting with the expansion of the Board from Mr Peter Marks and Dr Graham Kelly, to Mr John Moore (Independent Director and Executive Chairman), Mr Marcus Frampton (Independent and Non-Executive Director) and Dr Rüdiger Weseloh (Independent and Non-Executive Director). Preparation of a Prospectus also has been undertaken in readiness for a proposed listing on ASX in the second half of this year.

There was important progress across the three main R&D programs, with significant progress made in the identification of a lead candidate in the Company's two main programs – the PCSK9 inhibitor program and the neuroprotectant program. The Company remains strongly of the view that it has identified two



potentially major new therapeutics and shortly will be in a position to take both drug candidates on their journey into the clinic.

¹ By radiotherapy we mean multiple forms of radiotherapy, including radionuclides such as ¹⁷⁷Lu-PSMA-617

² The aim is to achieve registration / marketing authorisation for multiple stages of prostate cancer

³ With current standard of care treatment for sarcoma being chemotherapy, the aim is to achieve registration / marketing authorisation for Veyonda[®] in combination with chemotherapy

⁴ Body, A., Pranavan, G., Hsiang Tan, T., Slobodian P. (2018). Medical management of metastatic prostate cancer. Australian Prescriber; 41:154–9

⁵ These incentives include grants, tax incentives, research design assistance, FDA fee waivers, extended patent life and 7-year market exclusivity

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About Noxopharm

Noxopharm is a clinical-stage Australian drug development company with offices in Sydney and New York. The Company has a primary focus on the development of Veyonda[®] and is the major shareholder in Nyrada Inc, a spin-off company developing a pipeline of non-oncology drugs.

About Veyonda[®]

Veyonda[®] (previously known as NOX66) is a suppository dosage formulation of the experimental anti-cancer drug, idronoxil, that leads in the body to the formation of a proprietary pro-drug form. Idronoxil specifically inhibits the ability of cancer cells to respond to stress, such as that induced by radiation, leading to loss of pro-survival signaling via sphingosine-1-phosphate. Idronoxil is also a STING agonist, activating the body's innate and adaptive immune systems.

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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 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 announcement are accurate and undue reliance should not be placed upon such statements.

Appendix 4C

Quarterly report for entities subject to Listing Rule 4.7B

Introduced 31/03/00 Amended 30/09/01, 24/10/05, 17/12/10, 01/09/16

Name of entity

NOXOPHARM LIMITED

ABN

50 608 966 123

Quarter ended ("current quarter")

30 June 2019

Consolidated statement of cash flows	Current quarter \$A'000	Year to date (12 months) \$A'000
1. Cash flows from operating activities		
1.1 Receipts from customers		
1.2 Payments for		
(a) research and development	(1,556)	(6,164)
(b) product manufacturing and operating costs	-	-
(c) advertising and marketing	(18)	(83)
(d) leased assets	-	-
(e) staff costs	(1,273)	(4,371)
(f) administration and corporate costs	(1,037)	(3,011)
1.3 Dividends received (see note 3)	-	-
1.4 Interest received	104	194
1.5 Interest and other costs of finance paid	(7)	(18)
1.6 Income taxes paid	-	-
1.7 Government grants and tax incentives	487	3,751
1.8 Other (Listing process costs)	-	-
1.9 Net cash from / (used in) operating activities	(3,300)	(9,702)
2. Cash flows from investing activities		
2.1 Payments to acquire:		
(a) property, plant and equipment	-	(7)
(b) businesses (see item 10)	-	-
(c) investments	-	-

Consolidated statement of cash flows	Current quarter \$A'000	Year to date (12 months) \$A'000
(d) intellectual property	-	-
(e) other non-current assets	-	-
2.2 Proceeds from disposal of:		
(a) property, plant and equipment	2	2
(b) businesses (see item 10)	-	-
(c) investments	-	-
(d) intellectual property	-	-
(e) 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	2	(5)

3. Cash flows from financing activities		
3.1 Proceeds from issues of shares	-	-
3.2 Proceeds from issue of convertible notes	-	-
3.3 Proceeds from exercise of share options	-	75
3.4 Transaction costs related to issues of shares, convertible notes or options	-	(17)
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	-	58

4. Net increase / (decrease) in cash and cash equivalents for the period		
4.1 Cash and cash equivalents at beginning of quarter/year to date	6,225	12,612
4.2 Net cash from / (used in) operating activities (item 1.9 above)	(3,300)	(9,702)
4.3 Net cash from / (used in) investing activities (item 2.6 above)	2	(5)
4.4 Net cash from / (used in) financing activities (item 3.10 above)	-	58

Consolidated statement of cash flows		Current quarter \$A'000	Year to date (12 months) \$A'000
4.5	Effect of movement in exchange rates on cash held	(17)	(53)
4.6	Cash and cash equivalents at end of quarter	2,910	2,910

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	2,824	1,147
5.2	Call deposits	-	5,001
5.3	Bank overdrafts	-	-
5.4	Other		
	- business debit cards	86	77
	- bank balances (held in trust)	-	-
5.5	Cash and cash equivalents at end of quarter (should equal item 4.6 above)	2,910	6,225

6. Payments to directors of the entity and their associates

- 6.1 Aggregate amount of payments to these parties included in item 1.2
- 6.2 Aggregate amount of cash flow from loans to these parties included in item 2.3
- 6.3 Include below any explanation necessary to understand the transactions included in items 6.1 and 6.2

Current quarter \$A'000
283
-

Director fees and salary for executive director and related parties.

7. Payments to related entities of the entity and their associates

- 7.1 Aggregate amount of payments to these parties included in item 1.2
- 7.2 Aggregate amount of cash flow from loans to these parties included in item 2.3
- 7.3 Include below any explanation necessary to understand the transactions included in items 7.1 and 7.2

Current quarter \$A'000
-
-

8. Financing facilities available <i>Add notes as necessary for an understanding of the position</i>	Total facility amount at quarter end \$A'000	Amount drawn at quarter end \$A'000
8.1 Loan facilities	-	-
8.2 Credit standby arrangements	-	-
8.3 Other (please specify)	-	-
8.4 Include below a description of each facility above, including the lender, interest rate and whether it is secured or unsecured. If any additional facilities have been entered into or are proposed to be entered into after quarter end, include details of those facilities as well.		

9. Estimated cash outflows for next quarter	\$A'000
9.1 Research and development	1,000
9.2 Product manufacturing and operating costs	100
9.3 Advertising and marketing	45
9.4 Leased assets	-
9.5 Staff costs	1,250
9.6 Administration and corporate costs	500
9.7 Other (provide details if material)	-
9.8 Total estimated cash outflows	2,895

10. Acquisitions and disposals of business entities (items 2.1(b) and 2.2(b) above)	Acquisitions	Disposals
10.1 Name of entity	N/A	N/A
10.2 Place of incorporation or registration	-	-
10.3 Consideration for acquisition or disposal	-	-
10.4 Total net assets	-	-
10.5 Nature of business	N/A	N/A

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.

Sign here: 
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(Company secretary)

29 July 2019
Date:

DAVID FRANKS

Print name:

Notes

1. The quarterly report provides a basis for informing the market how the entity's activities have been financed for the past quarter and the effect on its cash position. An entity that wishes to disclose additional information is encouraged to do so, in a note or notes included in or attached to this report.
2. If this quarterly 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 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.