



Date: 30 July 2018

Sydney, Australia

ASX: NOX

Noxopharm Limited

ABN 50 608 966 123

**Registered Office
and**

Operational Office:

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Gordon NSW 2072
Australia

Board of Directors

Mr Peter Marks

Chairman

Non-Executive

Director

Dr Graham Kelly

Chief Executive Officer

Managing Director

Dr Ian Dixon

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ASX Limited
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APPENDIX 4C – JUNE 2018 QUARTER

Sydney, 30 July 2018: Noxopharm (ASX: NOX) today releases its Appendix 4C for the quarter ended 30 June 2018, as well as providing guidance on the next 18 months.

This report is presented in the context of the Company's overriding objective to use its lead pipeline drug, NOX66, to make standard radiotherapy and cytotoxic chemotherapy more effective for patients with most forms of cancer. The Company's goal is to see NOX66 become a standard of care treatment in the management of cancer.

The development of a drug that enhances radiotherapy in particular has long been a goal of medical research, but that goal remains unrealised with no universally effective and safe drug being brought to market to date.

Radiotherapy and cytotoxic chemotherapies share the same problem of inflicting damage in a non-specific way, harming both target and non-target cells alike. This results in their dosages (and thus their effectiveness) needing to be restricted. The concept of radio-enhancement is to make current dosages of radiation kill more cancer cells without increasing the damage to healthy cells.

Noxopharm has the objective of NOX66 being the first universally-acting and well-tolerated radio-enhancer to reach the market.

Noxopharm is running two separate radio-enhancing programs known as DARRT and LuPIN, each targeting a different way of using radiotherapy, with the DARRT program being the way the Company is looking to achieve marketing approval for NOX66.

Overview

The Company in mid-2018 is a quarter of the way into a 2-year clinical program embracing the 2018 and 2019 calendar years.

2018

This year has a focus on late-stage prostate cancer. There are 2x Phase 1 studies (DARRT-1 and LuPIN-1) with 5 main objectives:

1. To provide proof-of-concept of radio-enhancement by NOX66 in late-stage prostate cancer
2. To demonstrate a meaningful clinical response that is likely to result in extended survival in those patients
3. To identify the side-effect/safety profile of NOX66 + radiotherapy
4. To confirm the optimal therapeutic dosage (which may differ between the 2 applications)
5. To provide guidance on the design and size of the next phase of clinical studies.

2019

This year will have three confirmed major objectives.

The first is to take the DARRT program into a final study intended to lead to its approval for marketing (registration study). We expect this to be a multi-national study across North America, Europe, Australia and Asia (see details later).

The second is to extend the DARRT program into lung cancer and brain cancer.

The third is to conduct a Phase 2 Lu-PIN study.

Details

1. DARRT Program.

DARRT is the **D**irect and **A**bscopal **R**esponse to **R**adio**T**herapy program. It involves adding NOX66 therapy to radiotherapy being used to treat late-stage, metastatic disease. The primary intention of radiotherapy in that situation is to be palliative, seeking to provide temporary relief of symptoms such as pain. Typically, this involves irradiating between 1 and 2 larger tumours. The objective of adding NOX66 to that treatment is to shift the outcome in as many patients as possible from a temporary palliative outcome towards the chance of a far more durable and possibly curative outcome.

A *direct response* is one in which the irradiated tumours respond more completely to the radiotherapy. The active ingredient in NOX66, idronoxil, has proven in pre-clinical studies to increase the cancer-killing effect of radiotherapy between 2-3 times. This effect is thought to be responsible for a *direct response* effect.

An *abscopal response* is one in which the non-irradiated tumours (the tumours outside of the radiation zone) also respond, offering the potential of eliminating all tumour cells within the body on a permanent basis. This effect is thought to be related to the ability of idronoxil to stimulate the body's immune cells (natural killer cells) that fight cancer cells.

The Company regards the *abscopal response* as the primary outcome from the DARRT program. Abscopal responses are extremely rare in radiotherapy, even with current immuno-oncology drugs, with a response rate in late-stage prostate cancer in the 10-20% range being regarded as highly significant.

(i) DARRT-1

The DARRT-1 or PROSCART Study (Prostate Cancer Radio-enhancing Study) is currently using 8 sites in Australia, New Zealand and Georgia. It is a Phase 1b study in men with metastatic, castrate-resistant prostate cancer. The patients receive external beam radiotherapy to 1-2 tumours daily for between 5-10 days; NOX66 is given daily for 21 days. Over the last quarter, the study successfully completed the treatment of the first 8 patients comprising 4 treated with 400 mg NOX66 and 4 with 800 mg. Q3 is expected to see the next 4 patients (1200 mg NOX66) complete their treatment, with the final 12 patients (to receive the optimal NOX66 dosage) then completing their treatment by the end of October 2018.

On 21 March 2018 the Company reported on the outcome of using the DARRT treatment approach in 2 patients with late-stage cancer on a compassionate use basis. In one case of prostate cancer, a dosage of 1200 mg NOX66 resulted in a complete abscopal response of both soft tissue and bone metastases; in another case of leiomyosarcoma (a rare and poorly responsive cancer), a dosage of 800mg NOX66 resulted in a partial abscopal response in lung secondaries from an abdominal primary tumour. Based on that clinical experience, the Company anticipates that the therapeutic dose of NOX66 in this setting is between 800-1200 mg daily.

The Company anticipates reporting on the first 8 patients in DARRT-1 in August once their 12-week scans have been reviewed. Thereafter, the 1200 mg cohort should be reported on in Q4 2018.

(ii) DARRT-2

This is a repeat of DARRT-1 but in patients with late-stage lung cancer. It will be a Phase 2 multi-national, single-arm study involving a minimum of 40 patients. DARRT-2 currently is being planned, with an anticipated commencement in early-2019.

(iii) DARRT and Brain Cancer

The success of idronoxil in pre-clinical studies in sensitising both glioblastoma multiforme (GBM) and diffuse intrinsic pontine glioma (DIPG) brain cancer cells to radiation, and the confirmed ability of NOX66 to deliver idronoxil across the blood-brain barrier of animals, is behind the

Company's goal of bringing NOX66 into the clinic as a radio-enhancer in the treatment of primary brain cancers in both adults and children. Both programs have entered their final stages of pre-clinical testing, with the Company anticipating commencing a Phase 1 study in adult patients in H1 2019.

(iv) DARRT-Registration Study

This is an expanded version of DARRT-1 in late-stage prostate cancer patients. It will be a multi-national study planned in conjunction with major regulatory bodies (US, UK and EC) and intended to commence in H2 2019. A CRO has been engaged and a US Advisory Board convened in August 2018 to initiate the planning process.

2. LuPIN Program

The LuPIN program (Lutetium-PSMA In combination with NOX66) involves the use of NOX66 to enhance the cancer-killing effect of radiation injected intravenously, as opposed to the externally-delivered radiation in the DARRT program.

Specifically, LuPIN relates to the use of intravenous brachytherapy radiotherapy (¹⁷⁷lutetium-PSMA-617) (or Lu-PSMA) in men with metastatic castrate-resistant prostate cancer. Lu-PSMA is an experimental drug that has been licensed to another biotechnology company, Endocyte Inc, and currently is the subject of a global Phase 3 registration study.

The LuPIN-1 study is an investigator-initiated Phase 1 study being conducted at St Vincent's Hospital (Sydney), with NOX66 and Lu-PSMA being supplied by their respective companies.

The objective of Lu-PSMA therapy is to deliver radioactivity directly to prostate cancer cells through the bloodstream once the disease develops into multiple secondary tumours, leaving the cancer too advanced and too scattered to be targeted by traditional radiotherapy. A full course of treatment involves 6 injections over 36 weeks. While promising, the dilution of the radioactivity dose throughout the body restricts the ability of the radioactivity to kill larger tumours. This means that many patients either relapse before they finish a full course of treatment or relapse soon after completing the course.

Noxopharm is using NOX66 with the aim of increasing the response rate to Lu-PSMA, with more patients hopefully being able to complete their full course of therapy, as well as having a longer-lasting response.

The LuPIN-1 study is a safety and efficacy sighting study in 16 patients, testing 2 different dosages of NOX66. The first cohort of 8 patients (400 mg NOX66) have either completed or are nearing completion of their treatment; treatment of the second cohort of 8 patients (800 mg NOX66) has commenced. Recruitment of all 16 patients is anticipated to be completed during Q3 2018, with completion of treatment by mid-2019.

As LuPIN-1 is an investigator-initiated study, the release of data is at the discretion of the clinicians running the study.

3. Pre-Clinical Programs

In addition to the above clinical programs, the Company is conducting a range of R&D programs across 3 main areas:

(i) Further R&D in support of clinical programs

A range of studies have been commenced this quarter designed to provide data to support both the registration process and the eventual marketing of NOX66. These studies include understanding the mechanism of action of NOX66 as an enhancer of radiation, and in particular the mechanisms underlying an abscopal response. This is taking the Company into novel and potentially ground-breaking areas of science.

(ii) Brain cancer

Pre-clinical studies are underway to support the use of NOX66 in combination with radiotherapy in the treatment of primary brain cancer in both adults and children. On 5 July 2018, the Company announced that idronoxil, the active ingredient in NOX66, successfully enhanced the killing effect of radiotherapy on DIPG cancer cells. DIPG is a highly aggressive and poorly managed primary brain cancer in children.

(iii) Later generation drugs

The Company initiated studies in Q2 2018 designed to produce a second-generation form of NOX66 in a non-suppository dosage formulation. The Company is aiming to have at least one new dosage form in a pre-clinical program by the end of 2018.

4. Nyrada Inc

Noxopharm currently holds a 66.7% shareholding in this US registered public entity. Noxopharm continues to provide logistical support to Nyrada as that company continues its drug development programs in cardiovascular and neurological health.

5. Funding

On 3 March 2018 the Company announced the successful placement of 12m shares to sophisticated and institutional investors at a price of \$0.90 per share, to raise \$10.8M (before costs). The Company finished the 2017-2018 financial year with group consolidated cash reserves of \$12.612 million which, in combination with the anticipated Federal Government R&D Rebate Scheme funds, are expected to provide the Company with sufficient funds to continue its current planned business activities and to complete the clinical and pre-clinical activities that it has underway and plans to commence before the end of 2018. The current funding puts the Company in a strong position to continue with both its clinical and development programs for the remainder of 2018 and into 2019.

6. Pre-commercialisation

With NOX66 about to head into its final testing phase, it is timely that the Company have clear strategies leading up to that drug's commercialisation.

The current clinical and pre-clinical programs are aimed at putting the Company in a position to:

- gain marketing approval for NOX66 for at least 1 indication within 4 years
- commence negotiations with strategic partners ahead of a global roll-out of NOX66.

Specifically:

- the Company sees its DARRT program in late-stage (metastatic castrate-resistant) prostate cancer as the primary route to market. The current timetable is for this study to start in mid-2019. Depending on the length of follow up required by the regulators, we anticipate the study concluding in mid- to late-2021, with final data being presented for review by regulators in early-2022.
- the extension of the DARRT program into lung cancer and brain cancer is being undertaken with 3 outcomes in mind: (i) the opportunity to pursue a registration study if the data is sufficiently compelling, (ii) the opportunity to gain Orphan Drug status (see later), and (iii) the generation of additional clinical data to support marketing of the drug post-registration.
- in the case of the LuPIN program, the Company is reliant on the licensee of Lu-PSMA gaining marketing approval for that drug in due course, with 2022 a likely timeframe for that to happen. In the meantime, Noxopharm will take its LuPIN treatment program into a Phase 2 study in preparation for Lu-PSMA achieving marketing approval.

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About NOX66

NOX66 is an innovative dosage formulation of the experimental anti-cancer drug, idronoxil, developed specifically to preserve the anti-cancer activity of idronoxil in the body and to enhance its drug-like behaviour. Idronoxil is a kinase inhibitor that works by inhibiting a range of enzymes including sphingosine kinase and PI3 kinase that regulate cell pro-survival mechanisms and which are over-expressed in cancer cells, as well as inhibiting external NADH oxidase Type 2 (ENOX 2) which is responsible for maintaining the transmembrane electron potential (TMEP) in the plasma membrane of cancer cells and whose expression is limited to cancer cells. Inhibition of these enzymes results in disruption of key downstream pro-survival mechanisms including resistance mechanisms, sensitizing the cancer cell to the cytotoxic effects of chemotherapy drugs and radiotherapies. Idronoxil also increases the activity of human NK cells.

About Orphan Drug Designation

Orphan Drug Designation by the U.S. FDA provides orphan status to those drugs intended for the treatment of rare diseases/disorders that affect fewer than 200,000 in the U.S., or that affect more than 200,000 persons but are not expected to recover the costs of developing and marketing a treatment drug. Benefits include waiver of the New Drug Application fee (\$2.2M), tax credits to the value of 50% of the cost of clinical development, and 7-year market exclusivity.

About Noxopharm

Noxopharm is a clinical-stage Australian drug development company with offices in Sydney and Hong Kong. The Company has a primary focus on the development of drugs to sensitise cancer cells to radiotherapy and chemotherapy. NOX66 is the first pipeline product, with later generation drug candidates under development.

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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 2018

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	(1,483)	(5,303)
(b) product manufacturing and operating costs	-	-
(c) advertising and marketing	(6)	(55)
(d) leased assets	-	-
(e) staff costs	(1,109)	(2,999)
(f) administration and corporate costs	(569)	(1,727)
1.3 Dividends received (see note 3)	-	-
1.4 Interest received	12	63
1.5 Interest and other costs of finance paid	(5)	(8)
1.6 Income taxes paid	-	-
1.7 Government grants and tax incentives	28	911
1.8 Other (Listing process costs)	-	-
1.9 Net cash from / (used in) operating activities	(3,132)	(9,118)
2. Cash flows from investing activities		
2.1 Payments to acquire:		
(a) property, plant and equipment	(9)	(309)
(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	-	-
(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	(9)	(309)

3. Cash flows from financing activities		
3.1 Proceeds from issues of shares	4,264	16,496
3.2 Proceeds from issue of convertible notes	-	3,990
3.3 Proceeds from exercise of share options	-	-
3.4 Transaction costs related to issues of shares, convertible notes or options	(391)	(1,000)
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	3,873	19,486

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	11,880	2,553
4.2 Net cash from / (used in) operating activities (item 1.9 above)	(3,132)	(9,118)
4.3 Net cash from / (used in) investing activities (item 2.6 above)	(9)	(309)
4.4 Net cash from / (used in) financing activities (item 3.10 above)	3,873	19,486

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		
4.6	Cash and cash equivalents at end of quarter	12,612	12,612

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	2,521	8,141
5.2	Call deposits	10,001	3,700
5.3	Bank overdrafts		
5.4	Other		
	- business debit cards	90	39
	- bank balances (held in trust)	-	-
5.5	Cash and cash equivalents at end of quarter (should equal item 4.6 above)	12,612	11,880

6. Payments to directors of the entity and their associates

Current quarter \$A'000
294
-

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

Director fees and salary for executive director and related parties.

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

Current quarter \$A'000
-
-

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

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.		

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9. Estimated cash outflows for next quarter	\$A'000
9.1 Research and development	(1,886)
9.2 Product manufacturing and operating costs	-
9.3 Advertising and marketing	(20)
9.4 Leased assets	-
9.5 Staff costs	(730)
9.6 Administration and corporate costs	(360)
9.7 Other (provide details if material)	-
9.8 Total estimated cash outflows	(2,996)

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: 
(Company secretary)

30 JULY 2018
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.