



**Date: 12 November 2019**

**Sydney, Australia**

ASX Limited  
20 Bridge Street  
SYDNEY NSW 2000

#### **DARRT-1 INTERIM DATA PRESENTED TO CONFERENCE**

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- 57% of men (8/14) respond to a combination of NOX66 and external beam radiotherapy with stable disease or better at 6-months
  - Substantial pain relief achieved in 43% patients at 6-months
  - Evidence of off-target response in non-irradiated tumours
  - NOX66 to enter multi-national DARRT-2 study based on evidence of meaningful anti-cancer effect
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**Sydney, 12 November 2019:** Noxopharm (ASX: NOX) confirms the presentation of clinical data concerning NOX66 (Veyonda®) to the 46<sup>th</sup> Annual Scientific Meeting of the Clinical Oncology Society of Australia (12<sup>th</sup>-14<sup>th</sup> November 2019).

DARRT-1 involves a total of 25 treated patients. The conference data concerns the end-of-study outcome for the 14 men originally enrolled in the first arm of the study and who have completed their 6-month review. **The 6-month data on the final 11 patients is due to be released late-November 2019.**

DARRT-1 involves men with late-stage prostate cancer (metastatic castrate-resistant disease) with no remaining treatment options where NOX66 is being used in combination with external beam radiotherapy. The aim is to use the radio-enhancing and immune-stimulating properties of NOX66 to combine with radiotherapy in a well-tolerated way to provide better symptom (pain) relief, stabilization or reduction of disease activity, and longer survival as key objectives.

The data being presented to the conference by Noxopharm CMO, Gisela Mautner MD PhD, clearly indicates that NOX66 is meeting the first two objectives:

- 6/14 (43%) experienced a pain response (>30% reduction in pain) including 2 who were pain-free
- 8/14 (57%) showed a response radiographically (RECIST) with 1 partial response and 7 stable disease
- the partial responder showed progressive shrinkage of both irradiated and non-irradiated tumours over the 6-month study.



The effect on the all-important overall survival outcome will be determined in DARRT-2, with the Company confident of achieving this primary objective based on the high proportion of men seen in DARRT-1 to be experiencing an anti-cancer effect of at least 6-months' duration.

Noxopharm Executive Chairman and CEO, Graham Kelly PhD, commented, "Prostate cancer is second only to lung cancer as a cause of cancer-related deaths in men and there is an urgent need to develop treatment options once current therapies fail. This conference data goes a long way to suggesting that NOX66 can meet that need. Our focus now is getting NOX66 into a multi-national study next year where we can test its effect on overall survival."

The final statistical report, including full radiographic assessment of response in irradiated and non-irradiated tumours (abscopal responses), will be announced in Q1 2020.

The full poster can be viewed in the attached PDF file.

**About COSA**

The Clinical Oncology Society of Australia Scientific Annual Meeting (ASM) is Australia's premier cancer meeting, held over three days each year, usually in November. The ASM is a multidisciplinary meeting, inviting participation from doctors, nurses, allied health professionals and scientists working in cancer care nationally and internationally. A different state hosts the ASM each year, with a specific theme and focus on a specific cancer type. In 2019, the theme is urological cancers.

**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.

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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.

# Phase 1b Study of NOX66 in Combination with Radiotherapy in Patients with Late-Stage Metastatic Castration-Resistant Prostate Cancer (DARRT-1 Study)

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## Background

- NOX66 is a novel formulation of idronoxil designed for rectal administration which is currently under clinical investigation in combination with chemotherapy and radiation therapy (RT)
- NOX66 is designed to protect idronoxil from rapid metabolism and elimination, allowing for therapeutic levels of idronoxil to remain in the body
- A Phase 1b study of NOX66 as monotherapy and in combination with chemotherapy (carboplatin) showed NOX66 to be well tolerated. Here we present interim data from dose escalation cohorts 1, 2 and 3

## Study Objectives

The DARRT-1 (Direct and Abscopal Response to Radiotherapy) study aims to determine the tolerability and examine signals of efficacy of NOX66 in combination with low-dose RT in men with late-stage metastatic castration-resistant prostate cancer (mCRPC).

## Study Methodology

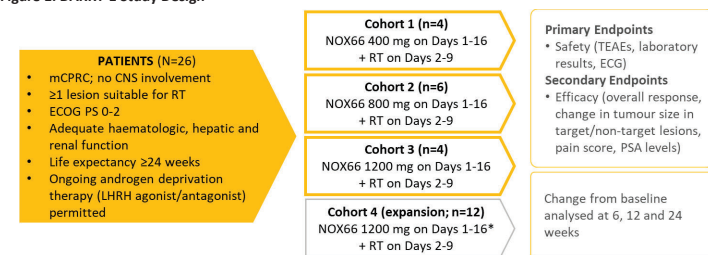
- A phase 1b dose escalation and dose expansion trial in men with late-stage mCRPC (Table 1; ClinicalTrials.gov Identifier NCT03307629)
- Fourteen patients were included in the dose-finding arm (4-6 patients per cohort; 400 mg, 800 mg or 1200 mg NOX66); an additional 12 patients were enrolled into the expansion arm (n=12; 1200 mg NOX66 daily for 14 days) (Figure 1)
- Recruitment commenced in March 2018, at eleven centres in Australia (5), New Zealand (1) and Georgia (5)
- All patients received NOX66 daily for 14 days and RT (20 Gy) in 5 fractionated doses and were assessed at 6, 12 and 24 weeks with follow up to 24 months

Table 1. Key Inclusion and Exclusion Criteria

Key Inclusion Criteria	
Historically confirmed prostate cancer	
Metastatic disease evidenced by either CT/MRI imaging or bone scan	
Objective evidence of disease progression	
One symptomatic lesion suitable for radiation therapy	
Key Exclusion Criteria	
Tumour involvement of the central nervous system	
Concurrent systemic chemotherapy or biological therapy	
Any situation where the use of suppository therapy is contra-indicated or impractical	

- The primary endpoint was safety as assessed by the frequency of treatment-emergent adverse events (TEAEs), laboratory results and electrocardiograms (ECGs)
- Secondary endpoints included radiographic response as assessed by RECIST v1.1, change in tumour size in both target and non-target lesions, pain response measured by the Brief Pain Inventory (BPI) scale (≥30% reduction) and prostate-specific antigen (PSA) response (≥50% reduction)

Figure 1. DARRT-1 Study Design



\* The 1200 mg dose for Cohort 4 was selected by the Study Steering Committee based on the interim safety and tumour response data from Cohorts 1, 2 and 3  
 CNS = central nervous system; ECG = electrocardiogram; ECOG PS = Eastern Cooperative Oncology Group Performance Status; LHRH = luteinizing hormone-releasing hormone; mCRPC = metastatic castration-resistant prostate cancer; PSA = prostate-specific antigen; RT = radiation therapy; TEAEs = treatment-emergent adverse events

## Study Results

- The median age of Cohort 1 was >4.5 years above the median of Cohorts 2 and 3 (Table 2)
- The ECOG performance status at baseline was 1 in most patients (n=11) and 0 in three patients (Table 2)

Table 2. Baseline Characteristics

Characteristics	COHORT 1	COHORT 2	COHORT 3
	400 mg NOX66 + RT (n=4)	800 mg NOX66 + RT (n=6)	1200 mg NOX66 + RT (n=4)
Median age, years	74.0	67.5	69.5
Median weight, kg	83.3	71.5	95.1
ECOG	0	1 (16.6%)	2 (50.0%)
	1 (100%)	5 (83.3%)	2 (50.0%)

- Eleven of the 14 enrolled patients received at least one dose of NOX66 in the dose escalation part of the study and have completed at least 24 weeks of follow-up
- 57.1% of patients experienced a TEAE (Table 3)
- TEAEs considered related to NOX66 alone were mild (Grade 1) cases of dry mouth, stomatitis and oral mucositis; mild (Grade 1) fatigue was considered related to both NOX66 and radiation; none of the 4 Grade ≥3 TEAEs were considered related to study drug
- Three patients in the 800 mg dose cohort died due to disease progression occurring ≥30 days after the last NOX66 dose; none of the deaths were considered by the Investigator to be related to study drug

Table 3. Treatment-Emergent Adverse Events

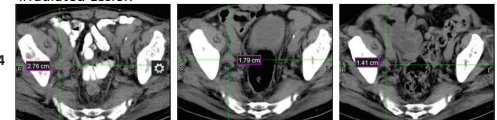
TEAEs	Cohort 1	Cohort 2	Cohort 3	Overall n = 14
	400 mg NOX66 + RT n = 4	800 mg NOX66 + RT n = 6	1200 mg NOX66 + RT n = 4	
All	2 (50.0)	4 (66.7)	2 (50.0)	8 (57.1)
Related to NOX66	1 (25.0)	1 (16.7)	0 (0.0)	2 (14.3)
Related to RT	1 (25.0)	0 (0.0)	1 (25.0)	2 (14.3)
≥Grade 3	0 (0.0)	3 (50.0)	1 (25.0)	4 (28.6)
Deaths (Disease progression)	0 (0.0)	3 (50.0)	0 (0.0)	3 (50.0)

- Nine patients (64%) achieved a partial response or stable disease by Week 12; 8 patients (57%) maintained their response from Week 12 to 24 (Table 4)
- The patient with an overall partial response had a 50% size reduction in both the irradiated index lesion and a distant lesion (Figure 2)

Table 4. Overall Response According to RECIST Criteria (V1.1)

	Cohort 1	Cohort 2	Cohort 3	Overall n = 14
	400 mg NOX66 + RT n = 4	800 mg NOX66 + RT n = 6	1200 mg NOX66 + RT n = 4	
<b>Number evaluable at Week 12</b>	4	4	3	11
Partial Response	0	1	0	1
Stable Disease	3	2	3	8
Progressive Disease	1	1	0	2
<b>Number evaluable at Week 24</b>	4	3	3	10
Partial Response	0	1	0	1
Stable Disease	2	2	3	7
Progressive Disease	2	0	0	2

Irradiated Lesion



Non Irradiated Lesion

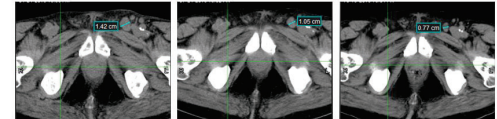
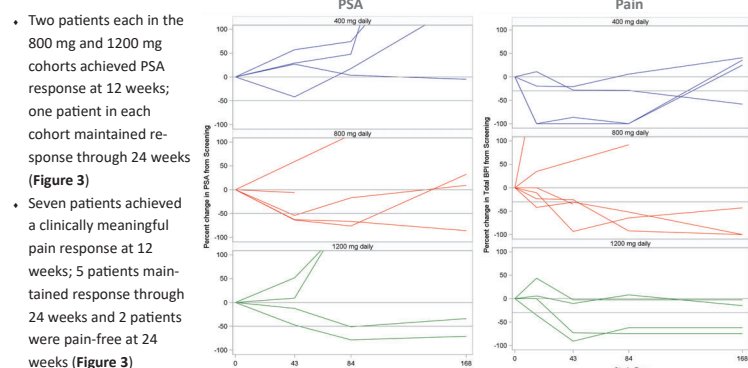


Figure 2. Radiographic Scan of an Irradiated and Non-irradiated Lesion at Baseline, 12 Weeks and 24 Weeks

Figure 3. PSA Change and Pain Score Change from Screening to 24 Weeks for Evaluable Patients



## Conclusions

- NOX66 combined with low-dose RT was well tolerated and appeared to stabilise disease for 6 months in the majority of patients
- The analysis of the 1200 mg NOX66 expansion Cohort 4 is ongoing

## Acknowledgements

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