

Date: 15<sup>th</sup> January 2020

Sydney, Australia

ASX Limited 20 Bridge Street SYDNEY NSW 2000

#### **Noxopharm Corporate Presentation**

**Sydney, 15<sup>th</sup> January 2020:** Noxopharm (ASX: NOX) is pleased to provide shareholders and the market the attached Noxopharm corporate presentation "Corporate & Clinical Overview".

This document is being used by Noxopharm for presentation during meetings with investment banks, fund managers and other attendees of the JP Morgan Healthcare Conference in San Francisco, California.

The presentation can be found at www.noxopharm.com

Graham Kelly, CEO and Chairman of Noxopharm has approved the release of this document to the market.

#### 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<sup>®</sup> and is the major shareholder in Nyrada Inc.

www.noxopharm.com

Investor & Corporate Enquiries: Prue Kelly M: 0459 022 445 E: info@noxopharm.com Company Secretary: David Franks T: +61 2 9299 9690 E: <u>David.Franks@automicgroup.com.au</u>

Media queries: Catherine Strong Citadel-MAGNUS T: 02 8234 0111 E: <u>cstrong@citadelmagnus.com</u>



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# **Noxopharm Limited**

Veyonda®

**Corporate & Clinical Overview** 15<sup>th</sup> January 2020



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Veyonda<sup>®</sup>

DARRT

Veyonda®

Noxopharm is seeking to bring Veyonda<sup>®</sup> to market as a first-inclass drug that boosts the efficacy of radiotherapy in prostate cancer





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### **Executive Summary**



- Australian biotech company listed on Australian Securities Exchange (ASX:NOX)
- Oncology focus
- Proprietary drug Veyonda<sup>®</sup>
- First-in-class inhibitor of sphingosine-1-phosphate
- Intended as adjunct to radiotherapy
- > 2 active clinical trials studying improved efficacy of radiotherapy in late-stage **mCRPC**:
  - (Phase 1b) DARRT, Veyonda<sup>®</sup> + external beam radiotherapy
  - (Phase 2a) LuPIN, Veyonda<sup>®</sup> + <sup>177</sup>Lu-PSMA-617
  - Strong clinical signals achieved in both trials
- Preparing for Phase 2 DARRT clinical trial
- Unique dual market opportunity for Veyonda<sup>®</sup> in late-stage prostate cancer space
- ~30% equity in Nyrada Inc., a promising listed subsidiary focused on novel small molecule drugs (ASX:NYR)
- > Experienced board and management team, strong technical & commercial experience

Noxopharm believes that its DARRT and LuPIN treatments will become standard of care for late-stage prostate cancer, offering patients and doctors two new treatment options



## **Company Details**



Noxopharm Limited (Dec 2019)		Board and Key Management		
Listed on Australian Securities	Exchange (ASX:NOX) Aug 2016	Dr Graham Kelly. PhD	Chairman & CEO	
Shares on issue	130m	lan Dixon. PhD, MBA	Non-Executive Director	
Share Price	A\$0.40	Peter Marks. MBA, BEc, LLB	Non-Executive Director	
Market Cap	A\$52m	Alex Hunter. <i>MBA, BE</i>	Chief Commercial Officer	
Cash	A\$3.5m	Greg Ambra. MS	SVP North American Ops	
Convertible notes	A\$5.2m	Dr Gisela Mautner. MD-PHD, MPH, MBA	Chief Medical Officer	
		Dr John Wilkinson. <i>PhD</i>	Chief Scientific Officer	
		Shawn Van Boheemen. BBus MCom	Chief Financial Officer	



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### **Veyonda**<sup>®</sup>



#### How Veyonda® works

- The active ingredient in Veyonda<sup>®</sup> is the experimental anti-cancer drug, idronoxil
- The molecular target of idronoxil is the pan oncogene, Ecto-Nox disulfide-thiol exchanger Type 2 (ENOX2)
- A principal downstream consequence of ENOX2 inhibition is downregulation of sphingosine-1-phosphate (S1P)
- S1P is a key secondary messenger, activating five S-1-P receptors that play critical roles in pro-survival signalling and immune cell function
- Pro-survival signalling includes cell growth, DNA repair and multi-drug resistance mechanisms
- Immune cell function includes a negative feed-back mechanism that blocks inflammatory response/immune cell trafficking in order to dampen an immune response following inflammation
- Most cancers over-express S1P levels, effectively blocking the ability of the body to mount inflammatory and immune responses against cancer cell growth
- By removing this block, Veyonda<sup>®</sup> helps to restore the body's inherent ability to fight cancer tumours

#### Patent and IP

- Veyonda<sup>®</sup> is a Noxopharm registered trade name
- Noxopharm has lodged 6 patent families around Veyonda<sup>®</sup>, the first of which has entered the national examination phase in 80 countries

#### Veyonda ®

- Veyonda<sup>®</sup> (previously known as NOX66) is the Company's proprietary oncology drug currently in Phase 1b and Phase 2a clinical trials
- Final results from the DARRT-1 study show that Veyonda<sup>®</sup> in combination with EBRT achieved a durable and meaningful anticancer response in a high proportion of late-stage prostate cancer patients in a well tolerated way
- Interim results from the LuPIN study suggest that Veyonda<sup>®</sup> is also boosting the response to <sup>177</sup>Lu-PSMA-617 (Novartis), enabling more men to complete their full course of radiation therapy, again, in a well tolerated way

#### Veyonda<sup>®</sup> boosts radiation in two ways

- 1. Palliative external radiotherapy
  - DARRT clinical trials underway
- 2. Palliative internal radiotherapy
  - LuPIN clinical trial underway



**DARRT** Veyonda<sup>®</sup> + EBRT



LuPIN Veyonda<sup>®</sup> + <sup>177</sup>Lu-PSMA-617



### **DARRT** - a novel radiation therapy enhancer



#### DIRECT RESPONSE

At a minimum, Veyonda® is expected to lead to better DIRECT response to radiotherapy by functioning as a radio-enhancer





ABSCOPAL RESPONSE

The best expected outcome would be an improved

Complete resolution

Partial abscopal Complete abscopal response response

The key to the success of the DARRT treatment is a combination of two actions:

- First: expose a small number (1 or 2) of individual tumours to low-dose (20 Gy) radiation. Low-dose is critical because the goal is to damage the tumour, not to destroy all cells including beneficial cells such as those responsible for inflammation and immune responses—these cells need to be preserved. The key to DARRT is initiating an inflammatory response that serves as a trigger to an immune response
- Second: the presence of idronoxil in all tumours boosts the pro-inflammatory (STING) effect of the radiation in the irradiated tumours as well as restoring local immune function in all tumours, promoting an allof-body immune response leading to an anti-cancer effect in all tumours in what is known as an abscopal response.

#### **DARRT-1: Headline Conclusions**

- 25 men started the Phase 1b DARRT-1 study; 4 withdrawals = 21 remaining in the study
- 16 alive and completed the study, with 15 radiographically assessable by RECIST
- Primary end-point of safety met with no significant or dose-limiting toxicities
- Secondary end-point of efficacy achieved

#### At 6-month follow up:

- 11/21 (53%) had progressive disease or died (unrelated to treatment)
- Anti-cancer response achieved as evidenced by:
  - Stable disease or better (RECIST) 10/15 (66%)
  - PSA Response 5/16 (31%) 0
  - Pain Response 10/16 (62%)

A durable and meaningful anti-cancer response was achieved at 6-months in 48% of men with endstage progressive prostate *cancer* with no remaining treatment options



### DARRT-2



#### DARRT-2 Trial Design

- Phase 2 clinical trial protocol development under way
- Men with mCRPC post-taxane and post-enzalutamide/abiraterone
- In combination with best supportive treatment/best standard of care
- Multiple sites, multi-national
- Single course (5 fractionated doses) of radiotherapy with repeat cycles of Veyonda<sup>®</sup>
- Compared to the single treatment cycle in DARRT-1, the repeat cycles expected to provide an additional monotherapy anti-cancer effect with potential for an increase in overall anti-cancer effect
- Medical advisory boards established
- Anticipated regulatory submissions late-2020

#### Potential Indicative Trial Design



# NOXOPHARM

#### **Anticipated endpoints**

- Key primary endpoint: Overall survival at 12-months
- Secondary endpoints:
  - Progression-free survival (radiographic, clinical, PSA)
  - RECIST response
  - pain response (BPI-SF)
  - Health-related quality of life
  - ✤ Safety and tolerability
  - Health economics

#### **DARRT-2** Timeline

- Clinical protocol planning has commenced with medical advisory board input
- Trial commencement date subject to current planning, targeted for early 2021

### LuPIN



#### Aim of the LuPIN study

A major aim of the LuPIN trial is to see if Veyonda<sup>®</sup> can boost the effectiveness of <sup>177</sup>Lu-PSMA-617 radiation therapy so that more men are able to complete their full course of treatment (up to 6 cycles) before their cancer progresses and they need to stop treatment

#### What is <sup>177</sup>Lu-PSMA-617

<sup>177</sup>Lu-PSMA-617 is an experimental radioactive drug that was the subject of a US\$6 billion series of acquisitions by Novartis in 2018 and currently is in a Phase 3 registration study expected to finish in 2020

#### About LuPIN

- LuPIN is an Investigator-Initiated Phase 1b/2a, single-arm, open label study being conducted at St Vincent's Hospital, Sydney
- The study is enrolling 56 men with PSMA-positive mCRPC that has progressed after docetaxel, cabazitaxel and either abiraterone and/or enzalutamide Rx
- Men receive intravenous <sup>177</sup>Lu-PSMA-617 at 6-weekly intervals; up to 6 cycles providing no progression based on PSA; Veyonda<sup>®</sup> dosed days 1-10 each cycle.
- Phase 1b arm was dose-escalation: 400 mg (8 patients), 800 mg (8 patients), 800 mg (16 patients) of Veyonda<sup>®</sup> to establish the safety of the combination treatment
- Based on evidence of efficacy and good tolerability, the trial progressed to a Phase 2a expansion arm of 1200 mg (24 patients) of Veyonda<sup>®</sup> intended to establish the dose-response effect of increasing Veyonda<sup>®</sup> levels in treatment safety and efficacy

#### **Results so far**

- Preliminary data published in September 2019 demonstrated that the three endpoints used to measure anti-cancer effect all showed a benefit from combining Veyonda<sup>®</sup> with <sup>177</sup>Lu-PSMA therapy
- <u>PSA response</u> refers to a fall in PSA levels in blood of greater than 50%. This is accepted by oncologists as a surrogate marker of disease activity.
- Adding Veyonda<sup>®</sup> to <sup>177</sup>Lu-PSMA therapy almost doubled the PSA response (69% with Veyonda<sup>®</sup> vs 36% with <sup>177</sup>Lu-PSMA alone)
- <u>Progression-free survival (PFS)</u> is a measure of the time from the start of treatment until the disease progresses. PFS quadrupled through the addition of Veyonda<sup>®</sup> (8.4 months vs 2.0 months with <sup>177</sup>Lu-PSMA alone)
- <u>Treatment duration</u>. The addition of Veyonda<sup>®</sup> meant that the number of men able to start the 4th treatment cycle tripled to 69% from 21% with <sup>177</sup>Lu-PSMA alone
- The combination therapy also was well tolerated, pointing to Veyonda<sup>®</sup> being safe to use in combination with intravenous radiotherapy

In summary, combination therapy of Veyonda<sup>®</sup> and <sup>177</sup>Lu-PSMA-617 shows benefits to patients well above that achieved with <sup>177</sup>Lu-PSMA-617 therapy alone and underscores the Company's confidence in Veyonda<sup>®</sup> eventually becoming a standard drug in the management of prostate cancer



# **Indicative Clinical Program Timing**



DARRT -1 complete, final statistical results	Indicative Clinical Program Timing		DecQ2019	MarQ2020	JunQ2020	SepQ2020	DecQ2020	MarQ2021	JunQ2021	SepQ2021	DecQ2021	
due March 2020	DARRT-1 Phase 1 clinical trial complete Phase 1 statistical report	Dec Q 2019 Mar Q 2020	•	•								
DARRT-2 protocol development under way	DARRT-2 Protocol Development/CRO appoin't •Medical advisory board consultation •Appoint CRO Commence trial (indicative) DARRT-2 trial under way (indicative)	now- Sep Q 2020 Early 2021 2021 onwards						<b>◆</b>				
DARRT-2 clinical trial indicative commencement early	LuPIN Trials complete Commercial partnerships	Dec Q 2020 2020 & 2021					•					



2021

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# **Market Opportunity**



Noxopharm believes Veyonda® has potential use in most forms of solid cancer

Noxopharm believes the fastest, lowest risk path to market for Veyonda<sup>®</sup> is as a treatment for **mCRPC** 

*mCRPC* currently is treated palliatively. Noxopharm is intended to go beyond palliation and provide a meaningful, durable and well tolerated anti-cancer effect

2019 Prostate Cancer	Australia	USA
New cases of Prostate Cancer diagnosed	19,500	175,000
Deaths from Prostate Cancer	3,300	31,600

#### **Market Opportunity**

- Noxopharm believes Veyonda<sup>®</sup> has potential applications in most forms of solid cancer as both a radio-enhancer and chemo-enhancer
- Noxopharm has selected radio-enhancement (DARRT regimen) in metastatic prostate cancer (mCRPC) as the path to first market approval:
  - DARRT-1 has shown that Veyonda<sup>®</sup> provides a meaningful anti-cancer effect including cessation of tumour growth in about half of mCRPC patients, and considerable (average 80%) pain relief
  - o Management of mCRPC is a major unmet need, with palliative treatment the current standard of care
  - o The need is predicted to grow with increasing longevity and a growing global middle class
  - Ease of enrolment due to high disease incidence and 12-months end-points (limited life expectancy of typically 6-9 months) suggests relatively short trial duration
  - o Potential high demand and low drug costs could result in blockbuster revenue
  - A number of recent multi-billion dollar deals in the mCRPC space (see table below)

Recent acquisitions	Buyer	Seller	Price range
XTANDI® mCRPC (2016)	Pfizer	MEDIVATION	US\$14 billion
<sup>177</sup> Lu-PSMA-617 mCRPC (2018)	U NOVARTIS	ENDOCYTE	US\$2.1 billior
<sup>177</sup> Lu-PSMA-617 & others mCRPC (2018)	U NOVARTIS	A d v a n c e d Accelerator Applications	US\$3.9 billior



### Nyrada Inc.



Nyrada is a U.S.-registered spin-off subsidiary of Noxopharm

Nyrada will list on the Australian Securities Exchange (ASX:NYR) on 16 Jan 2020

Focusing on novel small molecules for major nononcology indications

#### NYRADA

- Nyrada is a pre-clinical stage, drug company specialising in the development of novel small molecule drugs pertaining to the underlying pathological processes involved in cardiovascular, neurodegenerative and chronic inflammatory diseases
- The Company's vision is to become a high growth pharmaceutical company specialising in drug discovery where few if any, effective or well-tolerated therapies exist
- The Company has four current drug development programs:
  - Cardiovascular: A PCSK9 inhibitor for the treatment of high blood LDL-cholesterol levels in patients poorly responsive to, or unable to take statin drugs
  - Neuroprotection: A neuroprotectant drug to improve patient outcomes and prevent long-term disability in patients with ischaemic stroke and traumatic brain injury
  - Inflammation/pain: A drug to treat pain associated with peripheral nerve damage (such as sciatica), and
  - $\circ$  Inflammation/autoimmunity: A drug to treat autoimmune diseases such as psoriasis

Board and Key Management	
John Moore	Non-executive Chairman
Dr Graham Kelly PhD	Founder, Non-executive Director
Peter Marks	Non-executive Director
Marcus Frampton	Non-executive Director
Rudiger Weseloh PhD	Non-executive Director
Christopher Cox	Non-executive Director
James Bonnar	Chief Executive Officer
Benny Evison PhD	Chief Scientific Officer



### **Investment Highlights**



#### Noxopharm Investment Highlights

- Significant clinical milestones over next 12 months from DARRT and LuPIN trials
- Potential standard of care: Noxopharm believes that its DARRT and LuPIN treatments have the potential to become standard of care for late-stage prostate cancer where treatment currently is palliative
- Potential dominant position: Company in unique position of having two potential treatments for late-stage mCRPC, providing a likely dominant position in a critical sector
- DARRT marketing approval: With planning now in progress for DARRT-2 pivotal trial, Company within reach of Veyonda<sup>®</sup> generating significant revenue
- LuPIN treatment: Current LuPIN clinical trial suggesting that Veyonda<sup>®</sup> is at least doubling the anti-cancer activity of <sup>177</sup>Lu-PSMA-617, a drug candidate the subject of a US\$6 billion series of acquisitions in 2018
- Broader market opportunity: Approval of Veyonda<sup>®</sup> for mCRPC cancers (DARRT & LuPIN), including early-stage prostate cancer, likely to substantially increase the commercial value of the Company
- Equity in Nyrada provides additional corporate value

	USA	Australia	
Contact Details	Greg Ambra – Senior V-P North America Operations +1 732 595 7508 greg.ambra@noxopharm.com	+61 429 854 390 graham.kelly@noxopharm.com Alex Hunter – Chief Commercial Officer	
		+61 467 570 063 alex.hunter@noxopharm.com Dr Gisela Mautner – Chief Medical Officer	
		+61 499 005 012 gisela.mautner@noxopharm.com	

