

Date: 5 March 2019 Sydney, Australia

**ASX: NOX** 

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Mr John Moore

Non-Executive Director

#### NEW CORPORATE PRESENTATION RELEASED

SYDNEY, 5 March 2019: Noxopharm (NOX: ASX) today releases an updated corporate presentation ahead of non-deal roadshow presentations planned over the coming month in the U.S., Hong Kong and China. This is part of the Company's efforts to raise its profile in the global investment community ahead of planned release of key clinical data over the next 5 months.

#### **About Noxopharm**

Noxopharm is a clinical-stage Australian drug development company with offices in Sydney, New York and Hong Kong. The Company has a primary focus on the development of drugs based on an flavonoid chemical structure, with Veyonda® the first pipeline product. Three other drug candidates for non-oncology indications are under development in a subsidiary company (Nyrada Inc).

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## We have a single objective:

To make Veyonda® (a radio-enhancing/immune-enhancing drug)

a standard companion drug

- → for all forms of radiotherapy
- → across most forms of solid cancer

in order to deliver

- → more potent and more curative responses to radiotherapy
- → at lower, better tolerated dosages of radiotherapy

and in so doing

→ provide a transformative leap forward in the treatment of many cancers



## Veyonda® - A New Improved Formulation of Idronoxil

**Veyonda®** delivers a proprietary <u>pro-drug</u> form of idronoxil\* that delivers continuous anti-cancer activity for 12 hours

**Veyonda**® provides clinical benefit where earlier formulations did not

**Veyonda**<sup>®</sup> is a convenient-to-use, self-administered dosage form given twice daily to provide continuous 24-hour cover

\* Patents pending





### Examples of how a radio-enhancer might be used in prostate cancer

Stage of cancer

**Veyonda**® + Radiotherapy (RT)

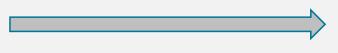
Potential benefits

Early-stage, operable

Early-stage, inoperable or recurrence post-prostatectomy

Late-stage, palliative

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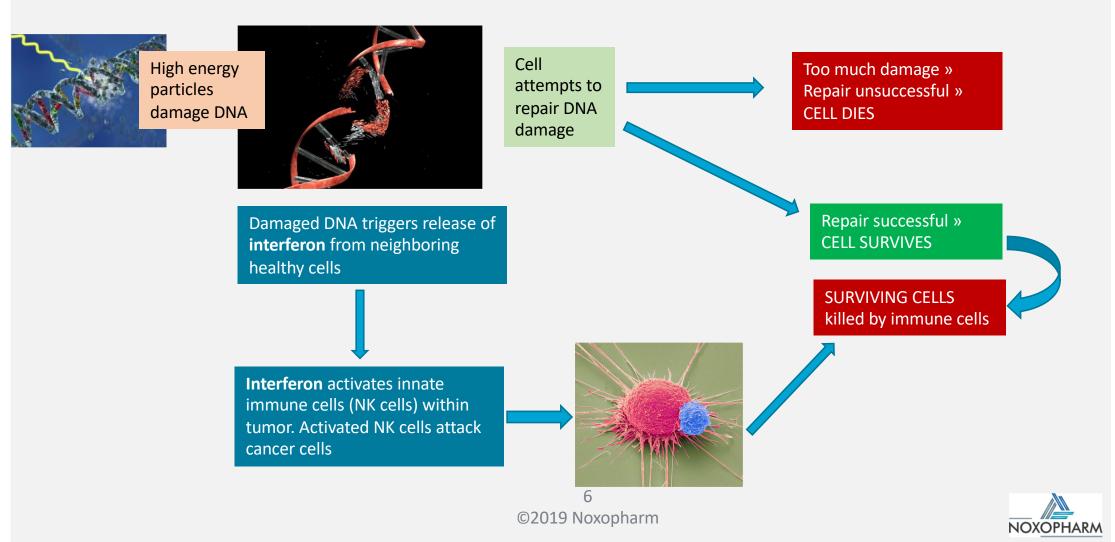


Avoidance of surgery and attendant side-effects

- Reduction in RT dosage to minimise pelvic tissue damage
- Delay in start of castration therapy
- Better pain and symptom relief
- Delay in tumour progression



## **How radiotherapy works**



# How *Veyonda*® radio-enhances

BLOCKS DNA REPAIR MECHANISMS



attempts to repair LNA clamage

Repair unsuccessful CELL DIES

Damaged DNA triggers release of interferon from neighboring healthy cells

FEWER CELLS SURVIVE

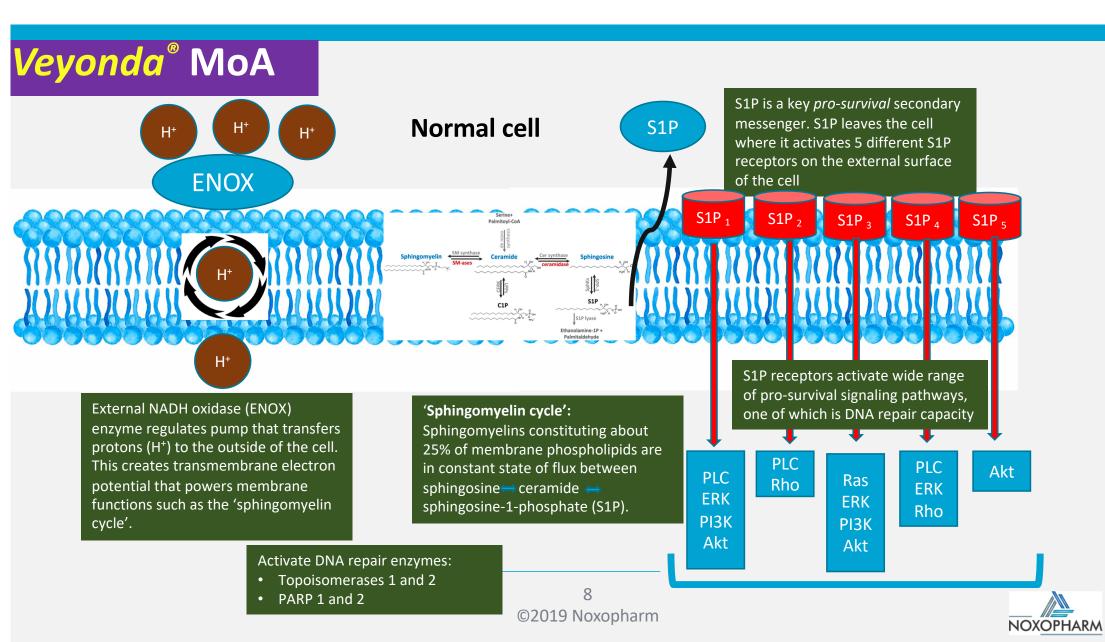
**Veyonda®** BOOSTS INTERFERON RESPONSE

SURVIVING CELLS more effectively killed by amplified immune response

**INCREASED ACTIVITY OF IMMUNE CELLS** 







#### *Veyonda®* MoA **Cancer cell** Human cells express RNA for two Declining S1P levels deprive S<sub>1</sub>P forms of ENOX - ENOX1 and ENOX2. S1P receptors of activation ENOX2 protein only expressed on cancer cells where it dominates over ENOX2 ENOX1 S1P<sub>4</sub> S1P<sub>5</sub> S1P<sub>3</sub> H<sup>+</sup> Sphingosine kinase function inhibited Idronoxil (Veyonda active ingredient) by elevated proton levels. Ceramide only binds to ENOX2. ENOX2 (pro-apoptotic) levels rise and S1P inhibition leads to accumulation of (pro-survival) levels fall. protons in plasma membrane. Key pro-survival signaling pathways

DNA repair enzyme activity inhibited

PI3K PI3K Akt

NOXOPHARM

down-regulated

Akt

## *Veyonda*® + Radiotherapy

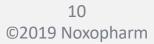
Potential use across broad range of radiotherapy practice



Externally-delivered radiotherapy



Internally-delivered radiopharmaceuticals





### **Clinical Programs**

### **DARRT**

Direct and Abscopal Response to Radio-Therapy

## LuPIN

<sup>177</sup>Lutetium-PSMA In Combination With VeyoNda

### Initial focus on late-stage prostate cancer

- Metastatic, castrate-resistant disease
- Post-docetaxel and abiraterone/enzalutamide
- No remaining standard treatment options
- Progressive disease
- Anticipated survival of > 3 months
- Patient eligible for palliative treatment



## **DARRT**

### Direct and Abscopal Response to Radio-Therapy

### Rationale

- 1. Use of palliative (low) dose of radiation minimizes damage to innate immune cells within the irradiated lesion.
- 2. Veyonda® amplifies radiation-induced DNA damage in cancer cell by:
- blocking cell division, thereby exposing the DNA to greater damage, and
- blocking the ability of the cancer cell to repair that damage
- 3. Amplified radiation-induced DNA damage then:
- Increases likelihood of irradiated cancer cell dying
- Enhances response of local innate immune cells

### Objectives

**Local effect.** Greater shrinkage of the irradiated target lesion (DIRECT RESPONSE)

<u>Systemic effect</u>. An anti-cancer response in non-target, non-irradiated lesions stemming from enhanced innate immune and epigenetic responses in the irradiated lesion (ABSCOPAL RESPONSE)



## **DARRT**

### Direct and Abscopal Response to Radio-Therapy



External Beam RT or Stereotactic Body RT

- Patients with multiple lesions and at least 2 measurable lesions
- Irradiate 1 lesion\*
  (20-25 Gy in 5 fractionated doses)
- > Veyonda® (600 mg bid) 10 days beginning Day -5
- > Assessments at 6, 12 and 24 weeks
  - PSA
  - Pain Score
  - QoL Score
  - Time to progression
  - RECIST\* (where possible)

<sup>\*</sup>Only patients in part 1 needed to have one measurable lesion as per RECIST v1.1



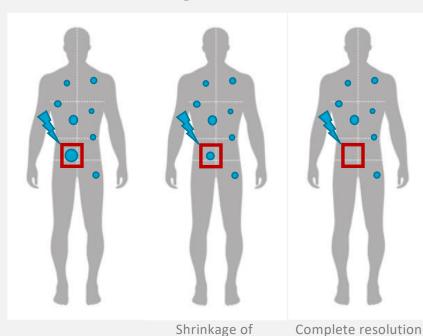


# **DARRT**

### Direct and Abscopal Response to Radio-Therapy

#### **DIRECT RESPONSE**

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



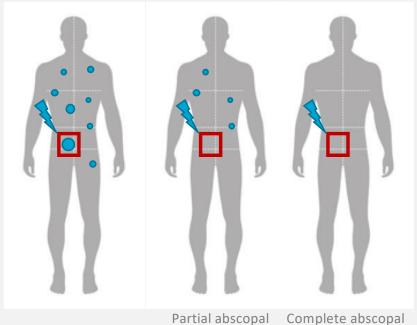
Irradiated tumor

of Irradiated tumor

#### 14 ©2019 Noxopharm

#### **ABSCOPAL RESPONSE**

The best expected outcome would be an improved DIRECT response, plus shrinkage of non-targeted lesions



response

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Complete abscopal response

NOXOPHARM

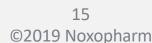
## **DARRT-1 Study**

#### **Details:**

- Phase 1b multi-national study (Australia, NZ, Georgia)
- Open label, single-arm study
- 24 patients; metastatic, castrate-resistant prostate cancer
- ❖ Veyonda® + external beam RT to 1 lesion\*
- ❖ Part 1: Dose-finding (constant RT dose)
  - 400 mg Veyonda (4 patients)
  - 800 mg Veyonda (4 patients)\*\*
  - 1200 mg Veyonda (4 patients)\*\*\*

Part 2: 1200 mg Veyonda

12 patients





<sup>\*</sup>Only patients in part 1 needed to have one measurable lesion as per RECIST v1.1

<sup>\*\*2</sup> patients were replaced

<sup>\*\*\* 1</sup> patient was not evaluable at 12 weeks

## **DARRT-1 Study**

### 12-week data for Part 1 patients:

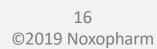
	<u><b>400 mg</b></u> n=4	<b>800 mg</b> n=4	1200mg n=4 (3 evaluable)
PSA response*	0	2	2
Pain response**	2	3	2
RECIST response***	4 SD	1 PR 2 SD 1 PD	3SD

<sup>\* &</sup>gt; 50% decline

24-week data Part 1 patients – late May 2019

12-week data Part 2 patients – July 2019

24-week data Part 2 patients – Q1 2020





<sup>\*\* &</sup>gt; 30% decline

<sup>\*\*\*</sup> aggregate of all measurable lesions

## **DARRT-1 Study**

#### **Interim conclusions:**

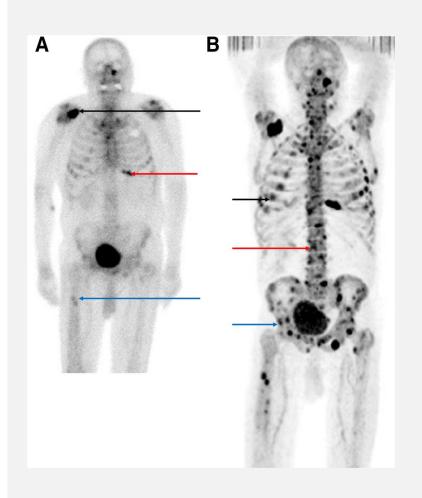
- ❖ Veyonda® + palliative dosages of radiotherapy well tolerated
- 400 mg dose of **Veyonda**® sub-therapeutic
- ❖ No notable difference between 800 and 1200 mg doses
- ❖ In the 7 evaluable patients in the 800 and 1200 mg cohorts\*
  - 4/7 achieved PSA falls >50%
  - 5/7 achieved decrease in pain levels >30%
  - 1/7 showed partial response (RECIST) and 5/7 showed stable disease

The significant reductions in PSA, pain levels and halt in tumour growth suggests potential off-target responses at 3 months in men with advanced mCRPC.

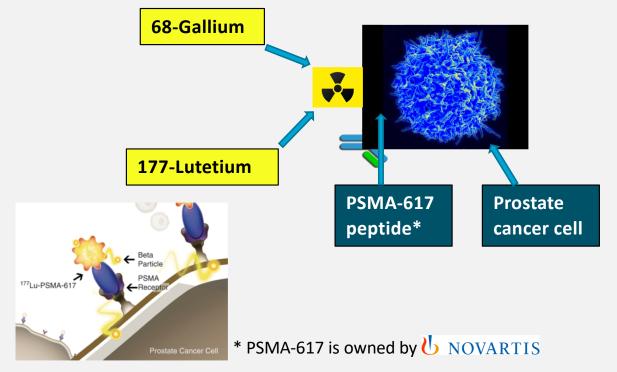


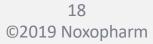
## LuPIN

### <sup>177</sup>Lutetium-PSMA-617 In Combination With VeyoNda



Aim of <sup>177</sup>lutetium-PSMA-617 therapy is to deliver a low dose of radiation to all cancer cells within the body







## LuPIN

# <sup>177</sup>Lutetium-PSMA-617 In Combination With VeyoNda

### Rationale

Objectives

- 1. Use of radiopharmaceutical maximises interaction between **Veyonda**® and radiation in the broad spread of cancer cells throughout the body.
- 2. Veyonda® amplifies radiation-induced DNA damage in cancer cell by:
- blocking cell division, thereby exposing the DNA to greater damage, and
- blocking the ability of the cancer cell to repair that damage
- 3. Amplified radiation-induced DNA damage then:
- Increases likelihood of irradiated cancer cell dying
- Enhances response of local innate immune cells
- 1. To achieve higher response rates, with more patients able to complete the 6-course Lu-PSMA treatment without relapsing
- 2. To achieve greater depth of response as measured by PSA levels
- To achieve more durable responses as measured by improved time to progression and overall survival.



## LuPIN-1 Study

- Phase 1/2 study; investigator-initiated; Australia
- > Open label, single arm
- PSMA-positive, late-stage mCRPC patients
- ➤ 6 courses of <sup>177</sup> lutetium-PSMA-617 administered intravenously every 6 weeks
- ➤ Veyonda® administered for 10 days starting Day-2 each course
- > 8 patients 400 mg Veyonda®; 24 patients 800 mg Veyonda®
- > 30/32 patients enrolled 1 March 2019\*



<sup>\*</sup>Clinical data from first 8 patients (400 mg dose cohort) to be presented at SNMMI Conference, Anaheim, June 2019.

## Planned Expanded Clinical Study Program 2019-2020

#### **DARRT - mCRPC**

- Late-stage mCRPC patients eligible for palliative therapy
- Phase 2 (adaptive), USA
- Double-blind, 2-arm study
- End-points: PSA response, pain response, QoL, PFS

#### DARRT – rare cancers

- Rare cancers eligible for palliative therapy
- Phase 1, Australia
- Open label, single arm
- End-points: genetic markers of response, RECIST, PFS

#### Veyonda® + immuno-oncology drug

- NSC lung cancer patients
- No remaining standard treatment options; failure to respond to checkpoint inhibitors
- Phase 1b, open label, single arm, Australia
- End-points: Safety, RECIST, PFS

**Priority** High Low



## External radiotherapy in cancer (all forms) treatment\*

	Africa	Asia Pacific	Europe	Latin America	North America
Population	1070	4108	893	601	350
No. radiation centres	140	2590	1430	620	2790
No. radiotherapy courses	0.4M	3.3M	1.9M	0.6M	0.9M
Cost per course (US\$)	1,300	2,120	3,490	2,080	7,050

**RADIO-ENHANCER OPPORTUNITY** 

Total 7.1 M courses of radiotherapy = **US\$70 billion** 

(US\$10K per course)





## **Key metrics**

Number of Shares	<b>121.9M</b> : Free float 66.8%
Market Cap (1 March 2019)	AU\$53M
IPO price	20 cents
12 month high/low	\$1.64/0.36
Cash position	AU\$ 9.6M (31 Dec 2018)















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