



19 October 2017

Sydney, Australia

## ASX: NOX

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#### Board of Directors

##### Mr Peter Marks

Chairman  
Non-Executive  
Director

##### Dr Graham Kelly

Chief Executive Officer  
Managing Director

##### Dr Ian Dixon

Non-Executive  
Director

ASX Limited  
20 Bridge Street  
SYDNEY 2000

## October 19<sup>th</sup> Open Briefing Corporate Presentation

Noxopharm Limited (ASX:NOX) is pleased to provide the market with today's Corporate Presentation to an open forum.

Noxopharm CEO, Dr Graham Kelly, will give an update on:

- The progress and timetable of NOX66 clinical trials
- Plans and expectations for the next 3-6 months
- The proposed non-oncology subsidiary, Nyrada Inc

#### 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 radiotherapy.

#### About Noxopharm

Noxopharm is an Australian drug development company with offices in Sydney, Melbourne and Hong Kong. The Company has a primary focus on the development of drugs to address the problem of drug-resistance in cancer cells, the major hurdle facing improved survival prospects for cancer patients. NOX66 is the first pipeline product, with later generation drug candidates under development. The Company also has initiated a pipeline of non-oncology drugs.

#### Investor & Corporate Enquiries:

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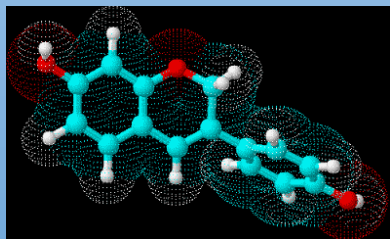
## **Forward Looking Statements**

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.



**ASX: NOX**

# NOX: Unique opportunities



## Idronoxil

- ❖ Kills all forms of cancer cells
- ❖ Sensitises to chemotherapy
- ❖ Sensitises to radiotherapy

? Monotherapy

? Chemo-sensitiser

? Radio-sensitiser



Radio-sensitiser

NOX66

NOX66

NOX66

NOX66

Idronoxil-C  
*IV*

Idronoxil-C  
*Pessary*

3<sup>rd</sup>  
generation

Non-oncology

Ability to deliver drugs across Blood-Brain and Blood-Nerve barriers



NYRADA Inc

## Radiotherapy vs chemotherapy

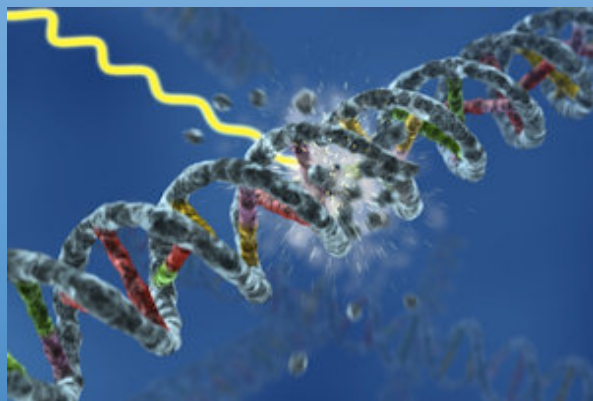
- more effective way of killing cancer cells
- more likely to be curative (early tumours)
- shorter treatment course (2 vs 20 weeks)
- fewer side-effects
- tumours within the 1 patient can have different mutations .. problem for targeted drugs



# Limitations of radiotherapy

## 1. Action is indiscriminate

Radiation does NOT discriminate between a cancer cell and a healthy cell

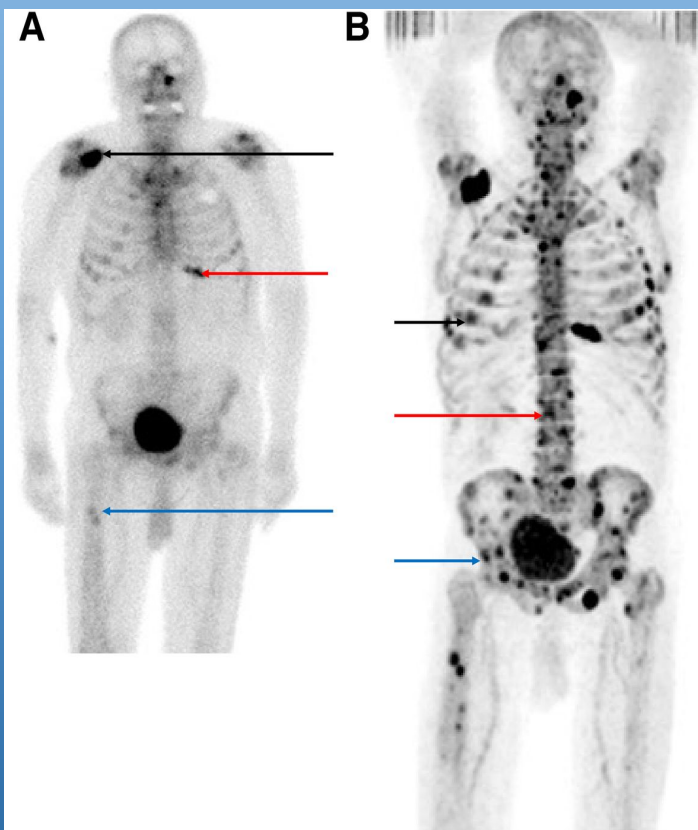


Radiation physically breaks DNA strands

Radiation dose needs to be limited in order to avoid excessive killing of healthy tissue  
*plus*  
limit to amount of total radiation body should be exposed to

# Limitations of radiotherapy

## 2. Metastatic cancer too extensive



Metastatic cancer can be associated with multiple (dozens / 100s) small tumours known as micro-metastases.

Tumours seen on scans can be just 'tip of the iceberg'.

A few larger tumours can be irradiated. But whole-of-body radiation to capture all micro-metastases not feasible.

# NOX66

## FIRST-IN-CLASS RADIOSENSITISER

- SENSITISES ONLY CANCER CELLS (NOT HEALTHY CELLS) TO RADIATION
- DOES NOT CREATE ANY MORE DAMAGE...IT WORKS BY BLOCKING ABILITY OF THE CELL TO REPAIR THE EXISTING DAMAGE
- ALLOWS THE DOSE OF RADIATION TO BE LOWERED TO MORE TOLERABLE LEVELS
- NO KNOWN SIDE-EFFECTS OF NOX66 OTHER THAN FATIGUE
- POTENTIAL TO BE USED WITH ALL FORMS OF RADIOTHERAPY



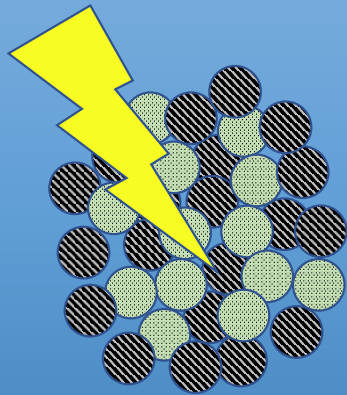
**NOX66**

**CLINICAL PROGRAM**

# **DARRT Program**

**[Direct and Abscopal Response to RadioTherapy]**

direct  
sensitisation



Tumor exposed to radiation



Radio-sensitive cells die  
Less radio-sensitive survive

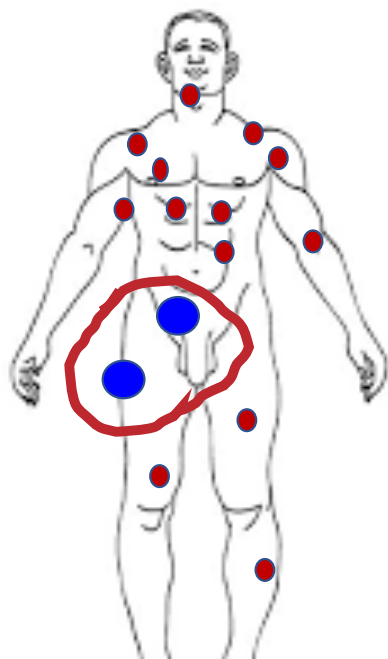


+ NOX66

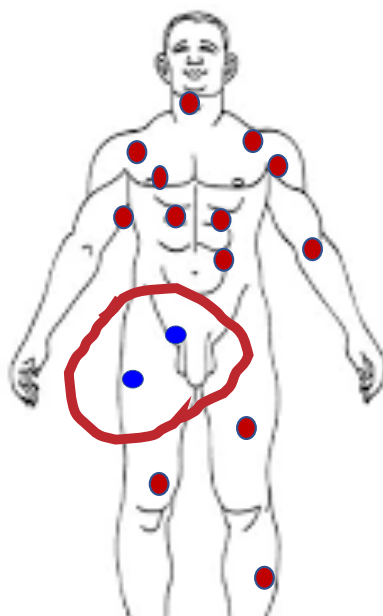
Most or all cancer cells die

# DARRT Program

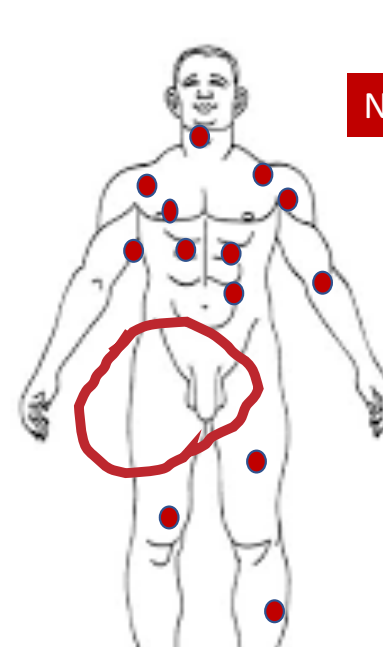
direct  
sensitisation



Palliative radiotherapy



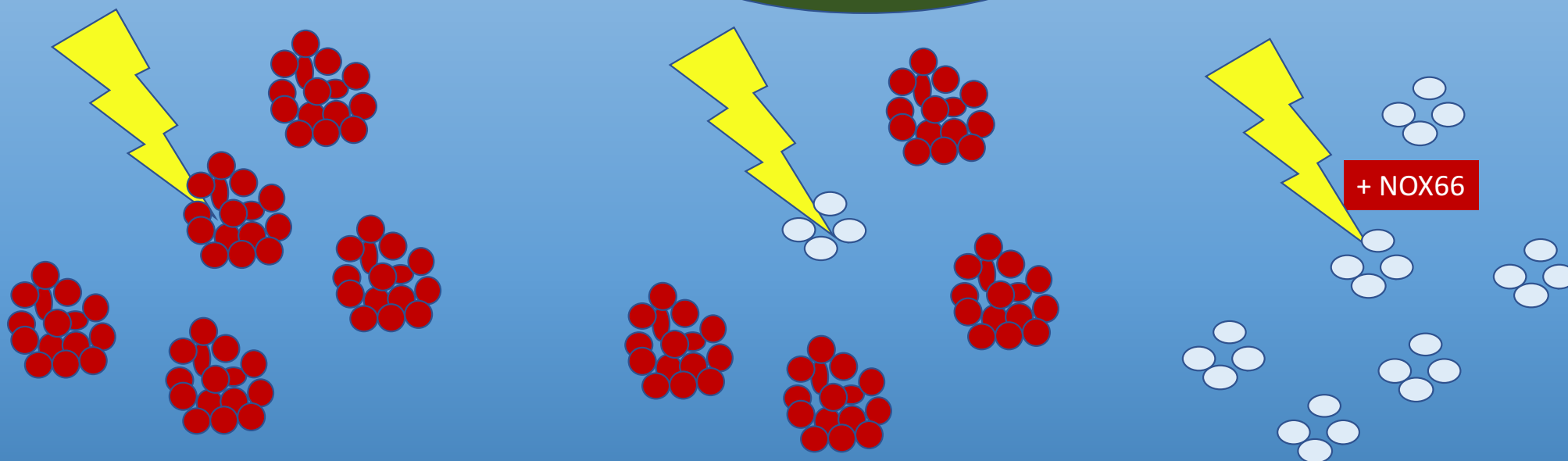
Shrinkage of irradiated  
tumours



Complete resolution of  
irradiated tumours

# DARRT Program

Abscopal response



Individual tumor exposed to radiation

**Normal response:**

- Irradiated tumor dies
- Non-irradiated tumors unaffected

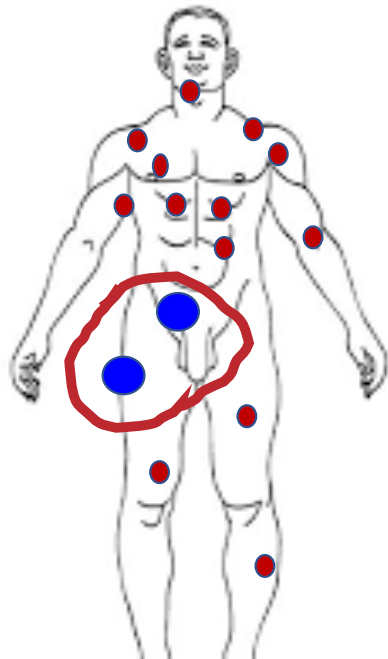
**Abscopal response:**

- Irradiated tumor dies
- Non-irradiated tumors also die

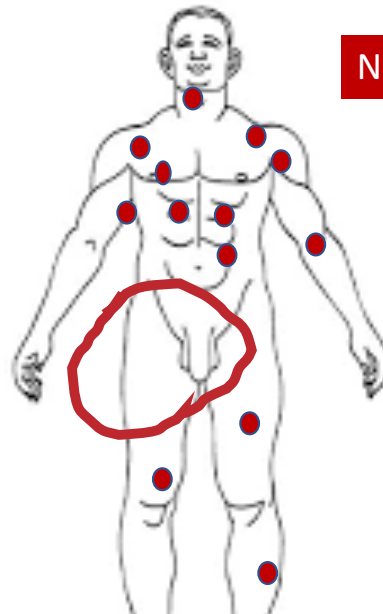
# DARRT Program

Noxopharm

Abscopal response



Palliative radiotherapy

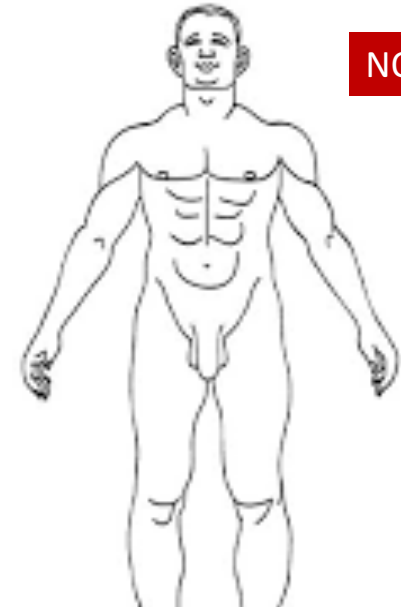


Complete resolution of irradiated tumours

+

NOX66

+



Complete resolution of non-irradiated tumours

+

NOX66

# DARRT Program

**Extremely rare**

**8 case reports**

**Complete/permanent response**

**Range of tumour types**

**ABSCOPAL  
RESPONSE**

# DARRT Program

Mechanism - *unknown*

## Theory 1

**Immune response:**  
Release of tumour antigens from injured cancer cells initiates vaccine-like effect

ABSCOPAL  
RESPONSE

## Theory 2

**Epigenetic effect:**  
Release of miRNA from dying cancer cells initiate suicide genes in non-irradiated cells

# DARRT

## Phase 1b 'proof-of-concept' Clinical Program

- 1** NOX66 + External beam radiotherapy responses:
  - Direct effect only
  - Direct effect + abscopal effect
- 2** NOX66 + External beam radiotherapy + chemotherapy in event of direct response only
- 3** NOX66 + Brachytherapy (internalised radiotherapy)



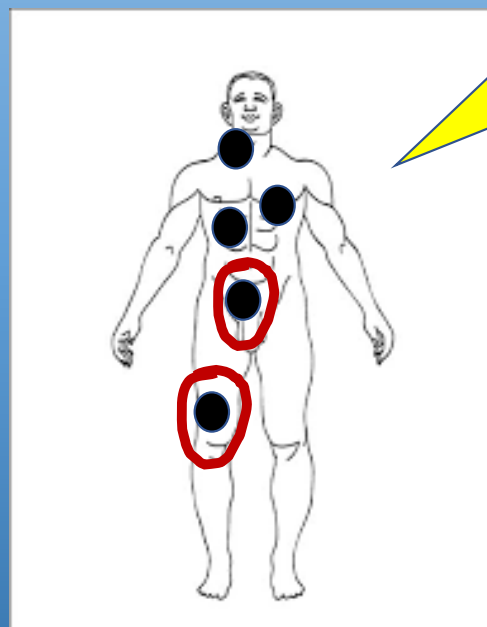
# DARRT

## Phase 1b 'proof-of-concept' Clinical Program

1

Late-stage cancer.  
No treatment options

2-5 measurable lesions



1-3 lesions irradiated.  
(Palliative dose)

At least 1 lesion NOT irradiated

NOX66 daily for 10-14 days

- Measure: response (RECIST) in measurable lesions at 6 weeks, 3- and 6-months

# DARRT Primary *proof-of-concept* study

1

Noxopharm

Q4 2017	Q1 2018	Q2 2018	Q3 2018	Q4 2018
<b>NOX66-002A: Prostate Cancer 24 Patients, 5 Centres (Australia)</b>				
	Review of Interim data	Study design. Site recruitment.	Approvals	
				<b>Phase 3 registration study. Multi-national.</b>

Q4 2017

Q1 2018

Q2 2018

Q3 2018

Q4 2018

**Open Label  
Common & Less Common Cancers  
30 patients, 8-10 Centres (Aust, NZ, Europe)**

**Open Label  
Rare Cancers  
up to 200 patients, 50 centres, multi-national**

# DARRT

## Phase 1b Clinical Program



**Common Cancers** – incidence  $>12$  in 100,000  
**eg. colorectal; lung; breast; prostate; melanoma**

**Less Common Cancers** – incidence 6-12 in 100,000  
**eg. brain, liver, thyroid, head and neck; stomach; pancreas; kidney; ovary**

**Rare Cancers** – incidence  $<6$  in 100,000  
**Approx. 200 types; most sarcomas**

# DARRT

## NOX66 + Radiotherapy + chemotherapy

- ❖ Phase 1b/2a study
- ❖ Stage 4 solid cancers
- ❖ NOX66 + carboplatin
- ❖ 16 patients

- QUESTIONS:**
- ❖ Can NOX66 make carboplatin-resistant tumors respond to carboplatin?
  - ❖ Can chemo dose be reduced to non-toxic levels?

1x NOX66 per day



Carboplatin (low)

Oct 2017\*

Carboplatin (high)

Dec 2017

2x NOX66 per day



Carboplatin (low)

Jan 2018

Carboplatin (high)

March 2018

\* ESMO (Madrid)  
Sept 11 2017  
4/5 patients with stable disease at 3 months

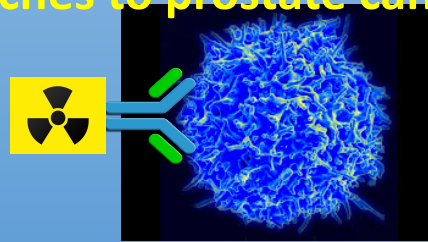
\* ESMO Asia (Singapore)  
Nov 17-19 2017  
Update

brachytherapy

Radioactive ligand

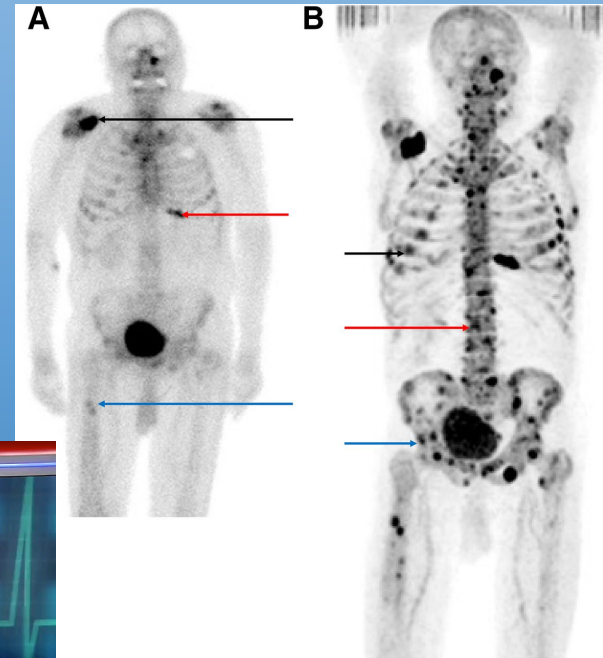


Attaches to prostate cancer cells



$^{177}\text{Lu}$ lutetium isotope

Antibody (peptide) against PSMA (prostate specific membrane antigen)



# DARRT

## Sensitisation of $^{177}\text{Lu}$ -PSMA-617 brachytherapy

3

brachytherapy

**Collective experience in > 200 patients**

Late-stage prostate cancer cases following failure of standard therapy

- About 20% show no meaningful response
- About 60% show partial response
- About 20% show strong or complete response

Summary =- promising therapy, but radiation effect incomplete and short-lived in majority of patients.

# DARRT

## Sensitisation of <sup>177</sup>Lutetium-PSMA-617 brachytherapy

3

brachytherapy

### LUPIN (LuPSMA –Idronoxil) Study St Vincent's Hospital, Sydney

- Metastatic castrate-resistant prostate cancer following standard therapy
- PSMA-expressing cancer (majority of cases)

- 15 patients

- 4x monthly cycles
- Each cycle = LuPSMA injection + NOX66 daily for 10 days
- <sup>68</sup>Gallium-PSMA and PSA levels before each cycle
- 3-, 6- and 12-month complete reviews

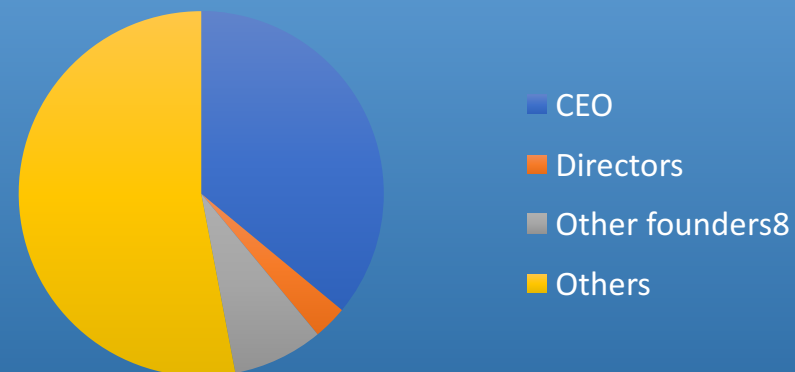
#### Objectives:

- Safety of LuPSMA + NOX66
- Response – PSA, scans and GaPSMA imaging
- Pain scores, QoL
- Progression-free survival
- Overall survival



# Key metrics .....

<b>Shares outstanding</b>	<b>107M</b> : 60M free; 47M escrowed (Sept 2018)
<b>Other</b>	22.5M options (\$0.30) (2021)
<b>Market Cap (18.8.2017)</b>	\$37M
<b>IPO price</b>	20 cents
<b>Last traded</b>	43 cents
<b>Cash position</b>	AU\$ 6 M



# Key Messages

WE EXPECT TO KNOW BY END OF 2017 OF THE SUCCESS OF OUR MISSION

WE AIM TO BE IN A REGISTRATION STUDY BY END OF 2018

WE AIM TO HAVE MARKETING APPROVAL BY 2022

A SUCCESSFUL OUTCOME IS A MAJOR SHARE OF THE \$100 BILLION ONCOLOGY DRUG MARKET

REALISTIC POTENTIAL TO BECOME STANDARD OF CARE DRUG IN MANY CANCERS

- ✓ Lean operation
- ✓ Experienced team

- ✓ A number of key inflection points anticipated within next 12 months

- ✓ Multiple shots on goal

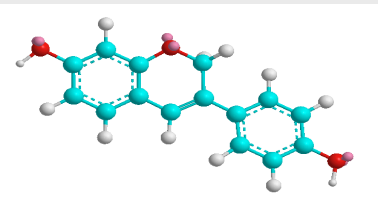


A Noxopharm subsidiary  
US-based (New York)

Non-oncology drug development

- Neurodegenerative diseases
- Hypercholesterolaemia

# NOX66... why it works



**Idronoxil**

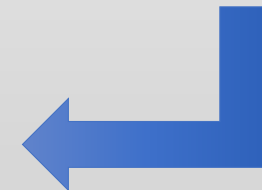


**LIPROSE**  
(Lipid Protective Shield)

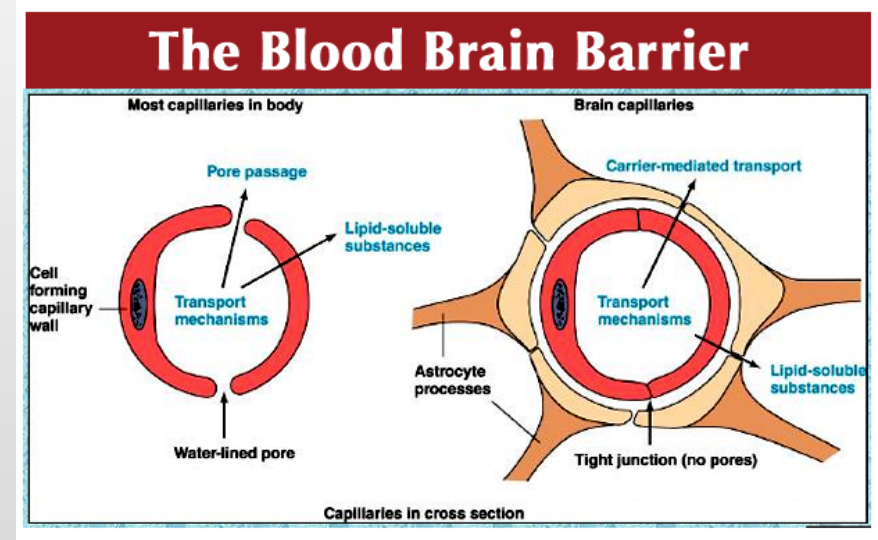


**idronoxil-c**

- Protects drug from inactivation
- Time in body extended >10x
- Crosses blood-brain barrier (pre-clinical)



# Brain, spinal cord and peripheral nerves have protective barrier



LIPROSE technology enables certain chemical classes of drugs to cross this barrier

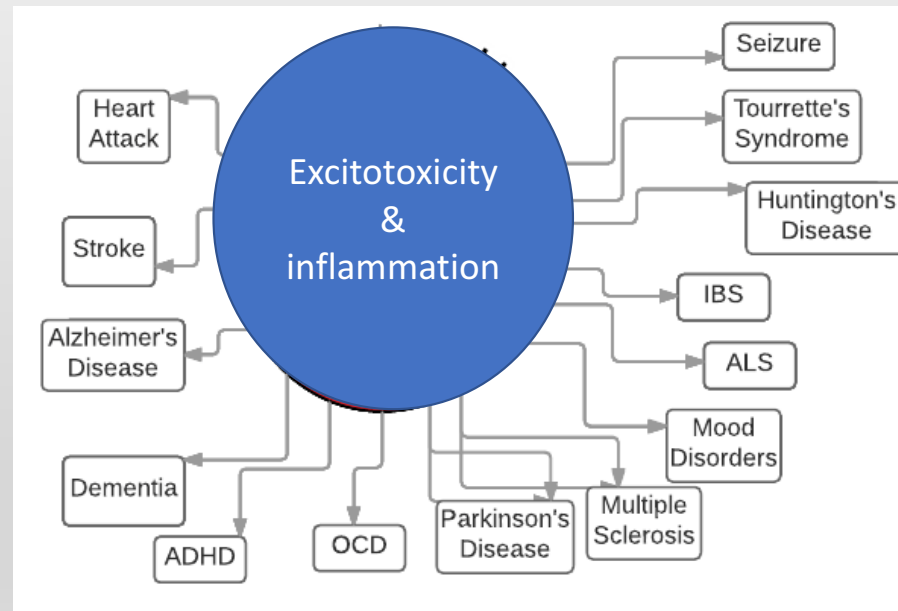
# Two underlying pathologies of neurodegeneration

## Excitotoxicity

Death of healthy brain cells from over-stimulation by neurotransmitters dumped from dying brain cells

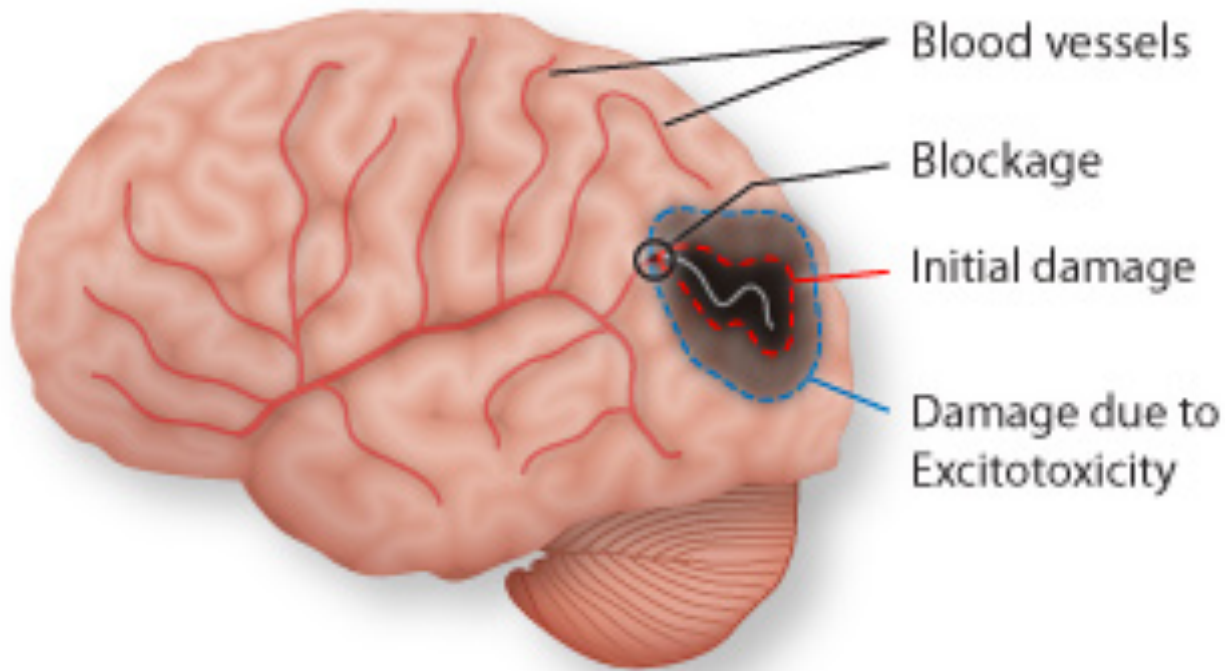
## Inflammation

Interference to normal nerve cell function by inflammation. Associated with demyelination of nerves.



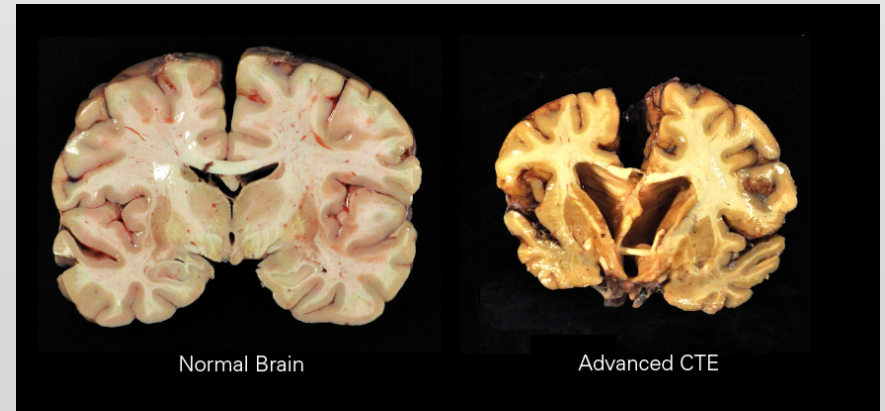
**NYX-104**

# *An inhibitor of excitotoxicity*



Stroke

## Repeated concussion



Chronic traumatic encephalopathy

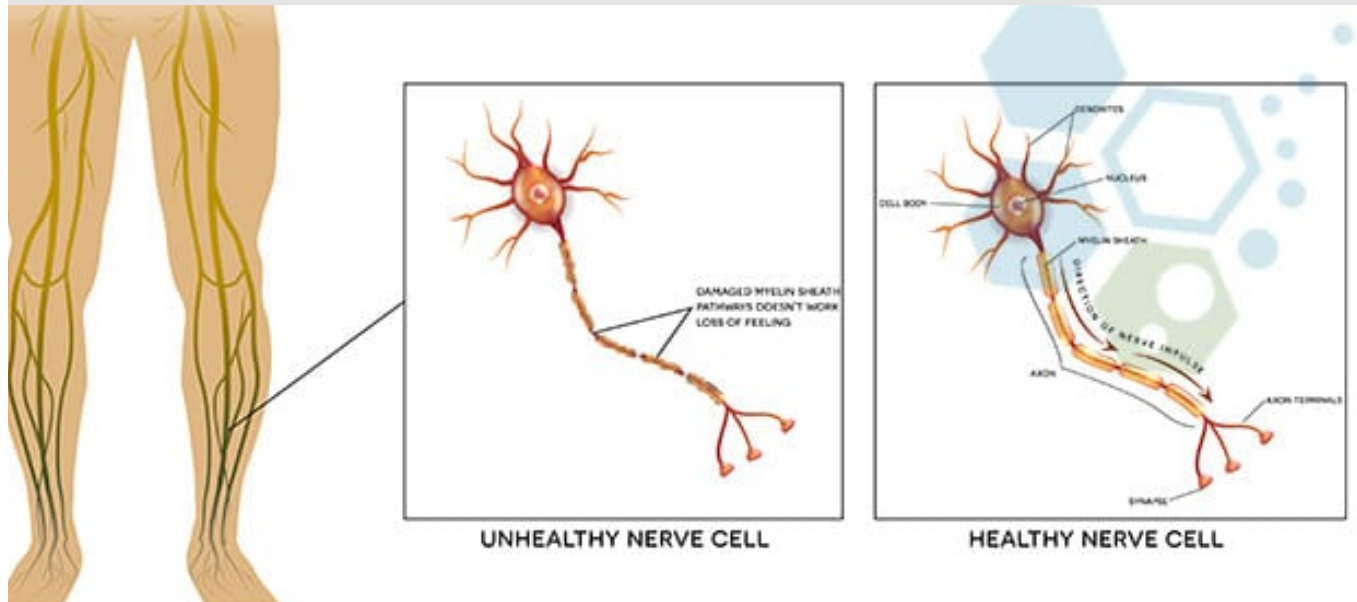
# NYX-205

# An inhibitor of neuro-inflammation

## Targeting peripheral neuropathy

Incidence in US estimated at 20 million:

- Diabetes
- Alcohol abuse
- Chemotherapy



### Typical Peripheral Neuropathy Symptoms

- ✓ Loss of Feeling
- ✓ Freezing
- ✓ Tingling
- ✓ Hyper Sensitivity
- ✓ Sharp Jabbing Pain
- ✓ Burning Sensation
- ✓ Numbness



## NYX-330

## *An inhibitor of LDL cholesterol*

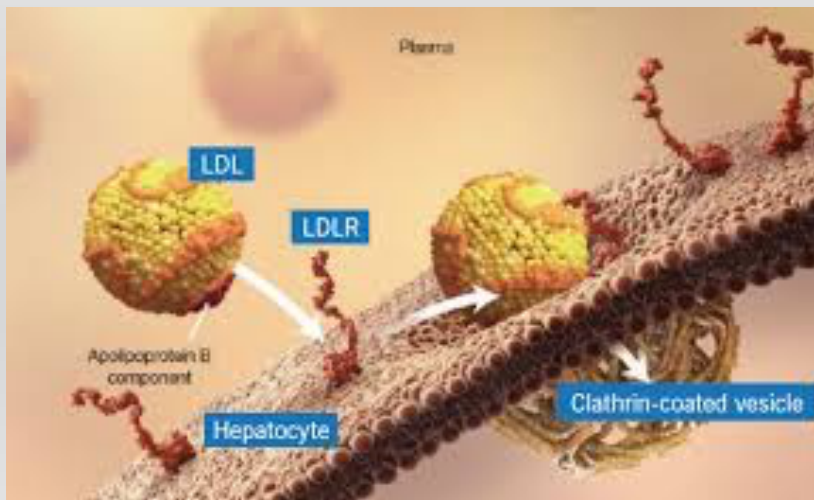
LDL cholesterol associated with increased risk of heart attack and stroke

US\$40 billion 'statin' drug market now largely generic

**PCSK9** identified as superior drug target as statin drugs achieve target LDL-C

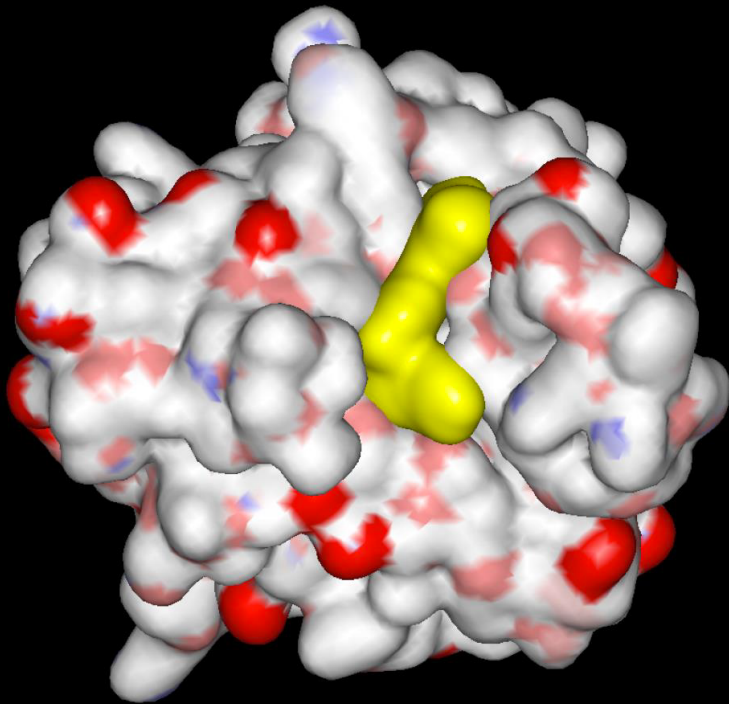
levels in only 1 in 3 people

**PCSK9** declared an unsuitable target for small molecule drug. Amgen develops monoclonal antibody. **Repatha** comes to market in 2015. \$15,000 p.a.



## NYX-330

## *An inhibitor of LDL cholesterol*



Australian chemists identify suitable binding site on PCSK9 for attachment of small molecule.

**NYX-330** effectively blocks binding of PCSK9 to LDL-cholesterol.

Appropriate drug-like behaviour in mice.

Pre-clinical program underway.

The logo for Nyrada inc features the company name in white text on a red, tilted rectangular background. The word "Nyrada" is in a large, sans-serif font, and "inc" is in a smaller font below it. The red background is tilted clockwise.

Nyrada  
inc

For NOX shareholders, Nyrada means:

Development of 2 drug assets in a non-dilutive way

Acquisition of a 3<sup>rd</sup> drug asset without dilution

Allowing NOX to focus on its considerable oncology opportunity

Value-adding to early-stage assets that otherwise would remain undeveloped

Owning 67% of something potentially very valuable

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