



5 September 2022

Sydney, Australia

Presentation to E&P Small Caps Health Care Conference

Nyrada Inc (ASX: NYR) is pleased to provide shareholders and the market generally with the attached presentation that will be given by Nyrada CEO, James Bonnar, at the E&P Small Caps Health Care Conference on 7 September 2022.

The presentation provides an overview of the Company's two lead drug development programs and an update on their progress as they advance towards Phase I first-in-human studies.

-ENDS-

About Nyrada Inc

Nyrada is a preclinical stage, drug discovery and development company, specialising in novel small molecule drugs to treat cardiovascular and neurological diseases. The Company has two main programs, each targeting market sectors of significant size and considerable unmet clinical need. These are a cholesterol-lowering drug and a drug to treat brain injury, specifically traumatic brain injury and stroke. Nyrada Inc. ARBN 625 401 818 is a company incorporated in the state of Delaware, US, and the liability of its stockholders is limited.

www.nyrada.com

Authorised by Mr. John Moore, Non-Executive Chairman, on behalf of the Board.

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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 Nyrada about circumstances and events that have not yet taken place. Although Nyrada 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 (including but not limited to the COVID-19 pandemic) that could cause the actual results, performance, or achievements to differ materially from those expressed or implied by the forward-looking statement.



Improving Lives Through Innovation

Corporate Presentation

James Bonnar - CEO
September 2022

ASX: NYR

Authorised by Mr. John Moore, Non-Executive Chairman, on behalf of the Board.

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Portfolio of Novel High Value Small Molecule Drugs

	Indication	Aim	Target Market (US)	Status
Cardiovascular NYX-PCSK9i Oral PCSK9 inhibitor	Cholesterol lowering	Best-in-class small molecule drug to disrupt and broaden the class in CV management	>18m Patients ¹	Phase I Study: H1 CY2023
Neurology NYR-BI02 TRPC 3/6/7 blocker	Brain Injury	First-in-class treatment to prevent secondary brain injury following moderate-severe TBI, concussion, or stroke	>3m Patients / year ²	Phase I Study: H1 CY2023

Commercially Focused Business Model

Focus Area

- **Novel small molecule treatments** for **serious and life-threatening diseases** where there is **unmet clinical need** and **large market share potential**

Development Objective

- Advance optimised drug candidates towards a **key value inflection point** of **confirming clinical safety and efficacy**

Growth Strategy

- **Build value** in lead drug assets by generating **clinical data** that **differentiates Nyrada's molecules as best-in-class**



Nyrada
inc

Cholesterol-Lowering Drug Program

Novel small molecule PCSK9 Inhibitor



Cholesterol-Lowering Market

Population, Problem, Opportunity



62.6 million

Americans have high cholesterol¹

56 million

between ages 40 and 75
treatment eligible

27.4 million

taking a statin¹

18.4 million

Unable to achieve
LDL-C target despite taking a statin¹

1 in 5 patients
statin intolerant³

Global Cholesterol Drugs Market

- USD 18.8 billion in 2021 (USD 14.7 billion statin drugs)⁴
- Est. sales revenue USD 30 billion by 2027 (**CAGR 8%**)⁵

Drivers of Market Growth

- Increasing rate of high cholesterol in patients
- Awareness of the benefits of cholesterol-lowering drugs
- New treatment options entering the market

Current PCSK9 Injectable Drugs

Expensive and Inconvenient



Effective when combined with statin treatment



Expensive US\$5,800 to US\$6,500 per year



Inconvenient for patient / poor compliance



Expensive to manufacture



Insurer / patient co-pay reluctance (US)

Competitive advantages
of a small molecule PCSK9 inhibitor



- **Patient convenience:** once per day oral treatment
- **Lower manufacturing cost**
- Dose form **can be combined with a statin** (single pill)

Development of Drug Candidate NYX-PCSK9i

Discovery to Clinical Lead

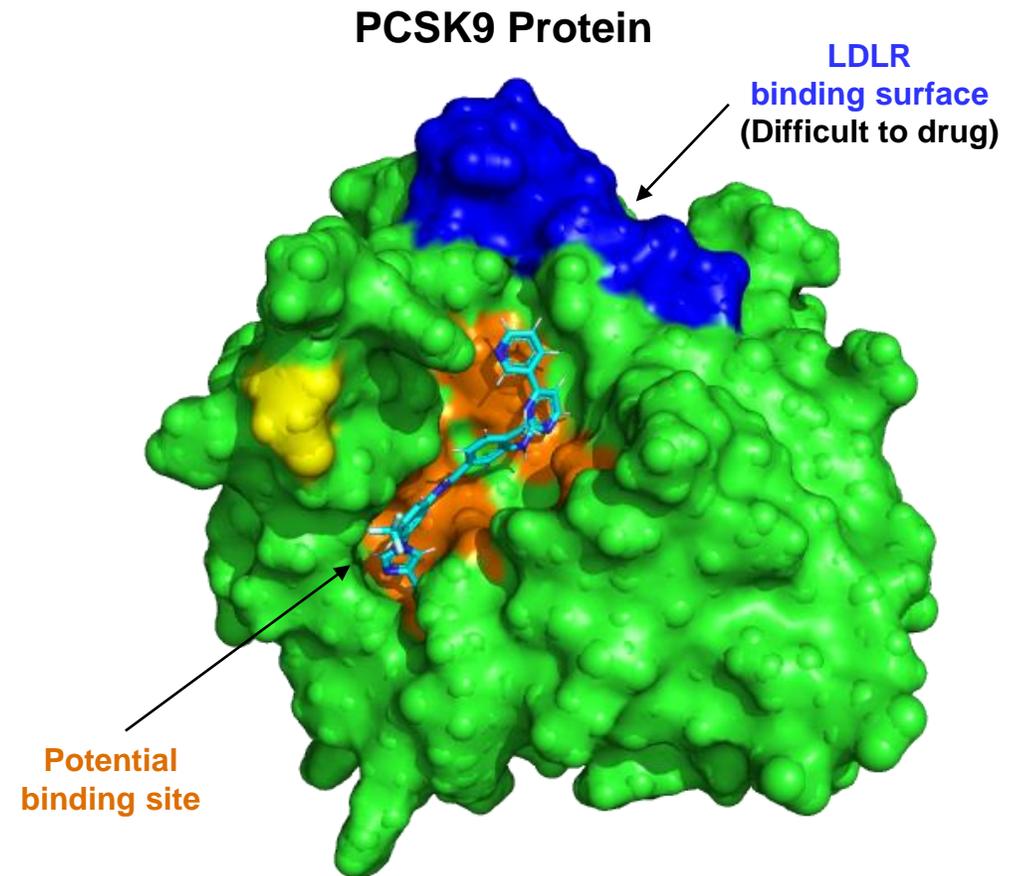


Target Product Profile

- Small molecule suitable for once per day oral dosing
- Sufficiently potent in lowering LDL-C
- Safety / toxicology profile consistent with chronic dosing
- PCSK9 validated CVD target

Development Overview

- Novel accessible binding site was identified
- Screening of 1,100 FDA-approved drugs and nilotinib (TASIGNA®) emerged as a hit
- Over 400 analogs modeled, synthesised and tested for PCSK9 binding affinity
- NYX-PCSK9i emerged as lead candidate with nanomolar PCSK9 binding affinity, good oral bioavailability and drug-like properties



Evison *et al.* Bioorg. Med. Chem. (2020) **28**: 115344

Benchmarking Efficacy

NYX-PCSK9i +/- Lipitor® in Transgenic Mouse Hyperlipidemia Model



Study Objective:

Determine if additive reduction in total cholesterol can be achieved with combination statin therapy

- APOE*3Leiden.CETP mouse hyperlipidemia model
- Mouse treated for 35 days (50 mg/kg BID NYX-PCSK9i)



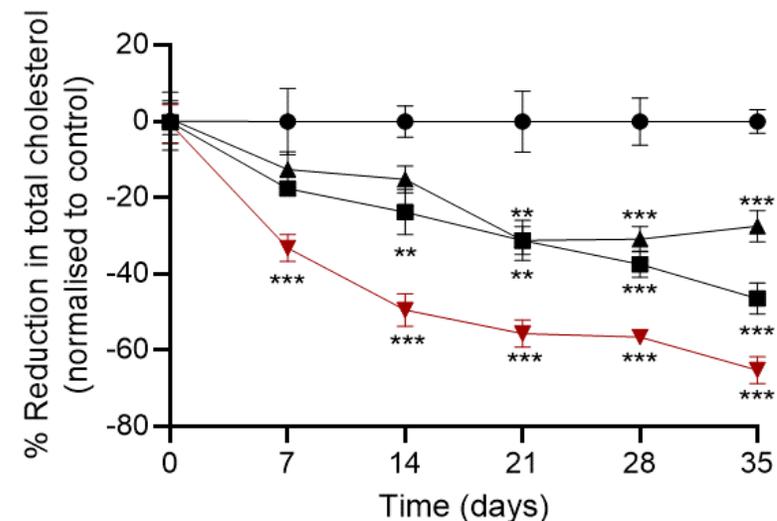
Results:

- NYX-PCSK9i + Lipitor® achieves 65% total cholesterol reduction
- No effect on body weight, food intake, liver enzymes

% Difference in plasma cholesterol versus vehicle control (p-value)

Time (days)	7	14	35
NYX-PCSK9i	-18% (0.066)	-24% (0.002)	-46% (< 0.001)
Lipitor®	-13% (0.275)	-15% (0.077)	-27% (< 0.001)
NYX-PCSK9i + Lipitor®	-33% (< 0.001)	-49% (< 0.001)	-65% (< 0.001)

bold = statistically significant



- Vehicle control
- ▲ Lipitor
- 50 mg/kg NYX-PCSK9i
- ▼ 50 mg/kg NYX-PCSK9i and Lipitor

Efficacy in Model of Atherosclerosis

NYX-PCSK9i in Human Tissue-Engineered Blood Vessel Model⁶



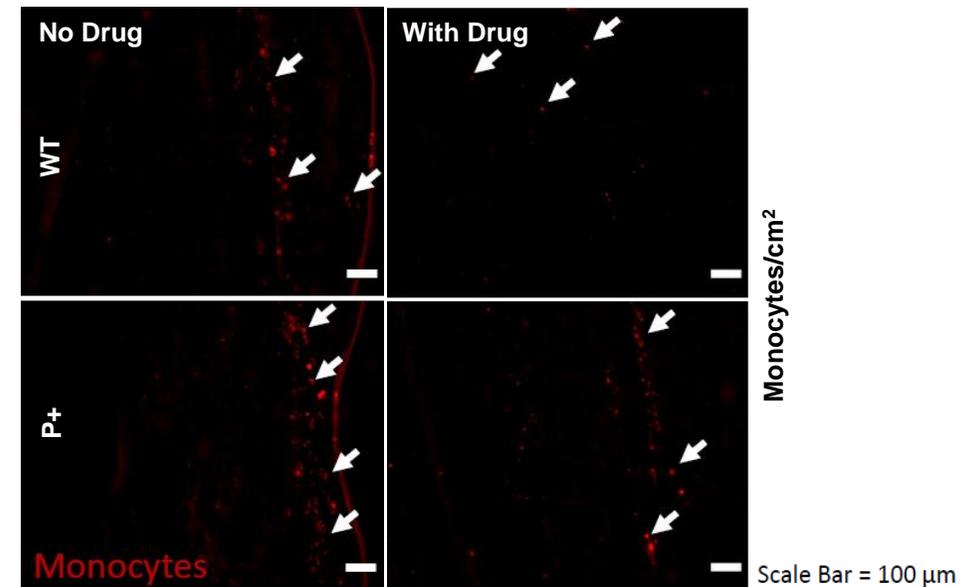
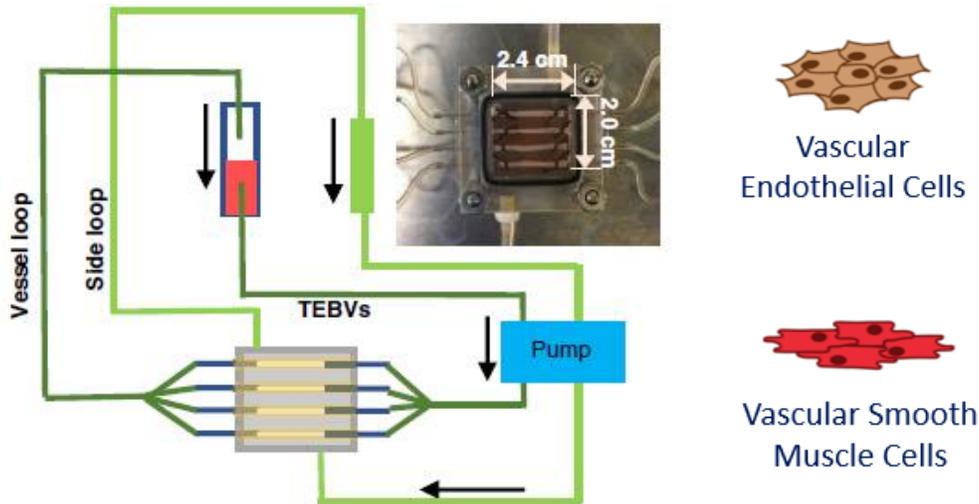
Study Design

- Researchers at Duke University (US) used human stem cells to create tissue-engineered blood vessels (TEBVs), replicating early features of atherosclerosis
- Evaluated the effect of PCSK9 inhibitor drug on inflammation and atherosclerotic plaque formation, a major cause of cardiovascular disease

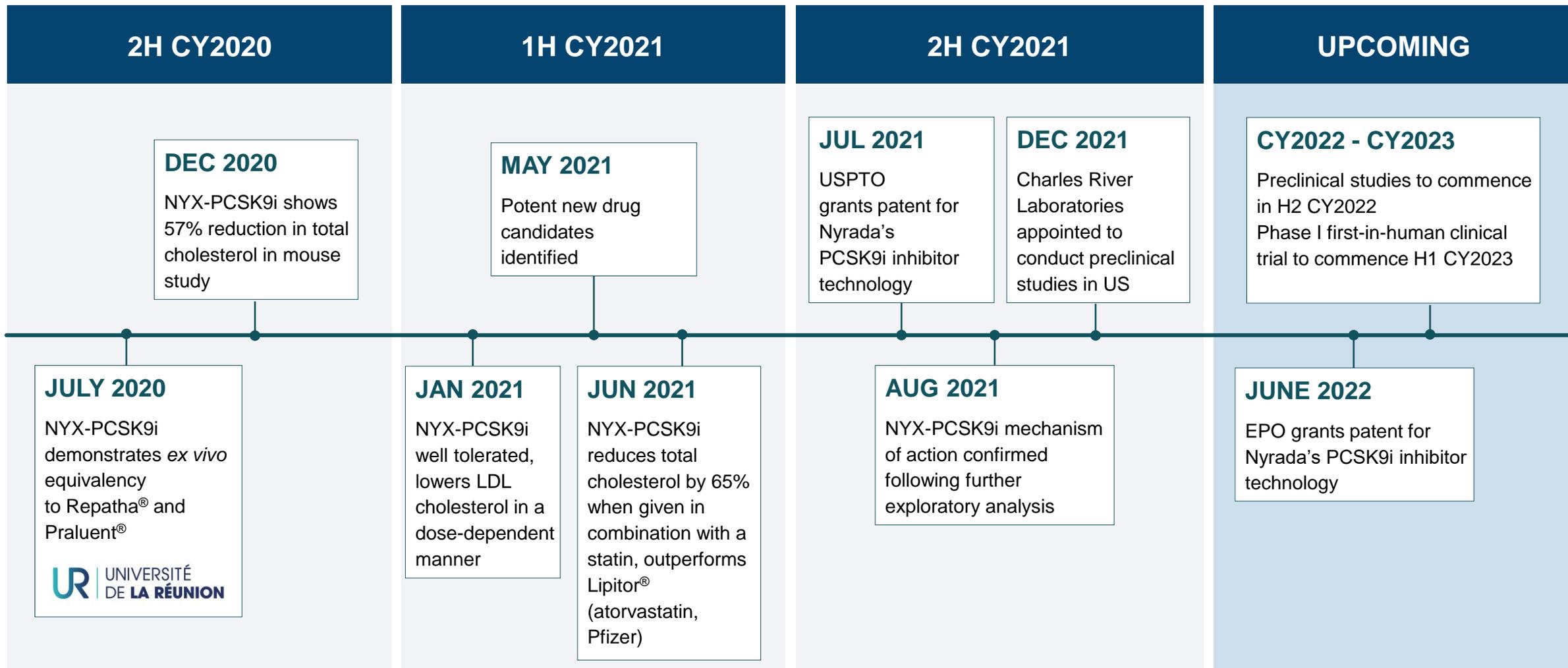


Results:

- Optimised analog of NYX-PCSK9i reduced cell adhesion (blocking atherosclerotic plaque formation)
- Nyrada's drug candidate reduced inflammatory response (cytokine levels) – a key driver of atherosclerosis
- Optimised analog of NYX-PCSK9i selected for Phase I



Program Milestones and Path to the Clinic





Brain Injury Drug Program

Novel small molecule TRPC 3/6/7 blocker



Brain Injury Market

Population, Problem, Opportunity



Each year

~5.5 million

People suffer a severe TBI⁷

55 million

People are living with the effects of medically treated TBI⁷

Each year

+12.2 million

suffer a stroke⁸

One drug class for stroke (tPA)
suitable for >15% of patients

TBI Treatment Market

- USD 6.7 billion sales revenue in 2020 (US, UK, Europe, Japan)⁹
- Sales revenue **CAGR 5%** to 2030⁹

Stroke Drug Market (tPA)

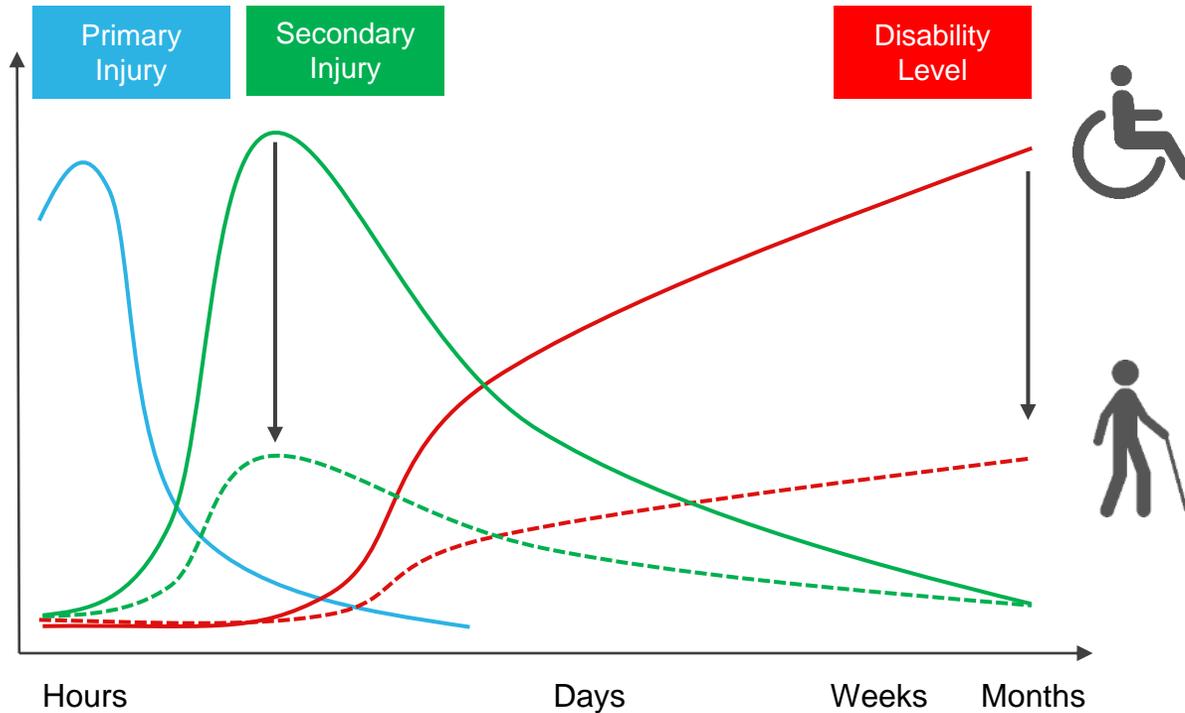
- USD 3.4 billion global revenue in 2018¹⁰
- Sales revenue **CAGR 7%** to 2027¹⁰

Problem and Opportunity

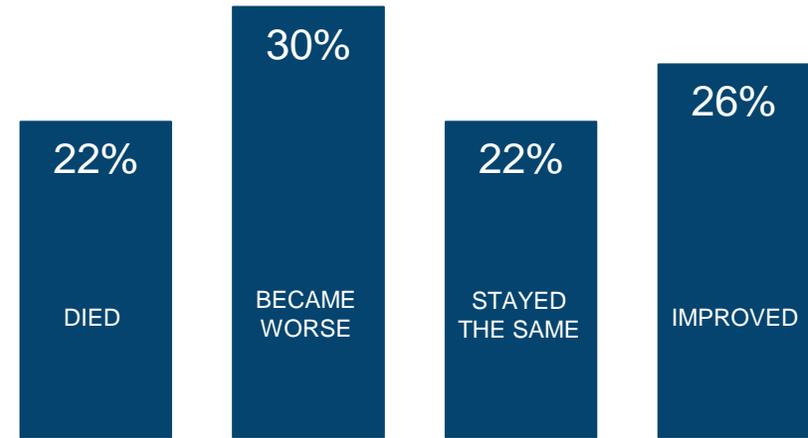
- **Unmet clinical need** with no approved drugs for TBI and limited treatment options for stroke
- **Effective treatment will improve patient outcomes and reduce high costs** associated with long-term care of brain injury survivors
- Moderate to severe TBI is an **orphan indication**

Nyrada is developing a first-in-class **neuroprotectant drug to prevent secondary injury**

Brain Injury Trajectory, Patient Outcomes, Treatment Aims



5-Year Patient Outcomes following TBI¹¹



Data are US population estimates based on the TBIMS National Database. Data refer to people 16 years of age and older who received inpatient rehabilitation services for a primary diagnosis of TBI.

Nyrada drug NYR-BI02
An acute 3-day intravenous treatment

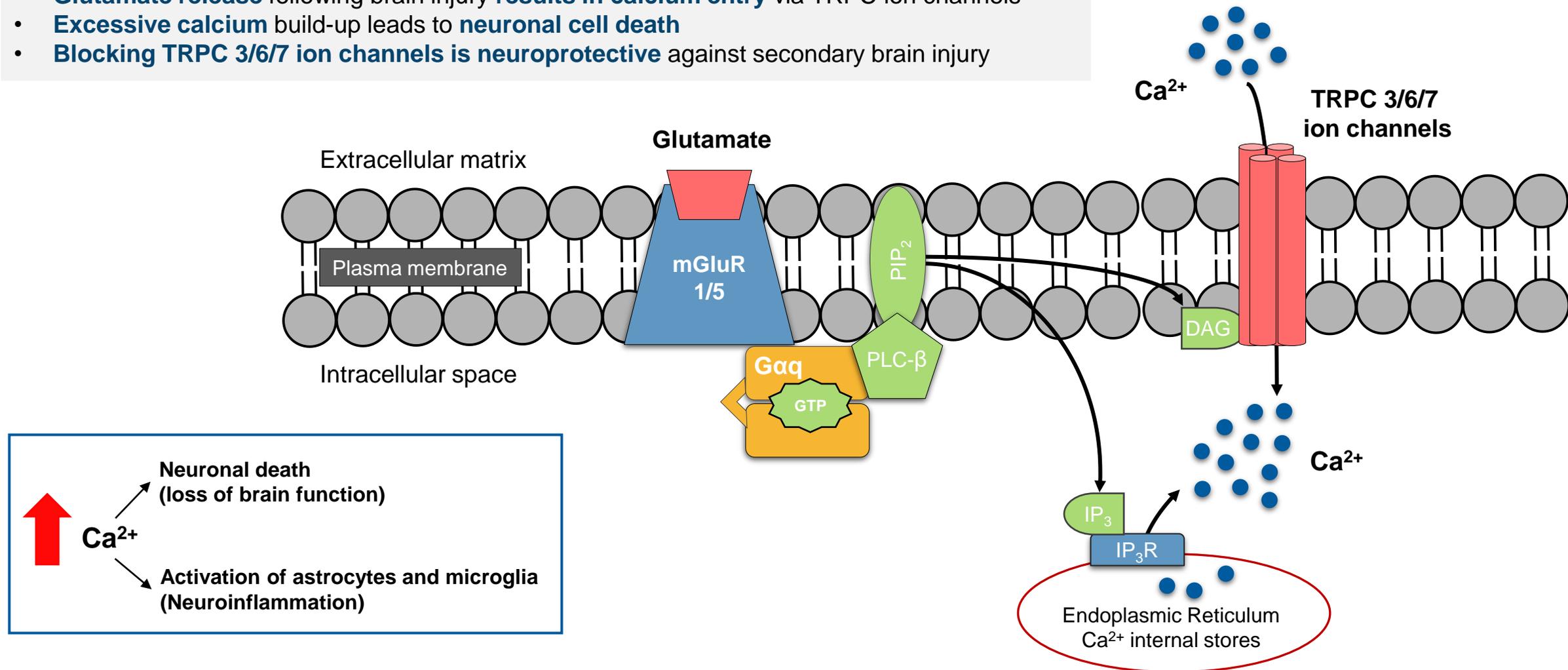


Reduce secondary injury resulting from TBI or stroke

- Improve survivability, limit disability
- Improve quality of life

TRPC 3/6/7 Ion Channels as a Therapeutic Target¹²

- **Glutamate release** following brain injury **results in calcium entry** via TRPC ion channels
- **Excessive calcium** build-up leads to **neuronal cell death**
- **Blocking TRPC 3/6/7 ion channels is neuroprotective** against secondary brain injury



Proof of Concept

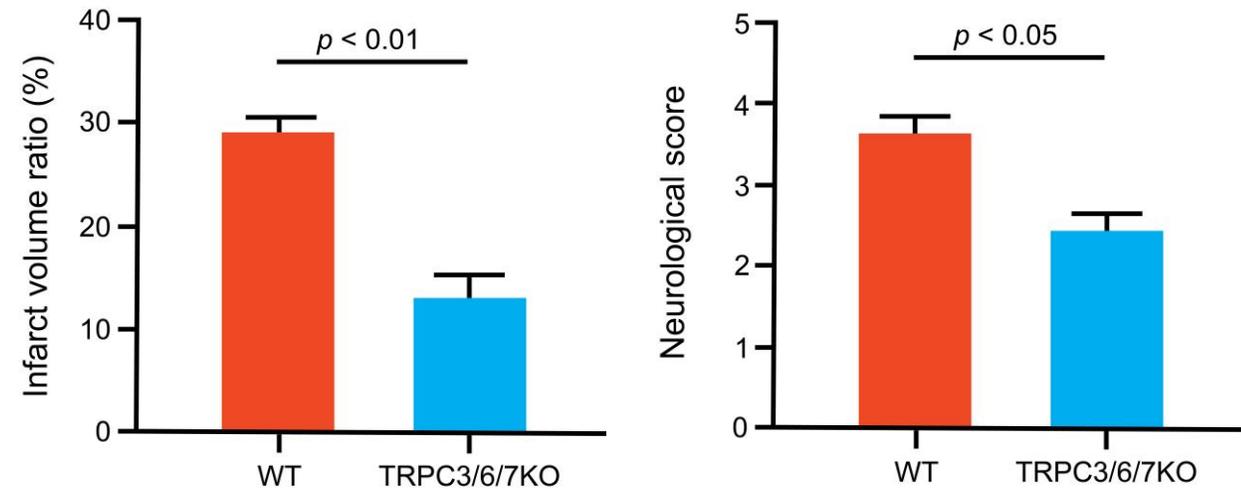
Knockout Model shows Neuroprotection



TTC Staining



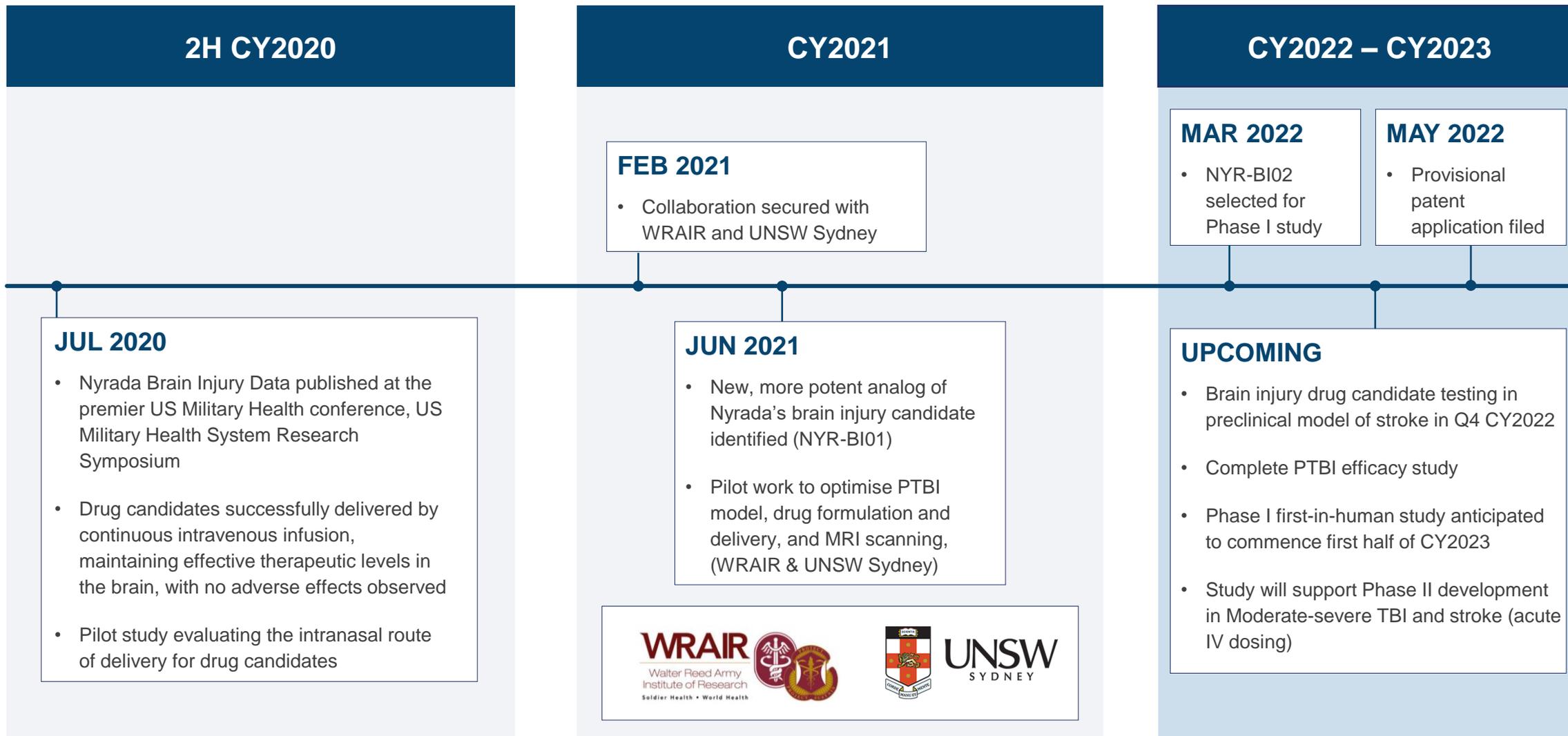
Functional Improvement following Brain Injury in TRPC 3/6/7 KO Mice¹³



Adapted from Chen et al. Mol. Neurobiol. 2017

- TRPC 3/6/7 KO mice have significantly **smaller lesion sizes** compared to WT
- TRPC 3/6/7 KO mice have significantly **better neurological score** compared to WT
- Nyrada molecule **NYR-BI02 blocks TRPC3/6/7 channels** ($IC_{50} = 0.6 \mu M$)
- **NYR-BI02 will be tested in models of TBI (WRAIR) and stroke CY2023**

Program Milestones and Path to the Clinic



Phase I Study Design

OBJECTIVES To assess the safety, tolerability, and pharmacokinetics of NYR-BI02

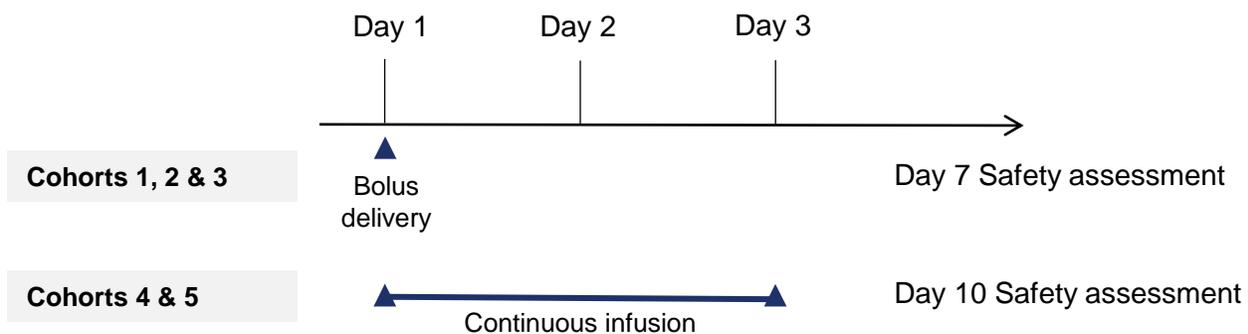
- DESIGN**
- Randomised, double-blind placebo – controlled, dose escalation design
 - 5 cohorts; 8 participants each cohort; 6:2 active and placebo treatments
 - 3 cohorts will be single ascending doses
 - 2 cohorts will be given continuous infusion doses

- PARTICIPANTS**
- Male and female healthy volunteers
 - 18 – 50 years age



Cohort number	Dose administered
1	Low dose single bolus
2	Medium dose single bolus
3	High dose
4	Low dose continuous infusion (72 hrs)
5	High dose continuous infusion (72 hrs)

- LOCATION & DURATION**
- Study will be conducted at a clinical trial centre in Australia
 - The study duration will vary between 1 – 4 days



*trial design subject to ethics approval



Corporate Snapshot

ASX:NYR

Key Metrics

Market capitalisation
(as at 2 September 2022) **A\$24.2M**

Share price
(as at 02 September 2022) **A\$0.155**

CDIs free float **156,008,700**

Cash at bank 30 June 2022:
• Adequate funding for Phase I studies **A\$10.8M**

ASX listing **January 16, 2020**

Management Team with Proven Industry Experience



James Bonnar - CEO

- Business executive with 25 years experience in healthcare companies in the UK, China, New Zealand, and Australia
- Experience in drug manufacture, preclinical development, clinical operations, regulatory affairs, and quality assurance
- Biotech experience spanning various therapeutic areas including cardiometabolic disease, neurodevelopment disorders, and brain injury



Cameron Jones - CFO

- Finance executive with experience as CFO and Company Secretary of ASX Listed and VC investee healthcare companies
- Supported several healthcare companies through IPOs, capital raisings and M&A transactions
- Managing Director of Bio101, financial services firm
- Chartered Accountant, Member of the Governance Institute of Australia and Registered Tax Agent



Dr Benny Evison - CSO

- More than 20 years experience in the discovery and development of small molecule inhibitors as therapies for various cancers, cardiovascular diseases and neurodegenerative diseases
- Obtained a PhD at La Trobe University (Melbourne, Australia) in biochemistry and molecular biology, and a postdoctoral fellowship in chemical biology at St Jude Children's Research Hospital, (Memphis TN)

High calibre Board with proven track record in realising the value of biotech companies:

- **John Moore**
Chairman
- **Christopher Cox**
Non-Executive Director
- **Marcus Frampton**
Non-Executive Director
- **Dr Rüdiger Weseloh**
Non-Executive Director
- **Dr Ian Dixon**
Non-Executive Director
- **Dr Gisela Mautner**
Non-Executive Director

Best-in-class small molecule PCSK9 inhibitor

- Oral, once per day dosing, patient convenience
- Manufacturing and cost advantages over biologics and peptides
- Can be administered with a statin to achieve additive therapeutic effect (monotherapy or combination)

First-in-class treatment to prevent secondary brain injury

- TBI and stroke
- Novel biological target – TRPC 3/6/7 ion channels
- Collaboration with WRAIR and UNSW - opportunity to pursue non-dilutive funding

Strong cash position

- A\$10.8M as at 30 June 2022
- Adequate funding for Phase I studies

References

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- 4 [Cholesterol Lowering Drug Market Research Report by Disease Type, Class of Drug, Distribution Channels, Region - Global Forecast to 2027 - Cumulative Impact of COVID-19, July 2022 and Global Statin Market – Industry Trends and Forecast to 2029, Data Bridge Market Research](#)
- 5 [Cholesterol Lowering Drug Market Research Report by Disease Type, Class of Drug, Distribution Channels, Region - Global Forecast to 2027 - Cumulative Impact of COVID-19, July 2022](#)
- 6 Adapted from Zhang et al. Nat Commun. 2020. 11(1): 5426 and modified from Nature cell biology, 17(8), 994-1003
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- 9 [Global Traumatic Brain Injury Market to 2030 - Insight, Epidemiology and Forecast by ResearchAndMarkets.com](#)
- 10 [Stroke Treatment Market Insight and Trends 2027 - TMR \(transparencymarketresearch.com\)](#)
- 11 'Moderate to Severe Traumatic is a Lifelong Condition', CDC publication available at: https://www.cdc.gov/traumaticbraininjury/pdf/moderate_to_severe_tbi_lifelong-a.pdf
- 12 Jeon J, Bu F, Sun G, Tian J, Ting S, Li J, Aronowski J, Birnbaumer L, Freichel M, and Zhu MX (2020). Contribution of TRPC Channels in Neuronal Excitotoxicity Associated With Neurodegenerative Disease and Ischemic Stroke. Front Cell Dev Biol. doi: [10.3389/fcell.2020.618663](https://doi.org/10.3389/fcell.2020.618663)
- 13 Chen X, Lu M, He X, Ma L, Birnbaumer L, and Liao, Y. (2017). TRPC3/6/7 knockdown protects the brain from cerebral ischemia injury via astrocyte apoptosis inhibition and effects on NF-small ka, CyrillicB translocation. Mol. Neurobiol. 54, 7555–7566. doi: [10.1007/s12035-016-0227-2](https://doi.org/10.1007/s12035-016-0227-2)



Brain Injury Solution
Animation



Cholesterol-Lowering
Animation



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