Annual General Meeting Presentation

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Chief Executive Officer

21 November 2022 | Sydney NSW

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

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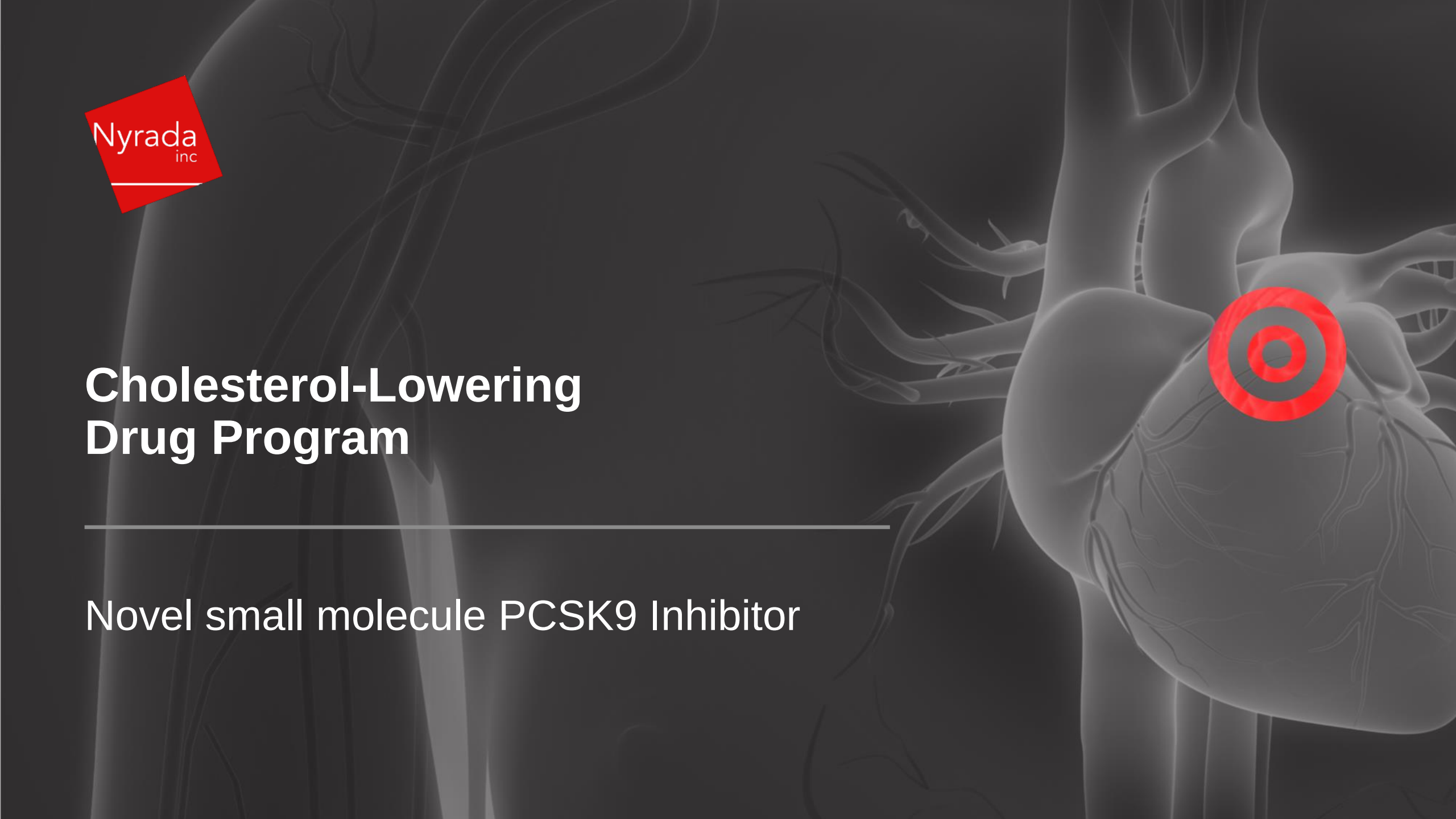
Commercially Focused Business Model

- **Novel drugs for life threatening conditions with:**
  - High unmet clinical need
  - Large market share potential
- **Transitioning to a clinical stage company:**
  - Lead Programs entering Phase I H1 CY2023
- **Strongly credentialed Board and Scientific Advisory Board:**
  - Track record of realising shareholder value
  - Deep industry and drug development expertise
- **Cash position of $9.9M (30 September 2022)**

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/IIa 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



Cholesterol-Lowering Drug Program

Novel small molecule PCSK9 Inhibitor

Cholesterol-Lowering Market

Population, Problem, Opportunity

62.6 million
Americans have high cholesterol[1]

56 million
between ages 40 and 75
treatment eligible

27.4 million
taking a statin[1]

18.4 million
Unable to achieve
LDL-C target despite taking a statin[1]

1 in 5 patients
statin intolerant[3]

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)

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

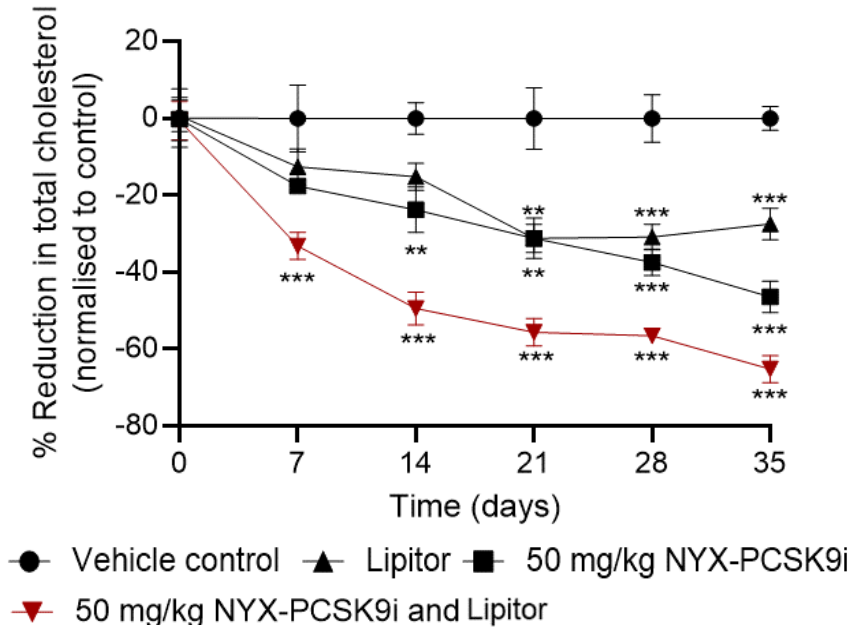
- APOE*3Leiden.CETP mouse hyperlipidemia model
- Mouse treated for 35 days (50 mg/kg BID NYX-PCSK9i)

Results:

- **NYX-PCSK9i + Lipitor® achieves 65% total cholesterol reduction**
- **No effect on body weight, food intake, liver enzymes**
- **Study published in *Journal of Lipid Research (Oct 2022)***

	% 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



Efficacy in Model of Atherosclerosis

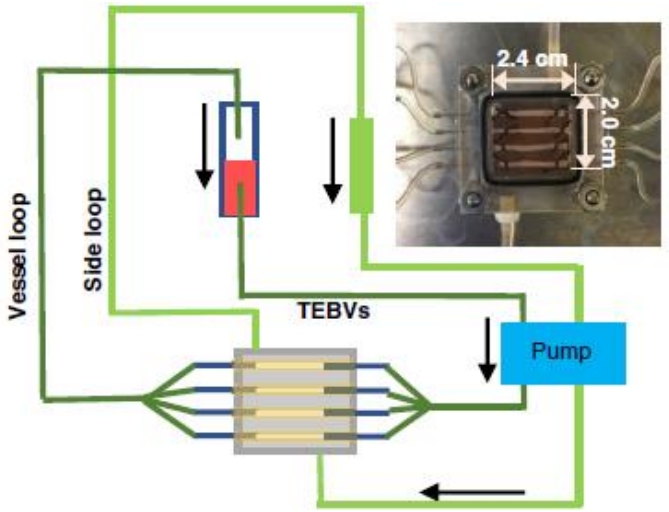
NYX-PCSK9i in Human Tissue-Engineered Blood Vessel Model[6]

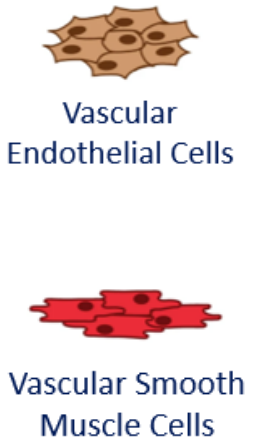
Study Design

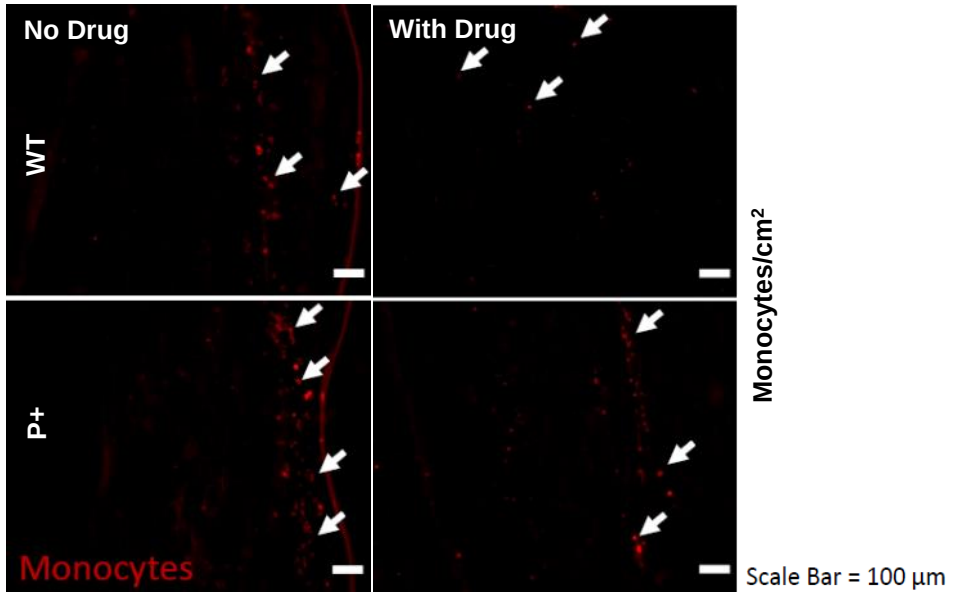
- Researchers at Duke University (US) used human stem cells to create tissue-engineered blood vessels (TEBVs), replicating early features of atherosclerosis
- Evaluated the effect of PCSK9 inhibitor drug on inflammation and atherosclerotic plaque formation, a major cause of cardiovascular disease

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**







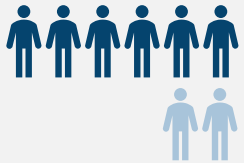
Phase I/IIa Study Design

OBJECTIVES

- Evaluate safety, tolerability, and pharmacokinetics of optimised NYX-PCSK9i in healthy volunteers and high cholesterol patients
- Exploratory evaluation of cholesterol metabolism in high cholesterol patients

PARTICIPANTS

- 8 cohorts (6 active: 2 placebo per cohort)
- **Cohorts 1-6**: 48 healthy volunteers
- **Cohorts 7,8**: 16 high cholesterol patients, 8 taking statins



Active arm

Placebo

DESIGN

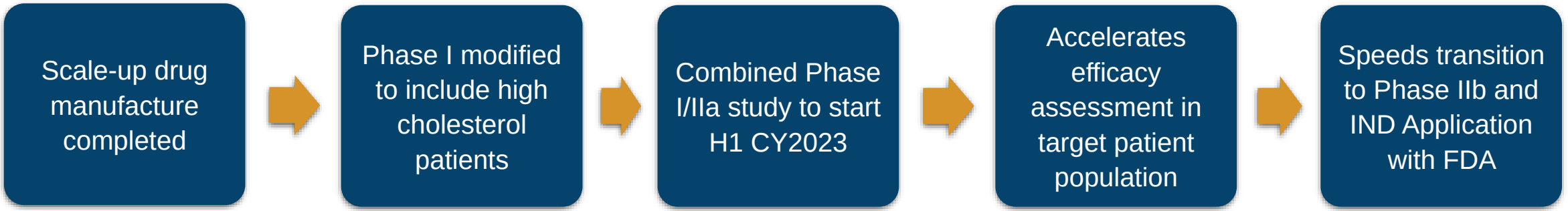
- Double-blind, randomised, placebo-controlled, dose escalation study
- **Healthy volunteers**:
  Single ascending oral dose (Cohorts 1-6)
- **High cholesterol patients**:
  Once daily oral dose over 14-day treatment period
  (Cohort 7 no statins, Cohort 8 statin co-treatment)
- Pharmacokinetic and pathology samples will be collected at selected time points over the trial period for all subjects.

LOCATION & DURATION

- Study will be conducted at a clinical trial centre in Australia in H1 CY2023
- The dosing period will be 1 day in healthy volunteers and 14 days in high cholesterol patients

*trial design subject to ethics approval

Acceleration of Clinical Program



- ☑ Smart and efficient use of capital
- ☑ Quick transition from Phase I/IIa to Phase IIb study, time saving of up to 12 months

Program Milestones

2H CY2020

DEC 2020

NYX-PCSK9i shows 57% reduction in total cholesterol in mouse study

JULY 2020

NYX-PCSK9i demonstrates *ex vivo* equivalency to Repatha® and Praluent®

UNIVERSITÉ DE LA RÉUNION

1H CY2021

MAY 2021

Potent new drug candidates identified

JAN 2021

NYX-PCSK9i well tolerated, lowers LDL cholesterol in a dose-dependent manner

JUN 2021

NYX-PCSK9i reduces total cholesterol by 65% when given in combination with a statin, outperforms Lipitor® (atorvastatin, Pfizer)

2H CY2021

JUL 2021

USPTO grants patent for Nyrada's PCSK9i inhibitor technology

DEC 2021

US CRO appointed to conduct preclinical studies in US

AUG 2021

NYX-PCSK9i mechanism of action confirmed following further exploratory analysis

2022 and Beyond

CY2022 - CY2023

Preclinical studies to commence in H2 CY2022
Phase I first-in-human clinical trial to commence H1 CY2023

JUNE 2022

EPO grants patent for Nyrada's PCSK9i inhibitor technology

OCT 2022

Efficacy study published in Journal of Lipid Research

JULY 2022

Nyrada's PCSK9 inhibitor blocks early stages of atherosclerosis in novel model at Duke University

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 TBI[7]

55 million

People are living with the effects of medically treated TBI[7]

Each year

+12.2 million

suffer a stroke[8]

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 2030[9]

Stroke Drug Market (tPA)

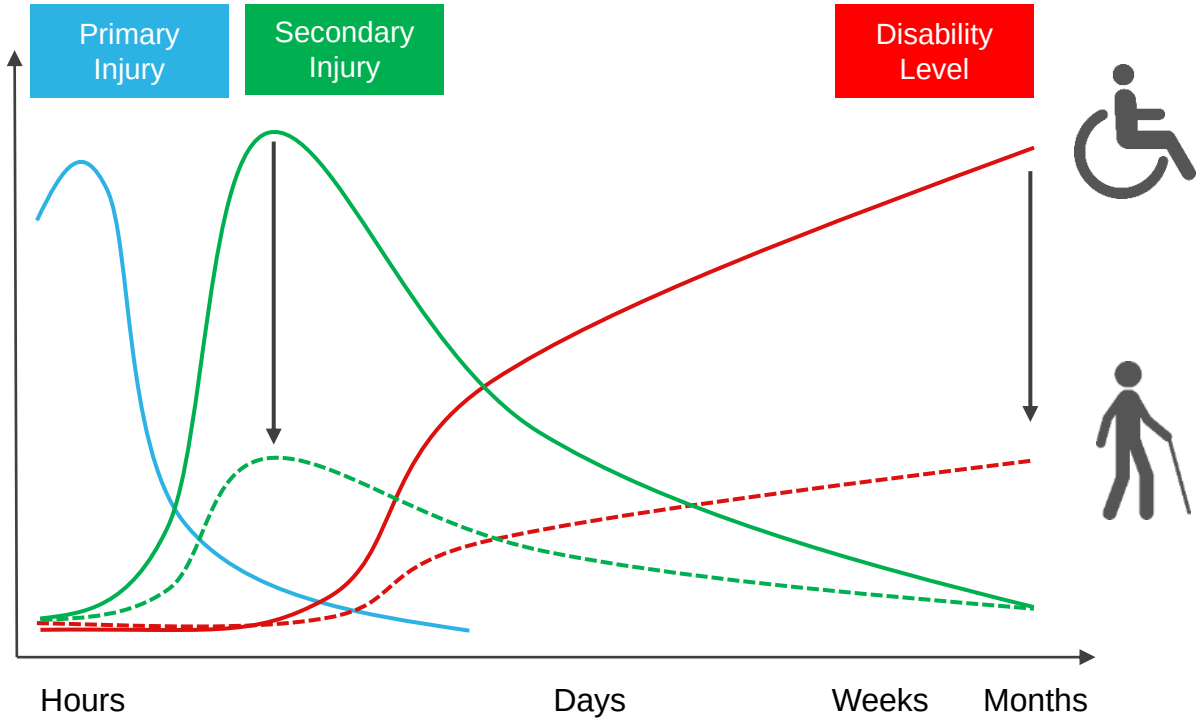
- USD 3.4 billion global revenue in 2018[10]
- Sales revenue **CAGR 7%** to 2027[10]

Problem and Opportunity

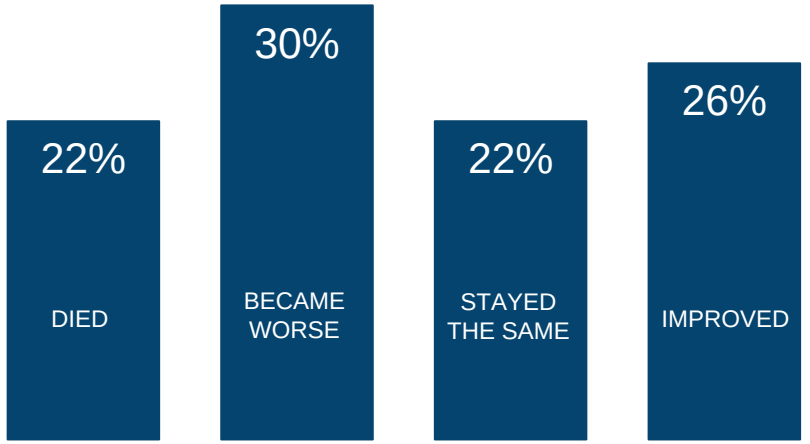
- **Unmet clinical need** with no approved drugs for TBI and limited treatment options for stroke
- **Effective treatment** will **improve patient outcomes** and **reduce high costs** associated with long-term care of brain injury survivors
- Moderate to severe TBI is an **orphan indication**

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 TBI[11]



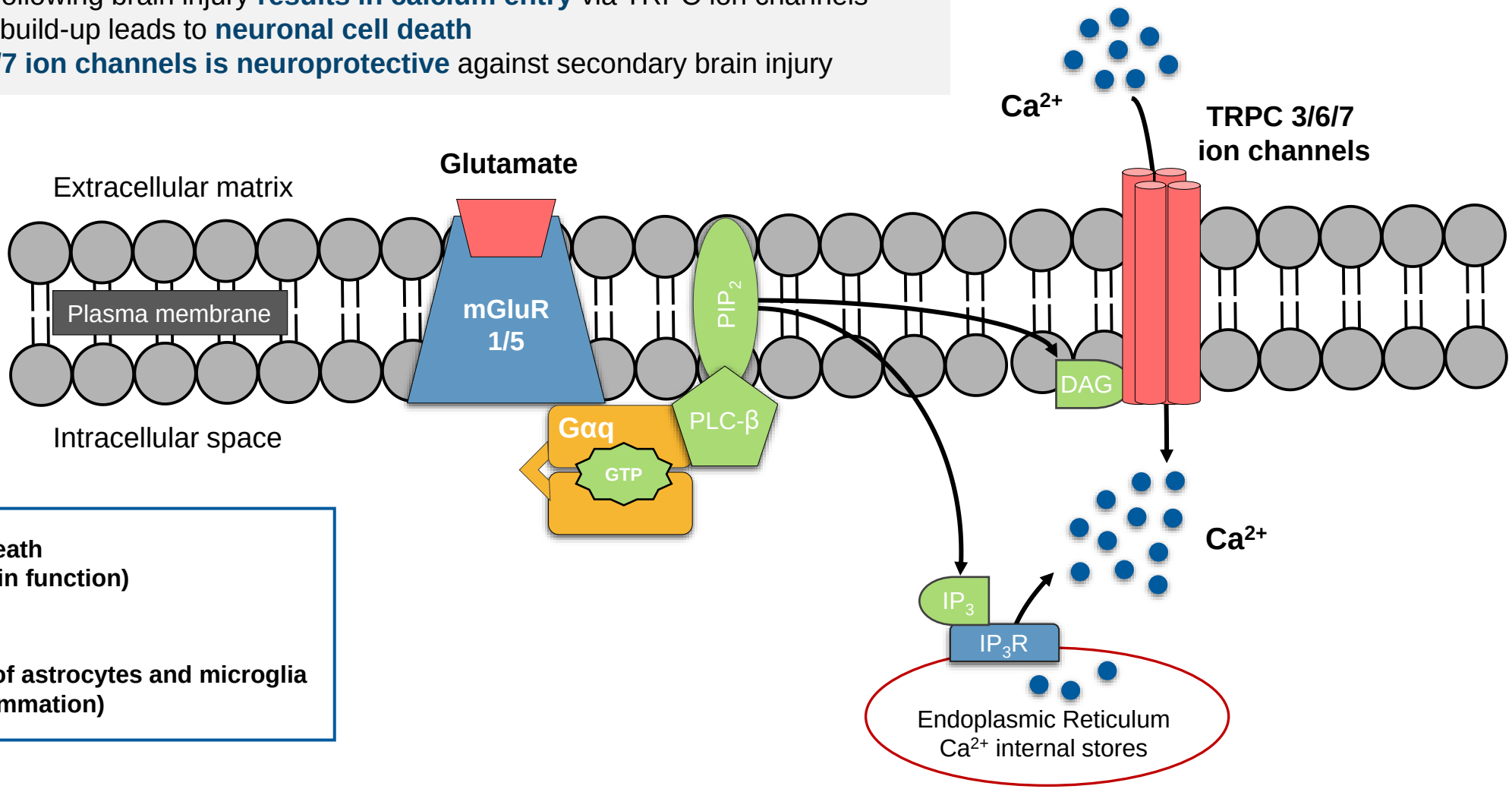
Data are US population estimates based on the TBIMS National Database. Data refer to people 16 years of age and older who received inpatient rehabilitation services for a primary diagnosis of TBI.

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 Target[12]

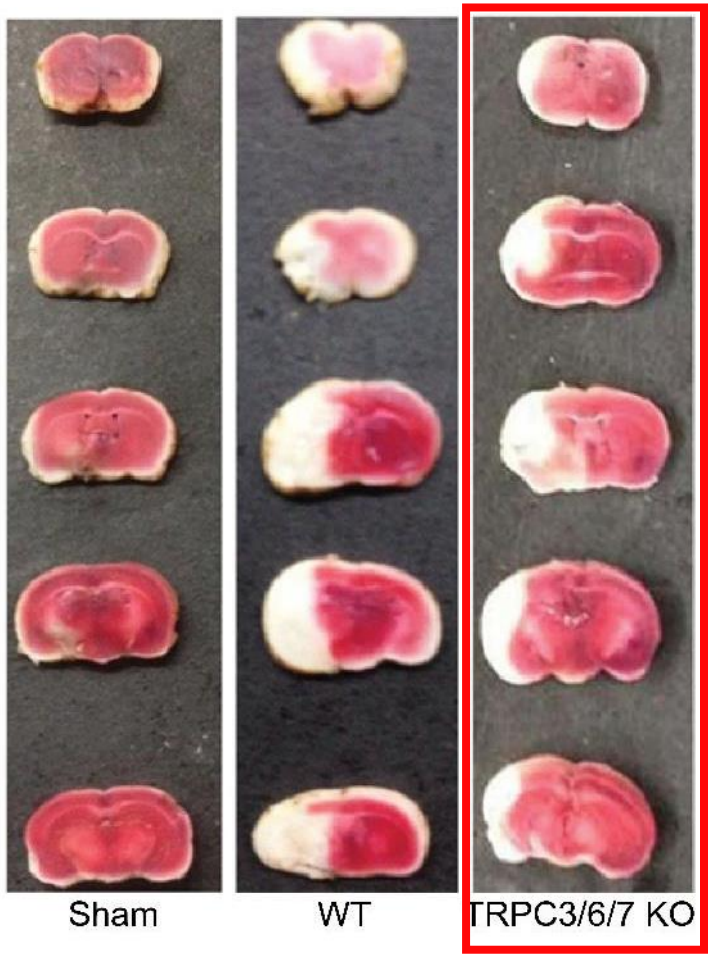
- **Glutamate release** following brain injury **results in calcium entry** via TRPC ion channels
- **Excessive calcium** build-up leads to **neuronal cell death**
- **Blocking TRPC 3/6/7 ion channels is neuroprotective** against secondary brain injury



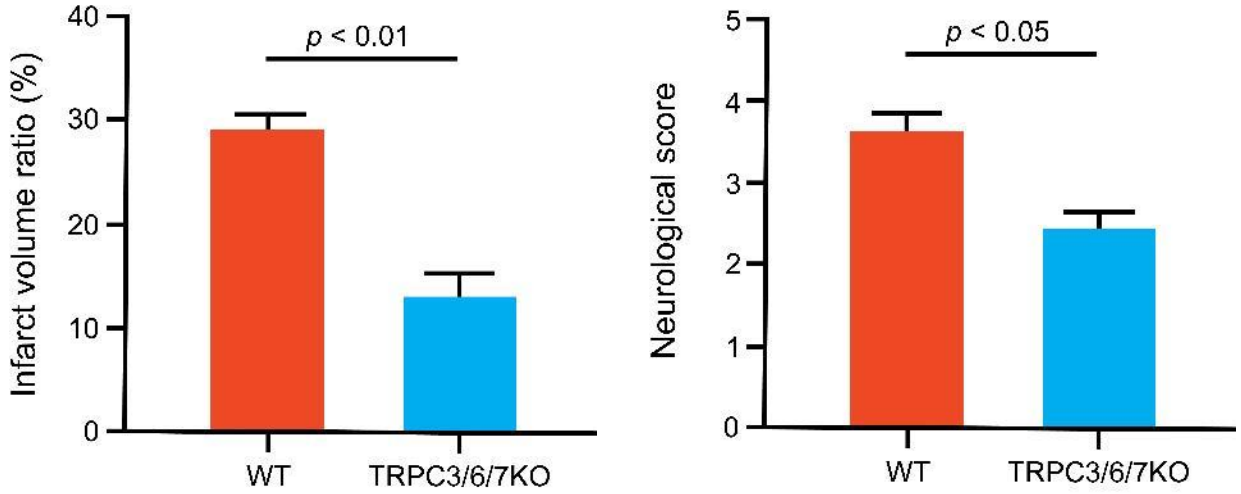
Proof of Concept

Knockout Model shows Neuroprotection

TTC Staining



Functional Improvement following Brain Injury in TRPC 3/6/7 KO Mice[13]



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 µM)
- **NYR-BI02 will be tested in models of TBI (WRAIR) and stroke CY2023**

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

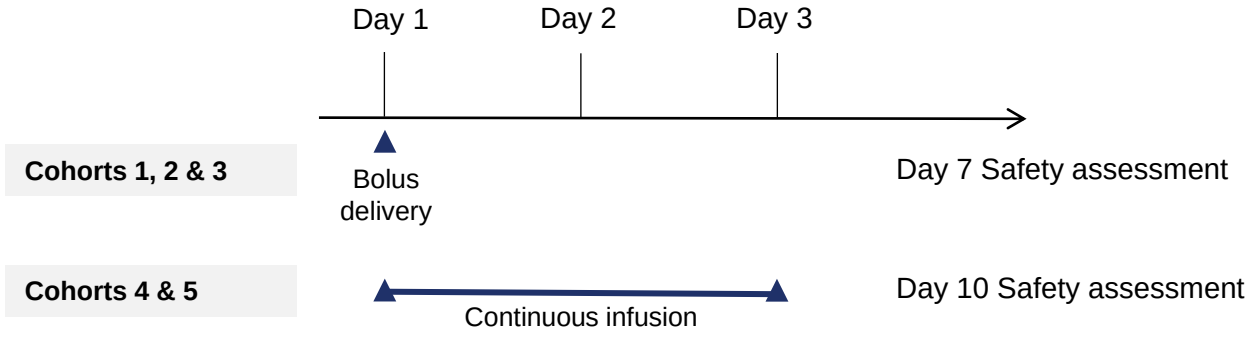
PARTICIPANTS

- 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 H1 CY2023
- The study duration will vary between 1 – 4 days



*trial design subject to ethics approval

Program Milestones

2H CY2020

JUL 2020

- Nyrada Brain Injury Data published at the premier US Military Health conference, US Military Health System Research Symposium
- Drug candidates successfully delivered by continuous intravenous infusion, maintaining effective therapeutic levels in the brain, with no adverse effects observed
- Pilot study evaluating the intranasal route of delivery for drug candidates

CY2021

FEB 2021

- Collaboration secured with WRAIR and UNSW Sydney

JUN 2021

- New, more potent analog of Nyrada's brain injury candidate identified (NYR-BI01)
- Pilot work to optimise PTBI model, drug formulation and delivery, and MRI scanning, (WRAIR & UNSW Sydney)

WRAIR Walter Reed Army Institute of Research Soldier Health • World Health

UNSW SYDNEY

CY2022 and Beyond

MAR 2022

- NYR-BI02 selected for Phase I study

MAY 2022

- Provisional patent application filed

UPCOMING

- Brain injury drug candidate testing in preclinical model of stroke in Q4 CY2022
- Complete PTBI efficacy study
- Phase I first-in-human study anticipated to commence first half of CY2023
- Study will support Phase II development in Moderate-severe TBI and stroke (acute IV dosing)

Targeting Non-Dilutive Funding

Walter Reed Army Institute of Research (WRAIR)

- Pursuing opportunities for post Phase I funding
- Potential support for clinical development available through *Transforming Research and Clinical Knowledge in Traumatic Brain Injury* (TRACK-TBI):
  - Access to >20 clinical trial sites at Level 1 Trauma Centres at US Hospitals
  - Close ties with US Department of Defense (DoD)
  - Pivotal in providing non-dilutive funding to support TBI drug development
- TBI continues to be primary focus of WRAIR and US DoD

WRAIR Walter Reed Army Institute of Research
Defense Health • Global Health

TRACK-TBI
Transforming Research and Clinical Knowledge in Traumatic Brain Injury
International Traumatic Brain Injury Research Initiative

Corporate Snapshot

ASX:NYR

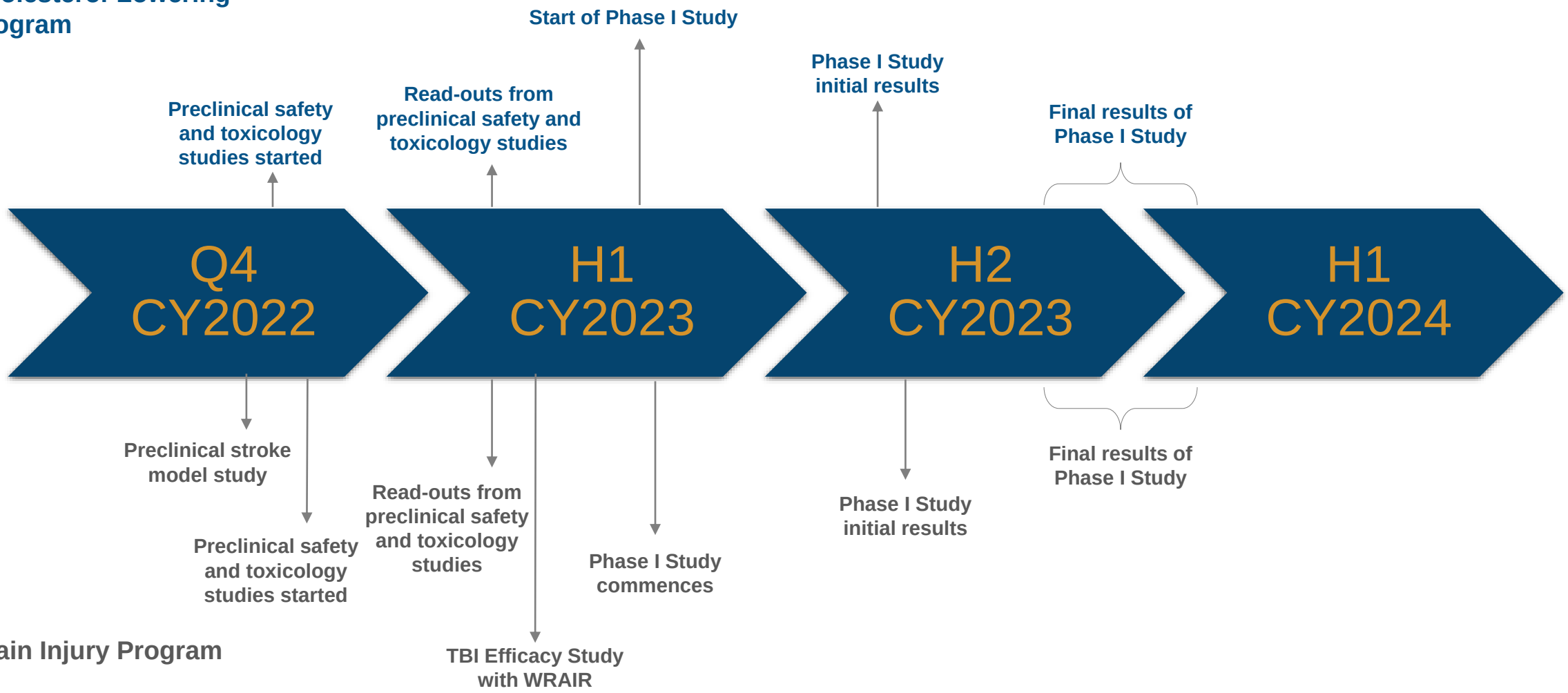
Corporate Overview

Key Metrics

Market capitalisation (as at 18 November 2022)	**A$18.7M**
Share price (as at 18 November 2022)	**A$0.12**
CDIs free float	**156,008,700**
Cash at bank 30 September 2022: • Funded to pursue Phase clinical development in CY2023	**A$9.9M**
ASX listing	**January 16, 2020**

Upcoming Newsflow*

Cholesterol-Lowering Program



Brain Injury Program

*Estimated timings and subject to change

FY2022 Financial Performance

Highlights

- Nyrada ended FY2022 with cash of $10.8M
- Cash position as at the end of Q1 FY2023 was $9.9M
- R&D Tax Incentive refund of ~$1.2M received in November 2022, further boosting capital resources
- Well funded to pursue Phase I clinical development in CY2023

Operating Results Summary

	FY2022 (A$)	FY2021 (A$)
R&D Costs	1,835,072	2,175,050
Corporate and admin expenses	699,653	895,839
Share-based payment expense	966,951	1,111,622
Professional services expense	338,841	509,842
Employment benefits expense	1,000,030	929,931

References

1 Wong ND et al. Prevalence of the American College of Cardiology/American Heart Association statin eligibility groups, statin use, and low-density lipoprotein cholesterol control in US. J Clin Lipidology. 2016

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3 Management of Statin Intolerance in 2018: Still More Questions Than Answers, Toth PP, Patti AM, Giglio RV, Nikolic D, Castellino G, Rizzo M, Banach M. Am J Cardiovasc Drugs. 2018 Jun;18(3):157-173

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

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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

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Brain Injury Solution Animation

Cholesterol-Lowering Animation