Bell Potter Healthcare Conference 2026

Building the Future of TRPC-targeted Therapies

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ASX:NYR

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



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Investment Highlights

Advancing first-in-class TRPC inhibitor with multiple near-term value catalysts



Platform asset with data supporting multiple indications

- Lead asset Xolatryp® targeting TRPC 3/6/7 ion channels with broad applicability across cardioprotection, neuroprotection and oncology
- Preclinical efficacy demonstrated in cardiac reperfusion injury, ischemic stroke, traumatic brain injury (TBI), anthracycline-induced cardiomyopathy and anti-tumour models
- Multiple development pathways across high unmet-need indications supported by a common and clinically validated target



Positive Phase I safety and pharmacokinetic data

- Phase I trial successfully completed in 48 healthy volunteers with all doses safe and well-tolerated
- No dose-limiting toxicities or serious adverse events observed
- Linear and predictable pharmacokinetics with rapid therapeutic exposure achieved within 10 minutes
- Supports launch of Phase II trials across multiple indications



Near term Phase IIa safety and efficacy data

- PROTECT-MI Phase IIa trial underway in cardiac reperfusion injury in STEMI patients undergoing PCI
- Five clinical trial sites currently activated in Australia
- Expanding the clinical site network to support recruitment. Four additional clinical trial sites committed across ANZ, with three currently onboarding and activation pending.
- Further site expansion opportunities are being evaluated to broaden recruitment reach.
- Safety review for first 8 patients expected in H2 CY26



High unmet need opportunity in reperfusion injury with large addressable market

- ~4 million PCI procedures performed globally each year with no approved cardioprotective therapies targeting reperfusion injury[1]
- Reperfusion injury may account for up to ~50% of total heart muscle damage (infarct size) following STEMI heart attack
- Potential to reduce infarct size and lower risk of heart failure, arrythmia, hospitalisation, and mortality
- US market is an estimated US$3bn opportunity



Strong IP & Uniquely Experienced Team

- Composition of matter patent protection supporting Xolatryp® platform development
- Leadership team with extensive and international experience across translational research and clinical drug development including at Neuren Pharmaceuticals, and other global clinical programs
- Board with proven track record across biotechnology, pharmaceuticals, commercialisation and capital markets



Multiple near-term catalysts

- Ongoing PROTECT-MI Phase IIa site activation and recruitment updates through CY26
- IND submission 1H27
- PROTECT-MI Phase IIa safety review of first 8 patients expected H2 CY26
- PROTECT-MI Phase II topline data anticipated in Q3/Q4 CY27
- Advancement of oncology, ischemic stroke and TBI programs

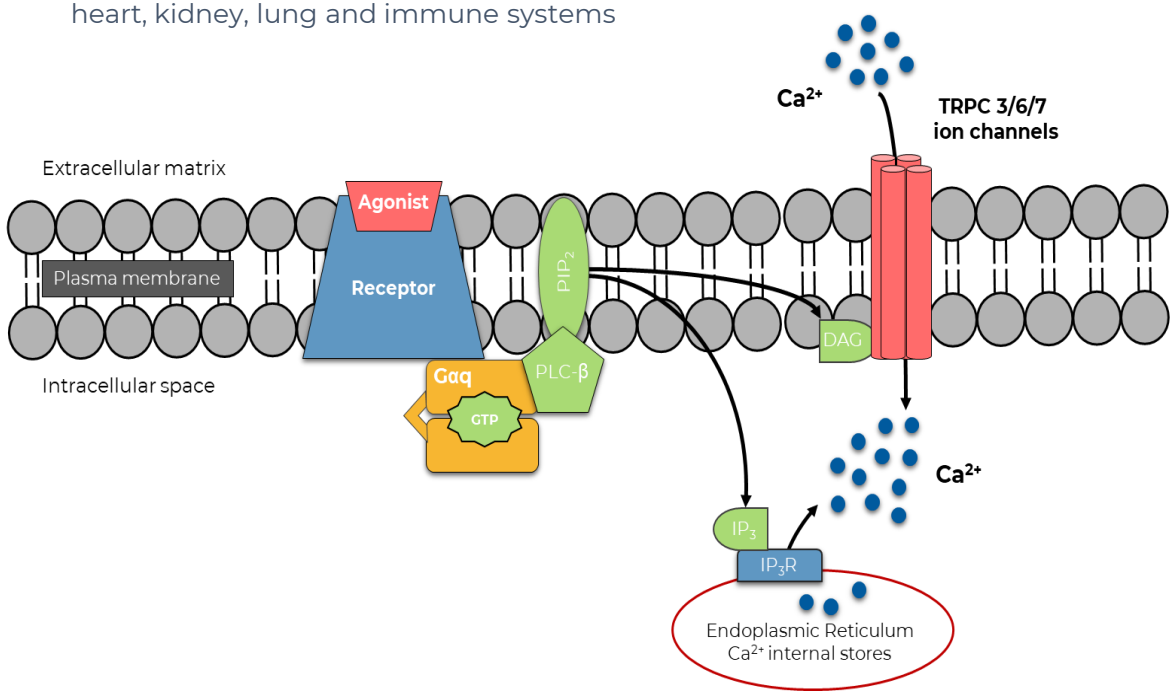
(1) Complex Percutaneous Coronary Intervention Market Outlook 2025-2034 - https://dataintelo.com/report/complex-percutaneous-coronary-intervention-market-report

Xolatryp® Mechanism of Action

Nyrada's lead candidate Xolatryp® is a clinically validated target and gatekeeper of calcium influx with broad therapeutic potential

Overview

- Xolatryp® is a third generation TRPC 3/6/7 channel inhibitor
- Highly differentiated and clinically-validated target with well understood mechanism-of-action
- TRPC ion channels act as an upstream control point for pathological Ca^{2+} influx, offering broad therapeutic potential relative to downstream pathway targets
- In normal state, TRPC maintains physiological ion channel equilibrium in brain, heart, kidney, lung and immune systems



Cardioprotection

TRPC3 TRPC6 TRPC7

- ↓ Cell death (preserve function)
- ↓ Oxidative stress
- ↓ Arrhythmia
- ↓ Fibrosis & Cardiovascular scarring
- ↓ Cardiac remodelling

Neuroprotection

TRPC3 TRPC6 TRPC7

- ↓ Cell death (preserve function)
- ↓ Inflammation (impaired regulation)
- ↓ Swelling
- ↓ Immune response

Oncology

TRPC3 TRPC6 TRPC7

- ↓ Cell proliferation & migration (metastatic spread)
- ↓ Drug resistance
- ↓ Cell invasion
- ↓ Tumour progression

TRPC Channels: Clinical Landscape & Validation

Growing industry investment supports the emergence of TRPC therapeutics

- Genetic validation and strong preclinical data have led to advancing clinical programs across cardiovascular, kidney, neurological and fibrotic diseases
- Both large pharma and biotech are now advancing TRPC-targeted therapies into Phase II/III trials, confirming clinical actionability

Clinical Landscape for TRPC Targeted Therapies

Company	Program/ Target	Indication	Phase	Status/Milestones
Boehringer Ingelheim	Apecotrep (BI 764198) TRPC6 inhibitor	Primary FSGS (kidney disease)	Phase III	• Phase II results published in The Lancet (Jan 2026). • 40% proteinuria reduction vs. placebo. Phase II. • (NCT07220083) now recruiting. • Phase II expansion to other proteinuric diseases underway.
Boehringer Ingelheim	BI 1358894 TRPC4/5 inhibitor	Major Depressive Disorder (MDD)	Phase II Completed	• Phase II dose-ranging trial completed (J Clin Psychiatry, Sept 2025). • Efficacy not demonstrated; drug well-tolerated. • Further development path under evaluation.
Bristol Myers Squibb	TRPC4/5 inhibitor program	Mood and anxiety disorder	Phase I	• Phase I SAD/MAD completed (2023). No publicly disclosed Phase II advancement to date.
Nyrada inc	Xolatryp® TRPC 3/6/7 inhibitor	Cardioprotection, Neuroprotection, Oncology	Phase II Recruiting	• PROTECT-MI Phase IIa trial recruiting STEMI patients. Interim safety review for first 8 patients expected Q3/Q4 CY26.

First TRPC Program to Reach Phase III

- Boehringer Ingelheim's Apecotrep is a first-in-class, oral, selective TRPC6 inhibitor in primary FSGS - a rare, progressive kidney disease with no approved targeted therapies. The Phase II trial (NCT05213624) enrolled 67 patients across 31 centres in 10 countries.
- **Study:** Phase II RCT, double-blind, placebo-controlled (NCT05213624)
- **Population:** Adults with primary FSGS or genetic TRPC6-mutation FSGS
- **Primary Endpoint**: ≥25% reduction in urine protein: creatinine ratio (UPCR)
- **Key Result:** 40% reduction in proteinuria (20mg dose) vs. placebo (p=0.002); published in The Lancet, January 2026
- **Next Step:** Phase III trial (NCT07220083) now recruiting (286 patients, 104-week study). Phase II expansion to other proteinuric kidney diseases also initiated.

This represents the most advanced clinical program targeting a TRPC channel and is a major near-term catalyst validating the class

Broad Therapeutic Potential Across TRPC Subtypes

Cardiovascular	Renal	Neurological / CNS	Oncology
Ischemia-reperfusion injury, heart failure, arrhythmias (TRPC3/6/7)	FSGS, diabetic kidney disease, proteinuric glomerular diseases (TRPC6)	MDD, anxiety, stroke, TBI, neurodegeneration (TRPC 3/4/5/6/7)	Cardioprotection and antiproliferative cancer treatment (TRPC 3,6,7)

Strong clinical validation: Boehringer Ingelheim's Apecotrep has become the first TRPC inhibitor to reach Phase III (FSGS, Jan 2026), validating TRPC6 as a disease target. Blue-chip pharma investment across multiple TRPC subtypes confirms the class as clinically actionable. Nyrada's Xolatryp® is the only program targeting TRPC 3/6/7 in cardioprotection, oncology and neuroprotection.

Xolatryp® in Cardiac Reperfusion Injury

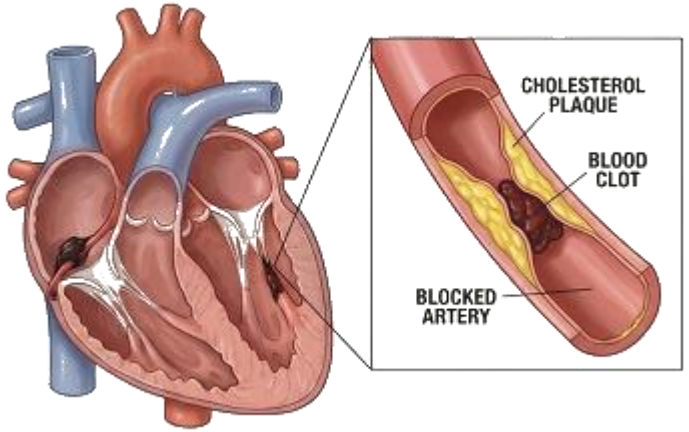
Well defined and uncontested $US3bn US market opportunity

Heart Attack (STEMI)

STEMI results in a hyper-activation of TRPC channels

Overview

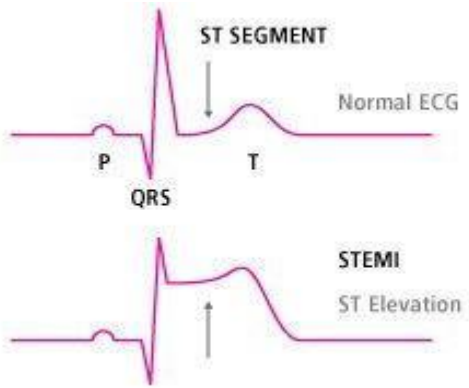
- Atherosclerotic plaque restricts blood flow to a region of the heart muscle resulting in Myocardial Infarction (MI) “Heart attack”
- Myocardium oxygen demand exceeds supply
  - **Within seconds**: Cells Shift towards emergency source of energy (anaerobic glycolysis)
  - **Within minutes**: Ion pumps fail, Ca^{2+} floods cardiac tissue → contractile dysfunction begins
  - **Within 20-40 minutes**: Irreversible cardiac cell tissue necrosis begins in the most oxygen deprived zones
- Release of cardiac biomarkers into the bloodstream (troponin I/T, CK-MB)
- Inflammatory response drives activation of fibroblast-drive scar tissue
- Compensatory hypertrophy of surviving tissue → driver of heart failure



Fatty cholesterol plaque builds up inside a coronary artery (the vessels supplying the heart with blood), forming a clot that completely blocks flow - starving heart muscle of oxygen.

STEMI

- STEMI (ST-elevation myocardial infarction) is a blockage
- Elevated ST segment on ECG
- Urgent reperfusion via Percutaneous Coronary Intervention (PCI) **required within ~90 minutes**
- ~30% of all MI cases; carry higher acute mortality
- ~7 million acute coronary syndrome (ACS) cases p.a. globally
- Compensatory hypertrophy of surviving tissue → driver of heart failure



An ECG (electrocardiogram) records the heart's electrical activity. In a normal heartbeat the ST segment is flat. In STEMI, the ST segment is elevated - signalling a complete blockage requiring immediate treatment.

Acute ST-Segment Elevation Myocardial Infarction (STEMI) - https://www.ncbi.nlm.nih.gov/books/NBK532281

Current Standard Treatment for STEMI Heart Attack

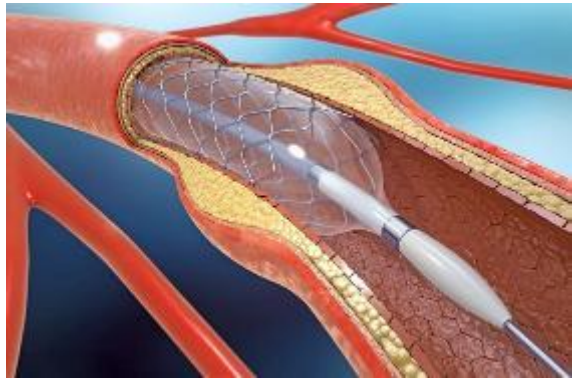
Up to ~50% of heart injury may be caused by reperfusion, representing a major remaining therapeutic challenge

Current Standard of Care for STEMI patients

- Percutaneous Coronary Intervention (PCI) is the standard of care for STEMI patients by early 2000s
- ~4 million PCI procedures p.a. globally[1]

The Clinical Paradox from PCI

- Although timely PCI restores coronary blood flow and limits ischemic injury, reperfusion itself can trigger additional myocardial damage
- The abrupt restoration of blood flow drives rapid Ca^{2+} overload, oxidative stress, mitochondrial dysfunction and inflammatory signalling
- **Reperfusion injury may account for up to ~50% of final infarct size** in STEMI patients following PCI[2]
- Despite strong mechanistic rationale, no approved pharmacological therapy currently exists to directly reduce reperfusion injury





Infarct size as a driver of heart failure risk and mortality

Review of multiple clinical studies show that reducing heart muscle damage lowers risk of heart failure hospitalisation[3]. Through 12 months:

- 5% reduction in infarct size → ~17% lower risk of heart failure hospitalisation
- 10% reduction in infarct size → ~31% lower risk of heart failure hospitalisation
- Patients with the largest infarcts have >7× higher risk of death or hospitalisation

Potential for Xolatryp® to reduce infarct size → clinically significant reduction in adverse cardiac events and improved quality of life

Phase III Roadmap – Faraday Pharmaceuticals

Primary Endpoint - Cardiovascular death or heart failure: the proportion of subjects who experience either cardiovascular mortality or a heart failure event, measured through 12 months

(1) Analyst Q&A: Coronary Balloon Catheters and the Global Market - https://idataresearch.com/analyst-qa-coronary-balloon-catheters-and-the-global-market
(2) Reducing myocardial infarct size: challenges and future opportunities - https://heart.bmj.com/content/102/5/341
(3) Relationship Between Infarct Size and Outcomes at 12 Months Following Primary PCI: Patient-Level Analysis From 10 Randomized Trials www.pubmed.ncbi.nlm.nih.gov/27056772/

PROTECT-MI: Phase IIa Trial

Phase IIa Cardiac Reperfusion Injury trial recruiting – 5 sites active, 5 patients dosed

PROTECT-MI is a Phase IIa randomised, double-blind, placebo-controlled study evaluating Xolatryp® in STEMI patients undergoing PCI

- Assesses safety, tolerability and preliminary efficacy in reducing myocardial infarction reperfusion injury
- 5 patients dosed as at 30 Oct 2026, progressing towards the 8th patient that triggers the first SRC meeting
- Liverpool Hospital exploring 24/7 recruitment to enable overnight and weekend screening
- Independent Safety Review Committee (SRC) meets after 8, 30, 60 and 90 patients dosed, with a market update after each; recruitment continues during reviews

Active sites (5)

- Nepean Hospital (NSW)
- Liverpool Hospital (NSW)
- Northern Health (VIC)
- Sir Charles Gairdner Hospital (WA)
- Royal Perth Hospital (WA)

Pending activation (4) – by end 2026

- Royal Adelaide Hospital (SA)
- Sunshine Hospital (VIC)
- Peninsula University Hospital (VIC)
- Aukland City Hospital (NZ)

Size	100 evaluable patients (drug:placebo randomisation 1:1)
Recruitment	5 dosed (30 Oct 2026); final patient dosed expected mid-2027
Sites	5 active, 4 pending (9 total). Additional ANZ, Singapore & HK sites under assessment
First patient dosed	July 2026
Top-line data timing	Q3/Q4 CY27
Primary endpoint	Safety and tolerability
Efficacy endpoints	• Cardiac MRI infarct size • Biomarkers, including Troponin I levels • Cardiac function • Incidence of arrhythmias of interest



STEMI Heart Attack – Large Uncontested Market Opportunity

US$3bn STEMI opportunity

US Market Opportunity

~750K
STEMI[1]
Annual STEMI incidence in the US

>80% ×

~600K
STEMI related PCI[1]
Estimated PCI procedures related to STEMI

×

US$5,000
Illustrative price[2]
Illustrative price per procedure

=

US$3bn
Total addressable market in the US

Potential future expansion into broader 4m global PCI procedure market
(~900k PCI's in the US alone)[3]

(1) Continuous quality improvement for prehospital STEMI improved triage rates and achievement of gold standard <90-min EMS-to-balloon time - https://pmc.ncbi.nlm.nih.gov/articles/PMC11905686/
(2) Based on TNKase (Tenecteplase) cost of ~US$5-10k
(3) Percutaneous Coronary Intervention (PCI) - https://www.yalemedicine.org/conditions/percutaneous-coronary-intervention-pci?utm

Catalysts

Multiple near-term milestones over the next 18 months

2H CY26

- PROTECT-MI Phase IIa execution: ongoing patient recruitment and site activations across Australian PCI-capable hospitals
- PROTECT-MI Phase IIa safety review committee assessment and data from first 8 patients
- Expansion of PROTECT-MI Phase IIa trial site network, adding hospitals in Australia, New Zealand and Southeast Asia
- Ongoing updates from preclinical oncology and cardioprotection studies
- Initiate development of next-generation orally dosed TRPC inhibitor

1H CY27

- PROTECT-MI Phase IIa execution: ongoing patient recruitment and site activation
- HREC submission for Phase Ib anthracycline combination safety study (cardiomyopathy and anti-cancer)
- Further preclinical translational oncology studies: Xolatryp in combination with standard of care cancer treatments
- Assessment of orphan drug potential in TRPC gain-of-function mutations
- Preclinical MCAO study read out
- Initiation preclinical GLP study to evaluate 24-hour dosing
- Initiation of Phase I to evaluate safety of 24-hour dosing in healthy human volunteers

2H CY27

- Phase IIa PROTECT-MI topline data readout
  - ➢ Positive data from Phase IIa PROTECT-MI would support partnering, larger Phase IIb/III planning, and broader platform validation for TRPC inhibition
- Ethics submission(s) for stroke Phase IIa study
- Continued development of next-generation orally dosed TRPC inhibitor
- Manufacturing and scale-up of clinical formulation candidate

Diversified Pipeline

Multiple compelling TRPC opportunities in indications of high unmet need

Applications	Target Indication	Pre-clinical	Phase I	Phase II	Phase III	Strategy and Upcoming Catalysts
Cardioprotection	Cardiac Reperfusion Injury Post STEMI			*Phase IIa Recruiting*		• Safety review in H2 CY26 • Topline data in Q3/Q4 CY27, positioning program to be 'deal ready'
Oncology	Adjunct Anthracycline + Anti-tumour Treatment	*Proof of concept demonstrated*	*Phase Ib ready*			• Phase Ib ready • Potential dual therapeutic action • Orphan drug potential – TRPC6 gain-of-function mutation
	Chemotherapy Induced Cardiomyopathy	*Proof of concept demonstrated*	*Phase Ib ready*			
Neuroprotection	Ischemic Stroke	*Preclinical efficacy demonstrated*	*Phase II ready subject to 2nd preclinical study*			• Additional preclinical model for Phase II ready
	Traumatic Brain Injury (TBI)		*Phase II ready*			• Phase II ready • Potential to pursue US Government non-dilutive funding and co-development

(1) Gain-of-Function Variant TRPC6 - https://www.ahajournals.org/doi/10.1161/CIRCGEN.125.005334

Key Links

- **Cardioprotection**
  - PROTECT-MI website - https://www.protect-mi.com
  - PROTECT-MI NIH Entry - https://bit.ly/4cB2fF9
  - FDA IND Feedback - https://bit.ly/4zyu9dZ
  - Phase IIa factsheet - https://bit.ly/4bcDlKj
  - Phase IIa update #4 - https://bit.ly/4A6N1kG
  - Preclinical cardioprotection study 1a - https://bit.ly/4sigwMZ
  - Preclinical cardioprotection study 1b - https://bit.ly/4rmOsXn
  - Preclinical cardioprotection study 2 - https://bit.ly/40jHpUg
- **Foundations**
  - US Patent Grant - https://bit.ly/4yUqMy
  - Phase I results - https://bit.ly/3Nt0GzH
  - Preclinical mitochondria stabilisation study - https://bit.ly/4yiZUHa
  - GLP study results - https://bit.ly/4d8VYkX
  - CSANZ Conference Poster - https://bit.ly/4A9ROmf
- **Oncology**
  - Preclinical cardiomyopathy study - https://bit.ly/4yR9BgD
  - Preclinical cardiomyopathy pilot study - https://bit.ly/4xJH3Fj
  - Preclinical anti-tumour study - https://bit.ly/49rWOa0
- **Neuroprotection**
  - Preclinical traumatic brain injury study - https://bit.ly/40fhrRT
  - Preclinical stroke study - https://bit.ly/4sygHmH
- **Corporate**
  - 1QFY2027 Quarterly update and cashflow - https://bit.ly/4sDWzRE
  - September 2026 Capital raise presentation slides - https://bit.ly/46FM9Xq
  - September 2026 placement results - https://bit.ly/4sA6kQC
  - October 2026 SPP results - https://bit.ly/3WnuJNk
  - November 2026 AGM Notice of Meeting - https://bit.ly/4ktLQHe