16 June 2026 Sydney, Australia

PROTECT-MI Phase IIa Clinical Trial Update

Highlights:

- Nyrada's PROTECT-MI Phase IIa clinical trial of Xolatryp® remains on track for completion in CY2027.
- Two additional sites nearing activation and Royal Perth Hospital selected to participate in the trial.
- Trial designed to assess safety and preliminary efficacy of Xolatryp in reducing heart tissue damage and improving heart function in patients suffering a heart attack.
- Activation of previously announced sites progressing and discussions continuing with additional prospective sites.

Nyrada Inc (ASX:NYR), a clinical stage biotechnology company focused on developing Transient Receptor Potential Canonical (TRPC) ion channel inhibitors to treat a range of medical conditions, today provides an update on its PROTECT-MI Phase IIa Clinical Trial.

Phase IIa Trial On Track

Nyrada's PROTECT-MI Phase IIa clinical trial remains on track for completion in CY2027.

As a first-in-patient study, the trial was designed to begin with in-hours recruitment at each site, allowing clinical teams to establish full familiarity with Xolatryp, protocol requirements, and trial workflow before scaling. This staged approach is common for first-in-patient cardiovascular studies.

Since activation of the first clinical trial site, close to 20 patients have been pre-screened. No patients have yet been enrolled. This is not a significant deviation from the trial plan. Pre-screened patients who did not proceed to enrolment largely reflected presentation outside pharmacy operating hours or protocol eligibility criteria, most commonly the upper age limit of 75 years. These factors were anticipated in the trial's scaling design.

Pathway to Accelerated Recruitment

As activated sites complete their initial in-hours phase, selected sites will move to storing Xolatryp directly in the cardiac catheterisation laboratory (Cath Lab), enabling 24-hour recruitment and capturing the proportion of eligible patients who present outside pharmacy hours. This transition, along with activation of further sites, are the primary drivers behind the Company's expectation of accelerating recruitment from the third quarter of CY2026.

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Expanding Site Network

Previously announced trial sites continue to progress through their respective Research Governance Office (RGO) approval processes. Two further sites are nearing RGO approval and are expected to activate soon thereafter. Site activation reflects completion of all key start-up activities, including governance approvals, site initiation, staff training, and receipt of Xolatryp and placebo.

Nyrada actively monitors recruitment performance across all participating sites. Subject to local governance approvals, the Company retains the flexibility to activate additional sites or discontinue underperforming ones, directing Company resources to the centres demonstrating the strongest recruitment potential.

Royal Hobart Hospital has withdrawn due to local resourcing constraints. However, the Company has also selected the participation of Royal Perth Hospital in the trial and is progressing discussions with several additional hospitals, including sites in New Zealand. This expansion is consistent with the multicentre design of the study and broadens and diversifies the recruitment base across centres.

Regulatory Progress

Preparation of Nyrada's Investigational New Drug (IND) application continues to advance, with submission to the US FDA targeted for the second half of CY2026.

Participating sites and trial status are publicly available through the U.S. National Library of Medicine clinical trial registry (NCT07362446), with further information available on the PROTECT-MI website.

Nyrada will continue to update the market on site activations, recruitment progress, and other material developments as the trial advances.

Further information on the PROTECT-MI Phase IIa clinical trial is provided in the Appendix.

-ENDS-

Appendix - Nyrada's PROTECT-MI Phase IIa Trial of Xolatryp®

Clinical Issue: Ischemia-reperfusion injury occurs following myocardial infarction (heart attack). The standard treatment following a heart attack is percutaneous coronary intervention (PCI), a procedure involving balloon angioplasty and stent implantation to reopen the occluded artery (or arteries) and restore blood flow to the heart.

- Although PCI treatment is a well-established and lifesaving procedure, the sudden return of oxygenated blood following PCI is paradoxically linked to irreversible cell damage in the heart muscle.
- This death of heart cells, ischemia reperfusion injury, occurs due to a vicious cycle of calcium overload when the blocked artery is manually opened. There is no way to avoid reperfusion injury.
- Approximately 5 million PCI procedures are performed globally each year (including about 50,000 in Australia), yet there are currently no approved therapies that address ischemia-reperfusion injury in this setting.

What is Xolatryp®

- Xolatryp is a small-molecule inhibitor of the calcium-permeable TRPC 3/6/7 ion channels.
- By limiting pathological calcium influx, Xolatryp is designed to help protect heart muscle cells from processes associated with irreversible injury, including mitochondrial dysfunction, ATP depletion, osmotic imbalance, and excess reactive oxygen species formation, which are known contributors to ischemia-reperfusion injury.

Preclinical data (cardioprotection signals)

In preclinical myocardial ischemia-reperfusion injury (IRI) animal models, Xolatryp showed:

- 86% cardioprotection with improved cardiac function and reductions in biomarkers (AST, LDH, Troponin I) when dosed at 30 mg/kg over 24 hours.
- 42% cardioprotection, 90% reduction in arrhythmias, and lower Troponin I levels when dosed at 9 mg/kg over 3 hours.

Phase I Clinical Trial data (healthy human volunteers)

- Phase I Clinical Trial (six cohorts; 48 participants, 36 active/12 placebo) met its primary endpoint, where all doses were shown to be safe and well-tolerated, with no dose-limiting or dose-related safety issues.
- Pharmacokinetics was also linear and predictable, with therapeutic levels reached within 10 minutes post start-of-infusion.

Phase IIa Clinical Trial plan: MI patients undergoing primary PCI

- Nyrada is undertaking a Phase IIa clinical trial of Xolatryp. Human Research Ethics Committee (HREC) approval was received in January 2026.
- The trial will be a randomised, double-blind, placebo-controlled, multicentre study in Australia to assess safety and preliminary efficacy in the target population.
- Although safety is the primary endpoint of this trial, multiple secondary efficacy endpoints are also being evaluated, including cardiac function, extent of cardiac injury, biomarkers such as Troponin I levels, and the incidence of arrhythmias of interest.

Population	First-time STEMI; primary PCI within 6 h of symptom onset
Patients Dosed	~100 evaluable patients (1:1 Xolaryp:placebo)
Intervention	IV Xolatryp for ~6 h at 3 mg/kg
Primary	Safety/tolerability (including cardiac-related safety)
Exploratory	Cardiac MRI infarct size, arrhythmias, Troponin I, PK, Day-30 PROs

Conclusion

- Nyrada's Phase IIa clinical trial represents a critical step to evaluate the potential of Xolatryp to modify injury to heart tissue and early clinical outcomes in heart attack patients.
- If successful, Xolatryp has the potential to become the first drug on the market to mitigate ischemia reperfusion injury, improving heart tissue integrity and function, thereby improving patient outcomes post-heart attack.

About Xolatryp®

- Xolatryp is a small-molecule inhibitor of TRPC3/6/7 channels designed to limit excessive Ca^{2+} entry related to multiple disease pathologies.

- A Phase I clinical trial to assess the safety, tolerability, and pharmacokinetics has been successfully completed and a Phase IIa clinical trial has commenced to assess the safety and preliminary efficacy of Xolatryp in reducing cardiac reperfusion injury in patients with ST-Elevation Myocardial Infarction (STEMI) undergoing PCI.

Key Details of Xolatryp® Phase IIa Clinical Trial

(Subject to Change)

Protocol Title (long)	A Randomised, Double-Blind, Placebo-Controlled, Study of Xolatryp in Patients presenting with STEMI undergoing primary PCI
Protocol Title (short)	A Study of Xolatryp in Patients presenting with STEMI undergoing PCI
Other Title	**P**revention of **R**eperfusion Injury **O**utcomes **T**hrough **E**ffective **C**ardioprotection **T**argeting **M**yocardial **I**nfarction (PROTECT-MI)
Study Description	A Phase IIa, prospective, randomised, double-blind, placebo-controlled, multi-centre study that will evaluate the safety, pharmacokinetics and exploratory efficacy of Xolatryp, in addition to standards of care, in ST-Elevation Myocardial Infarction (STEMI) patients with primary percutaneous coronary intervention (PCI) following 6 hours of continuous infusion.
Primary Objectives	• To evaluate the safety and tolerability of Xolatryp when delivered as an infusion in patients presenting with an acute STEMI undergoing primary PCI • To evaluate the cardiac related safety of Xolatryp when delivered as an infusion in STEMI patients undergoing primary PCI
Further Objectives including	• To determine the cardiac infarct size utilising cardiac MRI in participants with pre-PCI TIMI 0 or 1 flow in patients treated with Xolatryp compared patients treated with placebo • To determine the incidence of arrhythmias of interest in patients treated with Xolatryp compared patients treated with placebo • To determine the blood PK in patients treated with Xolatryp compared patients treated with placebo • To determine the relative difference in serum levels of Troponin I in patients treated with Xolatryp compared patients treated with placebo • To compare patient reported outcomes at Day 30 in patients treated with Xolatryp compared patients treated with placebo
Blinding Status	Double-blind, placebo-controlled, randomised, multi-centre.
Treatment Method	3 mg/kg as an intravenous infusion over 6-hours.
Number of Trial Subjects	~100 evaluable patients (1:1 Xolaryp:placebo)

Key Inclusion Criteria	• Informed consent • Male patients aged 40 to 75 years of age • Female patients aged 55 to 75 years of age, or women less than 55 years that have no possibility of being pregnant • Patient presents with first-time STEMI, scheduled to undergo primary PCI within 6 h of symptom onset • Confirmation of STEMI with ST-elevation at the J-point in two contiguous leads • Hemodynamically stable
Exclusion Criteria	• Prior major cardiac surgery • Known contraindication to CMR • History of clinically significant renal impairment • Body weight < 50 kg or > 120 kg • Pregnant females of childbearing potential or breastfeeding females • Any condition or significant clinical abnormality identified at the time of screening that, in the judgment of the Investigator or any sub-Investigator, would preclude safe completion of the study
Coordinating Principal Investigator	Professor William Chan MBBS (Hons), FRACP, FCSANZ, PhD
Contract Research Organisation	Accelagen Pty. Ltd. 785 Toorak Road Hawthorn East VIC 3123 Australia
ClinicalTrials.gov ID and Link	NCT07362446

About Nyrada Inc.

Nyrada Inc. is a clinical-stage biotechnology company focused on the discovery and development of innovative small-molecule therapies, specifically targeting Transient Receptor Potential Canonical (TRPC) ion channels. The company's lead candidate, Xolatryp®, has shown efficacy in preclinical cardioprotection, neuroprotection, and oncology models and has completed a first-in-human Phase I clinical trial. A Phase IIa clinical trial has commenced to assess the safety and preliminary efficacy of Xolatryp in reducing cardiac reperfusion injury in patients with ST-Elevation Myocardial Infarction (STEMI) undergoing PCI. Nyrada Inc. (ARBN 625 401 818) is incorporated in Delaware, US, with limited liability for its stockholders.

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