18 November 2025 Sydney, Australia

Nyrada Phase IIa Clinical Trial Update

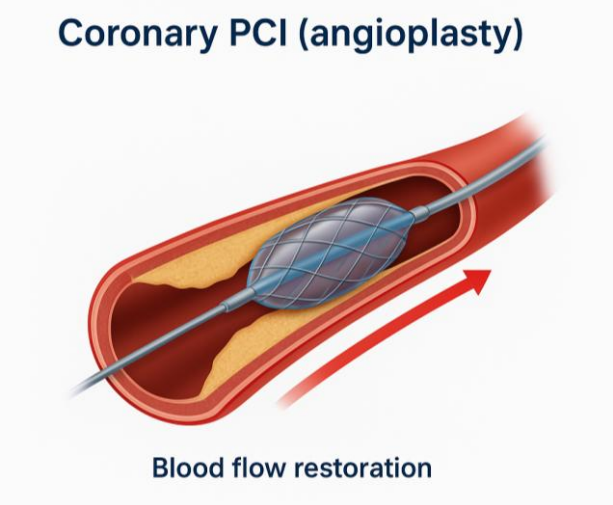
Highlights:

- Nyrada's Phase IIa Clinical Trial assessing the safety and preliminary efficacy of Xolatryp™ in cardioprotection on track to commence in March 2026.
- Human Research Ethics Committee (HREC) application now submitted.
- Professor William Chan engaged as Coordinating Principal Investigator.
- Accelagen engaged as Contract Research Organisation (CRO).

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 Phase IIa Clinical Trial.

As announced in July 2025 and following the successful completion of a Phase I clinical trial, Nyrada is progressing to a Phase IIa clinical trial to assess the safety and preliminary efficacy of Xolatryp in patients who experience ST-Elevation Myocardial Infarction (STEMI) and undergo Percutaneous Coronary Intervention (PCI).

STEMI is a severe type of heart attack occurring when there is blockage of a coronary artery, usually due to a blood clot forming on a ruptured atherosclerotic plaque. A PCI, often called angioplasty with stenting, is a minimally invasive procedure to restore blood flow in patients suffering a heart attack. It involves inserting a catheter (usually via the wrist or groin), inflating a balloon to open the blocked artery, and often placing a stent to keep it open.



While PCI remains the gold standard treatment for patients presenting with STEMI, it is also associated with myocardial ischemia reperfusion injury that occurs when blood flow is restored to the heart.

Despite significant clinical and research efforts, there are currently no effective therapies available to treat ischemia reperfusion injury. Myocardial ischemia reperfusion injury is also a significant market with around 900,000 PCI procedures performed annually in the US and a similar number in Europe. In 2024, there were approximately 50,000 PCI procedures performed in Australia, with the majority occurring in major public hospitals.

Nyrada's HREC submission, seeking approval to conduct its Phase IIa trial, has now been lodged. HREC's final decision is expected in February 2026 and, subject to approval, patient dosing is expected to commence in March 2026.

The trial will be a randomised, double-blind, placebo-controlled, multicentre study to assess the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary efficacy of Xolatryp in male and female patients of non-childbearing potential presenting with STEMI undergoing primary PCI. Approximately two hundred (200) patients will be dosed for this 1:1 drug to placebo trial.

Patient recruitment rates are a key determinant of the duration of the trial, and subject to patient recruitment rates, the trial is expected to conclude within 9 to 18 months of first patient dosing. Up to ten (10) hospitals across Australia will be involved in the trial. All selected hospitals will have dedicated coronary care units capable of performing PCI.

If recruitment does not proceed as quickly as planned, additional hospitals in Australia or internationally will be considered. Countries with similar regulatory frameworks, such as New Zealand, Singapore, and Canada, may be included if needed. Nyrada also plans to submit an Investigational New Drug (IND) application with the US Food & Drug Administration (FDA), allowing for potential expansion of the trial into the US if required.

Patients with a suspected heart attack attending a trial hospital will be invited to participate in the study. Those wishing to participate will be assessed for eligibility by the principal investigator (PI) at each trial site.

Once STEMI is confirmed by ECG and the decision is made to proceed with PCI, eligible patients will be randomly assigned to receive either an intravenous dose of Xolatryp or a placebo. As the trial will be blinded, neither the patient nor hospital staff will know which treatment each patient receives.

Treatment will commence prior to PCI where feasible. A key inclusion criterion for the study is that a patient presents with a first-time STEMI and is scheduled to undergo primary PCI within 6 hours of symptom onset.

Following treatment, patients will undergo standard assessments for safety and exploratory efficacy outcomes. Patients who were identified as having a complete or near complete blockage of their coronary artery will be invited to have an additional cardiac MRI scan to measure infarct volume.

The safety of Xolatryp will be evaluated in all treated patients. For other for endpoint evaluations, additional stratification of patients is predefined in the protocol to ensure the trial has adequate precision.

Xolatryp is currently being manufactured and is expected to be ready in January 2026. Other study start-up activities, in collaboration with Accelagen, are also underway.

A synopsis of the Phase IIa trial protocol that has been submitted to HREC is appended in Appendix 1. This protocol is subject to change.

Professor William Chan will be the Coordinating Principal Investigator. Professor Chan is Head of Cardiac Catheterisation Laboratories at Western Health and leader of the Interventional Services Program.

About Xolatryp™

Xolatryp, previously called NYR-BI03, is a small molecule that inhibits calcium ion influx via TRPC 3/6/7 channels. By limiting pathological calcium entry, it helps protect mitochondrial function and reduces ischemia reperfusion injury associated with acute myocardial infarction (AMI).

A Phase I clinical trial assessing the safety, tolerability, and pharmacokinetics has been completed, and a Phase IIa clinical trial focusing on safety and preliminary efficacy is scheduled to begin in the first quarter of calendar 2026. This upcoming study will enrol patients with AMI who are undergoing PCI.

- ENDs

Appendix 1 - 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
Study Description	A Phase 2A, 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	Approximately 200 patients will be dosed (100 active, 100 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 Sunshine Hospital, Western Health, Melbourne
Contract Research Organisation	Accelagen Pty. Ltd. 785 Toorak Road Hawthorn East VIC 3123 Australia

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 both cardioprotection and neuroprotection, and has just completed a first-in-human Phase I clinical trial. Nyrada Inc. (ARBN 625 401 818) is incorporated in Delaware, US, with limited liability for its stockholders.

www.nyrada.com

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