14 July 2025 Sydney, Australia

Final Nyrada Phase I Clinical Trial Cohort to Commence

Highlights:

- Cohort 6 approved to commence, marking the final stage of Nyrada's Phase I clinical trial of Xolatryp™.
- Safety Review Committee for Nyrada's Phase I clinical trial has cleared progression following review of safety and pharmacokinetic data from Cohort 5.
- Cohort 5 received the highest concentration to date via a 3-hour intravenous infusion – the human equivalent dose that showed 42% cardioprotection in a preclinical study.
- No safety concerns were identified in Cohort 5, with no dose-limiting toxicities or adverse effects reported.

Nyrada Inc (ASX:NYR), a clinical-stage drug discovery and development company focused on innovative Transient Receptor Potential Canonical (TRPC) ion channel inhibitors, today provides an update on its Phase I clinical trial.

Nyrada Advances to Final Cohort in Phase I Clinical Trial of Xolatryp™

Nyrada is pleased to announce the commencement of Cohort 6, the final dosing group in its Phase I clinical trial of Xolatryp. This milestone follows a review by the Safety Review Committee (SRC), which evaluated safety and pharmacokinetic data from Cohort 5.

Participants in Cohort 5 received Xolatryp at a human equivalent dose and exposure duration matching that used in the May 2025 3-hour preclinical cardiac efficacy study, where a 42% level of cardioprotection was observed. This dose level was approximately 2.5 times higher than that administered in Cohort 4. Importantly, no safety signals, dose-limiting toxicities, or unexpected adverse effects were reported, consistent with findings from earlier cohorts.

With SRC clearance secured, the study now progresses to Cohort 6, where participants will receive the same concentration of Xolatryp as in Cohort 5, but for a 6-hour infusion period. This effectively doubles the total dose. This extended exposure is expected to generate critical data that will provide Nyrada with greater flexibility in designing its upcoming Phase II study.

The trial is being conducted under the amended trial protocol approved by the Human Research Ethics Committee and is registered with the US National Institutes of Health. A summary of the protocol is provided in Appendix 1.

Nyrada will continue to provide regular updates throughout the study, with final readouts anticipated in the September 2025 quarter.

About Xolatryp™

Nyrada is developing Xolatryp (previously known as NYR-BI03), a first-in-class small-molecule cardioprotection and neuroprotection therapy. Xolatryp has demonstrated preclinical efficacy as an acute treatment following ischemic stroke, traumatic brain injury (TBI) and acute myocardial infarction (AMI). A Phase I clinical trial is currently underway to assess the safety, tolerability, and pharmacokinetics of Xolatryp in healthy human volunteers.

In July 2025, Nyrada announced that the first five cohorts of its Phase I clinical trial had been successfully completed. Dosing of the sixth and final cohort will commence imminently, with data and analysis to be compiled for the trial's Safety Review Committee's assessment. Final clinical trial readouts are expected in the September quarter of 2025.

In May 2025, Nyrada announced the results of a follow-up preclinical coronary heart disease study. This study showed that Xolatryp provided 42% cardioprotection when administered continuously for only 3 hours. In addition to protecting the irreplaceable heart tissue and reducing injury biomarker levels, the incidence of arrhythmias, including ventricular fibrillation and ventricular tachycardia, the leading causes of sudden cardiac death, was significantly reduced.

In April 2025, Nyrada announced the results of a preclinical traumatic brain injury study, which showed that Xolatryp provided a statistically significant (p = 0.043) neuroprotective effect following a penetrating traumatic brain injury. This study was undertaken in collaboration with the Walter Reed Army Institute of Research and UNSW Sydney.

In October 2024, Nyrada announced the results of a preclinical coronary heart disease study, which showed that Xolatryp provided an 86% cardioprotective effect following myocardial ischemic-reperfusion injury, a leading cause of tissue damage when blood flow is restored to the heart after injury. Further supporting efficacy data were provided through echocardiography assessment that showed significant improvements in heart function and structure following Xolatryp treatment.

In February 2024, Nyrada announced preclinical stroke study results showing that Xolatryp achieved a statistically significant neuroprotective effect, rescuing 42% of brain tissue in the penumbra region of treated animals.

-ENDS-

Appendix 1 - Key Details of Xolatryp (NYR-BI03) Phase I Clinical Trial

Protocol Title	A Phase I, Double-Blind, Placebo-Controlled, Randomised, First in Human, Dose Escalation Study to Assess the Safety, Tolerability, and Pharmacokinetics of NYR-BI03 in Healthy Participants, When Administered as an Infusion for up to 6 hours
Primary Endpoints	To evaluate the safety and tolerability of NYR-BI03 in healthy volunteers, when administered as an intravenous infusion for up to 6 hours
Secondary Endpoints	To determine the blood pharmacokinetics of an intravenous dose of NYR-BI03 in healthy volunteers when administered as an intravenous infusion for up to 6 hours
Blinding Status	Double-blind, placebo-controlled, randomised
Treatment Method	Up to 6-hour intravenous infusion
Number of Trial Subjects	Up to approximately 48 participants will be enrolled (8 participants per cohort for 6 cohorts)
Inclusion Criteria	• Informed consent • 18 to 50 years of age • Male or female • Weight 50 to 105 kilograms • Healthy as determined by a medical history
Exclusion Criteria	• Pregnancy • Allergy or hypersensitivity to formulation or ingredients • Any evidence of organ dysfunction • Liver function or blood clotting tests outside the approved range • Drug and alcohol abuse • Prescription medications taken within 14 days prior to dosing • Psychiatric disorder • Blood donation within 12 weeks prior to dosing • Vaccination or immunisation within 30 days prior to dosing
Trial Location	Scientia Clinical Research The Bright Building Level 5, Corner of Avoca and High Street Randwick NSW 2031 Australia
Principal Investigator	Dr Christopher Argent Scientia Clinical Research
Contract Research Organisation	Southern Star Research Level 1, 1 Merriwa Street Gordon NSW 2072 Australia
Trial Duration	Estimate completion in the quarter ended September 2025

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 neuroprotection and cardioprotection, positioning it for 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.

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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 that could cause the actual results, performance, or achievements to differ materially from those expressed or implied by the forward-looking statement.