NYRADA INC (ASX:NYR)

Equity Research Report – 31 July 2025

Capital Structure	
Current price per CDI	A$0.37
CDIs on issue	210,917,037
Market capitalisation	A$78.0m
Options outstanding*	44,100,000
Total CDIs and options	254,433,700

*Includes 2m 40c, 2m 60c, 2m 90c options expiring 29/06/2026 and 5m 13.5c, and 2m 20c options expiring 30/06/2027 and 31/12/2027, respectively, held by Canary Capital Pty Ltd

Major Shareholders (as at 31 July 2025)	
Mark Azzi	15.94%
Altnia Holdings (Ian Dixon)	4.70%
Kyriaco Barber Pty Ltd	3.39%
John Moore	3.35%
Celtic Capital PTE Ltd	1.90%

Key People

- John Moore – Non-Exec. Chairman
- James Bonnar – CEO
- Christopher Cox – Non-Exec. Director
- Dr Rüdiger Weseloh – Non-Exec. Director
- Dr Gisela Mautner – Non-Exec. Director
- Marcus Frampton – Non-Exec. Director
- Dr Ian Dixon – Non-Exec. Director

Key Achievements To Date

- Preclinical coronary heart disease study results announced in May 2025 proved that Xolatryp provided 42% cardioprotection and reduced associated arrhythmias by 88%
- Results from a recent penetrating TBI study reported in April 2025 showed Xolatryp's significant neuroprotective effect
- Successfully dosed all 6 cohorts as part of a Xolatryp Phase I clinical trial, with commitment being made for a Phase IIa trial

Research Team

Nathan Oyet – Head of Research

Stuart Craigie – Associate Director

Introduction. Nyrada Inc. (ASX:NYR) is a clinical-stage Australian biotechnology company developing small-molecule therapies targeting critical unmet needs in neuro- and cardioprotection. Its lead candidate, Xolatryp™, is a first-in-class Transient Receptor Potential Canonical (TRPC) ion channel inhibitor designed to mitigate secondary brain injury after stroke and traumatic brain injury (TBI). Additionally, Xolatryp reduces heart muscle damage and improves cardiac function following myocardial ischemia-reperfusion injury (MIRI) and associated arrhythmias.

Breakthrough Preclinical Success. In a recent preclinical coronary heart disease study, continuous administration of Xolatryp over three hours provided 42% cardioprotection and reduced the incidence of ventricular arrhythmias by 88% within the first hour following MIRI. Additionally, in a recent penetrating TBI study conducted in collaboration with the Walter Reed Army Institute of Research, Xolatryp provided a statistically significant (p = 0.043) neuroprotective effect following a penetrating TBI.

Successful Phase I Clinical Trial Cohort Dosage. NYR has completed the dosage of all 6 cohorts as part of the trial that aims to evaluate the safety and tolerability of Xolatryp. Notably, no safety signals, toxicities, or unexpected adverse events have been reported to date. A safety and pharmacokinetic review will be conducted by the SRC once all data is available, and a final clinical study report is expected to be completed in the coming months. NYR has also committed to starting a Phase IIa clinical trial in the first quarter of 2026.

Market-First Opportunity. Despite a total addressable market for TBI and cardiac injury projected to reach US$41.8 billion by 2032, there are currently no FDA-approved treatments for these conditions. Subject to positive clinical trial results, Nyrada is well-positioned to fill this void, providing a first-mover advantage in a large market with minimal competition.

A Promising Biotech Company Underappreciated by the Market. Xolatryp has demonstrated exceptional preclinical efficacy for neuro and cardioprotection in addition to a Phase I clinical trial nearing completion, positioning it as a potential first-in-class therapy addressing unmet medical needs. With upcoming clinical milestones expected to drive a stock revaluation, NYR's current market cap of A$78.0m appears notably discounted, indicating significant upside potential.

COMPANY OVERVIEW

Nyrada Inc. (ASX:NYR) is a clinical-stage Australian biotechnology company focused on the discovery and development of innovative small-molecule therapies, specifically targeting Transient Receptor Potential Canonical (TRPC) ion channels. These ion channels are a subfamily of calcium-permeable ion channels that play a central role in cellular survival and death mechanisms across the brain, heart, and other tissues. Among these, TRPC3 and TRPC6 have emerged as key regulators of calcium homeostasis during acute stress events, including stroke, traumatic brain injury (TBI), and myocardial infarction. Targeting these channels presents a compelling therapeutic opportunity, one that Nyrada is pursuing with its lead candidate, Xolatrypqu (formerly named NYR-BI03).

Xolatryp is a first-in-class neuro- and cardioprotective drug designed to selectively inhibit TRPC3/6/7. It has demonstrated strong preclinical efficacy across its three lead indications - stroke, traumatic brain injury (TBI), and myocardial infarction - and is currently being evaluated in a first-in-human Phase I clinical trial.

MYOCARDIAL ISCHEMIC REPERFUSION EXPLAINED

Overview

Myocardial ischemia-reperfusion injury (MIRI) occurs when blood flow is restored to the heart muscle after an ischemic event (e.g., myocardial infarction), paradoxically causing additional damage. While reperfusion is critical to salvage tissue, it triggers oxidative stress, inflammation, microvascular dysfunction, and electrical instability, exacerbating cardiac injury and increasing the risk of arrhythmias.

Pathophysiology

Myocardial ischemic reperfusion is driven by several mechanisms:

- **Oxidative Stress:** Rapid reintroduction of oxygen generates excessive reactive oxygen species (ROS), damaging cardiomyocytes and destabilising cardiac electrical activity.
- **Inflammation:** Neutrophil infiltration and cytokine release impair endothelial function, contributing to tissue damage.
- **Calcium Overload & Mitochondrial Dysfunction:** Dysregulated calcium levels trigger mitochondrial permeability transition pore (mPTP) opening, leading to cell death and promoting arrhythmias.
- **Microvascular Dysfunction:** The “no-reflow” phenomenon prevents effective tissue perfusion, worsening ischemia.
- **Electrical Instability & Arrhythmias:** Ischemia and reperfusion disrupt ion balances (e.g., potassium, calcium), creating re-entry circuits and ectopic foci. This can lead to life-threatening ventricular arrhythmias, such as ventricular tachycardia or fibrillation, particularly within hours of reperfusion.

Epidemiology and Unmet Medical Need

MIRI is a major complication of myocardial infarction, affecting millions undergoing percutaneous coronary intervention (PCI), such as angioplasty or thrombolysis. Arrhythmias, a frequent consequence of MIRI, significantly contribute to sudden cardiac death post-infarction. Despite advances in interventional cardiology, no FDA-approved drugs specifically target MIRI or its associated arrhythmias. Current treatments focus on revascularisation and supportive care (e.g., anti-arrhythmic drugs, beta-blockers), leaving a critical gap in therapies for myocardial protection and arrhythmia prevention.

STROKE EXPLAINED

Overview

Stroke occurs when the blood supply to a part of the brain is interrupted or reduced, depriving brain tissue of oxygen and nutrients. This leads to the rapid death of brain cells and subsequent neurological impairment. There are two main types: ischemic (caused by a blockage) and hemorrhagic (caused by bleeding).

Pathophysiology

Ischemic stroke (87% of cases) occurs when a blood clot or embolus blocks brain blood flow. This triggers a cascade of damage, including energy failure, excitotoxicity, oxidative stress, inflammation, and cell death. Hemorrhagic stroke results from bleeding in or around the brain. Secondary brain injury processes play a significant role in the progression of damage after the initial injury. These include excitotoxicity, neuroinflammation, oxidative stress, and a compromised blood-brain barrier.

Epidemiology and Unmet Medical Need

Stroke is a leading cause of death and disability worldwide, with an estimated 15 million people experiencing a stroke annually. Of these, approximately 5 million die, and another 5 million are left permanently disabled. While treatments like thrombolytics and thrombectomy help in acute ischemic stroke, they are time-sensitive and benefit only a small subset of patients. No therapies target secondary brain injury, which continues after the initial stroke.

TRAUMATIC BRAIN INJURY EXPLAINED

Overview

Traumatic Brain Injury (TBI) is a complex medical condition caused by an external mechanical force that disrupts the normal functioning of the brain. TBI can result from various incidents, including falls, motor accidents, and sports injuries. The severity ranges from mild (concussion) to severe, with outcomes varying based on injury extent.

Pathophysiology of TBI

The primary injury occurs at impact, leading to contusions, lacerations, and diffuse axonal injury. Long-term damage is driven by secondary mechanisms, including:

- **Excitotoxicity:** Excessive release of excitatory neurotransmitters can result in neuronal cell death.
- **Neuroinflammation**: The brain's immune response to trauma can exacerbate tissue damage.
- **Oxidative Stress:** The production of reactive oxygen species can damage cellular structures, including membranes, proteins, and DNA.
- **Blood-Brain Barrier (BBB) Disruption:** Trauma can compromise the integrity of the BBB, allowing harmful substances to infiltrate the brain and worsen inflammation.
- **Ischemia and Hypoxia:** Reduced blood flow and oxygen delivery to the brain can lead to further neuronal injury.

Epidemiology and Unmet Medical Need

TBI is a leading cause of death and disability, with millions of cases annually. According to the World Health Organisation, it's expected to surpass other diseases as a major cause of death by 2030. Current treatment focuses on supportive care, with no FDA-approved drugs addressing TBI's underlying mechanisms.

TRPC CHANNELS EXPLAINED

Overview

TRPC channels are activated in response to physiological stressors such as ischemia, inflammation, and excitotoxicity. When triggered, they allow calcium and other cations to enter the cell. This calcium influx acts as a powerful cellular switch, initiating a cascade of intracellular signals that regulate inflammation, programmed cell death, metabolism, and tissue repair. While a controlled calcium signal is essential for healthy cell function, excessive calcium influx, as commonly occurs during acute injury, can overwhelm the cell's protective mechanisms and lead to irreversible damage.

Backed By Research

The role of TRPC channels in injury-induced cell death has been validated through extensive preclinical research. In a landmark 2016 study conducted by researchers at Huazhong University of Science and Technology, genetically engineered mice lacking TRPC3, TRPC6, and TRPC7 channels, a model known as triple knockout mice, where all three genes have been deactivated, exhibited dramatically reduced cardiac damage following ischemia-reperfusion injury. These triple knockout animals showed significantly smaller infarct sizes and reduced markers of cardiomyocyte apoptosis, highlighting TRPC channels as key mediators of calcium-driven tissue injury in the heart.

Similar findings have been reported in neurological models. In a 2023 UNSW-led study published in Translational Stroke Research, knockout mice lacking TRPC3 or the broader set of TRPC1/3/6/7 channels demonstrated strong neuroprotection following induced brain injury. The study showed that TRPC channels, when activated via G protein-coupled receptors, drive pathological calcium influx and excitotoxicity in neurons and glia. Inhibition or genetic deletion of these channels significantly reduced lesion size and dendritic degeneration, underscoring their role in secondary brain injury after stroke or trauma.

Relevance to Humans

Although these findings are based on mouse models, the underlying cellular pathways, particularly those governing calcium regulation and programmed cell death, are biologically equivalent between mice and humans. For this reason, mouse studies remain a gold standard for modelling acute injury mechanisms and evaluating drug targets before moving into human trials. In the case of TRPC channels, their structural and functional roles are well-preserved across species, making these results especially promising from a translational perspective.

Nyrada's Drug Development Strategy

NYR's lead drug candidate, Xolatryp, targets TRPC3/6/7 activity after injury to prevent harmful calcium overload while preserving normal cell signalling. This approach addresses a key driver of cell death across organ systems, with the potential to reduce secondary damage and improve neurological and cardiac outcomes. It is supported by a strong scientific foundation and has clear relevance to large, underserved markets in acute care.

DRUG DEVELOPMENT PROCESS

To ensure that new medications are safe and effective for public use, pharmaceutical regulators (e.g. FDA, EMA and TGA) oversee a comprehensive drug development process that comprises five key steps as described below:

1. Discovery and Development

Research for a new drug begins in the laboratory. Scientists identify potential compounds and conduct initial tests to determine their effects. This stage involves understanding the disease, identifying targets, and developing compounds that may influence these targets.

2. Preclinical Research

Before testing a drug in humans, it undergoes preclinical research, which includes laboratory and animal studies to assess its safety and biological activity. These studies help to evaluate the drug's potential toxicity and efficacy.

3. Clinical Research

If preclinical results are promising, the drug enters clinical research, where it is tested on humans in three phases. These phases are designed to ensure that the drug is safe and effective for its intended use. Before administering the drug to humans, some regulatory authorities, like the FDA, require the submission of an Investigational New Drug (IND) application.

- **Phase 1:** A small group of healthy volunteers or patients is administered the drug to assess its safety, dosage range, and side effects.
- **Phase 2:** The drug is given to a group of target patients to evaluate its effectiveness and further assess its safety.
- **Phase 3:** The drug is administered to a group of target patients to confirm its effectiveness, monitor side effects, and compare it to commonly used treatments.

4. Regulatory Review and Approval

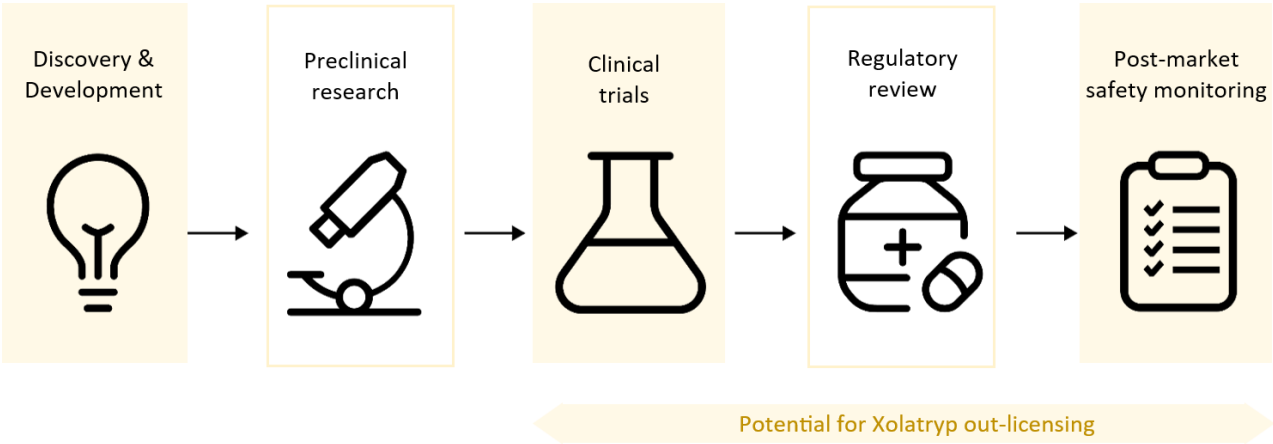
After successful clinical trials, the drug sponsor submits a New Drug Application to the relevant regulatory authority. The authorities review teams then thoroughly examine all of the submitted data related to the drug and make a decision to approve or not to approve it.

5. Post-Market Drug Safety Monitoring

Once a drug is approved and available to the public, the regulatory authority usually continues to monitor its safety. This includes reviewing reports of adverse events, conducting additional studies if necessary, and ensuring that the drug's benefits outweigh its risks.

NYR is making significant strides in its drug development journey, with Phase I clinical trials for Xolatryp nearing completion. Alongside successfully showcasing its efficacy in a model of stroke, Xolatryp also showed efficacy in a model of heart attack, demonstrating Xolatryp's potential in both neuro- and cardioprotection. As the drug progresses through clinical trials and toward post-market safety monitoring, NYR anticipates opportunities for out-licensing Xolatryp. Importantly, the company can license drugs for specific applications as they get developed while simultaneously advancing R&D in additional applications.

Xolatryp is progressing through the drug development process with potential for out-licensing



Source: FDA, Nyrada Inc

CARDIOPROTECTION PROGRAM

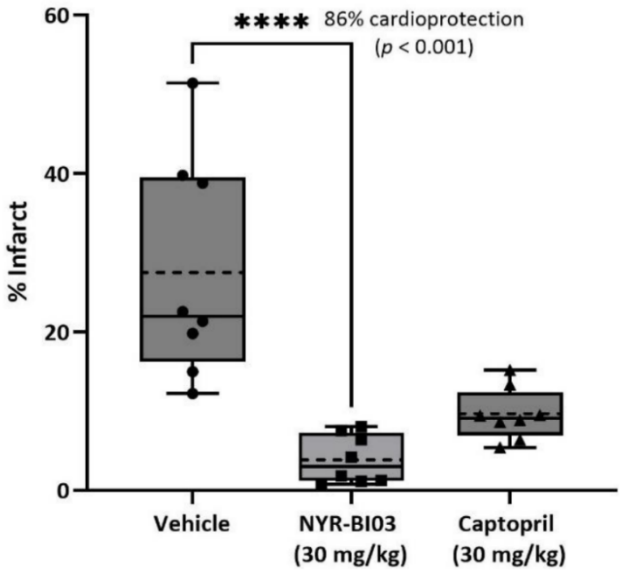
Preclinical Coronary Heart Disease Study

On 1 October 2024, NYR announced positive preclinical results for Xolatryp in MIRI. The preclinical rat study showed Xolatryp provided significant cardioprotection, reducing cardiac tissue damage by 86% ($p < 0.001$, n=8) following MIRI - a major cause of heart damage after blood flow restoration.

The study demonstrated Xolatryp's strong efficacy in limiting cardiovascular damage following acute MIRI. Xolatryp notably outperformed captopril, an established FDA-approved ACE inhibitor traditionally used in managing post-ischemic events and used in the study as a positive control. By surpassing the performance of the current standard treatment, Xolatryp showcases promising potential as a novel therapeutic intervention for patients experiencing acute MIRI.

These preclinical results validate the drug candidate's robust protective mechanisms and signal potentially significant therapeutic and commercial opportunities for NYR in the cardiovascular treatment landscape.

In a recent preclinical study, Xolatryp reduced cardiac tissue damage by 86% after myocardial infarction



Source: Nyrada Inc

Supplementary Cardioprotection Preclinical Studies

On 23 October 2024, NYR announced supplementary results from its preclinical coronary heart disease study. The supplementary data confirmed that Xolatryp prevents loss of function resulting from MIRI following myocardial infarction (heart attack) in rats. In this supplementary data:

- Xolatryp delivered a substantial 43% increase in left ventricular ejection fraction ($p < 0.0001$), a key indicator of heart pumping ability, significantly improving overall cardiac function.
- A 50% increase in fractional shortening ($p = 0.0002$) was observed, indicating that Xolatryp preserved the heart's contractile strength and prevented damage to the left ventricle.
- Left ventricular dimensions were reduced by 13% during diastole ($p = 0.0072$) and 22% during systole ($p = 0.0006$), highlighting Xolatryp's role in preventing harmful stretching of the heart muscle.

- Xolatryp also increased left ventricular posterior wall thickness by 25% (p = 0.0346), reinforcing the structural integrity of the heart and potentially improving resilience against further injury.
- The levels of three key blood biomarkers that elevate in response to ischemia-reperfusion injury to the heart were assessed. Xolatryp reduced the levels of AST by 42% ($p < 0.05$), LDH by 45% (p = 0.0285) and Troponin I by 32% (ns due to low sample size).

Currently, no FDA-approved therapies specifically target ischemia-reperfusion injury. The results further validate Xolatryp's effectiveness in addressing ischemia-reperfusion injury related to heart attacks, enhancing the company's potential to fill this critical treatment gap.

Rat Heart Sample Images

The images below depict sections of rat heart tissue from four groups: normal, damaged from ischemia-reperfusion, Xolatryp-treated, and Captopril-treated (current standard therapy) for visual comparison. Red-stained areas represent metabolically active tissue, while grey-stained areas indicate dead tissue. These images clearly demonstrate that damaged heart tissue treated with Xolatryp showed significantly better outcomes compared to both the control and Captopril-treated groups.

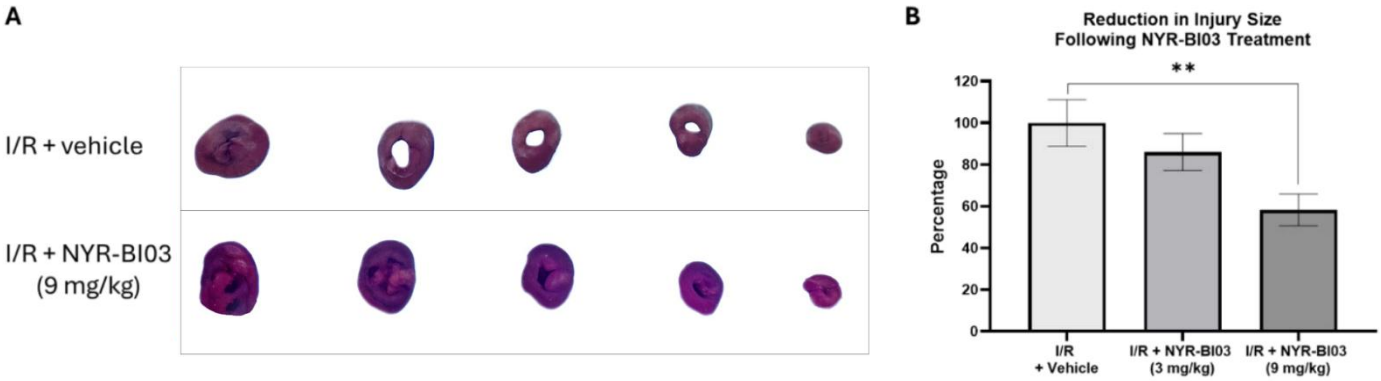
Source: Nyrada Inc

Preclinical Cardiac Arrhythmia Study

On 8 May 2025, Nyrada released results of a preclinical study in rats, which showed that the company's Xolatryp drug provides strong cardioprotection when administered as a short-duration intravenous infusion following myocardial infarction (heart attack). The study showed that Xolatryp provided 42% cardioprotection when administered continuously for 3 hours. This latest study builds upon the company's previous preclinical study in October 2024, and showed significant reductions in both heart muscle injury size and Troponin I, a key cardiac injury biomarker.

This study also showed that animals treated with Xolatryp had reduced incidence of ventricular arrhythmias (a condition where the heart beats at an irregular or abnormal rate, too fast, too slow, or with an irregular rhythm), which is a leading cause of sudden cardiac death following a heart attack. Animals treated with Xolatryp had an 88% reduction in ventricular arrhythmias at 1 hour and a 90% reduction at 3 hours (p = 0.04 at 1 hour and p = 0.01 at 3 hours, less than 0.05 is statistically significant).

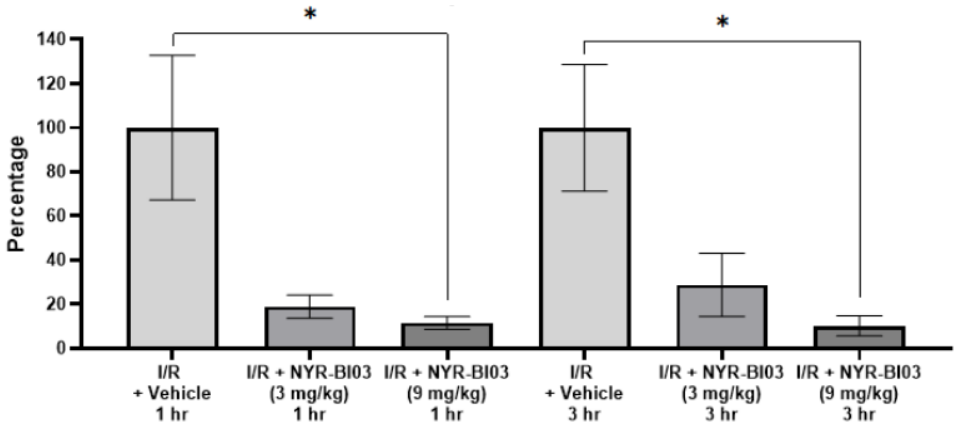
A dose-dependent reduction in heart injury was observed following Xolatryp treatment



Source: Nyrada Inc

The study utilised the same rodent model from the October 2024 study, but the animals were administered at doses of 9.0 mg/kg of Xolatryp over 3 hours following acute myocardial ischemia (occurs when the heart muscle doesn't get enough blood and oxygen due to restricted blood flow which can lead to a heart attack). Cardioprotection was confirmed with a short duration treatment compared with vehicle (placebo) with a 42% reduction in tissue death following heart attack (p = 0.008, less than 0.05 is statistically significant). This result is highly significant because it shows that the drug works over a shorter time period compared to the previous study, which involved administration over 24 hours.

Reduction of Ventricular arrhythmias following heart attack



Source: Nyrada Inc

Limited Competition in the Cardioprotection Market

Our analysis identified only one notable competitor to NYR in the cardioprotection market: Infensa Bioscience, an Australian biotechnology company. Infensa is developing a novel class of inhibitors derived from spider venom, designed to protect the heart and brain following stroke and myocardial infarction. These inhibitors function by blocking acid-sensing ion channel 1a (ASIC1a), a key driver of acid-induced cell death in both cardiac and neural tissues. Currently, Infensa remains in the preclinical stage of development.

The scarcity of competitors in the cardioprotection space underscores both the novelty and potential value of NYR's lead candidate, Xolatryp. With few alternative treatment options in development, NYR is well-positioned to capitalise on this emerging market and establish a competitive advantage in addressing a critical unmet medical need.

NEUROPROTECTION PROGRAM

Program Overview

Nyrada's lead candidate for its Brain Injury Program, Xolatryp, is a Transient Receptor Potential Canonical (TRPC) ion channel blocker with a novel mechanism of action designed to provide neuroprotection for stroke and traumatic brain injury (TBI) patients.

TRPC channels, located in cell membranes, regulate non-selective positive ion flow, influencing neuronal excitability, neurotransmitter release, and gene expression. Overactivation of these channels during neuronal injury leads to calcium overload, a key factor in cell death and brain damage. By blocking TRPC channels, Xolatryp aims to prevent excessive calcium influx, protecting neurons and mitigating the severity of brain injury in stroke and TBI.

Preclinical Stroke Study

In early 2024, Nyrada commenced a preclinical study on Xolatryp to assess its effectiveness in preventing secondary brain injury after a stroke. The company announced on 28 February 2024 that the study demonstrated significant neuroprotection, with Xolatryp reducing secondary brain injury in the penumbra region by an average of 42% (p = 0.0213).

The study, conducted in collaboration with UNSW Sydney, used a photothrombotic stroke model in test animals. Treatment with Xolatryp began 30 minutes post-injury and continued via intravenous infusion for 72 hours. MRI analysis confirmed the drug's efficacy, with no adverse effects observed. Currently, no FDA-approved treatments exist for secondary brain injury, highlighting Xolatryp's promising potential.

Good Laboratory Practice (GLP) Studies

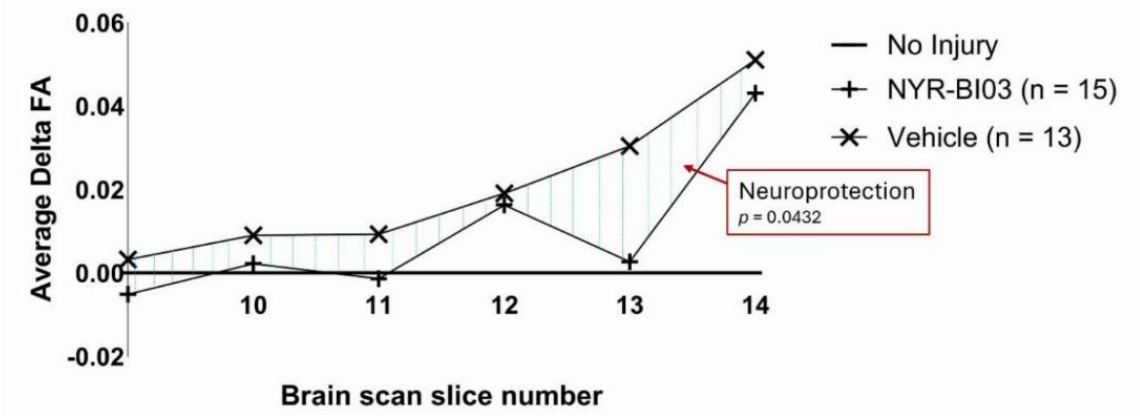
Following the preclinical stroke study results reported in February 2024, NYR commenced Good Laboratory Practice (GLP) studies in late March 2024 to assess the preclinical safety and toxicology of Xolatryp, a critical step necessary to progress to human studies. GLP studies typically involve two animal species to ensure reliable and consistent data. Nyrada selected rats and dogs to compare safety profiles, enhancing confidence in human applicability. A total of 8 studies were conducted, with the results from the final study being announced on 16 October 2024. Following the conclusion of the GLP safety studies, on 31 December 2024, NYR announced the submission of its Phase I first-in-healthy human volunteer clinical trial regulatory package for review by the Human Research Ethics Committee (HREC). HREC approval was received on 7 February 2025.

Preclinical Walter Reed TBI Study

In 4Q FY24, NYR commenced a collaborative TBI study with the Walter Reed Army Institute of Research (WRAIR) and UNSW Sydney. The study evaluated the neuroprotective efficacy of Xolatryp in a preclinical model using WRAIR's proprietary rodent model, designed to replicate severe head injuries experienced by military personnel. The study evaluated 28 test animals that received a continuous intravenous infusion of either Xolatryp or a vehicle control over 48 hours. In line with NYR's previous preclinical stroke research, UNSW performed high-resolution magnetic resonance imaging (MRI) using its advanced small animal imaging facility to assess brain tissue integrity.

On 7 April 2025, NYR announced that its study demonstrated strong neuroprotective effects of Xolatryp in reducing secondary TBI. Using a validated WRAIR model, animals treated with Xolatryp showed statistically significant improvements (p = 0.043 via ANOVA) compared to those receiving a vehicle control. Advanced MRI analysis across six consecutive brain sections near the injury site revealed that the treated group maintained tissue integrity closer to that of uninjured brains. This was measured by comparing the deviation in fractional anisotropy (delta FA), with values closer to zero indicating less damage.

Brain tissue treated with Xolatryp preserved its integrity, closely resembling that of healthy, uninjured tissue



Source: Nyrada Inc

Neuroprotection Market Landscape Presents Significant First-Mover Advantage

The neuroprotection market remains largely underdeveloped, with no existing FDA-approved treatments for mitigating secondary brain damage following TBI or stroke. Despite the significant unmet clinical need, only a handful of companies are actively pursuing neuroprotective therapies, reinforcing NYR's strong positioning in this emerging market. One such competitor is Argenica Therapeutics Limited (AGN:ASX), an Australian biotechnology company focused on reducing brain tissue death after stroke and other neurological injuries. Its lead candidate, ARG-007, a peptide-based therapy for acute ischemic stroke, is currently undergoing a Phase II clinical trial.

Similarly, Astrocyte Pharmaceuticals, a U.S.-based biotech, is developing small-molecule neuroprotective therapies for TBI, stroke, concussions, and neurodegenerative diseases. Its lead candidate, AST-004, is in Phase I human safety trials. Another player in the space is Cellvation Inc, a clinical-stage biopharmaceutical company developing CEVA-102, a cellular therapy targeting neuroinflammation associated with TBI. CEVA-102 remains in preclinical development.

The limited number of competitors highlights the significant white-space opportunity in neuroprotection, where NYR is well-positioned to become a first mover. With few companies actively developing treatments and no approved standard of care, NYR's innovative approach has the potential to establish a foothold in this market.

CLINICAL TRIALS

Phase I Clinical Trial

Overview. The study, which commenced in March 2025, aims to evaluate the safety, tolerability, and pharmacokinetics of Xolatryp. The study is a randomised, placebo-controlled trial which initially comprised five cohorts, each consisting of eight healthy volunteers - six receiving the active drug and two receiving a placebo. Dosing began at low concentrations, with dosage levels gradually increasing in subsequent cohorts. Participants received an intravenous dose of Xolatryp or placebo over three hours, followed by a 48-hour monitoring period for safety assessments and pharmacokinetic blood sampling. NYR's trial site operator, Scientia Clinical Research, managed participant recruitment.

Cohort Dosage. On 31 March 2025, NYR announced that the first cohort of participants in its Phase I clinical trial had been dosed and discharged. Two sentinel participants were dosed initially, one receiving Xolatryp and the other receiving a placebo. Sentinel dosing is a standard safety measure incorporated in first-in-human trials. Following a review of safety data from these initial sentinel doses, the remaining participants in the cohort were subsequently dosed. In total, six participants received Xolatryp and two received a placebo in this double-blind, randomised, placebo-controlled, dose-escalation study. All doses, whether active treatment or placebo, were administered via a three-hour infusion.

Clinical Trial Protocol Amendment. On 4 June 2025, following the successful dosing of cohort 3, NYR announced that it had received approval from the HREC to amend the Phase I clinical trial protocol. The modifications allowed the evaluation of a higher dosage and extended treatment duration, reflecting the strong safety and tolerability profile observed across all cohorts dosed thus far. As a result, the Phase I study was expanded to include six cohorts.

Completion of Dosage. On July 21, 2025, NYR announced the successful completion of dosing across all six cohorts in its ongoing clinical trial. Progress remained consistent throughout the study, with the Safety Review Committee (SRC) authorising advancement through each cohort following favourable safety and pharmacokinetic assessments. Notably, no safety signals, dose-limiting toxicities, or unexpected adverse events have been reported to date. A comprehensive safety and pharmacokinetic review will be conducted by the SRC once all data is available. All the data will then be analysed in preparation for the final clinical study report, expected in the coming months.

Strategic Refocus

Xolatryp has demonstrated strong preclinical efficacy across three key indications: stroke, TBI, and acute myocardial infarction (AMI). While academic studies suggest broader therapeutic potential, NYR has opted to concentrate its efforts on cardioprotection. This decision is driven by the robust preclinical cardiac data and the limited availability of non-dilutive funding for TBI in the U.S. Accordingly, the company will direct the majority of its financial and human resources toward advancing Xolatryp's development in cardioprotection.

Concurrently, Nyrada remains committed to progressing its stroke and TBI programs. The company will also continue to evaluate new pipeline opportunities and pursue non-dilutive funding avenues in Australia, the U.S., and other key markets.

Phase II Trial

Overview. With the Phase I trial of Xolatryp nearing completion, on 23 July 2025, NYR announced its commitment to a Phase IIa clinical trial. The Phase IIa trial design seeks to evaluate Xolatryp as a first-in-class intravenous therapy to limit heart muscle damage and prevent arrhythmias during ischemia and after reperfusion in patients with ST-Elevation Myocardial Infarction (STEMI) that undergo Percutaneous Coronary Intervention (PCI).

Study Design. NYR's planned Phase IIa trial will enrol up to 150 STEMI patients in Australia to assess two dosage levels of Xolatryp, administered via infusion for up to six hours. The trial is expected to begin in Q1 2026, pending completion of the ongoing Phase I study and HREC approval.

The primary endpoint is safety, with secondary endpoints focused on early signals of functional cardiac outcomes. These are supported by strong preclinical data, GLP-compliant safety and toxicology studies, and encouraging results from Nyrada's near-complete Phase I trial in healthy volunteers. The company is currently finalising the Phase IIa design and will provide further details once cost estimates are confirmed.

MARKET OVERVIEW

Stroke Market

Each year, 15 million people worldwide experience a stroke, with 5 million losing their lives and another 5 million left permanently disabled, creating significant challenges for families and communities[1]. Despite the apparent need for effective treatments, there is only one approved drug class for stroke suitable for <15% of patients, which is tissue plasminogen activator (tPA). Driven by innovation in treatment options, the global stroke treatment market is expected to grow at a 7.5% CAGR to US$58.09 billion in 2031 from US$32.57 billion in 2023[2].

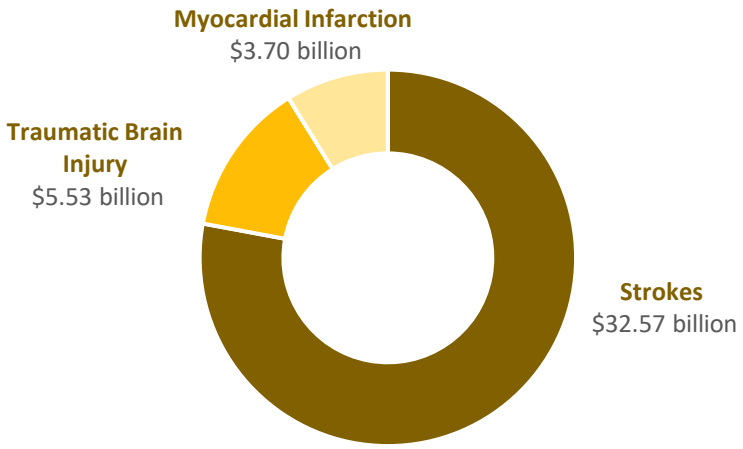
Traumatic Brain Injury Market

An estimated ~5.5 million people are suffering severe TBI annually, with ~55 million living with the effects of medically treated TBI[3]. It is clear that effective treatment can significantly enhance patient outcomes and lower the substantial costs linked to the long-term care of brain injury survivors. However, there is currently no FDA-approved treatment available on the market. Continued advancements in available treatments are expected to drive the growth of the global TBI treatment market from US$3.46 billion in 2022 to US$5.53 billion in 2030[4].

Myocardial Infarction Market

Globally, 15-20 million people suffer myocardial infarction annually, with a 15% mortality rate within 30 days[5]. Among survivors, 20-30%—particularly those experiencing cardiac arrest—develop acquired brain injury due to oxygen deprivation during arrest and reperfusion injury post-resuscitation. This leads to cognitive, neurological, or motor impairments, creating a significant unmet need. The market for myocardial infarction therapies, projected to reach US$3.7 billion by 2032, offers substantial growth potential. Xolatryp, targeting brain injury post-myocardial infarction, represents a transformative opportunity to address this gap, improve patient outcomes, and reduce long-term disability burdens.

Xolatryp is capitalising on a total market opportunity that is expected to reach US$41.8 billion in 2032



Source: See footnotes 2, 4 and 5

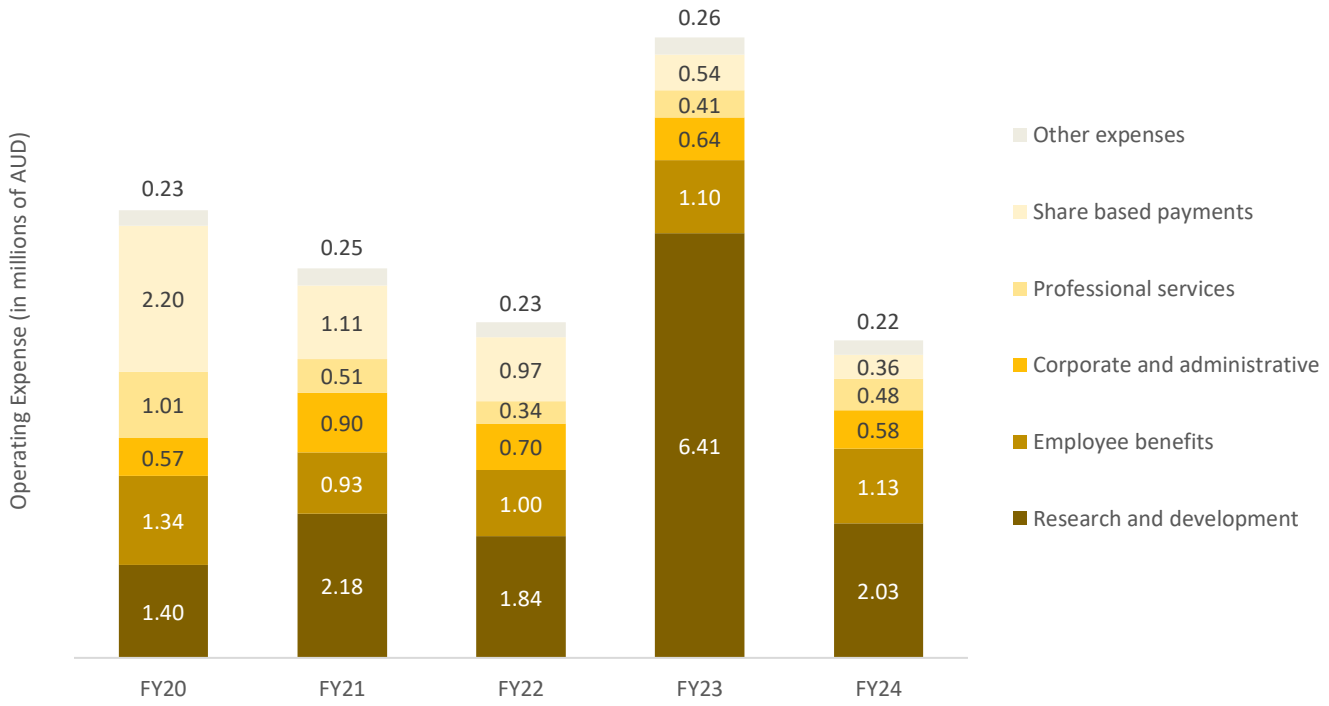
[1] World Health Organisation - Stroke, Cerebrovascular accident
[2] Data Bridge Market Research - Global Stroke Market Size, Share, and Trends Analysis Report
[3] National Academies of Sciences, Engineering and Medicine – Traumatic Brain Injury
[4] Global Traumatic Brain Injuries Treatment Market – Industry Trends and Forecast to 2030
[5] Spherical Insights - Global Myocardial Infarction Market Size To Grow USD 3.7 Billion By 2032

FINANCIAL OVERVIEW

Financial Performance

In FY24, NYR's operating expenses totalled A$4.8m, marking a substantial 49% decrease from A$9.4m in FY23. Of this, A$2m (42%) was allocated to R&D activities, primarily focused on preclinical studies exploring the cardio and neuroprotective potential of Xolatryp. This R&D expenditure represented a significant drop compared to A$6.4 million in FY23. Employee-related costs remained a key expense category, with A$1.2m spent on employee benefits and A$358,000 on share-based payments. Notably, NYR's operating expenses in FY24 were largely offset by a surge in R&D grant revenue, which increased to A$3.2m from A$1.4m in the previous year.

NYR's operating expenditure has continued to moderate whilst investment in R&D activities has remained strong



Source: Nyrada Inc

With NYR set to commence clinical trials for Xolatryp in the second half of FY25, we anticipate the company will allocate a significant portion of its operating expenses to research and development. We also expect the company to continue to efficiently recoup its investments in R&D activities through claiming government R&D incentives.

Financial Position

In the latest quarter, Q3 FY25, NYR had a cash balance of ~A$2.9m and no debt on its balance sheet. This implies that the company has a strong net cash position of ~A$2.9m. In the past 4 quarters, NYR has had a quarterly operational cash burn of ~A$1.57m, excluding cash received from government grants and tax incentives. Including cash received from R&D grants, NYR's quarterly cash burn is significantly lower at A$1.26m. We believe that the cash balance held by NYR should give the company approximately 9 months of operational runway.

Corporate Structure

NYR currently has 210.3 million CHESS Depositary Interests (CDIs) outstanding, which, at a price of A$0.37, results in a market capitalisation of ~A$78.0m. With A$2.9m in cash and no debt, the company's enterprise value stands at A$80.97m.

In AUD	
Market Capitalisation	$78,039,304
CDIs on Issue	210,917,037
Debt	-
Cash	$2,931,000
Enterprise Value	$75,108,304

BOARD OF DIRECTORS

John Moore (Non-Executive Chair)

John Moore is an experienced executive with a diverse background in leadership roles across various industries. John's prior experience includes serving as CEO of Acorn Energy from 2006 to 2015. During his tenure, the CoaLogix business was acquired for US$11m and later sold for US$101m. Additionally, the Comverge business was listed in the US before being sold to Constellation Energy. Prior to Acorn Energy, John was a Partner and CEO of Edson Moore Healthcare Ventures, where he oversaw the acquisition of sixteen drug delivery investments from Elan Pharmaceuticals for US$148m. John holds a Bachelor of Arts from Rutgers University in the US.

Christopher Cox (Non-Executive Director)

Christopher Cox is a Co-Founder and Managing Partner of Population Health Partners since April 2020. He is also a Senior Attorney and retired Partner at Cadwalader, Wickersham & Taft LLP, where he led the Corporate Department and served on the Management Committee. With expertise in mergers and acquisitions, restructurings, spin-offs, and complex financing, Chris was seconded from 2016 to 2019 to The Medicines Company as Executive Vice President and Chief Corporate Development Officer, overseeing business development and strategy. Earlier in his career, he was a partner at Cahill Gordon & Reindel LLP. Currently, Chris is the CEO of Symphony Capital Holdings, LLC, a private investment firm with interests in biotechnology, network security, and entertainment.

Rüdiger Weseloh Ph.D (Non-Executive Director)

Rüdiger Weseloh is the Executive Director of Business Development at EMD Serono, Inc. in Rockland, MA, USA. Over his 18-year tenure, he has led more than 80 transactions for the healthcare division of its parent company, Merck KGaA, Darmstadt, Germany. His deal-making expertise spans the entire drug development value chain, with a focus on oncology, rheumatology, neurodegenerative diseases, and fertility. Prior to joining Merck KGaA, Rüdiger spent five years as a Biotech and Pharma Equity Analyst at Gontard & Metallbank AG in Frankfurt and Sal. Oppenheim in Cologne/Frankfurt. Earlier in his career, he conducted three years of postdoctoral research at the Max Planck Institute for Experimental Medicine in Göttingen. Additionally, he served for five years on the Supervisory Board of Cytotools AG in Freiburg, Germany.

Marcus Frampton (Non-Executive Director)

Marcus Frampton is the Chief Investment Officer of the Alaska Permanent Fund Corporation (APFC), a US$80 billion sovereign wealth fund for the State of Alaska. In this role, he oversees APFC's investment team and leads all portfolio investment decisions within the strategic framework set by the Board of Trustees.

Frampton joined APFC in 2012, bringing a diverse background in investment banking, private equity, and asset management. He began his career as an Investment Banking Analyst and Associate at Lehman Brothers (2002–2005) before transitioning to private equity investing at PCG Capital Partners (2005–2010). He later served as an executive at LPL Financial, a private equity-backed portfolio company, from 2010 to 2012.

Dr Gisela Mautner (Non-Executive Director)

Gisela Mauntner is a seasoned international business leader with extensive experience in pharmaceutical product development, corporate strategy, and commercial execution in competitive global markets. She currently serves as CEO and Managing Director of Noxopharm Ltd (ASX:NOX). Throughout her career, Gisela has held senior roles at Amgen, Bayer, Siemens Medical Solutions, and Merck/MSD, driving both commercial and scientific success. She has a strong global network in the pharmaceutical industry and has held key leadership positions within the Australian Pharmaceutical Physicians Association (APPA, now MAPA), including President, Vice President, and Treasurer. She also represents Australia in the International Federation of Associations of Pharmaceutical Physicians (IFAPP).

Dr Ian Dixon (Non-Executive Director)

Dr Dixon holds a PhD in biomedical engineering from Monash University and an MBA from Swinburne University. He brings extensive technical and entrepreneurial expertise in founding, scaling, and managing technology-driven companies, with a strong focus on the commercial potential and challenges of early-stage drug development. In 2011, he co-founded Cynata Inc., now a subsidiary of ASX-listed Cynata Therapeutics Ltd (ASX: CYP), which is advancing the Cymerus stem cell therapy for conditions such as osteoarthritis, ARDS, and critical limb ischemia.

KEY MANAGEMENT PERSONNEL

James Bonnar (Chief Executive Officer)

James brings over 25 years of global experience in the Life Sciences industry, including preclinical research, clinical operations management, CMC (Chemistry, Manufacturing and Controls), Regulatory Affairs, and Quality Assurance. Before joining Nyrada, James was at Neuren for eleven years across various roles, including as the Director – Clinical Operations, where he oversaw clinical development for drugs in the areas of TBI and neurodevelopmental disorders. Prior to that, he worked in diabetes research, GMP manufacturing, and drug formulation development.

Dr Benny Evison Ph.D. (Chief Scientific Officer)

Benny brings to Nyrada expertise in advancing drug compounds from the discovery phase into clinical trials in humans. After earning a Bachelor of Medical Science with Honours and a PhD from La Trobe University, his doctoral research identified a novel mechanism of action for Pixantrone, a drug used to treat non-Hodgkin's lymphoma. Seeking international experience, Benny became a postdoctoral fellow at St. Jude Children's Research Hospital in Memphis, where his work on DNA repair-targeting drugs enhanced chemotherapy effectiveness. Inspired by his time with critically ill children, he returned to Australia as one of Nyrada's founding scientists, driving impactful research and development.

INVESTMENT THESIS

Clear Business Strategy

Nyrada is focused on drug discovery and developing innovative new treatments for which there is a large unmet clinical need and substantial market potential. The company aims to develop best-in-class drugs focusing on neuroprotection (TBI) and cardioprotection (MIRI). Nyrada's lead drug candidate – Xolatryp – has demonstrated strong preclinical efficacy in protecting the brain from secondary injury following stroke, in addition to strong

preclinical efficacy in protecting the heart following acute MIRI. The ability to leverage two applications from one drug candidate places Nyrada in a strong position to ensure commercial success via an economical and efficient pathway.

Nyrada has a well-defined strategy to maximise the value of its drug development pipeline through targeted out-licensing. Importantly, Nyrada's business model allows for licensing agreements based on specific indications and geographic markets, creating a flexible and scalable path to commercialisation. By pursuing this approach, Nyrada can leverage partnerships with larger pharmaceutical companies to handle manufacturing and distribution, enabling a capital-efficient strategy to monetise its R&D investments while focusing on further innovation.

High Barriers to Entry

The high barriers to entry in the markets NYR is targeting are illustrated by the presence of only 3 other competitors in the neuroprotection market and none in the cardioprotection market. This scarcity of competing development programs likely reflects both the scientific complexity of the field and the innovative nature of NYR's approach. The company's advanced position in this nascent space could translate into significant first-mover advantages and potential market exclusivity, pending successful clinical development.

The success of recent preclinical studies, such as the 2024 stroke and coronary heart disease trials, further underscores the efficacy of Xolatryp in providing neuroprotection and cardioprotection. This expanding body of evidence enhances Nyrada's intellectual property position by highlighting the distinctiveness and therapeutic potential of its compounds. Additionally, the nearly complete Phase I clinical trial is expected to yield further supportive data, which could form the basis for future patent applications.

During the first half of FY25, NYR submitted 'Composition of Matter' patent applications in key geographies, including Australia, Europe, and North America, to safeguard the chemical structure of its TRPC channel-blocking intellectual property. Once granted, these patents will ensure that NYR retains exclusive rights to its TRPC assets for at least 20 years from the submission date.

Expanding its patent portfolio in this manner will be critical to maintaining Nyrada's competitive advantage and securing long-term commercial opportunities in these high-value therapeutic areas.

Successful Management

The Nyrada Board and management team include leading figures in biotech, both here in Australia and the US, who have a proven track record of success in commercialising innovative technology. Nyrada's CEO, James Bonnar, a chemist by training, brings 25 years of broad professional experience in the biotech industry. He has worked in preclinical drug development, product manufacturing, regulatory affairs, and clinical-stage drug research, most recently for Neuren, overseeing the development of treatments for TBI and neurodevelopmental disorders.

The Nyrada Board is a diverse mix of successful international entrepreneurs and dealmakers with proven track records in the pharmaceutical industry. Christopher Cox was the Chief Commercial Officer for The Medicines Company which developed the cholesterol-lowering drug Inclisiran®, a program that was acquired by Novartis in late 2019 for US$9.7B. At the time, it was the largest ever acquisition of a company with a single drug in development. Chris has extensive industry contacts, and this is an obvious benefit for Nyrada.

Marcus Frampton is the CFO for the largest sovereign wealth fund in the US, the Alaska Permanent Fund, and has a proven record in identifying and backing successful biotech companies. Companies they have supported include Juno Pharmaceuticals, an Australian company focused on the supply of off-patent drugs to hospitals. Dr. Rüdiger Weseloh works in commercial development for Merck KGA in Germany so he has a lot of experience negotiating and securing deals with pharmaceutical companies.

Nyrada's Scientific Advisory Board comprises some of the world's most respected scientific thought leaders from Australia, the US, France, and Japan. The Chair of the board, Prof. Gary Housley, is the Chair in Physiology at the

University of New South Wales Sydney (UNSW) and is a founding director of the Translational Neuroscience Facility and has over 30 years of experience. Prof. Junichi Nabekura and Dr. Jim Palmer bring expertise in cardiovascular, neuroscience, and drug discovery programs, respectively.

Significant Investment Upside

At a market capitalisation of just A$78.0m, NYR appears significantly undervalued relative to its clinical progress, having successfully advanced through Phase I cohort dosage and now positioned to initiate Phase IIa trials. Furthermore, the neuroprotection and cardioprotection markets represent substantial, unmet medical needs, as there are currently no FDA-approved drugs with proven efficacy in these therapeutic areas. This positions NYR as a potential first mover, offering a meaningful competitive advantage over the limited number of players in the space. As the company progresses through clinical milestones and demonstrates further proof of concept, we anticipate that investor sentiment will shift, driving a revaluation of NYR's stock.

INVESTMENT RISKS

Clinical Development Risks

Nyrada's success heavily depends on the clinical progression of its lead candidate, Xolatryp. While preclinical studies have shown promising efficacy in neuroprotection and cardioprotection, and Phase I clinical trials have demonstrated Xolatryp's safety and tolerability thus far, there is no guarantee that these results will translate into regulatory approvals. The drug must demonstrate both safety and efficacy in upcoming Phase II and III trials before regulatory approval can be secured. Any failure, delay, or unexpected adverse effects in these trials could significantly impact the company's valuation and future prospects.

Availability of Funding

Nyrada is an early-stage biotechnology company with no commercialised products or revenue streams. Its financial position relies on external funding sources, including grants and potential equity raises. If funding is not secured on favourable terms, it could impact Nyrada's ability to execute its clinical development plans. However, the company currently has approximately 9 months of operational runway with A$2.9m in cash. We believe this level of runway will provide significant support for the upcoming Phase IIa clinical trial, a key milestone that could significantly enhance investor confidence and market valuation. Successful trial results would likely improve Nyrada's ability to secure additional funding on favourable terms, minimising shareholder dilution while ensuring continued progress through subsequent clinical phases.

Regulatory and Approval Risks

Following successful clinical trials, Xolatryp must navigate rigorous regulatory pathways in multiple jurisdictions, including approvals from the FDA and the Australian Therapeutic Goods Administration (TGA). Any setbacks in securing approvals could delay commercialisation and increase development costs.

However, Xolatryp is targeting conditions with significant unmet medical needs and no existing FDA-approved treatments, which may facilitate a more favourable regulatory pathway. Additionally, the strong preclinical efficacy and safety data provide a solid foundation for advancing into human trials. As the company progresses through clinical stages, further validation of Xolatryp's therapeutic potential will be critical in strengthening its regulatory submissions and increasing the likelihood of timely approvals.

Nyrada Inc is a Canary Capital-mandated company. Canary Capital Pty Ltd, its directors and associates own CDIs and options in Nyrada Inc.

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