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Sydney, Australia

Supplementary NYR-BI03 Studies Confirm Strong Cardioprotection

Highlights:

- Nyrada successfully completes supplementary preclinical studies, further supporting NYR-BI03's efficacy in treating ischemia-reperfusion injury associated with heart attack.
- Echocardiography assessment showed significant improvements in heart function and structure following NYR-BI03 treatment.
- Blood biomarkers of injury also showed significant improvements following NYR-BI03 treatment.
- No FDA-approved drugs specifically target ischemia-reperfusion injury, highlighting a significant unmet clinical need.
- Global market for myocardial infarction therapies to reach US\$3.7 billion by 2032¹.
- Phase I clinical trial for NYR-BI03 scheduled to commence in late 2024.

Nyrada Inc (ASX:NYR), a drug discovery and development company focused on innovative Transient Receptor Potential Canonical (TRPC) ion channel blockers, is pleased to announce the results from supplementary preclinical studies confirming its lead drug candidate, NYR-BI03 prevents loss of function resulting from myocardial ischemia-reperfusion (IR) injury following myocardial infarction (heart attack) in rats.

As [announced on 1 October 2024](#), in addition to its neuroprotection potential, NYR-BI03 has demonstrated the potential to address an additional critical unmet need in myocardial infarction treatment and improve patient outcomes. As previously reported, NYR-BI03 provided an 86% cardioprotective effect in a rat study, significantly reducing infarction, or heart tissue damage, following myocardial ischemia-reperfusion injury.

The supplementary studies announced today, utilising echocardiography, further reinforce the potential of NYR-BI03 to address this critical unmet need. In these supplementary studies:

- NYR-BI03 delivered a **substantial 43% increase in left ventricular ejection fraction** ($p < 0.0001$)², a key indicator of heart pumping ability, significantly improving overall cardiac function.
- A **50% increase in fractional shortening** ($p = 0.0002$)² was observed, indicating NYR-BI03 preserved the heart's contractile strength and prevented damage to the left ventricle.

¹ Spherical Insights, *Myocardial Infarction Market Report*.

² p value calculated using one-way ANOVA with a Holm-Sidak post-hoc analysis.



- **Left ventricular dimensions** were reduced by **13% during diastole** ($p = 0.0072$)² and **22% during systole** ($p = 0.0006$)², highlighting the NYR-BI03's role in preventing harmful stretching of the heart muscle.
- NYR-BI03 also increased **left ventricular posterior wall thickness by 25%** ($p = 0.0346$)², reinforcing the structural integrity of the heart and potentially improving resilience against further injury.
- The levels of three key blood biomarker markers that elevate in response to ischemia-reperfusion injury to the heart were assessed. **NYR-BI03 reduced the levels of AST by 42%** ($p < 0.05$)³, **LDH by 45%** ($p = 0.0285$)⁴ and **Troponin I by 32%** (ns due to low sample size).

Nyrada CEO James Bonnar commented: "The confirmation of significant cardioprotective effects from NYR-BI03 in preclinical studies represents another milestone for Nyrada. Heart attacks affect 15-20 million people globally each year, with up to 15% mortality within 30 days due to complications like heart failure. Additionally, up to 50% of heart tissue damage is caused by reperfusion injury, where restoring blood flow after a heart attack paradoxically causes further damage to the heart.

"The substantial improvements in heart function and structure shown in these supplementary studies are particularly encouraging as there are currently no FDA-approved therapies targeting ischemia-reperfusion injury.

"We are excited to advance NYR-BI03 into clinical trials and believe it has the potential to transform the standard of care for heart attack survivors."

Ischemia-Reperfusion Injury Market

Approximately 20-30% of patients who survive a heart attack, particularly those experiencing cardiac arrest, face some form of acquired brain injury. This occurs due to a lack of oxygen reaching the brain during cardiac arrest followed by reperfusion injury when blood flow is restored after resuscitation. This combination can result in cognitive, neurological, or motor function impairments.

NYR-BI03 has unique potential to fill this treatment gap by offering dual protection for both the heart and [brain from ischemia-reperfusion damage](#), helping prevent heart failure and neurological damage.

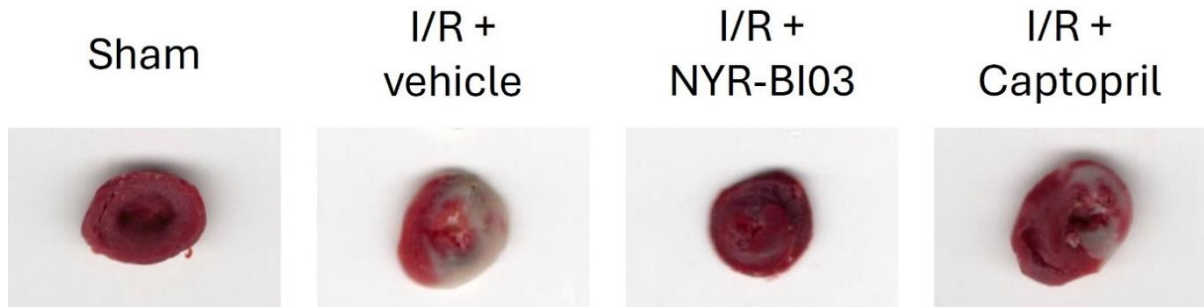
With a large unmet medical need and a market projected to reach US\$3.7 billion by 2032, NYR-BI03 represents a transformative opportunity in myocardial infarction therapy.

³ non-parametric t-test on ranked data between injury + vehicle and injury + NYR-BI03

⁴ t-test between injury + vehicle and injury + NYR-BI03



Rat Heart Tissue Samples Images



The above images show sections of rat heart tissue from sham (normal), injury plus vehicle (damaged), NYR-BI03 treated (protected), and injury plus Captopril (existing therapy) groups for visual comparison. Red and grey stained areas of the heart tissue indicate metabolically active and dead, respectively. The images visually highlight that outcomes for NYR-BI03 treated animals were superior to control and Captopril treated animals.

Looking ahead, Nyrada is preparing to begin a [Phase I clinical trial of NYR-BI03](#), with the study expected to commence by the end of 2024, subject to Human Research Ethics Committee (HREC) approval. This trial will assess the safety, tolerability, and pharmacokinetics of NYR-BI03 in healthy volunteers and provide crucial data to support both its cardioprotection and neuroprotection programs. The trial will run through 2025.

Glossary of Terms

Left ventricular ejection fraction is a measure of how well the heart is pumping blood, reflecting what percentage of blood is being pushed out of the heart's main pumping chamber (the left ventricle) with each heartbeat. If the ejection fraction is low, it means the heart is not pumping as effectively, which can be a sign of heart disease or damage, like after a heart attack. It is a key indicator of overall heart function.

Fractional shortening is a measure of how well the heart is pumping. It looks at how much the heart's main pumping chamber (the left ventricle) contracts during each heartbeat. In simple terms, it shows how much the heart "squeezes" to push blood out. A higher fractional shortening means the heart is pumping more effectively, while a lower value suggests the heart may be weakened or struggling to pump blood properly. It is an important indicator of heart health, especially after a heart attack or other heart conditions.

Left ventricular dimensions refer to the size of the heart's main pumping chamber, the left ventricle, both when it is relaxed (diastole) and when it is contracting (systole). These measurements reflect how well the heart is functioning.



Healthy left ventricular dimensions are key for normal heart function, and changes in these dimensions can signal heart problems or improvement in response to treatment.

- **During diastole** (relaxed state), a larger size could mean the heart is stretched out and weakened, which can happen after a heart attack or with heart disease.
- **During systole** (contracted state), a smaller dimension means the heart is effectively squeezing blood out, while a larger dimension may indicate the heart is not pumping as well as it should.

LDH: Lactate dehydrogenase, a general marker enzyme for tissue damage, found in many organs, including the heart.

AST: Aspartate transferase, an enzyme that indicates heart or liver damage.

Troponin I: Specific protein marker for heart muscle injury.

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About Nyrada Inc.

Nyrada Inc. is a 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, NYR-BI03, 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, USA, with limited liability for its stockholders.

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