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Sydney, Australia

Statistically Significant Neuroprotection Achieved in Nyrada's Preclinical Brain Injury Study

Highlights:

- Nyrada's lead Brain Injury Program drug candidate NYR-BI03 demonstrated strong efficacy in reducing injury in a preclinical study.
 - NYR-BI03 is a first-in-class therapy with a novel mechanism of action targeting significant market opportunity.
 - Supporting NYR-BI03's favourable safety profile, the current study had no drug-related adverse effects.
 - Good Laboratory Practice (GLP) safety testing to commence this current quarter.
 - Walter Reed Army Institute of Research (US Military) brain injury study to commence this current quarter.
 - Phase I clinical trial scheduled for the second half of the 2024 calendar year.
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Nyrada Inc (ASX: NYR), a drug discovery and development company specialising in novel small molecule therapeutics to treat neurological and cardiovascular diseases today announces positive results from its preclinical study evaluating the efficacy of its Brain Injury Program drug candidate NYR-BI03 in preventing secondary brain injury. The study showed a significant neuroprotective signal providing strong evidence of efficacy.

Nyrada CEO James Bonnar commented: "These study results mark a significant milestone in our Brain Injury program, providing strong evidence that our drug candidate NYR-BI03 has the potential to protect the brain from secondary injury. The magnitude of rescue achieved in this study is a compelling outcome and signals a significant therapeutic and market opportunity.

"This work is critical for our development pathway for NYR-BI03, giving us confidence as we advance it through to GLP safety and toxicology studies ahead of a first-in-human clinical trial currently planned to commence in the second half of this calendar year."



Nyrada Scientific Advisory Board Chair and Scientia Professor at UNSW Prof. Gary Housley commented: “These data on neuroprotection achieved by Nyrada’s NYR-BI03 pharmacological lead TRPC channel blocker map very well to our understanding of the substantial role of these channels in brain injury expansion. We have previously reported that transgenic animal models lacking these channels have less brain injury in the photothrombotic stroke model used here.”

Brain Injury Program

Nyrada’s Brain Injury Program is seeking to develop therapies to reduce the long-term disability associated with stroke or traumatic brain injury (TBI) by limiting the progressive cell death that occurs as secondary brain injury. Stroke and TBI are leading causes of death and disability worldwide¹.

Nyrada’s lead program candidate NYR-BI03 is a first-in-class therapy with a novel mechanism of action which limits secondary brain injury that occurs following a stroke or TBI.

NYR-BI03 has been developed to selectively block “Canonical” Transient Receptor Potential (TRPC) ion channels which are over-activated during brain trauma, causing calcium overload leading to brain cell death. At present, there are no FDA-approved drugs for the treatment of secondary brain injury.

Brain Injury Preclinical Study

Nyrada has completed a preclinical stroke study to assess the efficacy of NYR-BI03. The study showed a significant neuroprotective signal providing strong evidence of efficacy.

The study, conducted in collaboration with UNSW Sydney, involved inducing a focal ischemic stroke using a photothrombotic model² (a minimally invasive and reproducible way of inducing focal brain injury in test animals). A total of 16 test animals was treated with either NYR-BI03 or vehicle 30 minutes following the induced brain injury, with treatment conducted for 72 hours via continuous intravenous infusion.

Magnetic Resonance Imaging (MRI) was performed to quantify the brain injury in drug-treated and vehicle animals. These MRI data determined tissue damage in the penumbra region, the area of secondary brain injury that the NYR-BI03 neuroprotection drug targets.

These analyses were performed blinded, where the experimenter did not know if a particular animal received NYR-BI03 or vehicle.

¹ <https://www.nature.com/articles/s41598-024-52337-4>

² The Photothrombotic model of focal ischemia that was used in this study is described in Parmar et al. (2023) *TRPC Channels Activated by G Protein-Coupled Receptors Drive Ca²⁺ Dysregulation Leading to Secondary Brain Injury in the Mouse Model* - <https://link.springer.com/article/10.1007/s12975-023-01173-1>



Blood samples were also analysed for changes in the biomarker neurofilament light (NfL). NfL is a protein associated with neuron fibre tracts. Following a brain injury, neurons are damaged, and the NfL protein is released into the blood.

Stroke Study Results

The MRI brain imaging showed that a statistically significant (p value 0.021³) neuroprotection was achieved when animals received NYR-BI03 treatment. On average, NYR-BI03 therapy rescued 42% of the brain injury in the penumbra region seen in animals receiving vehicle.

NfL biomarker levels likely reflect this NYR-BI03 neuroprotection. The mean level for the NYR-BI03 animals was 41% lower than that of the vehicle control (p value 0.068⁴).

All animals survived the brain injury and drug treatment with no drug-related adverse effects reported. This builds upon NYR-BI03's good safety profile for continuous intravenous delivery in the sub-acute brain injury treatment interval.

Good Laboratory Practice Safety Studies

This confirmation of brain injury neuroprotection efficacy with the intended therapeutic route of administration enables the progression of NYR-BI03 to Good Laboratory Practice (GLP) studies this calendar quarter. These mandated GLP studies will assess the safety of the NYR-BI03 molecule in two animal species.

Although as part of the stroke study NYR-BI03 was shown to be well tolerated, the successful completion of a comprehensive battery of GLP studies is a necessary precondition to undertake a first-in-human clinical study (Phase I).

Walter Reed Army Institute of Research traumatic brain injury (TBI) study

Planning and preparation work for the Walter Reed TBI study has been completed. This study will assess the efficacy of NYR-BI03 in a penetrative brain injury model.

The Walter Reed study is expected to commence this calendar quarter, with the work continuing for approximately six months.

³ p value 0.021, Mann-Whitney Rank Sum Test.

⁴ p value 0.068, t-test.



Phase I Human Clinical Trial

Subject to the successful completion of GLP studies, the Company will commence a Phase I human clinical trial for NYR-BI03. The Company has already undertaken necessary planning and engaged a Contract Research Organisation for this purpose. The target commencement of a Phase I trial is the second half of the 2024 calendar year.

The data from the GLP studies and Phase I trial will support the Phase II trials of NYR-BI03 for both TBI and stroke indications.

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About Nyrada Inc

Nyrada is a drug discovery and development company specialising in novel small-molecule drugs to treat neurological and cardiovascular diseases. The Company has two main programs, each targeting market sectors of significant size and considerable unmet clinical need. These are a drug to treat brain injury, specifically traumatic brain injury and stroke, and a cholesterol lowering drug. Nyrada Inc. ARBN 625 401 818 is a company incorporated in the state of Delaware, US, and the liability of its stockholders is limited.

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