

16 June 2025 Sydney, Australia

#### **Non-Deal Investor Presentation**

**Nyrada Inc (ASX:NYR),** a clinical stage drug discovery and development company focused on innovative Transient Receptor Potential Canonical (TRPC) ion channel inhibitors provides the enclosed investor presentation in connection with a non-deal investor roadshow commencing on Monday 16 June 2025.

-ENDS-

#### **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, USA, with limited liability for its stockholders.

#### www.nyrada.com

Authorised by Mr. John Moore, Non-Executive Chair on behalf of the Board.

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# Investor Presentation

**June 2025** 

**Improving Lives, Offering Hope** 

#### **ASX:NYR**

Authorised by Mr. John Moore, Non-Executive Chair, on behalf of the Board.



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# About Nyrada

- Clinical stage drug discovery and development company focused on innovative small molecule Transient Receptor Potential Canonical (TRPC) ion channel inhibition.
- Lead drug candidate Xolatryp™ (previously known as NYR-BIO3) currently in Phase I safety and tolerability clinical trial
- Low-cost exploration for other indications.
- Lean operating model leveraging best in class third party service and research providers.
- Commercially focused business model, expert team, and impressive board with a track record of success.



# About Xolatryp™

- Third generation, small molecule TRPC ion channel inhibitor developed using rational drug design.
- > Previously known as NYR-BI03.
- Sound scientific foundation with underlying target proven in genetically modified mouse knock-out model.
- Blocks TRPC 3, 6 and 7 channels.
- Novel and well understood mechanism of action.
- Passes blood-brain barrier necessary for treatment of secondary brain injury, including following stroke and TBI.
- Protected by composition of matter patent application.



# One Drug

Xolatryp™

# Two Applications



Neuroprotection



Cardioprotection

# Three Markets



**STROKE** 

~US\$52.2 billion by 2030<sup>2</sup>

TRAUMATIC BRAIN INJURY

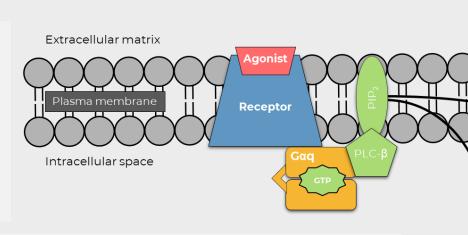
~US\$5.5 billion by 20304

**MYOCARDIAL INFARCTION** 

~US\$3.7 billion by 20325

## About TRPC Channel Inhibition

- Activation following injury results in calcium entry via TRPC ion channels
- Excessive calcium build-up leads to cell death
- Inhibiting TRPC 3/6/7 ion channels is neuro- and cardio- protective



Organ	Cell Type	TRPC Activation Effect	Xolatryp Inhibition Effect
Brain	Neurons	Calcium overload → neuron death	Reduces neuron loss, protects function
	Astrocytes	Impaired regulation → inflammation	Restores balance, reduces swelling
	Microglia	Excessive inflammation	Limits harmful immune response
Heart	Cardiomyocytes	Calcium overload → cell death, scarring	Prevents damage, improves contraction
	Endothelial	Impaired repair → poor blood flow	Enhances vessel repair, reduces inflammation
	Fibroblasts	Excessive scarring → stiff heart	Limits scarring, preserves flexibility

TRPC 3/6/7

Endoplasmic Reticulum Ca<sup>2+</sup> internal stores

## Phase I Clinical Trial

#### **Key Study Features**

- ✓ Primary Endpoints:
  - ✓ safety and tolerability of Xolatryp healthy volunteers, when administered as an intravenous infusion for up to 6 hours
- ✓ Secondary Endpoints:
  - ✓ blood pharmacokinetics of an intravenous dose of Xolatryp in healthy volunteers when administered as an intravenous infusion for up to 6 hours
- ✓ Double-blind, placebo-controlled, randomised.
- ✓ Up to approximately 48 participants (8 participants per cohort for 6 cohorts)

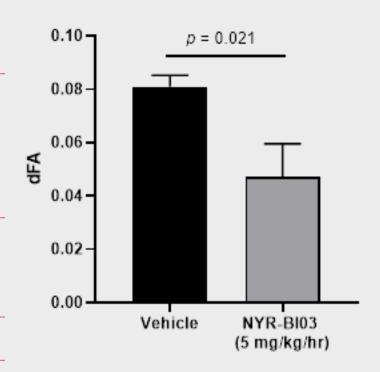
#### **Status**

- ✓ Cohort 4 (of 6) results reported.
- ✓ Cohort 5 to commence.
- ✓ Final trial results expected in quarter ending September 2025



## Ischemic Stroke

- Statistically significant neuroprotection from secondary brain injury
- MRI analysis undertaken by UNSW Sydney using a specialised technique known as fractional anisotropy (FA) to visualise structural damage in the penumbra.
- 42% neuroprotection was seen in the penumbra region of Xolatryp treated animals compared with vehicle treated animals.
- 41% decrease in NfL levels

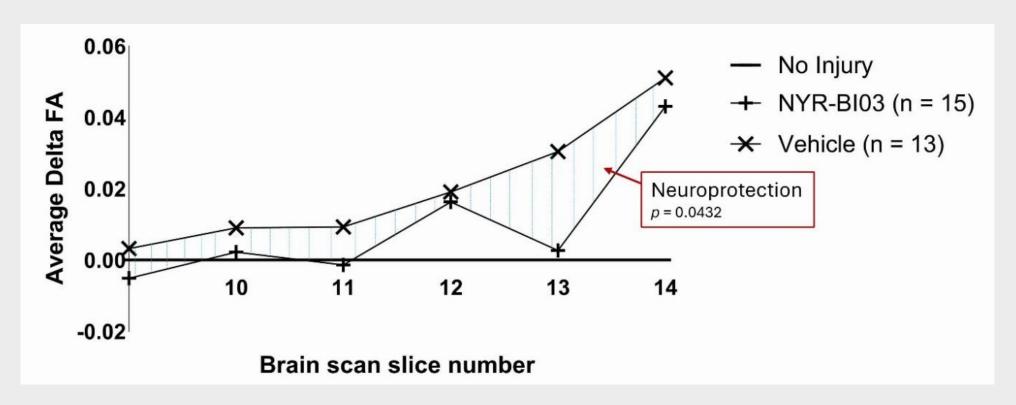




# Traumatic Brain Injury (TBI)



- Joint study with US Department of Defence (Walter Reed Army Institute of Research) and UNSW Sydney
- > Statistically significant neuroprotection



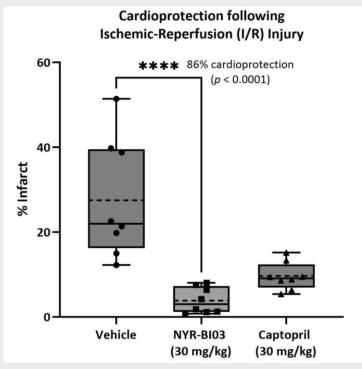




# Myocardial Infarction (1)

#### **Key Preclinical Results:**





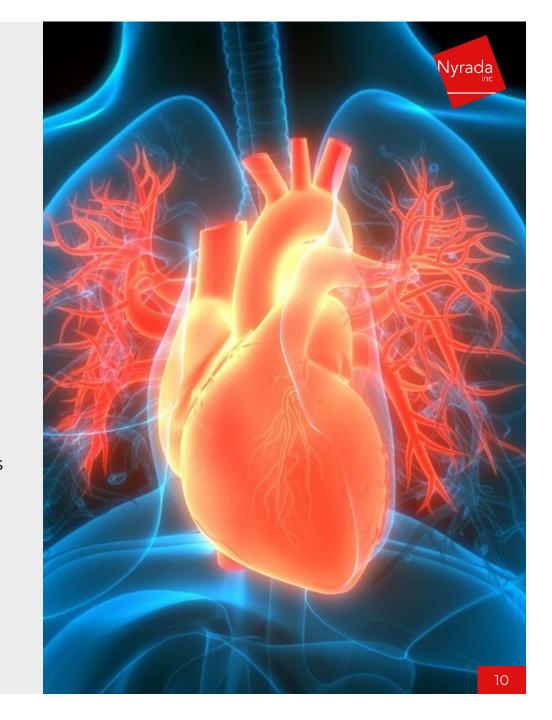
Xolatryp showed strong efficacy limiting cardiovascular damage resulting from myocardial ischemia-reperfusion (IR) injury

- 86% Cardioprotection
- 43% increase in left ventricular ejection fraction
- **50%** increase in fractional shortening

Key blood biomarker markers assessed

- 42% decrease in AST levels
- 45% decrease in LDH levels
- 32% decrease in Troponin I

**Superior efficacy** compared to FDA-approved, Captopril



# Myocardial Infarction (2)

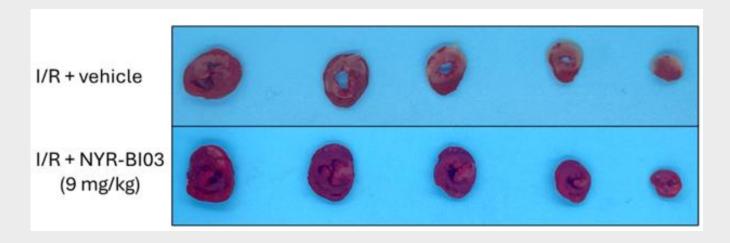
### **Key Preclinical Results:**

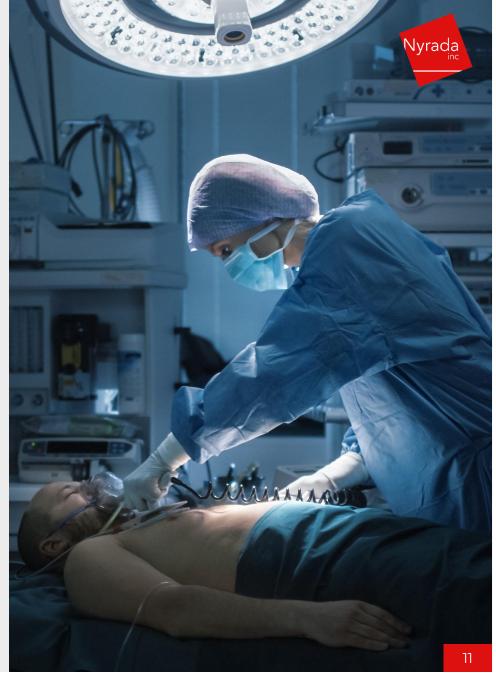
**Xolatryp** showed strong efficacy limiting cardiovascular damage resulting from myocardial ischemia-reperfusion injury when administered as a short-duration intravenous infusion

- 42% Cardioprotection
- 88% decrease in arrhythmias at 1 hour
- 90% decrease in arrhythmias at 3 hours

Key blood biomarker markers assessed

- 32% decrease in Troponin I
- 21% decrease in in ALT levels





## Conclusion

#### Summary

- Pioneering TRPC channel inhibition therapies.
- Xolatryp Phase I (safety and tolerability) clinical trial well advanced
- Xolatryp preclinical efficacy demonstrated in ischemic stroke, traumatic brain injury (TBI) and myocardial ischemia reperfusion injury
- AU\$4.76 million cash position at end March 2025

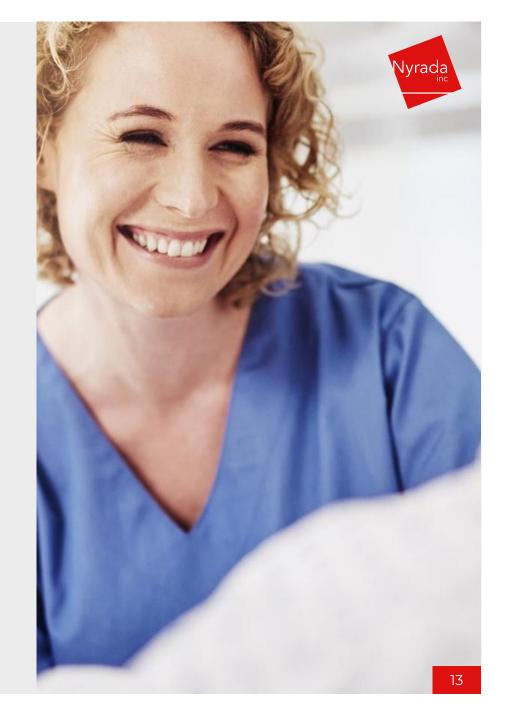
### News Flow/Catalysts

- 4QFY2025 Cashflow update June 2025
- FY2025 Audited accounts August 2025
- Final Phase I Clinical Trial Results September 2025
- Phase II Clinical Trial Target and Plan TBA



# Key Market Announcements

- Phase I Clinical Trial
  - Protocol Amendment June 2024
  - Cohort 3 Update May 2024
- Ischemic Stroke
  - > Preclinical Study February 2024
- Traumatic Brain Injury (TB()
  - Preclinical Study April 2025
- Acute Myocardia Ischemia
  - Preclinical Study October 2024
  - Supplementary Preclinical Study October 2024
  - Follow up Preclinical Study May 2025



# Appendices



## Vision and Strategy

#### **Our Vision:**

 to become a high-growth pharmaceutical company specialising in the discovery and development of novel treatments

#### **Our Strategy:**

to develop treatments for diseases where there
is an unmet clinical need, or where current
treatments are suboptimal, and to monetise the
value of these treatments through advancing
clinical drug candidates towards out-licencing.



# Large Market Opportunity – Myocardial Infarction

**Globally:** 

~15-20 million people suffer heart attack annually

~15% mortality within 30 days

No current FDA approved treatments targeting myocardial infarction-reperfusion injury

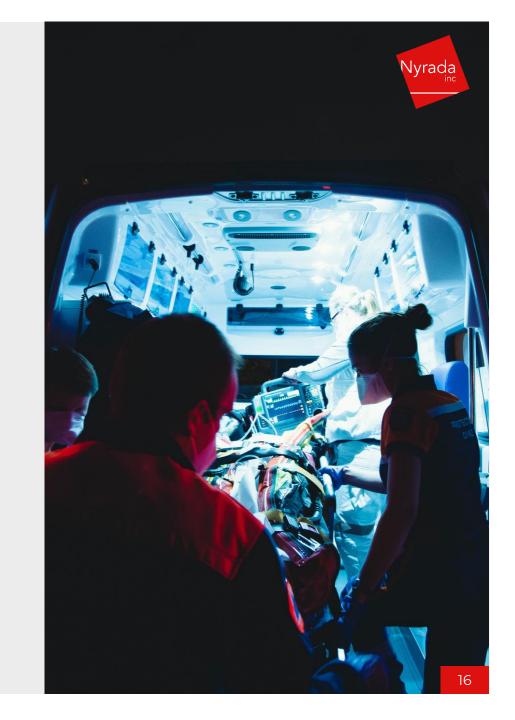
Effective treatment will improve patient outcomes and reduce high costs associated with long-term care of heart attack survivors.

#### Large and growing treatment market:

Currently ~US\$1.9 billion<sup>5</sup>

Growing ~6.8% CAGR<sup>5</sup>

Forecast ~US\$3.7 billion by 2032<sup>5</sup>



# Large Market Opportunity – Stroke

#### **Globally:**

**~15 million** people suffer strokes annually<sup>1</sup>

**~5 million**left permanently disabled<sup>1</sup>

One approved drug class for stroke suitable for <15% of patients (tPA - tissue plasminogen activator).

Effective treatment will improve patient outcomes and reduce high costs associated with long-term care.

#### Large and growing treatment market:

Currently ~US\$30.3 billion<sup>2</sup>

Growing ~7.5% CAGR<sup>2</sup>

Forecast ~US\$52.2 billion by 2030<sup>2</sup>



# Large Market Opportunity – Traumatic Brain Injury (TBI)

**Globally:** 

**~5.5 million**people suffer severe
TBA annually<sup>3</sup>

~55 million

living with effects of medically treated TBI<sup>3</sup>

No current FDA approved treatments

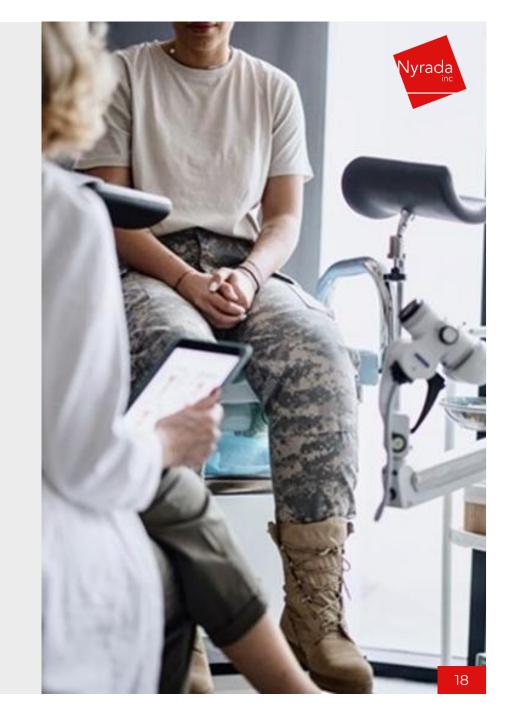
Effective treatment will improve patient outcomes and reduce high costs associated with long-term care of brain injury survivors.

#### Large and growing treatment market:

Currently ~US\$3.5 billion<sup>4</sup>

Growing ~6.2% CAGR<sup>4</sup>

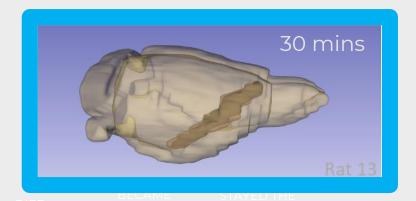
Forecast ~US\$5.5 billion by 2030<sup>4</sup>



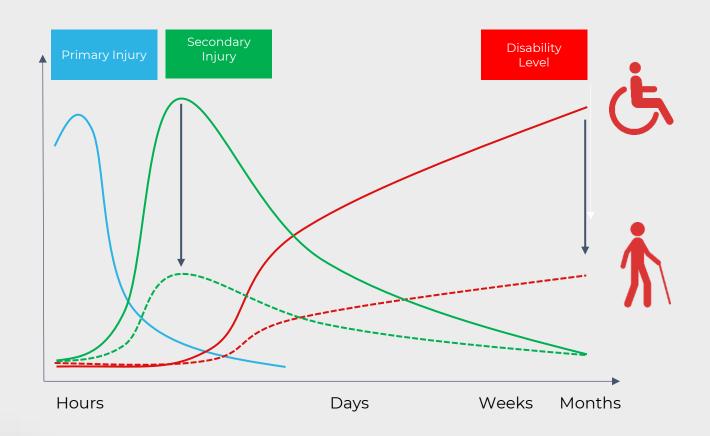
## Neuroprotection – Stroke and TBI



#### Serial reconstruction from MRI







**Nyrada drug Xolatryp** An acute 3-day intravenous treatment



#### Reduce secondary injury resulting from stroke or TBI

- Improve survivability, limit disability
- Improve quality of life

# Drug Development Cycle



## Discovery & Development



 $\longrightarrow$ 

## Preclinical research



Scientists study how
a disease affects
patients and look for
potential
compounds that
might help treat
these diseases

Once promising compounds are found, scientists begin to test the compounds in the lab and on animals

## Clinical trials



If the compounds pass preclinical tests, it is then tested on humans to confirm effectiveness, safety, and optimal dosage.

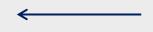
## FDA review



Post-market safety monitoring



After clinical trials, the company sends all data to the FDA so that they can review the drug's safety and effectiveness. After a drug is approved by the FDA, scientists continue to monitor both the drug's safety and effectiveness.



Potential for Xolatryp out-licencing



## References

- 1 World Health Organization <a href="https://www.emro.who.int/health-topics/stroke-cerebrovascular-accident/index.html#:~:text=Annually%2C%2015%20million%20people%20worldwide,cause%20is%20high%20blood%20pressure">https://www.emro.who.int/health-topics/stroke-cerebrovascular-accident/index.html#:~:text=Annually%2C%2015%20million%20people%20worldwide,cause%20is%20high%20blood%20pressure</a>
- 2 Databridge Market Research <a href="https://www.databridgemarketresearch.com/reports/global-stroke-market">https://www.databridgemarketresearch.com/reports/global-stroke-market</a> .
- 3 National Academy of Sciences <a href="https://nap.nationalacademies.org/catalog/25394/traumatic-brain-injury-a-roadmap-for-accelerating-progress">https://nap.nationalacademies.org/catalog/25394/traumatic-brain-injury-a-roadmap-for-accelerating-progress</a>
- 4 Databridge Market Research <a href="https://www.databridgemarketresearch.com/reports/global-traumatic-brain-injuries-treatment-market">https://www.databridgemarketresearch.com/reports/global-traumatic-brain-injuries-treatment-market</a>
- 5 Spherical Insights <a href="https://www.globenewswire.com/en/news-release/2023/05/30/2678779/0/en/Global-Myocardial-Infarction-Market-Size-To-Grow-USD-3-7-Billion-By-2032-CAGR-of-6-8.html">https://www.globenewswire.com/en/news-release/2023/05/30/2678779/0/en/Global-Myocardial-Infarction-Market-Size-To-Grow-USD-3-7-Billion-By-2032-CAGR-of-6-8.html</a>

