



25 May 2020

Sydney, Australia

## **Milestone Achieved in the Nyrada Brain Injury Program**

- Leads for two series of compounds with separate and distinct cellular targets shown in preclinical study to effectively block calcium ion build-up in cells, a key driver of secondary brain injury
- Both compounds shown to readily cross the blood-brain-barrier in an uninjured animal brain
- Levels above the anticipated therapeutic threshold achieved in the uninjured animal brain, with no observed adverse effects

**Sydney, 25 May 2020:** Nyrada Inc (ASX: NYR) provides an update on one of its leading programs for treatment of brain injury.

Nyrada has shown in a preclinical pharmacokinetic study that its lead candidate compounds can cross the blood-brain-barrier (BBB) in the intact uninjured animal brain.

The aim of the Nyrada Brain Injury program is a drug to reduce secondary brain damage following head trauma and stroke in order to improve survivability and patient outcomes.

Head trauma (motor vehicle accident, falls, sporting injury) and stroke are leading causes of hospital admissions and long-term rehabilitation service requirements. The Nyrada Brain Injury Program aims to prevent secondary brain injury by reducing the build-up of calcium ions in brain cells which causes the cells to die.

### **Reducing brain injury volume**

In an earlier preclinical proof-of-concept efficacy study in a model of stroke, the first-generation compound, NYX-104, was delivered as a suppository for five days following brain injury. It was found to significantly reduce the injury volume compared to control animals which received placebo (n=6 animals per treatment group, p=0.025).

### **Blocking calcium ion build-up**

Nyrada has since developed a more potent version of NYX-104 called NYX-242, which blocks calcium ion build-up in cells at three-times greater potency. In parallel with the development of NYX-242, Nyrada discovered a new generation of compounds with a different molecular target but considerably greater potency in blocking calcium, with the lead compound NYX-1010 broadening the Company's competitive advantage and commercial opportunity<sup>1</sup>.

### **Blood-brain-barrier penetration achieved**

In a separate preclinical pharmacokinetic study, Nyrada has shown that therapeutic concentrations of both NYX-242 and NYX-1010 can be detected in the healthy animal brain at 30 minutes following a

---

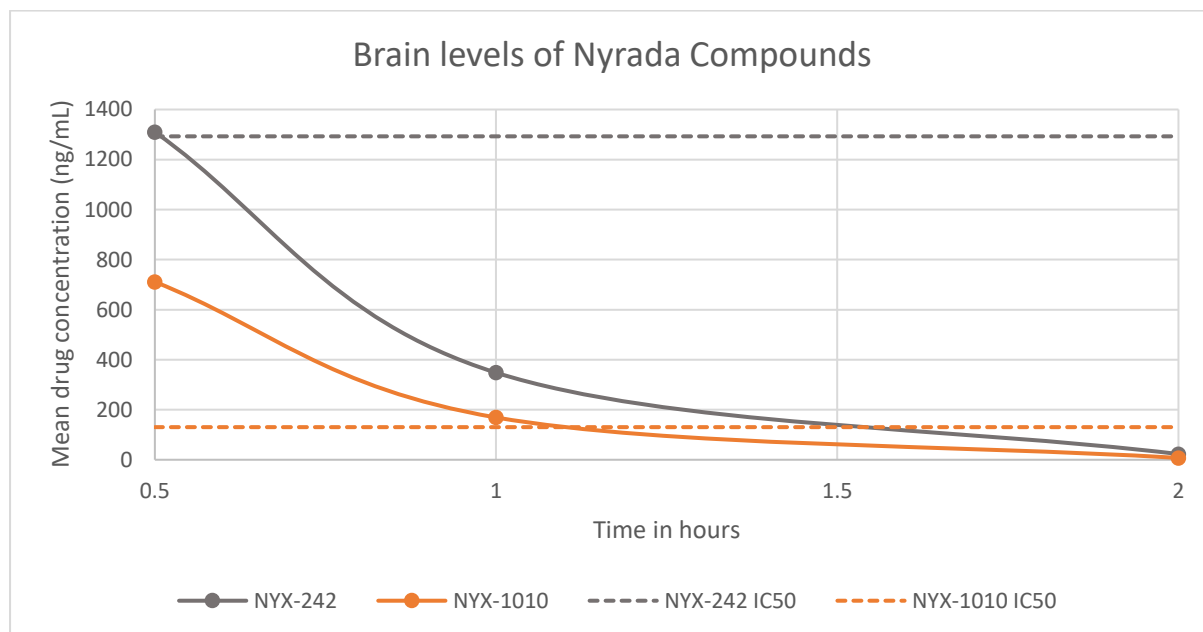
<sup>1</sup> See Nyrada April Newsletter



single intravenous dose (4.2 mg/kg, n=3 animals per timepoint, per arm). This is a significant finding as it shows that both drugs readily cross the intact BBB.

The BBB is a protective barrier between the components of the blood and the cells that form the brain tissue, keeping infection at bay in the healthy brain. However, this can pose a major roadblock in the development of drugs for treating brain disorders as a large proportion of drugs cannot cross this barrier and reach the desired target in brain tissue. Moreover, some drugs that can cross the BBB get readily pumped out and hence cannot accumulate in the brain tissue in sufficient quantity to be effective.

Figure 1 shows the quantity of NYX-242 and NYX-1010 detected in the brain over time and the corresponding IC<sub>50</sub> values for block of calcium ion build-up in cells. IC<sub>50</sub> refers to the concentration at which the compounds reduce calcium ion build-up in cells by 50% and reflects the anticipated therapeutic threshold. NYX-242 was detected in the brain at levels corresponding with the therapeutic IC<sub>50</sub> and NYX-1010 was detected in the brain at levels far exceeding the IC<sub>50</sub> (dashed lines) at the key 30-minute mark. It is anticipated that with continuous intravenous administration the therapeutic levels of both these compounds could be maintained for the duration of treatment.



**Figure 1:** The figure shows the average concentration of the two Nyrada compounds NYX-242 (grey) and NYX-1010 (orange) in the healthy animal brain, 0.5, 1 and 2 hours (n = 3 animals per timepoint) following a single intravenous dose (4.2 mg/kg). The dashed lines show the corresponding IC<sub>50</sub> of these compounds in blocking calcium ions.

Many drugs rely on the compromised BBB such as occurs in severe TBI and stroke to enter the brain. However, these drugs fail to show efficacy in milder forms of brain injury such as concussion, where the BBB is not as greatly compromised and may provide only localised neuroprotection in more significant brain injury cases. The Nyrada compounds do not rely on the breakdown of BBB, providing an advantage, as the compounds can be used for treatment of the full spectrum of TBI severity



including concussion. No adverse effects were observed in the animals in each arm of the study, indicating that the two compounds are safe and well-tolerated at the administered dose.

### **Next steps**

Follow-on studies are being undertaken to assess optimal dosing and drug levels in the brain following continuous intravenous administration, the preferred dosing method in the clinic for TBI and stroke patients, and intranasal administration, preferred for the treatment of concussion. The data will be reported in the coming weeks.

**Prof. Gary Housley, Chair of Nyrada’s Scientific Advisory Board said:** “Our Brain Injury program is advancing very well. These latest results show that we have two potent compounds that can easily cross the blood-brain-barrier at their anticipated therapeutic levels, or better. Next, we will conduct similar studies via intravenous and intranasal dosing which are preferred in a clinical setting.”

**Nyrada CEO, James Bonnar commented on the preclinical results:** “These latest data are an exciting step forward for Nyrada. Having two potent drug candidates that act on distinctly different targets to limit toxic calcium ion build-up in brain cells is a huge achievement. It provides a solid scientific foundation and greatly de-risks the Brain Injury program. Nyrada is well positioned to becoming a leader in the field of brain injury drug development.”

### **General**

Nyrada has a solid cash position having successfully raised \$8.5 million from its initial public offering in January 2020. In addition, the Company is actively pursuing a variety of non-dilutive funding and collaboration opportunities for the development of its product candidates. The Company also confirms that its operations and supply chains currently remain unaffected by the COVID-19 situation, although the Company is taking precautionary steps to help quarantine its business from any global fall-out.

### **About Nyrada Inc**

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

-ENDS-

*Authorised by Mr John Moore, Non-Executive Chairman, on behalf of the Board*

[www.nyrada.com](http://www.nyrada.com)

**Investor & Corporate Enquiries:**

Prue Kelly  
T: 0459 022 445  
E: [info@nyrada.com](mailto:info@nyrada.com)

**Company Secretary:**

David Franks  
T: 02 8072 1400  
E: [David.Franks@atomicgroup.com.au](mailto:David.Franks@atomicgroup.com.au)

**Media Enquiries:**

Catherine Strong  
Citadel-MAGNUS  
T: 02 8234 0111  
E: [cstrong@citadelmagnus.com](mailto:cstrong@citadelmagnus.com)

**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.