Nyrada Inc

Improving Lives, Offering Hope

Developing New Therapies for Cardiovascular & Neurological Disorders





Message from the CEO

I hope you and your families are safe and well.



As the six-month mark approaches since our IPO in January, we can look back on a successful first half of the year from a

corporate perspective. Despite the COVID-19 pandemic and disrupted social and economic environment, the Nyrada team has been working diligently on our two lead programs and are extremely pleased with the advances that have been made.

Significant progress has been made in the neuroprotection program with the important development of two novel compounds (NYX-242 and NYX-1010) that readily cross into the brain via the preferred route of administration for Stroke and Traumatic Brain Injury. These two compounds reach levels which we believe to be therapeutic and will be compared in a head-to-head animal model of brain injury and the best will be selected to take forward to the clinic to be evaluated in patients.

Our cholesterol-lowering drug program has also moved forward, with analogues delivering compounds with improved potency and drug-like properties which is highly encouraging to see. We look forward to moving these assets further towards the clinic in the coming months and expect to present further experimental data during the rest of the year, with the goal of having our first drug ready to enter the clinic in late 2021.

The Company's progress was very positive during our first few months and I am already looking forward to the remainder of 2020. I want to take this opportunity to wish everyone that follows Nyrada in one way or another our best wishes and thank you for joining us as we progress these exciting projects.

James Bonnar - Chief Executive Officer



Update on COVID-19

COVID-19 continues to have minimal impact on operations with our main CRO vendors in China and the US operating as usual. Currently, our drug synthesis vendor in India is also operating as usual, however, as a precautionary measure against future disruption, drug synthesis activities have increased in China.

Nyrada continues to safeguard against any potential future COVID-19 related setbacks by using multiple vendors across the globe, thus not being reliant on any one vendor or region









Status Update from the Bench

Updates for the Neuroprotection Program: Treatment for TBI & Stroke



- Further analogues have been synthesised, focusing on key structural features to improve the potency and half-life of the existing compounds.
- Preliminary PK study showed that the secondgeneration compounds NYX-242 and NYX-1010 can readily cross the blood-brain-barrier with intravenous delivery in animal models.
- Studies with continuous intravenous infusion are being conducted in animal models to assess drug levels in the brain. This is the preferred dosing regimen in the clinic for patients with stroke and traumatic brain injury (moderate to severe).

Updates for the Cholesterol-Lowering Program: PCSK9 inhibitor



- Med Chem program well advanced with more than 140 newly developed analogues designed, synthesised, and tested. Design of these analogues has focused on optimising key structural features, leading to improved potency and drug-like properties.
- Selection of the clinical candidate is on track and initiation of manufacturing scale-up activities for safety and toxicological testing is underway



Technology in Focus

Cholesterol-lowering program

The Company's cardiovascular program has been particularly busy in 2020, with minimal impact of COVID-19 on operations. Much of the activity has occurred within the program's medicinal chemistry campaign to identify a small molecule inhibitor of PCSK9, a key regulator of LDL or "bad" cholesterol levels in the blood. Medicinal chemistry is the design, optimisation, and development of chemical compounds for use as drugs. It is inherently a multidisciplinary subject, beginning with the synthesis of potential drugs and followed by studies investigating their interactions with biological targets (i.e. PCSK9). This helps us understand the positive medicinal effects of the drug, its metabolism, and any potential sideeffects.

This information is utilised to design and synthesise improved versions of the initial proof-of-concept drug in an iterative feedback process known as lead optimisation, that ultimately identifies the drug candidate suitable for clinical investigation (the clinical candidate).

Following successful safety studies, this is where the new drug is taken by people for the very first time.



Small molecule PCSK9 inhibitor overcomes longstanding challenge of an oral PCSK9 treatment The Nyrada medicinal chemistry (colloquially known as "Med Chem") program for the cardiovascular clinical area is currently in the lead optimisation stage and shortly we will be selecting our lead candidate for subsequent development towards the clinic.

Nyrada Inc has adopted an approach that involves the use of computational PCSK9-drug modelling to target changes to the lead drug that are intended to confer improved drug properties such as greater solubility, improved gut permeability and increased potency against PCSK9.

Nyrada Inc has synthesised more than 140 new compounds on its way to selecting an optimized clinical candidate that satisfies these requirements. The promising progress to date in identifying a clinical candidate has prompted

Nyrada Inc to begin investigations into the development of suitable dose forms for a clinical candidate drug, with current efforts focusing on a once daily oral delivery route.

This investigation will require considerable amounts of the clinical candidate to be synthesised, thus the Company is currently also investigating the upscaling process for its potential lead drug candidate.

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Image adapted from Evison et al. (2020) Bioorg. Med. Chem. 28 (6): 115344.

Nyrada Profile: Dr Benny J. Evison, Chief Scientific Officer

Tell us a bit about your background

I grew up on the Great Ocean Road in Victoria where I developed a curiosity about how the world worked, particularly all things biological. From there, I moved to Melbourne to study at La Trobe University where I obtained a Bachelor of Medical Science with Honours followed by a PhD. My PhD involved the identification of a potential new mechanism of action of a drug called pixantrone, which is currently used for the treatment of non-Hodgkin's lymphoma.

Following my PhD, I was keen to gain more training at an international level, so I moved to Memphis, Tennessee in the United States, where I was a postdoctoral fellow at St Jude Children's Research Hospital. My time there was very humbling as I spent a lot of time with kids who were very sick, mostly with cancer, and receiving treatment. It was a strong motivational factor to generate good science. In my time there, I worked on making drugs that targeted proteins involved in DNA repair to improve the activity of existing chemotherapies. Home called eventually, and I returned to Australia as one of the first employees of Nyrada Inc.

What do you most enjoy about working at Nyrada?

I really enjoy the notion of working towards a product that may one day have a positive impact on people's lives and their health, in much the same way as my time at St Jude. The cutting-edge nature of the science and the challenge it presents is something I also particularly enjoy.

Where do you see yourself in 5 years time?

I'm thoroughly enjoying my time here at Nyrada, so I certainly hope to remain here as the Company's CSO. In 5 years, I expect each of our current programs to be well advanced into the clinical phase of development or partnered out, so I'll be busy ushering in the next generation of compounds from the discovery phase into clinical trials to take their place. Nyrada has big plans for the future.



Authorised by Mr John Moore, Non-Executive Chairman, on behalf of the Board. Nyrada Inc. ARBN 625 401 818 Suite 3, Level 4, 828 Pacific Highway GORDON, NSW 2072