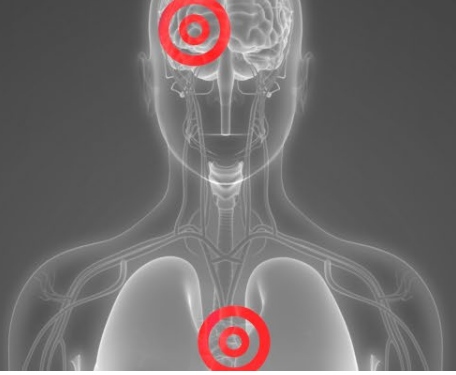
Nyrada Inc

Improving Lives, Offering Hope

Developing New Therapies for Cardiovascular & Neurological Disorders



Newsletter: 24 September 2020

Message from the CEO

I hope you and your families are safe and well.

This edition of the Nyrada newsletter centres on the Cholesterol-Lowering Program, providing an update on its status and the planned next steps, including some background to an efficacy study in a specialised mouse model of cholesterol which we are very excited about.

I would also like to take this opportunity to comment on the recent announcement of AstraZeneca's acquisition of Dogma Therapeutics' preclinical small molecule PCSK9 inhibitor program. This acquisition is an encouraging development for Nyrada as it demonstrates big pharma's interest in this space, even in preclinical/early-stage development programs. While deal terms have not been released, we do know something of the science behind the program from information in the public domain. Importantly, we know with certainty that the drug structures they are pursuing are different from Nyrada's and bind to a different site on the PCSK9 protein. This means that our patent family is separate and differentiated from theirs.

The strategy for our Cholesterol-Lowering Program is to confirm safety in a Phase I study and obtain an efficacy signal, as a way of maximising shareholder value before entering into a sale or license agreement with an industry partner. The Cholesterol-Lowering Program remains on track to enter the clinic in late 2021 with key efficacy data expected before the end of the year. This builds upon the excellent human cell model data released in July 2020.

The Brain Injury Program is also progressing well and we plan to announce further updates in the final quarter of 2020.

In terms of the COVID-19 pandemic and its impact on Nyrada, the team continues to work efficiently and effectively from home and there has been minimal disruption to operations at our key vendors.

On behalf of the Nyrada team, I want to offer everyone our best wishes, and thank you for your ongoing support.

James Bonnar - Chief Executive Officer

Corporate Information	
ASX Code	**NYR**
Funds Raised at IPO	**A$8.5m**
Share Price (at 23 Sep 2020)	**A$0.22**
Market Cap (at 23 Sep 2020)	**A$24M**
Cash-at-bank (at 30 June 2020)	**A$5.1M**

Scan QR Code to view 'Cholesterol Lowering Animation'

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Technology in Focus

Modelling human hypercholesteroleamia in a specialised transgenic mouse model

As previously reported on 6th July 2020, Nyrada has achieved encouraging efficacy data using its lead-like molecule NYX-PCSK9i. In a study using healthy human white blood cells (lymphocytes), NYX-PCSK9i was found to be efficacious in increasing surface expression of LDL receptors, as is necessary to lower cholesterol in patients. NYX-PCSK9i also worked just as well as the marketed monoclonal PCSK9 antibody drugs evolocumab (Repatha™, Amgen) and alirocumab (Praluent™, Sanofi/Regeneron). Whilst the further development of NYX-PCSK9i continues, Nyrada is working in parallel to show efficacy of its compound in an *in vivo* animal model.

Animal models are often used as a translational link between 'test tube' experiments and human clinical trials. We have already shown the efficacy of the NYX-PCSK9i in human cells, however in this study we are looking for proof-of-concept in the context of whole-system biology. Nyrada has chosen to use a specialised mouse model called the ApoE*3Leiden.CETP mouse model which has been specifically generated to possess human-like characteristics with respect to cardiovascular health. This model is very well regarded in the field, having been used for over 170 drug intervention studies by the pharmaceutical industry over the last 15 years. The ApoE*3Leiden.CETP mice will be treated with NYX-PCSK9i, in combination with or without a statin for 28 days. The effectiveness of NYX-PCSK9i to improve hypercholesterolaemia will be assessed via the measurement of lipid profile including total cholesterol and plasma triglycerides, liver function and plasma PCSK9 levels at regular intervals throughout the 4-week treatment period.

In order to run an *in vivo* efficacy study, Nyrada has been busy ensuring NYX-PCSK9i has an optimal pharmacokinetic profile. Promisingly, the compound is well tolerated and can be dosed at levels believed to be therapeutically optimal. Nyrada hopes to update the market with interim efficacy results from the *in vivo* study by the end of the year and final results in early 2021.

Did you know?

The transgenic ApoE*3Leiden.CETP mouse model Nyrada has chosen to use express three human genes to specifically model the human hyperlipideamia condition.

Did you know- the Leiden gene is named after the Dutch city Leiden? In 1994, scientist Björn Dahlbäck named the gene after a subset of patients living in Leiden, Netherlands who possessed the factor V Leiden mutation. Between 2 and 8 percent of people of European ancestry carry one copy of the Leiden mutation in each cell.

Industry News

AstraZeneca acquires oral PCSK9 inhibitor program from Dogma Therapeutics

Newly announced M&A activity has highlighted the value large pharma places on finding a small molecule PCSK9 inhibitor that can be given as an oral pill, to provide an alternative to antibody-based PCSK9 injectables.

AstraZeneca, a British multinational pharmaceutical and biopharmaceutical company has recently announced the acquisition of an oral PCSK9 inhibitor preclinical program from Dogma Therapeutics, which they aim to take into the clinic next year. While the deal value wasn't disclosed, AstraZeneca will pay Dogma Therapeutics upfront as well as downstream payments linked to global regulatory and commercial milestones.

This announcement validates the serious interest big pharma companies have in small molecule PCSK9 programs, such as Nyrada's. It also indicates their willingness to partner at an early stage in an asset's development.

At this stage, there is little detail in the public domain on the Dogma Therapeutics technology.

From the information available, Nyrada believes the Dogma Therapeutics compound is working via a mechanism that stops the secretion of the PCSK9 protein from the cell. In contrast, the Nyrada PCSK9i are directly targeting the binding of the PCSK9 protein to the LDLR **outside** the cell, this being more comparable to monoclonal PCSK9 inhibitors which also target PCSK9 protein in the blood. This distinction between inside, and outside, the cell is quite important in terms of drug development and biological function. By targeting the PCSK9 protein on the outside of the cell (i.e. in the blood), Nyrada believes it can achieve efficacy without the additional hurdle of having to penetrate the cell.

Overall, Nyrada is encouraged by AstraZeneca's acquisition and interest in cholesterol management and will continue to engage with the pharmaceutical industry while progressing to the clinic.

Nyrada Q&A

What are Nyrada's value drivers and potential milestones?

Nyrada expects to commence the first-in-human Phase1 study in late-2021 for the Cholesterol-Lowering Program and mid-2022 for the Brain Injury Program. In the lead up to Phase 1 clinical trials, Nyrada will be reporting further preclinical results for each program and expects to select a lead product candidate for the Brain Injury Program in H1 2021. For the Cholesterol-Lowering Program, Nyrada will continue to test and de-risk the recently selected lead drug candidate in preparation for clinical trials.

We also expect to be in a position to talk about potential collaborations soon.

Will Nyrada need more funding to reach the clinic?

For now, Nyrada is well funded with A$5.1M cash in the bank as at 30 June 2020. These funds will enable us to advance our cholesterol lowering drug into a Phase 1 Clinical Trial. We are, however, constantly assessing non-dilutive funding opportunities to ensure we have sufficient funding to support us well into the clinic.

How will Nyrada maximise value early via its business model?

Nyrada's focus is developing novel new treatments for areas of substantial unmet medical need. With prudent capital deployment, Nyrada de-risks its early stage assets and provides a licensing opportunity to large pharma companies before significant capital expenditure is required in later stage clinical trials. Nyrada limits company costs, reuses capital and reduces investor dilution via this business model.

We also seek to leverage shareholders' capital through non-dilutive sources of financing such as grants and tax incentives.

Why is Nyrada developing two dosage forms for the brain injury drug?

Nyrada is developing two dosage forms to provide treatment options for all forms of TBI and Stroke. The continuous intravenous injection is the preferred route for patients suffering from Stroke and moderate-severe TBI, while an intranasal route of delivery is preferred for the treatment of mild TBI and concussion injury, common in sports.

Nyrada Inc, 2020 Annual General Meeting

The Company's Annual General Meeting (AGM) will be held on Thursday 19 November 2020 at 10:00 am AEDT.

The location of the AGM is subject to COVID-19 restrictions, including regulatory requirements. Further details, including any hybrid or virtual meeting arrangements, will be confirmed closer to the AGM.

Following formalities, Nyrada's Non-Executive Chair, John Moore and CEO, James Bonnar will provide a corporate update on the Company's successful first eleven months since listing on ASX.

To receive electronic communications, shareholders are encouraged to contact the share registry, Automic Group:

- Visit: www.automicgroup.com.au
- Email: hello@automic.com.au
- Telephone: (Within Australia) 1300 288 664 (Outside Australia) +61 2 9698 5414

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

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