



6 July 2020

Sydney, Australia

Nyrada Cholesterol-Lowering Drug Study Results

- Nyrada PCSK9 inhibitor (NYX-PCSK9i) demonstrates equivalency to the two FDA approved monoclonal PCSK9 antibodies, Repatha® and Praluent®, in healthy human white blood cells
- Results confirmed both with, and without, the presence of a statin (Mevastatin), opening up the potential for NYX-PCSK9i to be used alone, or in combination with statin
- Nyrada has met significant scientific milestone in efforts to replace expensive ongoing injections with the first ever oral pill
- Combined sales for Amgen Repatha® and Regeneron/Sanofi Praluent® PCSK9 inhibitor injectables is in excess of US\$900 million in FY2019

Sydney, 6 July 2020: Nyrada Inc (ASX: NYR) is pleased to report encouraging preclinical results from its cholesterol-lowering program to develop a drug to treat hypercholesterolemia.

A study using healthy donor human white blood cells (lymphocytes) treated with Nyrada's PCSK9 inhibitor NYX-PCSK9i showed an increase in LDL receptor (LDLR) levels and demonstrated equivalency to marketed monoclonal PCSK9 antibody drugs evolocumab (Repatha®, Amgen) and alirocumab (Praluent®, Sanofi/Regeneron). Importantly, the results were confirmed both with and without the addition of a statin (Mevastatin), indicating the potential to develop a combined PCSK9-statin single-pill treatment for high LDL cholesterol.

Both Repatha® and Praluent® are used to treat patients with hypercholesterolemia and are delivered via subcutaneous injection. Repatha® generated sales of US\$661 million in FY2019 for Amgen, representing 20% growth from FY2018¹. Praluent® reached sales of US\$288 million in FY2019² for Regeneron/Sanofi.

Prof. Gilles Lambert, Nyrada Scientific Advisory Board Member commented: "Nyrada plans to develop an oral medication PCSK9 inhibitor for patients with high cholesterol giving them a more convenient option than regular injections. Today's results demonstrate that our PCSK9 inhibitor works just as well as the FDA approved injectable medications, Repatha® and Praluent® in this cell model, marking the achievement of an exciting scientific milestone for the Company. What is also exciting is that results occur both with and without a statin being present, opening up the potential for Nyrada's drug to be given on its own, or in combination with statin therapy."

James Bonnar, Nyrada CEO commented: "Having a drug candidate that works as well as the two market-leading monoclonal PCSK9 antibodies in a human cell model is a huge achievement. It represents a big step forward in our mission to develop the first-ever small molecule PCSK9 inhibitor to treat high cholesterol and provide a compelling cost-competitive and convenient treatment alternative to Repatha® and Praluent®. This advance will also be welcomed by the 70% of patients at risk of cardiovascular disease who take a statin but are still unable to reach their target LDL cholesterol level, and those patients who are statin-intolerant."

¹ <https://www.prnewswire.com/news-releases/amgen-2019-financial-results>

² <https://www.prnewswire.com/news-releases/regeneron-2019-financial-results>



Why is LDL Important to Health and what is the Role of PCSK9?

When the body has too much LDL (bad) cholesterol, it can accumulate on artery walls, restricting blood flow which can lead to heart attack and stroke.

LDL cholesterol is cleared from circulation by binding to LDL receptors (LDLR) on the surface of liver cells. PCSK9 is a naturally produced protein that plays a counter role in this regulation process. It does this by degrading the LDLR, lowering the number of receptors available to remove LDL cholesterol. This leads to increased levels of LDL cholesterol in the bloodstream.

Inhibition of PCSK9 function causes a beneficial increase in LDLR on the surface of cells, improving the body's ability to clear LDL cholesterol from the bloodstream.

Nyrada Drug NYX-PCSK9i Increases Cellular Levels of LDLR

In the presence of PCSK9, preservation of lymphocyte LDLR was observed in a dose-dependent manner by NYX-PCSK9i. This confirms NYX-PCSK9i inhibits the function of PCSK9 in degrading LDLR, as shown in the table below.

An 89% retention of LDLR from PCSK9-induced degradation was observed with NYX-PCSK9i at 4 μ M, and when NYX-PCSK9i was combined with Mevastatin, which increased LDLR levels, a 90% retention of that enhanced LDLR level was achieved.

	- Mevastatin		+ Mevastatin	
	% LDLR retention (with PCSK9 present)	p-value	% LDLR retention (with PCSK9 present)	p-value
No drug	51%	n/a	64%	n/a
NYX-PCSK9i (1 μ M)	53%	0.74	78%	0.13
NYX-PCSK9i (2 μ M)	64%	0.01	77%	0.06
NYX-PCSK9i (4 μ M)	89%	0.001	90%	0.003
alirocumab (Praluent®)	78%	0.002	88%	0.04
evolocumab (Repatha®)	84%	0.0009	89%	0.0001

bold = statistically significant

The statistical significance of the effect of NYX-PCSK9i at each dose versus vehicle (no drug) is shown as p-values.



Limitations of the reported testing include:

Additional testing as part of a development program would be required before NYX-PCSK9i would be proposed for human trials.

Glossary

LDL	Low-density lipoprotein cholesterol often referred to as “bad” cholesterol.
LDLR	Low-density lipoprotein receptor. This receptor binds to particles called low-density lipoproteins (LDLs), which are the primary carriers of cholesterol in the blood.
NYX-PCSK9i	NYX-PCSK9i is the Nyrada small molecule PCSK9 inhibitor, developed to bind to PCSK9, to increase LDLR levels and therefore reduce LDL cholesterol.
PCSK9	Proprotein convertase subtilisin/kexin type 9 (PCSK9), an enzyme predominantly produced in the liver. PCSK9 is a key player in plasma cholesterol metabolism.
Statistical significance	Statistical significance is a measure of how likely a test result is likely to be due to chance e.g. a p-value of 0.05 means there is a 5% likelihood that the result is a false positive and a 95% likelihood that it is real. A p-value of 0.0001 means there is a .01% likelihood that the result is a false positive and a 99.99% likelihood that the result is real. In general, the larger the study size, or the larger the effect, the lower the p-value.

General

Nyrada has a solid cash position having \$6.1 million in the bank on 31 March 2020. Also, 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 fallout.

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

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Forward-looking Statements

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