Nyrada Announces Further Encouraging Results from NYX-PCSK9i *In Vivo* Study

- New results from an exploratory arm in Nyrada's *in vivo* cholesterol efficacy study build on the 57% reduction in total cholesterol announced on 21 December 2020
- Additional laboratory test results confirm that LDL ("bad") cholesterol levels were lowered in a dose-dependent manner by NYX-PCSK9i
- No adverse effects were observed and NYX-PCSK9i was well-tolerated, as indicated by the evaluation of body weight, food intake, and liver function
- NYX-PCSK9i *in vivo* results compare favourably with historical *in vivo* trials of the statin, Lipitor®(Pfizer), and injectable PCSK9 monoclonal antibody, Praluent® (Sanofi/Regeneron), in the magnitude of total cholesterol reduction
- A follow-up, proof-of-concept study is planned to evaluate NYX-PCSK9i when combined with a statin, with results expected in mid-2021

Sydney, 25 January 2021: Nyrada Inc (ASX: NYR) is pleased to report new additional exploratory results of its *in vivo* cholesterol efficacy study, first announced on 21 December 2020. The study used a mouse model that has been genetically modified to mimic human-like characteristics concerning cholesterol metabolism and cardiovascular health (*APOE*3-Leiden.CETP* mouse model).

During the study, 30 mg/kg and 50 mg/kg dose levels were administered over 28 days, with a clear dose-dependent reduction in total cholesterol shown (as previously announced). Nyrada also ran an exploratory group in which animals were treated with 10 mg/kg for 14 days before the dose was increased to 75 mg/kg for the remaining 14 days. A large and rapid reduction in total cholesterol was observed from days 14-28 when the dose increased from 10 mg/kg to 75 mg/kg (see ***Figure 1*** and ***Table 1***). Further analysis of the lipoprotein fraction confirms that the reduction in cholesterol is LDL or "bad" cholesterol and that the reduction was dose-dependent (see **Lipoprotein Profile** on page 3).

Figure 1. *Total Cholesterol Reduction in APOE*3-Leiden.CETP Mice Treated with NYX-PCSK9i. In the exploratory group, mice were treated with 10 mg/kg NYX-PCSK9i on days 0-13 and with 75 mg/kg NYX-PCSK9i from days 14-28. (Data shown in red).*

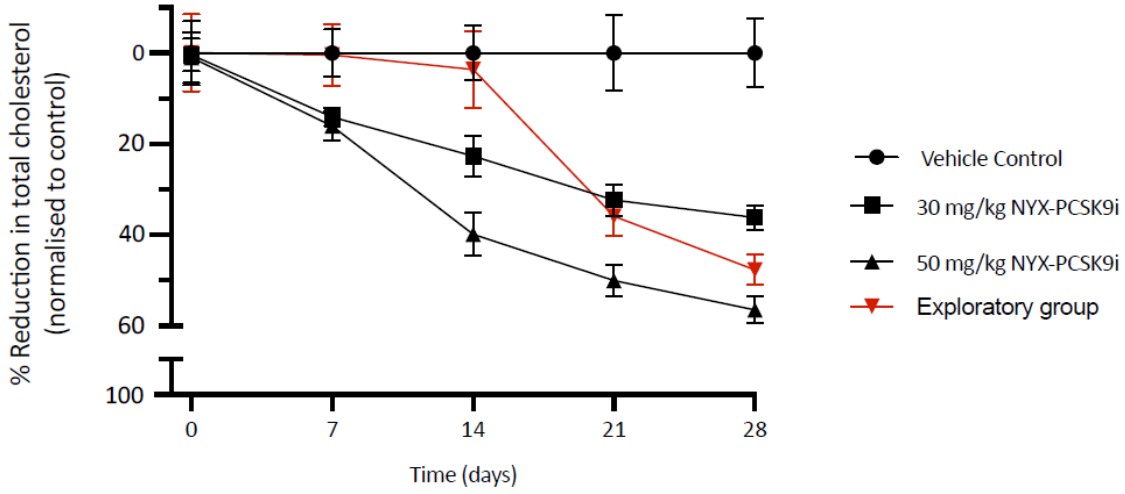


Table 1. *Percentage change in total cholesterol, when compared to vehicle control. There were 8 mice in each experimental group. P-values are shown in brackets, with significant p-values in bold.*

	% difference in plasma total cholesterol versus vehicle control (*p*-value)			
Time (days)	7	14	21	28
30 mg/kg NYX-PCSK9i	-14% **(0.05)**	-23% **(0.015)**	-32% **(0.002)**	-36% **(<0.001)**
50 mg/kg NYX-PCSK9i	-16% **(0.05)**	-40% **(<0.001)**	-50% **(<0.001)**	-57% **(<0.001)**
Exploratory 10 mg/kg	0% (0.95)	-4% (0.505)	-	-
Exploratory 75 mg/kg	-	-	-36% **(<0.001)**	-48% **(<0.001)**

No adverse effects were observed at any dose, and a reduction in cholesterol at the 75 mg/kg dose occurred more rapidly when compared with the 50 mg/kg group (see **NYX-PCSK9i Safety Profile Information** on page 3).

The additional results reported today show that Nyrada's lead product candidate NYX-PCSK9i does not affect the body weight, food intake, or liver function of treated animals (see charts on page 3), while greatly reducing LDL cholesterol levels (***Figure 1***, ***Table 1***, and the chart on page 3). The data supports the continued development of the Company's hypercholesterolemia clinical candidate towards the clinic. It also confirms the suitability of NYX-PCSK9i as a potential oral treatment that can be combined with a statin in a single pill for the large cohort of patients that cannot reach their targeted LDL cholesterol levels taking a statin alone.

"The new results build on the impressive cholesterol-lowering results announced in December. They provide further evidence of a clear dose-response and confirm that NYX-PCSK9i dramatically reduces LDL or "bad" cholesterol. The next step, in addition to conducting further safety testing, is to determine what level of enhancement can be achieved by combining NYX-PCSK9i with statin, in the same mouse model," **said James Bonnar, Nyrada CEO.**

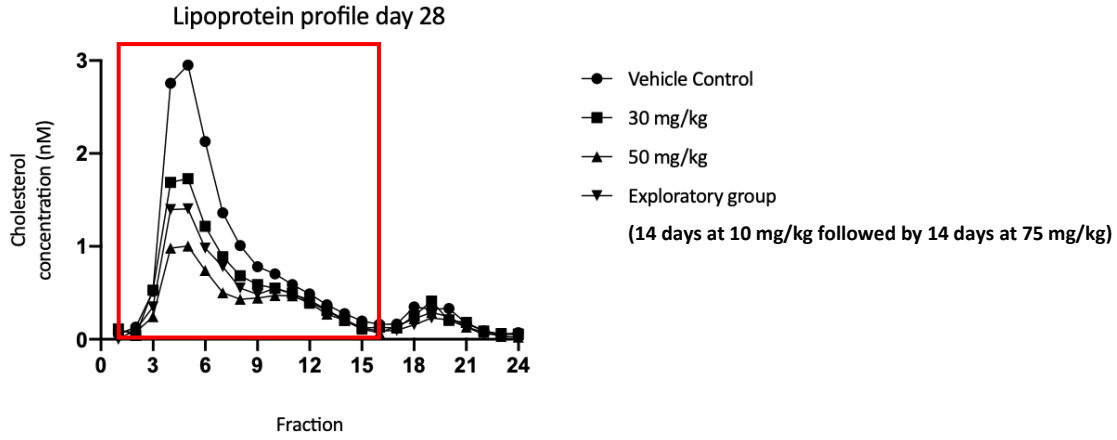
"The Nyrada team is excited to be working on the development of a small molecule PCSK9 inhibitor drug as the optimal treatment approach for reducing cholesterol. Such a drug will provide an effective, convenient, and cost-competitive treatment that would benefit the 70% of patients at risk of cardiovascular disease who are unable to reach their target LDL cholesterol level despite taking a statin[1]," Mr Bonnar added.

*"*What is most impressive about the results of this study is that it shows that NYX-PSCK9i, in a dose-dependent manner, can reduce LDL cholesterol by specifically targeting the PCSK9 protein. NYX-PSCK9i compound efficacy and safety that were initially established on human cells are now confirmed in *APOE*3-Leiden.CETP* mice, the animal model best suited to assess human lipoprotein metabolism *in vivo*," **said Professor Gilles Lambert, Nyrada Scientific Advisory Board Member and Professor in Cell Biology and Biochemistry at the University of La Réunion Medical School.**

[1] Wong ND *et al.* Prevalence of the American College of Cardiology/American Heart Association statin eligibility groups, statin use, and low-density lipoprotein cholesterol control. *J Clin Lipidol*. 2016;10(5): 1109–1118

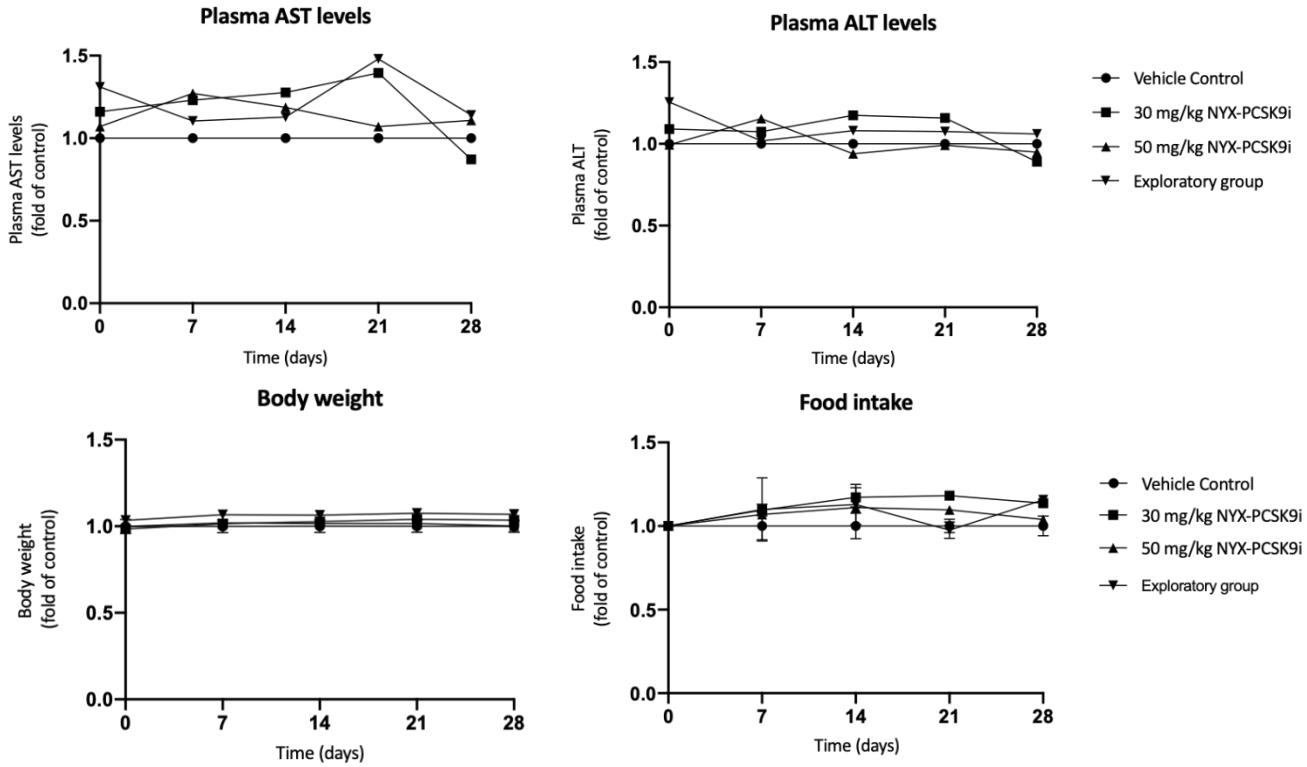
Lipoprotein Profile

Lipoprotein fraction analysis shows that the drug reduced LDL "bad" cholesterol (fraction less than 16, enclosed by the red box) in a dose-dependent manner (see chart below).



NYX-PCSK9i Safety Profile Information

Plasma levels of key liver enzymes AST and ALT were measured as markers of liver function. No elevation in AST or ALT levels was observed, consistent with normal liver function. Body weight and food intake were also measured as markers of overall health and appetite in animals. Treated and untreated animals had similar levels of food intake and body weight remained consistent throughout the 28-day study (please see charts below).



Next Steps

Further testing will explore the maximal effect of NYX-PCSK9i as a monotherapy and the potential enhancement effect when dosed in combination with a statin. The study is expected to commence in Q1 CY2021.

Nyrada anticipates announcing the results of this study in mid-2021. In the meantime, the Company has initiated larger-scale production of NYX-PCSK9i, ahead of preclinical regulatory studies to commence in Q1 CY2021.

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.

Glossary

In vivo	A medical test, experiment, or procedure that is done on (or in) a living organism such as a laboratory animal or human.
LDL	Low-density lipoprotein cholesterol, often referred to as "bad" cholesterol. This is defined as the lipoprotein fraction less than 16 (see the Lipoprotein Profile chart on page 3).
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 oral small molecule PCSK9 inhibitor, developed to bind to PCSK9 with the purpose to increase LDLR levels and thus 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 0.001 means there is a 0.1% likelihood that the result is a false positive and a 99.9% likelihood that the result is real. In general, the larger the study size, or the larger the effect, the lower the *p*-value.

-ENDS-

General

Nyrada has a solid cash position having A$5.2 million in the bank as at 30 September 2020. Also, the Company is actively pursuing a variety of non-dilutive funding and collaboration opportunities for the development of its drug candidates. The Company also confirms that its operations and supply chains currently remain unaffected by the COVID-19 pandemic.

About Nyrada Inc

Nyrada is a preclinical stage, drug discovery, and development company, specialising in novel small molecule drugs to treat cardiovascular and neurological 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, US, and the liability of its stockholders is limited.

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

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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.