



Nyrada Quarterly Activities Report & Appendix 4C

Highlights:

- **Cholesterol-Lowering Program:**
 - Preclinical safety and toxicology studies underway
 - Enhanced trial design for Phase I first-in-human study commencing in 1H CY2023:
 - Includes new cohorts of high cholesterol patients to assess exploratory efficacy in target population, in addition to healthy volunteers
 - Peer-reviewed paper on results from *in vivo* efficacy studies of NYX-PCSK9i published in the *Journal of Lipid Research*, conferring peer validation
- **Brain Injury Program:**
 - Ongoing preclinical stroke model study to be completed during Q4 CY2022
 - Preclinical *in vitro* safety and toxicology studies commenced
 - Phase I first-in-human study on track to commence 1H CY2023
- **Well-funded to pursue Phase I clinical development in CY2023, with cash balance of \$9.9M**

Nyrada Inc (ASX: NYR), a preclinical stage, drug development company specialising in novel small molecule drugs to treat cardiovascular and neurological diseases today provides its Quarterly Activities Report and Appendix 4C for the period ending 30 September 2022, and a summary of progress for its Cholesterol-Lowering and Brain Injury Programs.

Commenting on the quarter, Nyrada CEO, James Bonnar said: “Both the Cholesterol-Lowering and Brain Injury Programs continue to gain momentum as we get closer to starting our Phase I first-in-human studies next year. The team and I are focused on accelerating the pace of the clinical program for Nyrada’s Cholesterol-Lowering drug, to enable a quicker and more cost-effective transition to Phase II development.

“As part of this strategy, we have modified the cohorts in our Phase I protocol to include patients with high cholesterol, as well as healthy volunteers. By doing so, we will have an early indication of not only the safety and tolerability of our drug candidate in the target population, but also how well it lowers LDL-cholesterol levels. A selection of these new patients will also be on statins, and it is hoped we will see an additive effect from our drug candidate being taken in combination with a statin, resulting in an even greater reduction in LDL-cholesterol levels.



“It was also encouraging to see the team’s efforts recognised through the publication of a peer-reviewed paper in the Journal of Lipid Research, which covered the impressive preclinical results of *in vivo* efficacy studies of Nyrada’s cholesterol-lowering drug previously announced to shareholders,” Mr Bonnar added.

Preclinical Program Update

Cholesterol-Lowering Program – PCSK9 inhibitor

Preclinical Studies

A key focus during the quarter has been our preparatory work with Inotiv, the US Contract Research Organisation (CRO) appointed to conduct the required preclinical safety and pharmacology studies.

The method development and validation work is on track, with genotoxicity and *in vitro* safety pharmacology studies due to begin in November 2022, followed by *in vivo* toxicology and safety pharmacology studies.

Phase I Study

The primary objective of the planned Phase I study is to evaluate Nyrada’s drug candidate for safety and tolerability in healthy human volunteers. The Company has actively enhanced the Phase I clinical trial protocol to enable the inclusion of high cholesterol patient cohorts. This will inform on safety and efficacy in the target patient population, while also providing insights on drug-drug interactions in patients already on statins. Pleasingly, the new cohorts can be added to the trial design without adding significant expense to the program.

Information obtained from the expanded Phase I study lays the foundation for a faster transition to Phase II clinical development. The Phase I study is expected to commence in the first half of CY2023.

Efficacy Study Published in the Journal of Lipid Research

On 10 October, the Company announced the publication of a peer-reviewed scientific paper in the Journal of Lipid Research, authored by Nyrada’s Chief Scientific Officer, Dr. Benny Evison and Director of Preclinical Development, Dr. Alexandra Suchowerska.

The [paper](#) entitled, ‘*A novel, orally bioavailable, small-molecule inhibitor of PCSK9 with significant cholesterol-lowering properties in vivo*’, outlines the results of [previously announced](#) efficacy studies in hyperlipidemic APOE*3-Leiden.CETP mice, where NYX-PCSK9i was shown to reduce total cholesterol by 57%.



A [follow up study](#) showed the co-administration of NYX-PCSK9i with a statin further reduced total cholesterol. No adverse effects were identified and NYX-PCSK9i was well-tolerated at the efficacy doses used. This study was the first to show a combination treatment of a small-molecule PCSK9 inhibitor and a statin is highly effective in lowering LDL (“bad”) cholesterol.

Dr. Benny Evison has been selected to present the study’s findings at the 46th Annual Scientific Meeting of the Australian Atherosclerosis Society Inc, to be held in Melbourne between 23-25 November. Further opportunities to present the data are being explored, including overseas conferences.

Brain Injury Program

Preclinical Studies

Formulation Development

Formulation development work is being undertaken to ensure Nyrada can deliver a dose form suitable for intravenous drug administration of the Company’s lead product candidate. This is necessary for the required *in vivo* safety and toxicology studies, the planned Phase I trial and the preclinical stroke model study. This work has been initiated, with the results due in coming months.

Stroke Model Study

Preparations for this study are progressing well. It is expected to commence in the latter part of Q4 CY2022, with results expected early in the new year. The start of this study has been slightly delayed while the necessary formulation work for intravenous dosing is completed.

Safety Toxicology and Pharmacology Studies

Pleasingly, the *in vitro* safety and toxicology studies have commenced and the formulation development work necessary to ensure optimal drug delivery ahead of the *in vivo* studies, continues to advance.

Phase I Study

The Phase I study remains on track to commence in the first half of CY2023. It will be run in Australia with 40 healthy human volunteers participating.

The goal of this study is to assess the safety and pharmacokinetics of the Company’s lead brain injury drug candidate, NYR-BI02 in a randomised, double-blind, placebo controlled, single ascending dose escalating study in humans.



The study will support the development of Nyrada’s drug in both traumatic brain injury and stroke indications, significantly expanding the commercial opportunities available to the Company.

Corporate and Financial Summary

Cash Flow & Cash Position

Total cash operating outflows for the September 2022 quarter were approximately A\$1,283,000 (A\$781,000 million in the prior quarter). The Company anticipates cash outflows in future quarters will increase as both Programs progress toward and enter Phase I clinical trials.

Nyrada has a robust cash position of A\$9.9 million as at 30 September 2022 (A\$10.8 million as at 30 June 2022), ensuring the Company is well placed to pursue Phase I clinical development in CY2023 for its Brain Injury and Cholesterol-Lowering programs.

In accordance with Listing Rule 4.7C, payments made to related parties and their associates included in item 6.1 of the Appendix 4C was approximately A\$132,000 and included Director fees.

-ENDS-

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.

www.nyrada.com

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.

Appendix 4C

Quarterly cash flow report for entities subject to Listing Rule 4.7B

Name of entity

Nyrada Inc.

ABN

54 625 401 818

Quarter ended ("current quarter")

30 September 2022

Consolidated statement of cash flows	Current quarter \$A'000	Year to date (3 months) \$A'000
1. Cash flows from operating activities		
1.1 Receipts from customers	-	-
1.2 Payments for		
(a) research and development	(689)	(689)
(b) product manufacturing and operating costs	-	-
(c) advertising and marketing	-	-
(d) leased assets	-	-
(e) staff costs	(241)	(241)
(f) administration and corporate costs	(353)	(353)
1.3 Dividends received (see note 3)	-	-
1.4 Interest received	27	27
1.5 Interest and other costs of finance paid	-	-
1.6 Income taxes paid	-	-
1.7 Government grants and tax incentives	-	-
1.8 Other (provide details if material)	-	-
1.9 Net cash from / (used in) operating activities	(1,256)	(1,256)
2. Cash flows from investing activities		
2.1 Payments to acquire or for:		
(a) entities	-	-
(b) businesses	-	-
(c) property, plant and equipment	-	-
(d) investments	-	-
(e) intellectual property	-	-
(f) other non-current assets	-	-

Consolidated statement of cash flows		Current quarter \$A'000	Year to date (3 months) \$A'000
2.2	Proceeds from disposal of:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	-	-
	(d) investments	-	-
	(e) intellectual property	-	-
	(f) other non-current assets	-	-
2.3	Cash flows from loans to other entities	-	-
2.4	Dividends received (see note 3)	-	-
2.5	Other (provide details if material)	-	-
2.6	Net cash from / (used in) investing activities	-	-

3.	Cash flows from financing activities		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)	-	-
3.2	Proceeds from issue of convertible debt securities	-	-
3.3	Proceeds from exercise of options	-	-
3.4	Transaction costs related to issues of equity securities or convertible debt securities	-	-
3.5	Proceeds from borrowings	-	-
3.6	Repayment of borrowings	-	-
3.7	Transaction costs related to loans and borrowings	-	-
3.8	Dividends paid	-	-
3.9	Other (provide details if material)	-	-
3.10	Net cash from / (used in) financing activities	-	-

4.	Net increase / (decrease) in cash and cash equivalents for the period		
4.1	Cash and cash equivalents at beginning of period	10,816	10,816
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(1,256)	(1,256)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	-	-

Consolidated statement of cash flows		Current quarter \$A'000	Year to date (3 months) \$A'000
4.4	Net cash from / (used in) financing activities (item 3.10 above)	-	-
4.5	Effect of movement in exchange rates on cash held	302	302
4.6	Cash and cash equivalents at end of period	9,862	9,862

5.	Reconciliation of cash and cash equivalents at the end of the quarter (as shown in the consolidated statement of cash flows) to the related items in the accounts	Current quarter \$A'000	Previous quarter \$A'000
5.1	Bank balances	9,862	10,816
5.2	Call deposits	-	-
5.3	Bank overdrafts	-	-
5.4	Other (provide details)	-	-
5.5	Cash and cash equivalents at end of quarter (should equal item 4.6 above)	9,862	10,816

6.	Payments to related parties of the entity and their associates	Current quarter \$A'000
6.1	Aggregate amount of payments to related parties and their associates included in item 1	132
6.2	Aggregate amount of payments to related parties and their associates included in item 2	-
<i>Note: if any amounts are shown in items 6.1 or 6.2, your quarterly activity report must include a description of, and an explanation for, such payments.</i>		

The amount at 6.1 includes Director fees and salary (including superannuation) and consulting fees for directors and related parties.

Quarterly cash flow report for entities subject to Listing Rule 4.7B

7. Financing facilities	Total facility amount at quarter end \$A'000	Amount drawn at quarter end \$A'000
<i>Note: the term "facility" includes all forms of financing arrangements available to the entity. Add notes as necessary for an understanding of the sources of finance available to the entity.</i>		
7.1 Loan facilities	-	-
7.2 Credit standby arrangements	-	-
7.3 Other (please specify)	-	-
7.4 Total financing facilities	-	-
7.5 Unused financing facilities available at quarter end		-
7.6 Include in the box below a description of each facility above, including the lender, interest rate, maturity date and whether it is secured or unsecured. If any additional financing facilities have been entered into or are proposed to be entered into after quarter end, include a note providing details of those facilities as well.		

8. Estimated cash available for future operating activities	\$A'000
8.1 Net cash from / (used in) operating activities (item 1.9)	(1,256)
8.2 Cash and cash equivalents at quarter end (item 4.6)	9,862
8.3 Unused finance facilities available at quarter end (item 7.5)	-
8.4 Total available funding (item 8.2 + item 8.3)	9,862
8.5 Estimated quarters of funding available (item 8.4 divided by item 8.1)	7.9
<i>Note: if the entity has reported positive net operating cash flows in item 1.9, answer item 8.5 as "N/A". Otherwise, a figure for the estimated quarters of funding available must be included in item 8.5.</i>	
8.6 If item 8.5 is less than 2 quarters, please provide answers to the following questions:	
8.6.1 Does the entity expect that it will continue to have the current level of net operating cash flows for the time being and, if not, why not?	
Answer: N/A	
8.6.2 Has the entity taken any steps, or does it propose to take any steps, to raise further cash to fund its operations and, if so, what are those steps and how likely does it believe that they will be successful?	
Answer: N/A	
8.6.3 Does the entity expect to be able to continue its operations and to meet its business objectives and, if so, on what basis?	
Answer: N/A	
<i>Note: where item 8.5 is less than 2 quarters, all of questions 8.6.1, 8.6.2 and 8.6.3 above must be answered.</i>	

Compliance statement

- 1 This statement has been prepared in accordance with accounting standards and policies which comply with Listing Rule 19.11A.
- 2 This statement gives a true and fair view of the matters disclosed.

26 October 2022

Date:

By order of the Board

Authorised by:
 (Name of body or officer authorising release – see note 4)

Notes

1. This quarterly cash flow report and the accompanying activity report provide a basis for informing the market about the entity's activities for the past quarter, how they have been financed and the effect this has had on its cash position. An entity that wishes to disclose additional information over and above the minimum required under the Listing Rules is encouraged to do so.
2. If this quarterly cash flow report has been prepared in accordance with Australian Accounting Standards, the definitions in, and provisions of, *AASB 107: Statement of Cash Flows* apply to this report. If this quarterly cash flow report has been prepared in accordance with other accounting standards agreed by ASX pursuant to Listing Rule 19.11A, the corresponding equivalent standard applies to this report.
3. Dividends received may be classified either as cash flows from operating activities or cash flows from investing activities, depending on the accounting policy of the entity.
4. If this report has been authorised for release to the market by your board of directors, you can insert here: "By the board". If it has been authorised for release to the market by a committee of your board of directors, you can insert here: "By the [name of board committee – eg Audit and Risk Committee]". If it has been authorised for release to the market by a disclosure committee, you can insert here: "By the Disclosure Committee".
5. If this report has been authorised for release to the market by your board of directors and you wish to hold yourself out as complying with recommendation 4.2 of the ASX Corporate Governance Council's *Corporate Governance Principles and Recommendations*, the board should have received a declaration from its CEO and CFO that, in their opinion, the financial records of the entity have been properly maintained, that this report complies with the appropriate accounting standards and gives a true and fair view of the cash flows of the entity, and that their opinion has been formed on the basis of a sound system of risk management and internal control which is operating effectively.