



30 January 2023

Sydney, Australia

Nyrada Quarterly Activities Report & Appendix 4C

Highlights:

- **Cholesterol-Lowering Program:**
 - Preclinical safety and toxicology studies tracking well, *in vivo* studies underway
 - Phase I/IIa study in 1H CY2023 will assess safety and tolerability in healthy human volunteers as well as exploratory efficacy in high cholesterol patients
 - **Brain Injury Program:**
 - Collaboration with WRAIR & UNSW Sydney extended for further two years to CY2025
 - Preclinical *in vitro* safety and toxicology studies advancing well
 - Phase I first-in-human study on track to commence 1H CY2023
 - Results from preclinical stroke model study expected Q1 CY2023
 - **Well positioned to undertake Phase I studies in 1H CY2023, with cash balance of \$9.3M**
-

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 31 December 2022, including a summary of progress for its Cholesterol-Lowering and Brain Injury Programs.

Commenting on the quarter, Nyrada CEO, James Bonnar said: “I am proud of the team’s efforts to ensure we ended 2022 in a strong position, ahead of our drug development programs’ transitioning to the clinic during the first half of this year.

“Modifications to the Phase I/IIa clinical trial protocol for the Cholesterol-Lowering Program will provide early efficacy signals from Nyrada’s drug candidate in high cholesterol patients, saving up to 12 months and expediting the transition to Phase IIb clinical development.

“We have also extended our existing collaboration with WRAIR and UNSW Sydney for a further two years to January 2025. Nyrada continues to benefit from working alongside the specialist traumatic brain injury research teams at WRAIR and UNSW as our Brain Injury Program advances. The team and I are looking forward to delivering strong results in the year ahead,” **Mr Bonnar added.**



Preclinical Programs Update

Cholesterol-Lowering Program – Small Molecule PCSK9 Inhibitor

More than 62 million Americans have risk factors associated with cardiovascular disease and are therefore eligible for cholesterol-lowering treatment.¹ From this population, approximately 27 million take a statin drug, however, more than 18 million, or close to 70% are unable to achieve their safe target cholesterol level. With a global aging population, public need for new, more effective, and convenient cholesterol-lowering medication will only increase.

Nyrada has shown through preclinical studies that its small molecule PCSK9 inhibitor is able to significantly lower LDL (“bad”) cholesterol levels, while also increasing the number of LDL receptors which are responsible for removing cholesterol from the blood stream. This drug candidate is intended to be taken in the form of a pill, on its own or in combination with a statin, overcoming the inconvenience of expensive injectable PCSK9 inhibitors.

Globally, the Company continues to see growing interest in the development of oral PCSK9 inhibitors, which clinicians consider to be an optimal approach to LDL-cholesterol lowering as an adjunct to statin treatment.

Preclinical Studies

During the last quarter, formulation development work prior to initiation of animal toxicology studies was undertaken to ensure Nyrada’s cholesterol-lowering drug candidate can be dosed to achieve sufficiently high exposures. High dosing in toxicology studies is a requirement of regulators such as Australian human ethics committees and the US Food and Drug Administration, in order to provide acceptable data on the safety margin between efficacious and toxic dose levels.

Preclinical *in vitro* safety and toxicology studies also commenced at Nyrada’s US-based contract research organisation (CRO) partner, Inotiv, and are progressing well. Nyrada has been working closely with Inotiv over the Christmas and New Year holiday period to ensure the seamless progression of the eight Good Laboratory Practice (GLP) studies required by the regulators, ahead of applying for human ethics approval to start Phase I first-in-human studies. The first of the *in vivo* GLP studies commenced in early January.

Phase I/IIa Study

Nyrada’s Phase I/IIa study is on track to commence during the first half of this year. The primary objective of the study is to evaluate Nyrada’s drug candidate for safety and tolerability in healthy human volunteers. Recently announced modifications to the Phase I/IIa study design

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 in US. *J Clin Lipidology*. 2016.



to include cohorts of high cholesterol patients will also provide the Company with an early indication of the efficacy of Nyrada's drug candidate in the target patient population.

The inclusion of these cohorts will enable an accelerated path to a Phase IIb study than would typically be possible, a potential saving of up to 12 months. The new cohorts can be added to the trial design without adding significant expense to the program.

Brain Injury Program

Nyrada is developing a first-in-class neuroprotectant drug to prevent secondary brain injury, which occurs in the hours and days following the primary injury, leading to increased disability and reduced quality of life.

Each year, globally, more than 60 million people suffer a concussion or moderate to severe traumatic brain injury (TBI)², yet no FDA-approved treatment for secondary brain injury exists. For stroke the need is similar, with only limited treatment options available. Nyrada's brain injury drug candidate offers the potential to reduce the secondary injury, and therefore reduce patient mortality and disability and improve quality of life.

Two-Year Extension to Collaboration with Walter Reed Army Institute of Research (WRAIR) & UNSW Sydney

Post the quarterly period, Nyrada announced a two-year extension to its collaboration with WRAIR and UNSW, from February 2023 through to January 2025.

Changes made to the Collaborative Research and Development Agreement between the parties (Revised CRADA) will enable testing of Nyrada's brain injury drug candidate in a rodent model of penetrating traumatic brain injury (PTBI), which mimics the serious head injuries suffered by military service members. The study will measure the degree to which intravenous administration of Nyrada's drug leads to a reduction in injury size following a PTBI.

This work builds on the studies already completed under the original CRADA, which included an extensive pilot study run by WRAIR and UNSW to determine the most suitable model for testing Nyrada's brain injury drug.

By utilising a specialised MRI technique called fractional anisotropy (FA), the team at UNSW were able to quantify the sizes of the primary and secondary injury volumes in the WRAIR PTBI and controlled cortical impact (CCI) models. It was determined that the PTBI model was more consistent in producing a quantifiable secondary injury measurement compared to the CCI model using the FA method of assessment.

² National Academies of Sciences, Engineering, and Medicine 2022. Traumatic Brain Injury: A Roadmap for Accelerating Progress. Washington, DC: The National Academies Press. <https://doi.org/10.17226/25394>



This data formed the basis of the design for the TBI efficacy study and informed on the number of animals required to appropriately power the efficacy study.

Key Terms of the Revised CRADA:

- The TBI efficacy study will be undertaken in 1H CY2023 with the results expected in 2H CY2023.
- All work under the existing CRADA has been completed as part of an in-kind non-financial arrangement between Nyrada and WRAIR. Pursuant to the terms of the Revised CRADA, Nyrada will provide WRAIR with sufficient drug quantities to complete the study, and US\$150,000 to cover key costs associated with the work. In exchange, the studies will be undertaken by WRAIR personnel at WRAIR's specialist TBI research facility in the US.
- WRAIR and Nyrada will continue to work together to pursue non-dilutive funding opportunities to further progress the Company's Brain Injury Program.

Preclinical Studies

Formulation Development

The formulation development work necessary to ensure Nyrada can deliver an optimal dose form suitable for intravenous administration of our brain injury drug candidate is progressing well. This work is essential for the upcoming *in vivo* safety and toxicology studies, the scheduled Phase I trial and stroke model study.

Stroke Model Study

The efficacy of Nyrada's brain injury drug candidate is being evaluated in a well-established preclinical stroke model. This model was previously used by Nyrada to test the efficacy of its first-generation molecule, which showed a promising efficacy signal.

The Company previously indicated that this study would be undertaken in the latter part of Q4 CY2022, with results expected early in the new year. However, additional time has been required to progress the formulation development work, resulting in a slight delay to the commencement of the stroke model study. Nyrada now expects the results of the stroke model study to be available during the first quarter of this year.

The stroke study is outside of the work being undertaken as part of Nyrada's collaboration with WRAIR and UNSW. WRAIR's focus remains solely on developing a drug to mitigate the impact of TBI on military service members.



Safety Toxicology and Pharmacology Studies

The *in vitro* safety and toxicology studies have started and continue to advance as anticipated, with *in vivo* studies to follow. The required *in vitro* and *in vivo* preclinical studies will be used to evaluate the safety and tolerability of Nyrada's drug. Data from these studies will determine the safe starting dose for the Phase I study.

Nyrada recently completed an *in vitro* hERG ion channel study, which is designed to measure whether a drug candidate blocks hERG potassium channels. Blockage of these channels in patients can lead to a serious side effect of heart arrhythmia (irregular heartbeats). Pleasingly, activity of Nyrada's brain injury drug candidate on the hERG channel is within the acceptable range for the drug to be considered safe. The next step will be to further confirm our drug candidate's safety in an *in vivo* study.

Phase I Study

Expected to commence in the first half of this year, the Phase I study will evaluate the safety and pharmacokinetics of Nyrada's brain injury drug candidate. Structured as a randomised, double-blind, placebo controlled, single ascending dose escalating study in humans, it 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.

The study will be run in Australia with 40 healthy human volunteers participating.

Corporate and Financial Summary

Cash Flow & Cash Position

Total cash operating outflows for the December 2022 quarter were approximately A\$1.5 million (A\$1.3 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 strong cash position of A\$9.3 million as at 31 December 2022 (A\$9.9 million as at 30 September 2022), positioning the Company well 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\$146,000 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.

Investor & Corporate Enquiries:

Laura Vize
Investor Relations Manager
T: 02 9498 3390
E: info@nyrada.com

Company Secretary:

David Franks
T: 02 8072 1400
E: David.Franks@automicgroup.com.au

Media Enquiries:

Catherine Strong
Citadel-MAGNUS
T: 02 8234 0111
E: cstrong@citadelmagnus.com

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")

31 December 2022

Consolidated statement of cash flows	Current quarter \$A'000	Year to date (6 months) \$A'000
1. Cash flows from operating activities		
1.1 Receipts from customers	-	-
1.2 Payments for		
(a) research and development	(787)	(1,476)
(b) product manufacturing and operating costs	-	-
(c) advertising and marketing	-	-
(d) leased assets	-	-
(e) staff costs	(244)	(485)
(f) administration and corporate costs	(494)	(847)
1.3 Dividends received (see note 3)	-	-
1.4 Interest received	37	64
1.5 Interest and other costs of finance paid	-	-
1.6 Income taxes paid	-	-
1.7 Government grants and tax incentives	1,169	1,169
1.8 Other (provide details if material)	-	-
1.9 Net cash from / (used in) operating activities	(319)	(1,575)
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 (6 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	9,862	10,816
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(319)	(1,575)
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 (6 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	(199)	103
4.6	Cash and cash equivalents at end of period	9,344	9,344

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	9,344	9,862
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)	9,344	9,862

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	146
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)	(319)
8.2 Cash and cash equivalents at quarter end (item 4.6)	9,344
8.3 Unused finance facilities available at quarter end (item 7.5)	-
8.4 Total available funding (item 8.2 + item 8.3)	9,344
8.5 Estimated quarters of funding available (item 8.4 divided by item 8.1)	29.3
<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.

30 January 2023

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.