



21 January 2022

Sydney, Australia

Nyrada Quarterly Activities Report & Appendix 4C

Highlights:

- **Cholesterol-Lowering Program:**
 - Charles River Laboratories appointed to conduct safety pharmacology and toxicology studies in Nyrada's cholesterol-lowering drug in the US in 1H CY2022
 - Australian world-class clinical research centre will conduct Phase I first-in-human clinical trial, set to commence in 2H CY2022
 - Phase I dose escalation study will evaluate the safety, tolerability and efficacy of Nyrada's cholesterol-lowering drug candidate
 - PCT patent application filed in Dec 2021 for new generation cholesterol-lowering compounds, expanding protection of Nyrada's PCSK9 inhibitor technology
 - **Brain Injury Program:**
 - Nyrada's brain injury drug candidate to be tested in preclinical model of stroke in Q1 CY2022
 - Pilot Traumatic Brain Injury (TBI) preclinical study under Nyrada-UNSW Sydney-WRAIR collaboration progressing well to optimise efficacy study design
 - Phase I study to commence in 2H CY2022, evaluating safety and tolerability of Nyrada's drug in two indications, TBI and stroke
 - **Robust cash position of A\$11.1 million:** R&D tax incentive rebate of A\$1.3 million received in January 2022
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Nyrada Inc (ASX: NYR), a preclinical stage, drug development company specialising in novel small molecule drugs to treat cardiovascular and neurological diseases is pleased to provide its Quarterly Activities Report and Appendix 4C for the period ending 31 December 2021, and a summary of progress for its Cholesterol-Lowering and Brain Injury Programs.

Commenting on the quarter, Nyrada CEO, James Bonnar said: "Our drug development programs made good progress at the end of 2021, and we are excited to be advancing to the next stage as Nyrada begins to transition to a clinical drug development company in 2022.

"The Phase I clinical trial for the Cholesterol-Lowering Program will be the first time our drug candidate is evaluated in humans, representing a significant milestone for Nyrada. Furthermore, the Phase I clinical trial for the Brain Injury Program will support the



development of Nyrada’s drug in both TBI and stroke indications, significantly expanding the commercial opportunities available to the Company. The team and I look forward to keeping investors informed of our progress in what we expect will be an active and exciting year for Nyrada,” Mr Bonnar added.

Preclinical Program Update

Cholesterol-Lowering Program – PCSK9 inhibitor

Preclinical Studies

Nyrada has appointed Charles River Laboratories, Inc. (“Charles River”) to conduct the Company’s preclinical studies in the US in the first half of this year, ahead of a Phase I cholesterol-lowering trial in Australia. Charles River has supported the development of more than 80% of the drugs approved by the US Food & Drug Administration in the past three years.

The required preclinical studies will be used to evaluate the safety and tolerability of Nyrada’s drug in research models. This is a necessary part of the drug development process given Nyrada’s candidate has not been tested in humans. Data from these studies will determine the safe starting dose for the Phase I first-in-human study.

Phase I Study

The Phase I study will be a first-in-human, double-blind, randomised, dose escalation design evaluating the safety, tolerability, and pharmacokinetics of Nyrada’s leading drug candidate in approximately 56 healthy volunteers aged 18 to 50 years. The Company will also evaluate efficacy by measuring changes in LDL or “bad” cholesterol levels in the blood.

Nyrada’s drug candidate will be administered to participants as a once daily oral dose over the 14-day treatment period, to assess safety, tolerability, and efficacy. In the trial, participants will be split into 7 groups of 8, with each person in groups 1-5 receiving a single dose of Nyrada’s drug candidate or placebo, whilst healthy volunteers in groups 6 and 7 will receive a dose of Nyrada’s drug candidate or placebo over 14 days. Pathology samples and data will be collected at selected time points over the trial period for all groups.

Pending scale-up manufacturing of the drug and ethics committee approval of the trial protocol, recruitment and dosing of the first participant is expected to commence in 2H CY2022.

Patent Cooperation Treaty (PCT) Application

Nyrada’s medicinal chemistry program continued to generate further promising PCSK9 inhibitor analogues, which enabled the Company to file a PCT application for new generation PCSK9 inhibitor compounds in December 2021. A PCT application makes it possible to seek protection for an invention simultaneously in a large number of countries by filing a single “international”



patent application, instead of filing several separate national or regional applications. This application builds on the patent granted by the US Patent and Trademark Office, as announced on 30 July 2021, and the corresponding European Patent which is in the final stages of examination.

Brain Injury Program

Preclinical TBI Efficacy Study Progress

In the lead-up to the efficacy study with Nyrada's brain injury drug candidate, a pilot study is being conducted to optimise the design of the efficacy study. A key focus of this pilot study is to refine the location and extent of injury in each model and select optimal timepoints to assess a therapeutic effect of Nyrada's drug in preventing secondary brain injury.

Brain samples from the Controlled Cortical Impact (CCI) and Penetrating Ballistic Brain Injury (PBBI) models have been collected from the Walter Reed Army Institute of Research (WRAIR) and are currently undergoing assessment at the Translational Neuroscience Facility of UNSW, utilising their sophisticated MRI technology (T2-weighted and Fractional Anisotropy MRI) to establish the nature and extent of injury. This reflects brain imaging technology used in hospital emergency rooms.

The data from the pilot study will allow Nyrada to ascertain the number of animals that will be required to provide a meaningful assessment of the therapeutic effect of the Company's drug.

Testing Nyrada's Brain Injury Drug Candidate in Stroke

The efficacy of Nyrada's brain injury drug candidate will be evaluated in a well-established preclinical model of stroke during the first quarter of this year. The model is called the Photothrombotic Model of Ischemia, where localised clot formation is achieved in a specific brain region, leading to a stroke. This model was previously used by Nyrada to test the efficacy of its first-generation molecule, which showed a promising efficacy signal.

This work in stroke is outside of the studies 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.

A key advantage of the drug that Nyrada is developing is it can be administered to stroke and TBI patients in the same manner, by way of intravenous dosing over a 3-day period, which is matched to patient emergency hospital admission.

Phase I Study

Nyrada expects to commence a Phase I first-in-human study for its Brain Injury Program in the second half of CY2022. The Phase I study will be run in Australia and will evaluate the safety and tolerability of the Company's brain injury drug candidate.



Nyrada will provide an update on the preclinical studies with WRAIR and UNSW, as well selection of the contract research organisation and study design for the Phase I study in the first half of this year.

Corporate and Financial Summary

Cash Flow & Cash Position

Total cash operating outflows for the December 2021 quarter were approximately A\$1.3 million (A\$1.2 million in the prior quarter). The Company anticipates cash outflows in future quarters will increase as both Programs progress towards Phase I clinical trials.

Nyrada's cash position was A\$11.1 million as at 31 December 2021. Subsequent to the end of the quarter, the Company received a FY2021 R&D tax incentive refund of \$1.3 million, further boosting available capital resources. 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\$162,000 and included Director fees.

A summary of the operating cashflows for the twelve months ending 31 December 2021, compared with the proposed use of funds in Year 2 of Nyrada's Prospectus dated 26 November 2019 and Supplementary Prospectus dated 9 December 2019 is outlined below:

	Year 2 12-month period Per Prospectus (A\$)	12-month period ending 31 Dec 2021 (A\$)
Research & Development (R&D) - Salaries	1,500,000	928,000
R&D – Brain Injury program	1,000,000	910,000
R&D – Cholesterol-Lowering program	700,000	1,550,000
Other R&D	500,000	13,000
Repayment of part of the Noxopharm Loan	-	342,000
Working Capital	700,000	1,809,000
Government grants and tax incentives	-	(976,000)
Total	4,400,000	4,576,000

During the twelve-month period ending 31 December 2021, overall R&D spend remains broadly in line with the estimated use of funds as set out in the Prospectus and Supplementary Prospectus.



The estimated R&D Tax incentive inflows for FY19, FY20 and FY21 were not included in the use of funds statement and are partially funding the working capital requirements along with the Company's R&D programs.

Nyrada believes the working capital outflows are consistent with the requirements for an ASX listed biotech company of its size. As a result of last year's capital raise, the Company has sufficient cash reserves to complete Phase I studies in both its Brain Injury and Cholesterol-Lowering programs.

-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 2021

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	(541)	(1,043)
(b) product manufacturing and operating costs	-	-
(c) advertising and marketing	-	-
(d) leased assets	-	-
(e) staff costs	(236)	(464)
(f) administration and corporate costs	(539)	(1,004)
1.3 Dividends received (see note 3)	-	-
1.4 Interest received	2	4
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	(1,314)	(2,507)
2. Cash flows from investing activities		
2.1 Payments to acquire or for:		
(a) entities	-	-
(b) businesses	-	-
(c) property, plant and equipment	(2)	(2)
(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	(2)	(2)

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	-	(224)
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)	-	(45)
3.10	Net cash from / (used in) financing activities	-	(269)

4.	Net increase / (decrease) in cash and cash equivalents for the period		
4.1	Cash and cash equivalents at beginning of period	12,445	13,751
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(1,314)	(2,507)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	(2)	(2)

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)	-	(269)
4.5	Effect of movement in exchange rates on cash held	(24)	132
4.6	Cash and cash equivalents at end of period	11,105	11,105

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	11,105	12,445
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)	11,105	12,445

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	162
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) for directors and related parties.

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)	(1,314)
8.2 Cash and cash equivalents at quarter end (item 4.6)	11,105
8.3 Unused finance facilities available at quarter end (item 7.5)	-
8.4 Total available funding (item 8.2 + item 8.3)	11,105
8.5 Estimated quarters of funding available (item 8.4 divided by item 8.1)	8.5
<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.

21 January 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.