



27 July 2021

Sydney, Australia

Nyrada Quarterly Activities Report & Appendix 4C

Highlights:

- **Cholesterol-Lowering Program Update:**
 - *In vivo* efficacy study in a specialised mouse model showed NYX-PCSK9i reduced total cholesterol by 46% as a monotherapy and 65% in combination with the leading statin drug Lipitor® (atorvastatin, Pfizer)
 - NYX-PCSK9i selected as the preferred compound for safety pharmacology and toxicology studies to commence in H1 FY22
 - Phase I first-in-human study anticipated to commence mid-2022
 - **Brain Injury Program Progress:**
 - New lead drug candidate NYR-BI01 advances to efficacy studies in collaboration with the Walter Reed Army Institute of Research (WRAIR) and University of NSW
 - Testing of NYR-BI01 in WRAIR's Traumatic Brain Injury (TBI) animal model expected to start in Q1 FY22, with results expected before the end of the year
 - **Capital Raising Program Completed:** all resolutions approved at the June EGM, with the total program raising A\$11.5M to fund Phase I clinical trials in both Programs
 - **Robust cash position of A\$13.8 million:** including R&D tax incentive rebate of A\$1.0M
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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 30 June 2021, and an update on the progress of its Cholesterol-Lowering and Brain Injury Programs.

Commenting on the progress and outlook, Nyrada CEO James Bonnar said: "After a good quarter of preclinical progress and results, Nyrada is entering an exciting phase to complete the remaining studies before we start a first-in-human trial for our Cholesterol-Lowering Program in mid-2022. Our lead compound, NYX-PCSK9i outperformed the best-selling statin drug Lipitor® in our recent *in vivo* study to reduce total cholesterol by 47%, vs 27% for Lipitor® alone. This is an impressive result that bodes well for NYX-PCSK9i's selection as the optimal candidate to take into a Phase I study in 2022. The team and I look forward to reporting on the results of the upcoming safety pharmacology and toxicology studies later in the year.



“We also achieved an important milestone in our Brain Injury Program with NYR-BI01, our newly improved and highly potent drug candidate crossing the blood-brain-barrier at above therapeutic levels. This means our drug can reach the area of the brain damaged by traumatic brain injury. We are making solid gains in our preparations to evaluate NYR-BI01 in WRAIR’s TBI animal model, which we expect to report on before the end of the year,” Mr Bonnar added.

Preclinical Program Update

Brain Injury Program

In June, Nyrada announced the selection of a new analogue of its brain injury candidate, called NYR-BI01, to be taken forward into its collaboration studies with WRAIR. NYR-BI01 is a more potent and improved version of its predecessor, NYX-1010. This follows a pharmacokinetic study in which NYR-BI01 showed impressive drug-like characteristics and encouragingly, was able to cross the blood-brain-barrier at above therapeutic levels.

The TBI animal models to be used in the planned WRAIR studies are highly specialised and mimic moderate to severe injury in humans. Work is well underway by WRAIR and UNSW Sydney to determine the baseline injury signal in these models, using multiple MRI techniques, to establish endpoint measurements for therapeutic assessment. MRI is used as a common modality in the clinical setting to assess injury localisation and volume in patients, making the pilot study extremely relevant.

Following this pilot work, Nyrada anticipates testing of NYR-BI01 in the TBI models at WRAIR will commence in the third quarter of 2021, with the results of the study expected before the end of the year.

Cholesterol-Lowering Program – PCSK9 inhibitor

During the quarter, Nyrada reported results from an *in vivo* efficacy study in a specialised transgenic mouse model (APOE*3-Leiden.CETP) to evaluate NYX-PCSK9i in combination with a statin. The aim of the 5-week study was to determine if NYX-PCSK9i enhances the efficacy of a statin drug when co-administered.

Results from the study showed NYX-PCSK9i reduced total cholesterol by 46% as a monotherapy, and 65% when dosed in combination with the statin drug Lipitor® over the study period. This compares to the reduction achieved using Lipitor alone of 27%. Pleasingly, NYX-PCSK9i was well-tolerated with no significant changes in food intake, body weight, or liver function observed.

NYX-PCSK9i has been selected as the preferred compound for safety pharmacology and toxicology studies to commence in the second half of 2021, at an internationally recognised



Contract Research Organisation, with a Phase I first-in-human study anticipated to commence mid-2022.

Earlier medicinal chemistry work had revealed analogues NYX-PCSK9i-211 and NYX-PCSK9i-212 as two compounds more potent than NYX-PCSK9i, which led to their inclusion as additional arms of the study. NYX-PCSK9i-211 showed a 39% reduction by 14 days (compared with a 24% reduction by NYX-PCSK9i over the same period), however, the compound was not well-tolerated. Notwithstanding, NYX-PCSK9i-211 has the characteristics of a strong second-generation compound. NYX-PCSK9-212 showed a modest reduction in total cholesterol but did not reach statistical significance.

Nyrada has several promising compounds in its portfolio including NYX-PCSK9i-211 and continues to optimise and develop these through its medicinal chemistry program that runs in tandem with its primary preclinical studies.

Corporate and Financial Summary

Financing

At the Extraordinary General Meeting (EGM) held on 16 June, shareholders approved the issuance of CHES Depositary Interests (CDIs) to investors, Nyrada Directors, Management and advisors as part of the second tranche of Nyrada's Capital Raising Program. The second tranche raised A\$4.3 million, bringing the total funds raised through the Company's Capital Raising Program to A\$11.5 million.

The proceeds will be used to fund Phase I clinical trials of Nyrada's Cholesterol-Lowering and Brain Injury drug candidates, with the additional funds raised enabling further proof-of-concept studies evaluating existing drug candidates in additional therapeutic areas, to deliver shareholder value.

Cash Flow & Cash Position

Total cash operating outflows for the June 2021 quarter were approximately A\$1.6 million (A\$1.1 million in the prior quarter). Looking ahead, the Company expects cash outflows in future quarters to increase as both Programs progress towards Phase I clinical trials.

Nyrada's cash position was A\$13.8 million as at 30 June 2021. During the quarter, Nyrada received an R&D tax incentive rebate for the 2020 financial year of A\$976,372. In addition, A\$4.3 million was received following settlement of the second tranche of the Company's Capital Raising Program, bringing the total funds received to A\$11.5 million.



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\$103,000 and included Director fees.

A summary of the operating cashflows for the six months ending 30 June 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\$)	6-month period ending 30 June 2021 (A\$)
Research & Development (R&D) - Salaries	1,500,000	464,000
R&D – Brain Injury program	1,000,000	397,000
R&D – Cholesterol-Lowering program	700,000	1,018,000
Other R&D	500,000	13,000
Repayment of part of the Noxopharm Loan	-	342,000
Working Capital	700,000	806,000
Government grants and tax incentives	-	(976,000)
Total	4,400,000	2,064,000

During the six-month period ending 30 June 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 FY2019, FY2020 and FY2021 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 requirements for an ASX listed biotech company of its size. As a result of the recent 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.

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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.

ARBN

625 401 818

Quarter ended ("current quarter")

30 June 2021

Consolidated statement of cash flows	Current quarter \$A'000	Year to date (12 months) \$A'000
1. Cash flows from operating activities		
1.1 Receipts from customers	-	-
1.2 Payments for		
(a) research and development	(930)	(2,455)
(b) product manufacturing and operating costs	-	-
(c) advertising and marketing	-	-
(d) leased assets	-	-
(e) staff costs	(251)	(920)
(f) administration and corporate costs	(451)	(1,525)
1.3 Dividends received (see note 3)	-	-
1.4 Interest received	1	3
1.5 Interest and other costs of finance paid	-	-
1.6 Income taxes paid	-	-
1.7 Government grants and tax incentives	976	2,102
1.8 Other (provide details if material)	-	-
1.9 Net cash from / (used in) operating activities	(655)	(2,795)
2. Cash flows from investing activities		
2.1 Payments to acquire or for:		
(a) entities	-	-
(b) businesses	-	-
(c) property, plant and equipment	(5)	(5)
(d) investments	-	-
(e) intellectual property	-	-
(f) other non-current assets	-	-

Consolidated statement of cash flows		Current quarter \$A'000	Year to date (12 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	(5)	(5)

3.	Cash flows from financing activities		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)	4,297	11,501
3.2	Proceeds from issue of convertible debt securities	-	-
3.3	Proceeds from exercise of options	-	369
3.4	Transaction costs related to issues of equity securities or convertible debt securities	(216)	(216)
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		
	- Repayment of Noxopharm Loan (Noxopharm Loan was settled in full post the March 2021 Placement)	-	(342)
	- Other	-	45
3.10	Net cash from / (used in) financing activities	4,081	11,357

Consolidated statement of cash flows		Current quarter \$A'000	Year to date (12 months) \$A'000
4.	Net increase / (decrease) in cash and cash equivalents for the period		
4.1	Cash and cash equivalents at beginning of period	10,255	5,146
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(655)	(2,795)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	(5)	(5)
4.4	Net cash from / (used in) financing activities (item 3.10 above)	4,081	11,357
4.5	Effect of movement in exchange rates on cash held	75	48
4.6	Cash and cash equivalents at end of period	13,751	13,751

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	13,751	10,255
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)	13,751	10,255

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	103
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>		

7. Financing facilities <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>	Total facility amount at quarter end \$A'000	Amount drawn at quarter end \$A'000
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)	(655)
8.2 Cash and cash equivalents at quarter end (item 4.6)	13,751
8.3 Unused finance facilities available at quarter end (item 7.5)	-
8.4 Total available funding (item 8.2 + item 8.3)	13,751
8.5 Estimated quarters of funding available (item 8.4 divided by item 8.1)	21.0
<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.

27 July 2021

Date:

By 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.