



26 July 2022

Sydney, Australia

Nyrada Quarterly Activities Report & Appendix 4C

Highlights:

- **Cholesterol-Lowering Program:**
 - Nyrada's PCSK9 inhibitor shown to block the early stages of atherosclerosis in a novel human tissue-engineered blood vessel model of atherosclerosis
 - Preclinical safety and toxicology studies expected to commence Q3 CY2022
 - COVID-related lockdowns in Shanghai delay drug manufacture, Phase I first-in-human study expected to commence 1H CY2023
 - European Patent Office grants patent for novel compounds inhibiting PCSK9
- **Brain Injury Program:**
 - Biological target revealed as versatile TRPC ion channels
 - NYR-BI02 is a potent TRPC ion channel blocker, limiting excitotoxicity with potential to pursue multiple additional indications
 - Preclinical stroke model study results anticipated during Q3 CY2022
 - Preclinical safety and toxicology studies expected to commence Q3 CY2022
 - Phase I first-in-human study on track to commence in 2H CY2022
- **Strong financial position with cash balance of \$10.8M**
 - Sufficient funding for Phase I studies in both lead programs

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

Commenting on the quarter, Nyrada CEO, James Bonnar said: "I am pleased with the progress in advancing both our programs during the quarter, notwithstanding the challenges presented by the ongoing COVID-19 pandemic. Now that Shanghai has reopened, the team and I look forward to completing the scale-up drug manufacture process, ahead of the required preclinical and Phase I studies.

"We have already shown in preclinical studies that our PCSK9 inhibitor family of compounds are able to significantly lower LDL-cholesterol levels. Their ability to also stop the early stages of



atherosclerosis in a novel human-tissue engineered blood vessel model of the disease, developed by researchers at Duke University, is an exciting development in understanding broader applications for PCSK9 inhibitors, particularly as atherosclerotic plaque build-up is a major cause of cardiovascular disease.

“Additionally, we are pleased with initial study results announced last month indicating that our Brain Injury Program drug candidate, NYR-BI02, is a potent blocker for three of the TRPC channels and offers significant potential to treat multiple additional diseases involving TRPC ion channels. We are focused on finalising drug synthesis in order to test the efficacy of the molecule in a TBI model as well as in a model of ischemic stroke.

“In the coming months we will be reporting on the results of the preclinical stroke model study for the Brain Injury Program and providing updates on the progress of the preclinical safety and toxicology studies for the Cholesterol-Lowering Program,” Mr Bonnar added.

Preclinical Program Update

Cholesterol-Lowering Program – PCSK9 inhibitor

Evaluation of Nyrada’s PCSK9 Inhibitors in a Novel Model of Atherosclerosis

Results from a study run by researchers at Duke University Pratt School of Engineering (Duke), using select candidates from Nyrada’s PCSK9 inhibitor family of compounds was presented at the North American Vascular Biology Organisation (NAVBO) 2022 Vasculata conference in North Carolina on 19 July 2022.

The study aimed to determine if PCSK9 inhibitors attenuate inflammation in vascular cells in the early phases of atherosclerosis. In a human tissue-engineered blood vessel model of atherosclerosis, developed in the lab of Professor George Truskey, Nyrada’s PCSK9 inhibitor blocked the early stages of atherosclerotic plaque progression, including preventing monocyte adhesion and suppression of inflammatory cytokines, both of which are key mediators of the disease process.

It is the first time the model has been used to characterise the role of PCSK9 in the early phases of atherosclerosis and the potential for small molecule inhibitors of PCSK9 to block this process. The researchers at Duke intend to publish the findings of this study in a peer-reviewed paper.

Preclinical Studies

During the quarter, the scale-up manufacture of Nyrada’s lead cholesterol-lowering drug candidate for the program’s preclinical studies was delayed due to the extended COVID-related lockdown in Shanghai, China. Employees of the Shanghai-based contract manufacturing



organisation (CMO) engaged by Nyrada were unable to access laboratory worksites while the lockdown remained in place.

The required preclinical safety and toxicology studies are expected to commence in Q3 CY2022. Substantial efforts were made by the CMO to minimise the impact of the COVID-related lockdowns on drug manufacturing timelines, including the deployment of additional personnel and resources to recover lost time. As the delay impacted the availability of preclinical study slots at Charles River Laboratories, Inc., these studies will now be run at Inotiv, a US based contract research organisation (CRO).

Phase I Study

As a result of scale-up drug manufacturing delays caused by COVID-related lockdowns in Shanghai, the Phase I first-in-human study for Nyrada's Cholesterol-Lowering Program is expected to commence during the first half of CY2023.

The primary objective of the Phase I study is to evaluate Nyrada's drug candidate for safety and tolerability. A secondary endpoint will assess blood cholesterol levels in cohorts treated for 14 days with Nyrada's drug candidate as a preliminary indication of the drug's efficacy in humans.

Intellectual Property

The European Patent Office has formally granted the composition of matter patent for the Company's novel compounds inhibiting PCSK9, providing protection for Nyrada's intellectual property relating to its PCSK9 inhibitor technology until 16 March 2038. Nyrada now has patent protection for the compounds in both the US and European Union.

Brain Injury Program

Target Revealed

During the quarter, Nyrada revealed the biological target of its Brain Injury Program as a class of proteins known as the "Canonical" Transient Receptor Potential, or TRPC ion channels.

These channels are present on the surface of brain cells and allow calcium to enter the cell. While calcium is critical to cell survival, excess calcium triggers cell death pathways. Following an injury in the brain, the mechanisms that keep the calcium levels in-check fail as they rely on energy, which quickly depletes. After a brain injury such as a stroke, accident impact or concussion, the TRPC channels are constantly activated, allowing sustained calcium entry into the cells leading to cell death.

Nyrada's brain injury drug candidate NYR-BI02 is a potent blocker of three subtypes of the channel – TRPC3, TRPC6 and TRPC7, which are present in high levels in brain tissue. By targeting these channels, Nyrada's brain injury drug candidate is able to interrupt the sustained entry of



calcium into the cells and thereby reduce secondary brain injury. Presently, there are no FDA-approved small molecule blockers of TRPC 3, 6, 7 ion channels. NYR-BI02 is also able to cross the blood-brain-barrier, indicating it can reach therapeutic levels in the injured brain.

As part of its active intellectual property protection program, Nyrada has filed a provisional patent covering a library of molecules, including NYR-BI02, that block these channels. It is anticipated that the patent will have coverage firstly in Australia, followed by Europe and US.

Preclinical Studies

Stroke Model Study

The COVID-related lockdowns in Shanghai delayed the start of the preclinical stroke model study. With the re-opening of Shanghai, it is anticipated the results of the preclinical stroke model study will be available in Q3 CY2022.

Safety Toxicology and Pharmacology Studies

The required preclinical studies will be used to evaluate the safety and tolerability of Nyrada's lead brain injury drug candidate in research models. Data from these studies will determine the safe starting dose for the Phase I first-in-human study. The Company is in discussions with a number of CROs regarding the design and timing of these studies and a further update will be provided once these details are finalised. These studies are anticipated to begin in Q3 CY2022.

TBI Efficacy Study Progress

Nyrada will initially test the efficacy of its NYR-BI02 molecule as a TRPC 3, 6 and 7 channel blockers in a model of traumatic brain injury via its existing collaboration with the Walter Reed Army Institute of Research (WRAIR). With the initial pilot work at WRAIR and UNSW Sydney now complete, the study design for the efficacy study has been finalised.

The efficacy study will employ the penetrating ballistic brain injury (PBBi) model which has been developed by the WRAIR team to emulate penetrating head wounds on the battlefield. The study will involve dosing animals with a vehicle or NYR-BI02 in a blinded fashion and assessing the injury volume using a specialised MRI technique at UNSW Sydney.

The study will include assessment of blood biomarkers including GFAP and NF-L. MRI and blood biomarker assessments are commonly used in the clinical setting for diagnosis and prognosis purposes in TBI and stroke patients. The efficacy study will also incorporate assessment techniques commonly used in animal brain injury models.

The complex nature of this study requires WRAIR to contribute considerable resources to enable its completion. Like many large research organisations globally, the ongoing COVID-19 pandemic has had an impact on some project timelines. The progression of this study is largely



driven by availability of the necessary resources at WRAIR and is currently expected to start in the new year.

Delays to the start of the TBI efficacy study will not impact the commencement of the Phase I first-in-human study. These studies can be run in parallel.

Phase I Study

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

The Phase I study will be run in Australia and will evaluate the safety and tolerability of the Company's preferred brain injury drug candidate, NYR-BI02.

The trial participants will be split into 5 groups of 8, with 6 receiving the drug and 2 receiving a placebo. Cohorts 1 and 2 will be given a bolus single ascending dose, while cohorts 3, 4 and 5 will be given bolus and continuous infusion in ascending doses for 72 hours via intravenous infusion.

Blood samples will be drawn several times throughout the study period and analysed for drug levels. Participants will be monitored for clinical signs throughout the study duration.

Corporate and Financial Summary

Cash Flow & Cash Position

Total cash operating outflows for the June 2022 quarter were approximately A\$781,000 (A\$1.0 million in the prior quarter). The Company anticipates cash outflows in future quarters will increase as both Programs progress toward Phase I clinical trials.

Nyrada has a robust cash position of A\$10.8 million as at 30 June 2022 (A\$11.3 million as at 31 March 2022), providing the Company with sufficient cash reserves to complete Phase I studies for both 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\$139,000 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")

30 June 2022

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	(252)	(1,719)
(b) product manufacturing and operating costs	-	-
(c) advertising and marketing	-	-
(d) leased assets	-	-
(e) staff costs	(246)	(946)
(f) administration and corporate costs	(283)	(1,628)
1.3 Dividends received (see note 3)	-	-
1.4 Interest received	7	13
1.5 Interest and other costs of finance paid	-	-
1.6 Income taxes paid	-	-
1.7 Government grants and tax incentives	45	1,355
1.8 Other (provide details if material)	-	-
1.9 Net cash from / (used in) operating activities	(729)	(2,925)
2. Cash flows from investing activities		
2.1 Payments to acquire or for:		
(a) entities	-	-
(b) businesses	-	-
(c) property, plant and equipment	-	(4)
(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	-	(4)

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	11,333	13,751
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(729)	(2,925)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	-	(4)

Consolidated statement of cash flows		Current quarter \$A'000	Year to date (12 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	212	263
4.6	Cash and cash equivalents at end of period	10,816	10,816

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	10,816	11,333
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)	10,816	11,333

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	139
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.

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.</i>		
<i>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)	(729)
8.2 Cash and cash equivalents at quarter end (item 4.6)	10,819
8.3 Unused finance facilities available at quarter end (item 7.5)	-
8.4 Total available funding (item 8.2 + item 8.3)	10,819
8.5 Estimated quarters of funding available (item 8.4 divided by item 8.1)	14.8
<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 July 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.