ASX ANNOUNCEMENT 28 October 2021

September 2021 Quarterly Activity Report

Melbourne, Australia; 28 October 2021: Cynata Therapeutics Limited (ASX: "**CYP", "Cynata",** or the **"Company"**), a clinical-stage biotechnology company specialising in cell therapeutics, has today released its Quarterly Activity Report for the three-month period ended 30 September 2021.

Key highlights

- **Signed a Strategic Partnership Agreement (SPA) with Fujifilm: Cynata has regained development and commercialisation rights to CYP-001 for graft-versus-host disease (GvHD), agreed core terms of manufacturing services agreement, and (post close of the quarter) received payment of US$5m**
- **Strengthened intellectual property portfolio, with patents encompassing the Company's unique Cymerus™ mesenchymal stem cell (MSC) technology granted in the US, Canada and Russia**
- **Actively recruiting and treating patients in the Phase 3 osteoarthritis clinical trial and the MEND respiratory distress trial**
- **Subsequent to the quarter, the Data Safety Monitoring Board (DSMB) reviewed the initial data from the MEND trial, and recommended that the trial continue as planned**
- **Preclinical study showing the beneficial effects of Cynata's Cymerus MSCs in heart attacks was published in peer-reviewed journal, *Cytotherapy***
- **Appointment of Dr Jolanta Airey to the new position of Chief Medical Officer to drive Cynata's advanced clinical product pipeline**
- **Strong financial position with A$23.9m in cash as at 30 September 2021**

Dr. Ross Macdonald, Cynata's CEO and MD, said:

"I am pleased with the great progress we have made this quarter, as we continue to advance our clinical pipeline and execute on our strategic priorities. We currently have two active clinical trials underway, the Phase 3 osteoarthritis trial and the MEND respiratory distress trial, and a planned trial in diabetic foot ulcers expected to commence in the near term. Further, we are pleased to continue our long and fruitful relationship with Fujifilm through the new strategic partnership signed in September. In addition to being an experienced manufacturer of cell therapy products, Fujifilm is a major global conglomerate, with a significant presence in the biotechnology space. Our new partnership involves Cynata regaining the rights to CYP-001 in GvHD and we will use this opportunity to immediately implement a US regulatory strategy, adding another late-stage indication to our diverse and robust pipeline. We will continue to focus on generating robust clinical data, and we are confident in our ability to execute on our strategic priorities and deliver shareholder value."

Commercial update

Signed a SPA with Fujifilm

During the quarter, Cynata and Fujifilm entered into a new strategic partnership for Fujifilm to provide clinical and commercial manufacturing services for, and supply of, Cynata's Cymerus MSC products. Under the SPA, the parties have agreed to terminate the September 2019 licence agreement and to negotiate a manufacturing services agreement in good faith during a 90-day period, which will incorporate the detailed and agreed core terms for Fujifilm to manufacture Cynata's Cymerus therapeutic MSC products. Fujifilm has agreed to a new voluntary escrow over the ~8.1m shares it holds in Cynata. Cynata has regained all rights to CYP-001 for GvHD and subsequent to the quarter, received a US$5m payable to Cynata from Fujifilm (as part of the transaction). Cynata

will immediately commence implementation of a US development strategy for Cymerus MSCs, capitalising on the need for an effective and scalable MSC therapeutic product for acute GvHD. Cynata has already secured Orphan Drug Designation from the U.S. Food and Drug Administration (FDA) for CYP-001, potentially providing several commercially significant incentives. Current therapies for GvHD rely on inadequate treatment options, presenting a compelling opportunity for Cynata, with an estimated global market opportunity of US$600m.[1] The Company will engage with the FDA in the near term to conduct a Phase 2 GvHD trial in the US, leveraging the results of Cynata's previous ground-breaking Phase 1 trial in GvHD that met all safety and efficacy endpoints and received significant attention including a feature on the front cover of prestigious medical journal, *Nature Medicine*.

Strengthened intellectual property portfolio

Cynata has continued to advance its unique and proprietary intellectual property portfolio, generating protection in major markets of commercial importance. During the quarter, Cynata received a Notice of Allowance from the United States Patent and Trademark Office and from the Canadian Intellectual Property Office, for a patent application covering its proprietary Cymerus MSC technology. The US patent and the Canadian patent will extend to 2037 and 2034, respectively. Additionally, the Patent Office of the Russian Federation accepted two applications covering Cynata's Cymerus technology for which it intends to grant patents in late 2021, with expiration in 2037.

Clinical update

Multiple clinical trials currently underway

Active patient recruitment and treatment continues in the Phase 3 SCUlpTOR (structure-modifying treatment for medial tibiofemoral osteoarthritis) Osteoarthritis trial aiming to enrol a total of 440 patients with osteoarthritis of the knee. The trial is designed to assess the effect of CYP-004, Cynata's Cymerus mesenchymal stem cell (MSC) product for osteoarthritis, against placebo on clinical outcomes and knee joint structure over a two-year period. Osteoarthritis is a degenerative disease that occurs when the cartilage in affected joint(s) wears away, causing significant pain, inflammation and swelling. There is currently no cure for osteoarthritis and available treatments are centred on symptom management. Preclinical research suggests that MSCs have the potential to improve the underlying disease, and any product that might result in a tissue regenerative response will be a breakthrough in the global US$11.6bn osteoarthritis market.[2] The trial is sponsored by the University of Sydney and funded by an Australian Government National Health and Medical Research Council project grant, with full intellectual property and commercialisation rights to Cynata.

Recruitment and patient treatment in the MEND clinical trial is currently underway. The open-label randomised controlled clinical trial aims to investigate the safety and early efficacy of Cymerus MSCs in 24 adult patients admitted to ICU with respiratory failure, who meet the established criteria for Acute Respiratory Distress Syndrome (ARDS). ARDS, sepsis and cytokine release syndrome (CRS) have been identified as targets for this trial, as they present significant unmet medical needs and are manifestations of the excessive inflammatory responses typically seen in patients experiencing respiratory distress. The combined market opportunity of ARDS, sepsis and CRS is estimated to be over US$8bn.[3] Cynata's pre-clinical studies have shown that these conditions can

[1] Reflects GvHD market by 2030, Biospace "Acute Graft Versus Host Disease Treatment Market: Intravenous Segment to Expand at High Growth Rate" (23 August 2021).

[2]Reflects OA market by 2025; Persistence Market Research 2018 research report: "Osteoarthritis Treatment Market: Global Industry Analysis (2012-2016) and Forecast (2017-2025).

[3]Vasomune Therapeutics company announcement, 2018 (Reflects ARDS global market opportunity of US$2.5bn); GlobeNewswire, 2020 (Represents Cytokine Release Syndrome (CRS) global market opportunity of US$0.16m in 2017); GlobalData 2017 (Reflects Sepsis global market opportunity of US$5.9bn in 2026).

potentially be improved with Cymerus MSCs through modulation of the inflammatory reaction associated with these diseases. The trial is in collaboration with the Cerebral Palsy Alliance Research Institute and the COVID-19 Stem Cell Treatment Group. Subsequent to the quarter, Cynata announced the successful completion of a planned, routine review of the MEND clinical trial by the independent DSMB, consistent with good clinical practice in clinical trials. Pleasingly, the DSMB has recommended that the MEND trial continue as planned.

Publications

Beneficial effect of Cynata's MSCs in heart attacks published in peer-reviewed journal

A scientific paper describing the use of Cymerus MSCs in a model of myocardial infarction (heart attack), has been published in the peer-reviewed journal, *Cytotherapy*, the official journal of the International Society for Cell & Gene Therapy. The paper summarises the preclinical studies led by Associate Professor James Chong from the Westmead Institute for Medical Research in Sydney, which concluded that Cymerus MSCs were efficacious in the treatment of heart attacks. In the trial, rats were randomly assigned to receive Cymerus MSCs, bone marrow-derived MSCs or placebo control. Overall, the results showed that Cymerus MSCs achieved better therapeutic effects compared to conventional bone marrow-derived MSCs. This paper validates the importance of Cymerus MSCs in treating serious diseases and provides recognition of Cynata's potential ability to provide a scalable stem cell therapy for cardiac repair.

An article on MSCs as a treatment for acute GvHD, by Dr Kilian Kelly (Cynata's COO) and Professor John EJ Rasko AO, has been published in the peer-reviewed journal, *Frontiers in Immunology*. The paper concludes that there is a substantial body of evidence suggesting that MSCs have beneficial effects in treating acute GvHD, and that recent innovations may be capable of overcoming problems associated with inter-donor variability and functional changes associated with excessive culture expansion. Cynata's Cymerus MSC manufacturing process addresses the aforementioned challenges, as it derives all of its cell product from one donation from one donor, with essentially unlimited expansion, offering a commercially scalable solution.

Corporate update

Dr Jolanta Airey appointed to the new position of Chief Medical Officer

During the quarter, Cynata announced the appointment of Dr Jolanta Airey as Chief Medical Officer to drive Cynata's advanced clinical product pipeline, consistent with Cynata's growing trial activities and late-stage portfolio. Dr Airey has over 25 years' experience in respiratory, rheumatology, dermatology, biologicals, international markets and listed companies and is a highly experienced clinician. She is an accomplished biopharmaceutical executive who has led the successful development and commercialisation of pharmaceutical products, including novel biological agents. She was formerly Director, Translational Development at CSL Limited and has held a range of medical positions within biotech, pharmaceutical and clinical research companies.

Strong financial position

Cynata closed the quarter with A$23.9m in cash, as at 30 September 2021.

Subsequent to the quarter, Cynata received the US$5m fee payable by Fujifilm under the SPA, as announced on 18 October 2021.

Net operating cash outflows for the quarter totalled A$3.24m, primarily relating to increased expenditure on product development associated with increased clinical trial activity and product manufacture and a seasonal reduction in administration and corporate costs. In item 6 of the Appendix 4C cash flow report for the quarter, payments to related parties of approximately A$153k compromised of salary paid to the Managing Director and fees paid to Non-Executive Directors.

In September 2018 shareholders approved the grant of loans to Dr Stewart Washer and Dr Ross Macdonald to fund the exercise of their full quota of fully vested 2018 director options. The loans, which totalled $900,000 to each Director, did not involve any cash outflow given the funds were used for payment of the exercise price of the director options. The loans have now been repaid in full, resulting in Cynata raising proceeds of $2,000,000 (which includes $100,000 paid in cash directly by each Director upon exercise of the options), together with a total of $157,158 in interest on the loans paid by the Directors. Dr Washer and Dr Macdonald are among the top 10 shareholders in the Company.

Outlook

Current clinical trials and results

The ongoing Phase 3 trial in osteoarthritis has advanced, with the University of Sydney seeking to enrol a total of 440 patients. Following enrolment, each participant will receive injections of Cymerus MSCs (or placebo in the case of the control group) on three occasions over a one-year period and will continue follow ups for an additional year, with final results expected in 2024.

The ongoing MEND respiratory distress trial has also advanced, with a total of 24 adult patients expected to participate. The trial will involve 12 critically infected patients randomised to receive Cymerus MSC infusions, in addition to standard of care, while 12 patients will be randomised to the control group and will receive current standard of care only. Following successful completion of the DSMB review (subsequent to the end of the present quarter) and dependent upon patient enrolment rates, it is expected full enrolment will be completed before the end of 2021.

The Phase I DFU trial is expected to commence recruitment of 30 adult patients with DFU in 4Q CY21, subject to the completion of trial start up activities, which are presently underway. Patients will be randomly assigned to receive CYP-006TK (a polymer-coated silicon dressing seeded with MSCs) or standard care of treatment. Cynata has an exclusive license agreement with leading manufacturer of innovative biomedical coatings, TekCyte Pty Ltd, to utilise its wound dressing technology. The treatment period will be 4 weeks, and each patient will be evaluated for a total of 24 weeks.

A Phase 2 GvHD trial in GvHD will be an important late-stage addition to Cynata's active pipeline. Cynata will engage with the FDA to confirm the Phase 2 GvHD trial design to conduct the trial in the US.

In light of the Phase 2 GvHD trial, and the current exposure to the diabetes sector through the planned DFU trial, Cynata plans to divert future activities from the Phase 2 trial in critical limb ischemia (CLI) towards partnering opportunities, providing flexibility to accelerate Cynata's progress. Clinical trial planning for potential indications of idiopathic pulmonary fibrosis and renal transplantation has assumed a subordinated priority as resources have been re-focused on GvHD, DFU and the two ongoing clinical trials.

Strategic pathway

The new strategic partnership with Fujifilm ensures Cynata is in a strong position for commercialisation. Fujifilm Cellular Dynamics Inc (subsidiary of Fujifilm) developed the original iPSC line used in Cynata's Cymerus manufacturing process, and they are a leading cell therapy manufacturer. With the rights to CYP-001 in GvHD regained, Cynata can accelerate a US development strategy. Planning and trial design activities are underway for a Phase 2 GvHD trial that is expected to be conducted in the US, where Cynata has already secured Orphan Drug Designation. Cynata continues to focus on optimising and expanding its manufacturing capabilities to prepare for commercialisation.

-ENDS-

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Authorised for release by Dr Ross Macdonald, Managing Director & CEO

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About Cynata Therapeutics (ASX: CYP)

Cynata Therapeutics Limited (ASX: CYP) is an Australian clinical-stage stem cell and regenerative medicine company focused on the development of therapies based on Cymerus™, a proprietary therapeutic stem cell platform technology. Cymerus™ overcomes the challenges of other production methods by using induced pluripotent stem cells (iPSCs) and a precursor cell known as mesenchymoangioblast (MCA) to achieve economic manufacture of cell therapy products, including mesenchymal stem cells (MSCs), at commercial scale without the limitation of multiple donors.

Cynata's lead product candidate CYP-001 met all clinical endpoints and demonstrated positive safety and efficacy data for the treatment of steroid-resistant acute graft-versus-host disease (GvHD) in a Phase 1 trial. Planning for a Phase 2 clinical trial in GvHD is presently underway. Clinical trials of Cymerus products in osteoarthritis (Phase 3) and in patients with respiratory failure are currently ongoing. In addition, Cynata has demonstrated utility of its Cymerus technology in preclinical models of numerous diseases, including the clinical targets mentioned above, as well as asthma, heart attack, sepsis, acute respiratory distress syndrome (ARDS) and cytokine release syndrome.

Cynata Therapeutics encourages all current investors to go paperless by registering their details with the designated registry service provider, Automic Group.

Appendix 4C

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

Name of entity	
CYNATA THERAPEUTICS LIMITED	
ABN	**Quarter ended ("current quarter")**
98 104 037 372	30 SEPTEMBER 2021

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	(2,531)	(2,531)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	(94)	(94)
	(d) leased assets	-	-
	(e) staff costs	(403)	(403)
	(f) administration and corporate costs	(228)	(228)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	20	20
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**	**(3,236)**	**(3,236)**

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	200	200
3.7	Transaction costs related to loans and borrowings	-	-
3.8	Dividends paid	-	-
3.9	Interest on Director's Loan received	10	10
3.10	**Net cash from / (used in) financing activities**	**210**	**210**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	26,717	26,717
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(3,236)	(3,236)
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)	210	210
4.5	Effect of movement in exchange rates on cash held	221	221
4.6	**Cash and cash equivalents at end of period**	**23,912**	**23,912**

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	13,912	16,717
5.2	Call deposits	10,000	10,000
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)**	**23,912**	**26,717**

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	235
6.2	Aggregate amount of payments to related parties and their associates included in item 2	-

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.

7.	**Financing facilities** *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.*	**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.

N/A

8.	**Estimated cash available for future operating activities**	**$A'000**
8.1	Net cash from / (used in) operating activities (item 1.9)	(3,236)
8.2	Cash and cash equivalents at quarter end (item 4.6)	23,912
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	23,912
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	7.39

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.

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?

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?

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?

N/A

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.

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.

Date: 28 October 2021

Authorised by: .The Board of Directors
(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.