ASX ANNOUNCEMENT **25 October 2024**

September 2024 Quarterly Activity Report

Melbourne, Australia; 25 October 2024: Cynata Therapeutics Limited (ASX: **"CYP", "Cynata",** or the **"Company"**), a clinical-stage biotechnology company specialising in cell therapeutics, provides its Quarterly Activity Report for the three-month period ended 30 September 2024.

Key highlights:

- **Phase 2 clinical trial in acute graft-versus-host disease (aGvHD): recruitment continues; primary results expected by late 2025**
- **Phase 1 clinical trial in diabetic foot ulcer (DFU): patient visits complete; results expected late 2024/early 2025**
- **Phase 1 clinical trial in kidney transplantation: first patient enrolled; expect to be dosed in Q4 2024**
- **Cymerus™ MSCs shown to reverse pulmonary fibrosis and lung stiffness in preclinical pulmonary fibrosis study published in peer-reviewed journal**
- **Acquisition of wound dressing technology from TekCyte completed**
- **Phase 3 clinical trial in osteoarthritis: recruitment complete; results expected 1H 2026**
- **Cash balance of A$4.29m at end of quarter, R&D Tax Incentive rebate expected Q4 2024, forecast cash runway into H2 2025**

Research and Development Pipeline

CYP-001

CYP-001 is Cynata's Cymerus™ off-the-shelf iPSC[1]-derived MSC[2] product for intravenous infusion, which is currently in clinical development for two indications (aGvHD and kidney transplantation). The US FDA has granted Orphan Drug Designation[3] to CYP-001 for the treatment of aGvHD.

Phase 2 Clinical Trial in aGvHD – Recruitment Continues; Results Anticipated by Late 2025

aGvHD is a potentially life-threatening complication of bone marrow transplants or similar procedures. It arises when immune cells in the transplant (the graft) attack the recipient's tissues (the host) as "foreign". In this trial, CYP-001 is being investigated as a potential immune modulating treatment for aGvHD.

This global Phase 2 trial aims to enrol approximately 60 patients with High-Risk aGvHD (HR-aGvHD), who will be randomised to receive either steroids plus CYP-001, or steroids plus placebo. The Company is confident the trial will build on the success of its Phase 1 trial in GvHD, which generated positive safety and efficacy results and led to two publications in the prestigious peer-reviewed journal *Nature Medicine*.[4,5]

Patient enrolment is now approximately 20% complete. Although the rate of recruitment has accelerated substantially, following the opening of numerous additional clinical centres, the Company now anticipates enrolment continuing into 2025. Release of the primary results is still anticipated by late 2025.

Phase 1 Clinical Trial in Kidney Transplantation – First Patient Enrolled

Patients who receive a kidney transplant typically require long-term treatment with immunosuppressant drugs to prevent rejection of the transplanted organ. Immunosuppressants known as calcineurin inhibitors are effective at preventing rejection, but they are associated with very serious toxicities. In this trial, CYP-001 is being investigated as a potential immune modulating treatment in patients who have received a kidney transplant. If successful, this could facilitate dose reduction or withdrawal of calcineurin inhibitors, which would be expected to reduce or avoid toxicity.

This trial is being undertaken in collaboration with Leiden University Medical Centre (LUMC), the Netherlands, which will fund and manage the trial, under the leadership of Prof Ton Rabelink. Cynata will provide CYP-001 for use in the trial, while retaining full commercial rights to use the data.

Prof Rabelink and colleagues have previously published encouraging data from a clinical trial in which the patients' own MSCs were used in a similar way. They found that early tacrolimus (calcineurin inhibitor) withdrawal with MSC therapy was safe, without increased rejection of the transplanted organs, and concluded that this is a potentially useful approach after kidney transplantation.[6]

The first patient has been enrolled in this trial, and is expected to receive the first infusion of CYP-001 during Q4 2024. The trial aims to recruit a total of up to 16 patients who have undergone a kidney transplant. The first six patients will receive either one (n=3) or two (n=3) infusions of CYP-001, in addition to standard treatment. Subject to favourable safety review of the initial cohorts, a further ten patients will receive two infusions of CYP-001, followed by tacrolimus dose reduction.

CYP-006TK

CYP-006TK is Cynata's Cymerus™ iPSC-derived MSC topical wound dressing product candidate, which comprises MSCs seeded onto a novel silicone dressing.

Phase 1 Clinical Trial in DFU – Patient Visits Complete; Results Expected Late 2024/Early 2025

Due to reduced blood flow, patients with diabetes are at risk of developing non-healing wounds on the feet/lower limbs, which are also known as diabetic foot ulcers or DFU. In addition to causing severe pain and discomfort, DFU pose a significant risk of infection, and if treatment is unsuccessful, amputation may be necessary. In this trial, CYP-006TK is being investigated as a potential treatment to promote wound healing in patients with DFU.

This trial enrolled a total of 30 patients with DFU, who were randomised to receive either: (i) CYP-006TK treatment for four weeks, followed by standard of care treatment for the rest of the study; or (ii) standard of care treatment throughout the study.

Following completion of patient enrolment in April 2024, the last patient visit occurred in September 2024. Work is ongoing with the clinical centres and the Company's service provider partners to conclude data monitoring and clinical data management activities, followed by analysis of the data. The Company anticipates releasing results from the trial in late 2024 or early 2025.

In February 2024, the Company announced the outcome of analysis of wound surface area in the first 16 patients enrolled in the trial (n=8 per group), up to the 10-week follow-up time point. The median percentage reduction in wound surface area in the active CYP-006TK group after 10 weeks' follow-up was 87.6%, compared to 51.1% in the control group. These findings were consistent with the trend observed in the results from the first six patients enrolled in this trial (n=3 per group) up to Day 28, which were released in April 2023.

CYP-004

CYP-004 is Cynata's Cymerus™ off-the-shelf iPSC-derived MSC product for intra-articular injection (injection into a joint).

Phase 3 Clinical Trial in Osteoarthritis – Recruitment Complete; Patient Follow-up Ongoing

Osteoarthritis is a chronic inflammatory joint disease that causes pain and disability, which affects over two million people in Australia[7] and over 500 million people worldwide.[8] In this trial, CYP-004 is being investigated as a potential treatment to reduce pain, inflammation and cartilage degeneration in patients with osteoarthritis of the knee.

Known as the SCUlpTOR[9] trial, this randomised and placebo-controlled Phase 3 trial is being conducted by the University of Sydney, under the leadership of Professor David Hunter, with funding provided under an Australian Government National Health and Medical Research Council (NHMRC) project grant. The co-primary endpoints of the trial are (i) the proportion of participants achieving patient-acceptable symptom state (PASS) for knee pain at 24 months; and (ii) central medial femorotibial (cMFT) cartilage thickness change from baseline to 24 months, as assessed by magnetic resonance imaging (MRI).

Patient recruitment was completed in November 2023, with a total of 321 participants enrolled. In accordance with the study protocol, patients will be followed up for two years, to allow sufficient time for a potential disease modifying effect to be assessed. The Company anticipates that the last participant visit will occur around November 2025, with results expected in the first half of 2026.

Preclinical Pipeline

Publication of Study of Cymerus™ MSCs in Pulmonary Fibrosis Model

During the quarter (announced on 8 August 2024), a study of Cymerus™ MSCs in a preclinical model of pulmonary fibrosis was published in the peer-reviewed journal *Biomedicine & Pharmacotherapy*.[10] The study was conducted by Professor Chrishan Samuel (Monash Biomedicine Discovery Fellow and Head of the Fibrosis Laboratory, Department of Pharmacology at Monash University) in mice subjected to bleomycin (BLM)-induced pulmonary fibrosis, which mimics features of idiopathic pulmonary fibrosis (IPF) in humans.

IPF is a chronic lung disease of unknown cause, characterised by lung scarring and stiffening, which leads to a progressively worsening difficulty in breathing. There is no known cure, and the condition is often fatal, with a reported median survival of between two and five years from diagnosis.[11,12]

The study found that a single or double intravenous administration of Cymerus™ MSCs had beneficial effects, including:

- reduced lung inflammation
- reduced damage to cells in the lungs
- reduced several measures of lung fibrosis
- promoted the balance between enzymes that facilitate the breakdown of fibrosis
- reduced lung stiffness.

Corporate Update

Acquisition of CYP-006TK Wound Dressing Technology from TekCyte

During the quarter end (announced on 1 July 2024), the Company entered into an agreement with TekCyte Limited (TekCyte) to secure outright ownership of the underlying technology utilised in CYP-006TK, Cynata's Cymerus™ iPSC -derived MSC topical wound dressing product candidate. The technology is based on proprietary surface modification techniques, to produce polymer-coated dressings for the delivery of MSCs to wounds. This acquisition was completed on 31 July 2024, following completion of the assignment of the relevant intellectual property to Cynata. In consideration of this acquisition, Cynata issued shares to the value of $230,000 to TekCyte.

Intellectual Property Portfolio

Cynata continues to strengthen its robust intellectual property portfolio, which comprises several different in-licensed and Company-owned patent families.

During the quarter:

- A decision to grant was issued by the European Patent Office for a Cynata-owned patent application entitled "*Method for Treating Allergic Airways Disease (AAD/Asthma)*", which describes a method of use of Cymerus MSC products in treating diseases of the lungs and airways.
- A notice of allowance was issued by the Brazilian Patent and Trademark Office for a patent application entitled "*Colony Forming Medium and Use Thereof*", which relates to the optimisation of the Cymerus process by Cynata.

Finance

The Company closed the quarter with A$4.29m in cash. Net operating cash outflows for the quarter totalled A$1.91m.

In accordance with ASX rules, the "*Estimated quarters of funding available*" reported in item 8.5 of the Appendix 4C is calculated by dividing the cash at the end of the quarter by the net operating cash outflows in the previous quarter, and the result of this calculation is 2.2 quarters of funding available. The Company anticipates receiving its R&D Tax Incentive rebate in the coming quarter, and expects its cash runway to extend into the 2025-26 financial year.

In item 6 of the Appendix 4C cash flow report for the quarter, payments to related parties of approximately A$245k consisted of salary and bonus paid to the Managing Director and fees paid to Non-Executive Directors.

Outlook

During the remainder of this financial year, the Company anticipates the following milestones:

- Dosing of the first patient in the kidney transplantation trial
- DFU trial results
- Completion of enrolment in the GvHD trial
- Cohort A results from the kidney transplantation trial

Annual General Meeting

The Company's Annual General Meeting will take place at the Amora Hotel Riverwalk Melbourne, 649 Bridge Road, Richmond, VIC 3121 on 19 November 2024 at 10.00 am (AEDT).

-ENDS-

Authorised for release by Dr Kilian Kelly, CEO & Managing Director

CONTACTS: Dr Kilian Kelly, CEO & MD, Cynata Therapeutics, +61 (03) 7067 6940, kilian.kelly@cynata.com
Lauren Nowak, Media Contact, +61 (0)400 434 299, lauren@littlebigdeal.au

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. A Phase 2 clinical trial in GvHD under a cleared US FDA IND, as well as trials of Cymerus products in osteoarthritis (Phase 3), diabetic foot ulcers (DFU) and renal transplant are currently ongoing. In addition, Cynata has also demonstrated utility of its Cymerus technology in preclinical models of numerous diseases, including critical limb ischaemia, idiopathic pulmonary fibrosis, 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.

---

[1] iPSC = induced pluripotent stem cell
[2] MSC = mesenchymal stem (or stromal) cell
[3] Orphan Drug Designation qualifies Cynata for incentives including extended marketing exclusivity, tax credits and fee waivers.
[4] Bloor AJC, et al. Nat Med. 2020;26:1720–1725.
[5] Kelly K, et al. Nat Med. 2024;30:1556–1558.
[6] Reinders MEJ, et al. Am J Transplant. 2021;21:3055–3065
[7] Australian Institute of Health and Welfare. Chronic musculoskeletal conditions: arthritis. 14 December 2023.
[8] World Health Organization. Fact Sheet – Osteoarthritis. 14 July 2023.
[9] SCUlpTOR = Stem Cells as a symptom- and strUcture-modifying Treatment for medial tibiofemoral OsteoaRthritis
[10] Chakraborty A, et al. Biomedicine & Pharmacotherapy. 2024:178: 117259.
[11] Raghu et al, Am J Respir Crit Care Med. 2011;183(6):788-824.
[12] Zheng et al, ERJ Open Res. 2022 Jan; 8(1): 00591-2021.

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 2024

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	(1,081)	(1,081)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	(24)	(24)
	(d) leased assets (including premises)	-	-
	(e) staff costs	(610)	(610)
	(f) administration and corporate costs	(278)	(278)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	79	79
1.5	Interest and other costs of finance paid	-	-
1.6	Income taxes paid	-	-
1.7	Government grants and tax incentives	-	-
1.8	Other	-	-
1.9	**Net cash from / (used in) operating activities**	**(1,914)**	**(1,914)**

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)	1	1
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**	**1**	**1**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	6,205	6,205
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(1,914)	(1,914)
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)	1	1
4.5	Effect of movement in exchange rates on cash held	(3)	(3)
4.6	**Cash and cash equivalents at end of period**	**4,289**	**4,289**

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	1,289	1,205
5.2	Call deposits	3,000	5,000
5.3	Bank overdrafts	-	-
5.4	Other	-	-
5.5	**Cash and cash equivalents at end of quarter (should equal item 4.6 above)**	**4,289**	**6,205**

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	245
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)	(1,914)
8.2	Cash and cash equivalents at quarter end (item 4.6)	4,289
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	4,289
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	2.2

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: 25 October 2024

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.