ASX ANNOUNCEMENT

11 July 2018

# June 2018 Quarterly Report

**Melbourne, Australia; 11 July 2018:** Australian stem cell and regenerative medicine company, Cynata Therapeutics Limited (ASX: CYP or "the Company"), has today released its Appendix 4C Report for the three-month period to 30 June 2018 and is pleased to provide a review of operational progress during the period.

**Highlights**

- **Highly encouraging safety and efficacy 28-day data reported for Cohort B in Phase 1 GvHD trial**
  - **Overall Response rate of 86%**
  - **Complete Response rate of 57%**
  - **No adverse safety events or safety concerns**
- **Selection of cardiovascular disease as a new high-priority clinical target area**
  - **Planning underway for a Phase 2 clinical trial in critical limb ischemia (CLI)**
  - **CLI is a ~US$1.4billion/year commercial opportunity for novel MSC therapies**
- **Additional pre-clinical indications added to the exemplary product portfolio, including the use of MSCs in diabetic wound dressings and in the treatment of coronary artery disease (CAD)**
- **New development partnership with the *RCSI (Royal College of Surgeons in Ireland)* added after quarter end to investigate the use of Cymerus™ MSCs in the treatment of sepsis**
- **Patent portfolio strengthened with new patents awarded and applications lodged**
- **$5.2m investment from Fidelity International, providing additional funding to advance product development activities**

## Operational update

**GvHD Clinical Trial: Patient Cohort B Positive Efficacy and Safety Data at Day 28**

During the quarter, the final patient in Cynata's phase I clinical trial in acute steroid resistant GvHD was treated with Cynata's mesenchymal stem cell (MSC) product, CYP-001. The completion of the enrolment followed the very promising safety and efficacy data from the 28-day and 100-day analysis of the first cohort (Cohort A) announced in the prior quarter. The six-month data from Cohort A, released in June, reported continued positive safety and sustained survival rates of 87.5%, an outstanding outcome given the devastating nature of this disease.

The second and final cohort (Cohort B), received a higher dose of two infusions of CYP-001 administered once week apart. Each dose was two million cells per kilogram of body weight, up to a maximum of 200 million cells. The 28-day analysis of Cohort B was completed in June and delivered further positive safety and efficacy results.

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All seven patients treated with CYP-001 in Cohort B survived until Day 28. The Overall Response and Complete Response rates were 86% and 57%, respectively. Furthermore, a higher dose of CYP-001 administered in Cohort B elicited a faster response than the lower dose in Cohort A. By Day 28, Cohort A had a Complete Response rate of 12.5%, compared to 57% in Cohort B. Again, these findings are highly encouraging in view of the very poor outlook for patients with acute GvHD who have failed the standard treatment, i.e. steroids.

With recruitment now complete, the Company eagerly awaits the Primary Evaluation Period, 100-days after the final patient received the first infusion of CYP-001. Once this milestone is reached, the full report can be compiled.

**Further preclinical progress and development in other indications**

Cynata's Cymerus MSCs were investigated by the *Cooperative Research Centre for Cell Therapy Manufacturing (CTM CRC)* in a preclinical model of diabetic wounds with excellent results. Cynata's product resulted in significantly faster wound healing than bone-marrow MSCs derived from five different sources. *CTM CRC* is developing an active wound care dressing for the treatment of diabetic wounds that is seeded with MSCs or similar cells.

The primary outcome of the CTM CRC study was to measure the extent of skin restoration after three days and Cynata's MSCs were found to result in greater restoration than all other cells, with the only cell coming close to delivering the same result as Cynata's MSCs being MSCs from gingival fibroblasts or bone chips, both of which have major manufacturing and scalability challenges associated with them.

Cynata and the CTM CRM are in discussions regarding an extended collaboration, with a view to commencing a clinical trial using Cymerus MSCs with *CTM CRC's* wound dressing technology in human patients with diabetic foot ulcers.

Cynata also commenced a research collaboration with the *University of New South Wales (UNSW*) for the development of MSC therapies for the treatment of coronary artery disease (CAD). *UNSW* will develop methods for activating Cynata's MSCs using novel culture materials with the goal of enhancing blood vessel formation and improving blood supply to the heart in patients with CAD, which is currently the cause of most heart attacks and one third of deaths in people over the age of 35 in developed countries.

Post the quarter, the Company entered into a development partnership with the *RCSI (Royal College of Surgeons in Ireland)* to investigate the potential therapeutic use of Cymerus MSCs to treat sepsis. The studies will leverage the potential of the MSCs to direct the body's immune cells to kill bacterial during sepsis and to reduce the inflammation.

**Patent Portfolio Strengthened**

The *United States Patent and Trademark Office (USPTO)* granted a further patent covering aspects of Cynata's proprietary Cymerus platform. The patent granted is entitled 'Methods and materials for hematoendothelial differentiation of human pluripotent stem cells under defined conditions' and is owned by the *University of Wisconsin-Madison Alumni Research Foundation (WARF)* and is among the intellectual property licenced to Cynata.

Cynata also submitted a patent application to cover its Cymerus stem cell technology in the treatment of side effects related to the cancer treatment, CAR-T therapy. A preclinical study at the *University of Massachusetts* has demonstrated that Cymerus MSCs have the potential to improve the negative side-effects and adverse reactions of CAR-T therapy.

A Notice of Allowance was also received from *the European Patent Office (EPO)* for a patent covering the Cymerus technology in Europe. The patent is titled 'Generation of clonal mesenchymal progenitors and mesenchymal stem cell lines' and is also owned by *WARF* but licensed exclusively to Cynata. The patent is expected to be granted in September 2018.

## Corporate Update

During the June quarter, Cynata welcomed Fidelity International (Fidelity) to its shareholder register. *Fidelity* invested $5.2m through a share placement at $1.275 per share, representing a 4.5% premium to the closing price at the time of announcement. The investment took their existing holding to 10% and subsequently saw them become the largest shareholder of the Company.

The Company subsequently closed the June quarter with $12.2m in cash to continue to support its product development activities, that includes completing the current Phase 1 clinical trial in graft-versus-host-disease (GvHD) and commencing activities toward a Phase 2 clinical trial in critical limb ischemia (CLI).

Cynata has built a strong data set confirming the use of its Cymerus™ MSCs in preclinical studies of cardiovascular diseases and inflammatory complications, including CLI. As such, the Board and Management have made the decision to prioritise cardiovascular disease and to proceed toward a clinical in CLI and to continue to work with existing partners to further progress studies and generate supporting data in other cardiovascular indications.

## Outlook

**Cynata is looking beyond GvHD, at a range of target areas**

The positive safety and efficacy data from the GvHD clinical trial has provided a very strong platform that validates, in humans with GvHD, the clinical utility of the Company's Cymerus MSCs. This affords a great deal of confidence in the ability of CYP-001 to treat GvHD and a raft of other debilitating diseases and the data from the Phase I trial will enable Cynata to advance trials across its target disease portfolio.

**GvHD license option agreement with Fujifilm**

The primary evaluation period concludes with the 100-day analysis point. Post this point and following submission of the final study report, the 90-day review period provided by the licence option agreement with Fujifilm will begin. Should Fujifilm choose to exercise the option they will pay an initial USD3m upfront licence fee to Cynata for the exclusive worldwide licence for GvHD. Cynata could then potentially see a further AUD60m in milestone payments, as well as royalties on product sales.

**Critical limb ischemia Phase II trial in planning**

Cynata also has a strong set of preclinical data in a wide range of other potential drug indications and continues to focus on securing further licensing and partnership agreements to advance development. The Board has identified critical limb ischemia (CLI) as the next target indication to undertake phase II clinical trials following initial positive data in a preclinical study and strong supporting data in other cardiovascular diseases.

Following the $5.2m investment from *Fidelity International*, the Company closed the quarter with $12.2m in cash and is well funded to drive its product development programs and to further progress the commercialisation of its Cymerus platform.

**-ENDS-**

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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 that is developing a therapeutic stem cell platform technology, Cymerus™, originating from the University of Wisconsin-Madison, a world leader in stem cell research. The proprietary Cymerus™ technology addresses a critical shortcoming in existing methods of production of mesenchymal stem cells (MSCs) for therapeutic use, which is the ability to achieve economic manufacture at commercial scale. Cymerus™ utilises induced pluripotent stem cells (iPSCs) to produce a particular type of MSC precursor, called a mesenchymoangioblast (MCA). The Cymerus™ platform provides a source of MSCs that is independent of donor limitations and provides an "off-the-shelf" stem cell platform for therapeutic product use, with a pharmaceutical product business model and economies of scale. This has the potential to create a new standard in the emergent arena of stem cell therapeutics and provides both a unique differentiator and an important competitive position.

*+Rule 4.7B*

# Appendix 4C

# Quarterly report for entities subject to Lis ting Rule 4.7B

Introduced 31/03/00 Amended 30/09/01, 24/10/05, 17/12/10, 01/09/16

**Name of entity**

Cynata Therapeutics Limited

| **ABN** | **Quarter ended ("current quarter")** |
|---|---|
| 98 104 037 372 | 30 June 2018 |

| **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 | (597) | (3,352) |
| | (b) product manufacturing and operating costs | - | - |
| | (c) advertising and marketing | (124) | (525) |
| | (d) leased assets | - | - |
| | (e) staff costs | (109) | (472) |
| | (f) administration and corporate costs | (273) | (1,075) |
| 1.3 | Dividends received (see note 3) | - | - |
| 1.4 | Interest received | 37 | 161 |
| 1.5 | Interest and other costs of finance paid | - | - |
| 1.6 | Income taxes paid | - | - |
| 1.7 | Government grants and tax incentives | | |
| | - Export Market Development Grant | - | 46 |
| | - 2017 R&D Tax Incentive | - | 1,329 |
| 1.8 | Other (provide details if material) | - | - |
| **1.9** | **Net cash from / (used in) operating activities** | **(1,066)** | **(3,888)** |

| **2.** | **Cash flows from investing activities** | | |
|---|---|---|---|
| 2.1 | Payments to acquire: | | |
| | (a) property, plant and equipment | - | - |
| | (b) businesses (see item 10) | - | - |

| **Consolidated statement of cash flows** | | **Current quarter**<br>**$A'000** | **Year to date (12 months)**<br>**$A'000** |
|---|---|---|---|
| | (c) investments | - | - |
| | (d) intellectual property | - | - |
| | (e) other non-current assets | - | - |
| 2.2 | Proceeds from disposal of: | | |
| | (a) property, plant and equipment | - | - |
| | (b) businesses (see item 10) | - | - |
| | (c) investments | - | - |
| | (d) intellectual property | - | - |
| | (e) 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 shares | 5,195 | 5,195 |
| 3.2 | Proceeds from issue of convertible notes | - | - |
| 3.3 | Proceeds from exercise of share options | 175 | 644 |
| 3.4 | Transaction costs related to issues of shares, convertible notes or options | (366) | (370) |
| 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) | - | 150 |
| **3.10** | **Net cash from / (used in) financing activities** | **5,004** | **5,619** |

| **4.** | **Net increase / (decrease) in cash and cash equivalents for the period** | | |
|---|---|---|---|
| 4.1 | Cash and cash equivalents at beginning of quarter/year to date | 8,268 | 10,350 |
| 4.2 | Net cash from / (used in) operating activities (item 1.9 above) | (1,066) | (3,888) |
| 4.3 | Net cash from / (used in) investing activities (item 2.6 above) | - | - |

| **Consolidated statement of cash flows** | | **Current quarter**<br>**$A'000** | **Year to date (12 months)**<br>**$A'000** |
|---|---|---|---|
| 4.4 | Net cash from / (used in) financing activities (item 3.10 above) | 5,004 | 5,619 |
| 4.5 | Effect of movement in exchange rates on cash held | - | 125 |
| **4.6** | **Cash and cash equivalents at end of quarter** | **12,206** | **12,206** |

| **5.** | **Reconciliation of cash and cash equivalents**<br>at the end of the quarter (as shown in the consolidated statement of cash flows) to the related items in the accounts | **Current quarter**<br>**$A'000** | **Previous quarter**<br>**$A'000** |
|---|---|---|---|
| 5.1 | Bank balances | 8,706 | 3,768 |
| 5.2 | Call deposits | 3,500 | 4,500 |
| 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)** | **12,206** | **8,268** |

| **6.** | **Payments to directors of the entity and their associates** | **Current quarter**<br>**$A'000** |
|---|---|---|
| 6.1 | Aggregate amount of payments to these parties included in item 1.2 | 239 |
| 6.2 | Aggregate amount of cash flow from loans to these parties included in item 2.3 | - |

6.3 Include below any explanation necessary to understand the transactions included in items 6.1 and 6.2

Directors' fees, salaries including superannuation benefits, and professional consultancy fees. All payments are on normal commercial terms.

| **7.** | **Payments to related entities of the entity and their associates** | **Current quarter**<br>**$A'000** |
|---|---|---|
| 7.1 | Aggregate amount of payments to these parties included in item 1.2 | - |
| 7.2 | Aggregate amount of cash flow from loans to these parties included in item 2.3 | - |

7.3 Include below any explanation necessary to understand the transactions included in items 7.1 and 7.2

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| **8.** | **Financing facilities available**<br>*Add notes as necessary for an understanding of the position* | **Total facility amount at quarter end $A'000** | **Amount drawn at quarter end $A'000** |
|---|---|---|---|
| 8.1 | Loan facilities | - | - |
| 8.2 | Credit standby arrangements | - | - |
| 8.3 | Other (please specify) | - | - |

8.4 Include below a description of each facility above, including the lender, interest rate and whether it is secured or unsecured. If any additional facilities have been entered into or are proposed to be entered into after quarter end, include details of those facilities as well.

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| **9.** | **Estimated cash outflows for next quarter** | **$A'000** |
|---|---|---|
| 9.1 | Research and development | 1,936 |
| 9.2 | Product manufacturing and operating costs | - |
| 9.3 | Advertising and marketing | 83 |
| 9.4 | Leased assets | - |
| 9.5 | Staff costs | 209 |
| 9.6 | Administration and corporate costs | 213 |
| 9.7 | Other (provide details if material) | - |
| **9.8** | **Total estimated cash outflows** | **2,441** |

| **10.** | **Acquisitions and disposals of business entities (items 2.1(b) and 2.2(b) above)** | **Acquisitions** | **Disposals** |
|---|---|---|---|
| 10.1 | Name of entity | - | - |
| 10.2 | Place of incorporation or registration | - | - |
| 10.3 | Consideration for acquisition or disposal | - | - |
| 10.4 | Total net assets | - | - |
| 10.5 | Nature of business | - | - |

## 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.

Sign here: ..... Date: 11 July 2018

***Managing Director/CEO***

Print name: Dr Ross Macdonald

### Notes

1. The quarterly report provides a basis for informing the market how the entity's activities have been financed for the past quarter and the effect on its cash position. An entity that wishes to disclose additional information is encouraged to do so, in a note or notes included in or attached to this report.
2. If this quarterly 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 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.