ASX ANNOUNCEMENT

23 October 2018

September 2018 Quarterly Report

Melbourne, Australia; 23 October 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 September 2018 and is pleased to provide a review of operational progress during the period.

Highlights

- **Very successful 100-day (final) data reported for Phase 1 GvHD trial, with all end-points met**
  - Overall Response rate of 93%
  - Complete Response rate of 53%
  - No adverse safety events or safety concerns
- **Planning for Phase 2 trial in GvHD commenced with Fujifilm; trial expected to start in 2019**
  - Completion of a Pre-Development Meeting, led by Fujifilm, with the Japan Pharmaceuticals and Medical Devices Agency, to discuss the regulatory approval path for Cymerus™ mesenchymal stem cell (MSC) products in Japan
- **Planning continues to initiate a Phase 2 clinical program in critical limb ischemia, a US$1.4b commercial opportunity**
  - Further details to be announced during the upcoming quarter
- **Results of pre-clinical studies announced, supporting further applications of Cymerus MSCs:**
  - Cymerus MSCs demonstrated to have positive effect on cardiac function after a heart attack
  - Cymerus MSCs demonstrated to ameliorate the effects of Cytokine Release Syndrome (CRS) in immunotherapy cancer patients
- **New development partnership with the *Royal College of Surgeons in Ireland* to investigate the use of Cymerus MSCs in the treatment of sepsis**

Operational update

Phase 1 Clinical Trial in GvHD meets all safety and efficacy endpoints

Most excitingly this quarter, Cynata announced that its CYP-001 cell therapy for the treatment of steroid-resistant acute graft-versus-host disease (GvHD) met all safety and efficacy endpoints in its Phase 1 trial.

The Overall Response rate by Day-100 was 93%, with 14 out of 15 patients demonstrating an improvement in GvHD severity by at least one grade compared to baseline. The Complete Response rate by Day-100 was 53%, with GvHD signs and symptoms completely resolved in 8 out of 15 patients and the Overall survival at Day-100 was at least 87%. Importantly, no treatment-related serious adverse events or safety concerns were identified during the Primary Evaluation Period

As previously announced, one patient in Cohort A died after developing pneumonia, which is a common finding in recipients of bone marrow transplants and similar procedures. This death was not considered to be treatment-related. One patient in Cohort B withdrew from the trial to commence palliative care, which meant it was not possible to collect any further data regarding that patient as part of this trial. All other patients remained alive at Day 100.

The efficacy data following the completion of the Phase 1 trial supports the advancement of CYP-001 into a Phase 2 trial and validates the potential to generate safe and effective iPSC-derived MSC therapies.

In an interview with Cynata's Vice President of Product Development, Dr Kilian Kelly (available on the Company's website), the important implications of the Phase 1 trial are discussed.

A formal clinical study report (CSR) is now being prepared to support further clinical development and commercialisation of CYP-001 in GvHD. The CSR will be provided to Fujifilm pursuant to the license option agreement and upon receipt, Fujifilm will have 90 days to exercise its license option. The CSR is a very comprehensive report detailing all aspects of the trial, which must be prepared in compliance with international regulatory requirements[1]:

- The first stage of this process involves rigorous on-site review and verification of all data collected, to ensure data accuracy, as well as compliance with the clinical trial protocol and applicable regulations, in particular ICH Good Clinical Practice[2].
- Next, the database is locked and transferred to statisticians, who prepare a set of tables, figures and listings and (TFLs) using validated statistical software.
- The report text is then written on the basis of the TFLs, and subsequently reviewed by key stakeholders.
- Once complete, the CSR is subjected to further quality control checks, and finally it undergoes a publishing process to comply with regulatory electronic submission requirements.

On average, CSR preparation takes around four months from completion of patient data collection, and in some cases it can take more than one year[3]. Cynata expects to complete the GvHD trial CSR ahead of industry standard timelines.

Phase 2 Clinical Trial Programs

Planning for a Phase 2 clinical trial program in GvHD is currently underway, with a successful Pre-Development Meeting held with the Japan Pharmaceuticals and Medical Devices Agency (PMDA) in September. Pending further discussions with the PMDA and other regulatory agencies and other concerned parties the trial protocol will be finalised and a schedule developed and communicated to the market. A similar planning and communication process is also underway for the Company's other Phase 2 program, being in critical limb ischemia (CLI), as announced earlier this year.

Developments in Japan

Further to the positive trial results, Cynata has participated in a Pre-Development Meeting with PMDA, to discuss the regulatory approval path for Cynata's proprietary Cymerus™ mesenchymal stem cell (MSC) products in Japan. The meeting (as announced on 3 September 2018) was led by Fujifilm group and provided Cynata with valuable information about the Japanese regulatory framework for CYP-001 as well as for the broader product portfolio.

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[1] International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. ICH Harmonised Tripartite Guideline E3: Structure and Content of Clinical Study Reports. 1995.
https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E3/E3_Guideline.pdf

[2] International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. ICH Harmonised Guideline E6(R2): Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice. 2016.
https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2__Step_4_2016_1109.pdf

[3] Hamilton S. Effective authoring of clinical study reports: A companion guide. Medical Writing. 2014:23(2);86-92.

The reporting of excellent results from the Phase 1 trial and our meeting with the Japanese regulatory agency, PMDA, has attracted the attention of the media, particularly in Japan. Consistent with expectations that the partnership will proceed, subject to exercise of the license option, Fujifilm has indicated in response to media questions that Phase 2 clinical trials in GvHD should commence during 2019. It is notable that manufacturers may seek conditional marketing approval in Japan for stem cell therapeutic products after completion of Phase 2 clinical trials.

At the date of this report, Fujifilm has not exercised the license option to CYP-001 for GvHD. Cynata is encouraged that Fujifilm has confirmed publicly that its actively planning toward the further development of CYP-001 for GvHD.

Preclinical Progress and Development

During the quarter, Cynata continued to expand its portfolio of target indications and potential commercial opportunities through new collaborations and partnerships. Positive preclinical research has strengthened and expanded its data set to support further clinical trials. Consistent with its business model, the Company is actively seeking partners to assist in accelerating its pre-clinical programs into the clinic.

- ***Partnership with RCSI to investigate treatment of sepsis***

Cynata 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 bacteria during sepsis and to reduce the inflammation. The study is being co-funded by Cynata and the RCSI under the RCSI Strategic Industry Partnership Seed Fund. Sepsis is the most common cause of death in Intensive Care Units. It is implicated in 1 in 20 deaths in the population as a whole and up to 50% of all hospital deaths.

The project is led by Professor Gerard Curley, Chair of the Department of Anaesthesia and Critical Care at RCSI, and Consultant in Intensive Care Medicine at Beaumont Hospital, Dublin. Professor Curley has considerable expertise and a strong publication record in both sepsis and cellular therapies, and his research has been widely recognised globally.

- ***Positive data in pre-clinical study of heart attack***

The Company reported positive efficacy data from a study of Cymerus MSCs in a preclinical heart attack model in rats, conducted under the leadership of Associate Professor James Chong at the Westmead Institute for Medical Research, Sydney.

The primary endpoint of the study was fractional shortening (the ability of the heart to contract effectively that is indicative of overall cardiac function) at Day 28. An improvement in fractional shortening is indicative of recovery of the pumping function of the heart after a heart attack. Treatment with Cymerus MSCs resulted in an improvement in fractional shortening at Day 28, with the improvement being statistically significant compared to the placebo group. Cymerus MSC treatment also reduced left ventricular end-systolic diameter (LVESD) compared to either placebo or bone-marrow derived MSCs. LVESD reduction is associated with lower risk of further cardiac events. There is still a huge unmet medical need associated with heart attacks, which are the cause of over 8,000 deaths and more than 50,000 hospitalisations each year in Australia alone.

- ***Pre-clinical data shows Cymerus MSCs ameliorate the effect of Cytokine Release Syndrome in cancer immunotherapy patients***

In a study at the University of Massachusetts Amherst, Cynata's Cymerus MSCs were evaluated in a mouse model of Cytokine Release Syndrome (CRS), a potentially severe and life-threatening adverse reaction to cancer immunotherapy and can limit the ability to undergo immunotherapy treatment. The results suggest that administering a single dose of Cymerus MSCs before, during or even shortly after cancer immunotherapy treatment may provide significant therapeutic benefit and a straightforward way of limiting adverse CRS

reactions. Cynata intends to partner with companies developing cancer immunotherapies to evaluate the treatment approach in humans.

The positive preclinical data package adds to Cynata's growing number of successful pre-clinical studies and demonstrates the broad applicability of the Cymerus cell-manufacturing platform.

Outlook

In a very short period of time Cynata has progressed from a pre-clinical company to having two programs poised to enter Phase 2 clinical trials, with a combined market opportunity of around US$1.7 billion per annum[4]. The Company has a strong data package confirming the use of its Cymerus MSCs in preclinical studies and clear safety data from the phase I clinical trial in GvHD that can be leveraged to advance trials in other indications.

The Board and Management are targeting Phase 2 clinical studies in CLI and GvHD and are currently in the planning stages for these trials and will provide more definitive guidance once planning and scheduling has been completed. The growing and compelling data package is also assisting the Company in its partnering efforts which continue vigorously.

As noted above, the Company is now in the process of preparing the formal clinical study report (CSR) to support further clinical development and commercialisation of CYP-001 in GvHD. The CSR will be provided to Fujifilm pursuant to the license option agreement. Upon receipt, Fujifilm will have 90 days to exercise its license option that would see Fujifilm pay an initial US$3m upfront licence fee to Cynata for the exclusive worldwide licence for the product and a potential further ~A$60m in milestone payments, plus double-digit royalties on product sales. Fujifilm would also take on all development and commercialisation costs associated with progressing CYP-001 to market for GvHD.

The Company closed the September quarter with $10.9 million in cash to continue to support its product development activities, that includes pursuing phase 2 clinical trials in the treatment of GvHD and in CLI.

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CONTACTS:
Dr Ross Macdonald, CEO: Tel: 0412 119343; email ross.macdonald@cynata.com
Rosa Smith, Australia Media Contact, +61 (0) 475 305 047, rosa.smith@mcpartners.com.au
Laura Bagby, U.S. Media Contact, +1 312-448-8098, lbagby@6degreespr.com

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 and 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. Cynata plans to advance its Cymerus™ MSCs into Phase 2 trials for GvHD and critical limb ischemia. In addition, Cynata has demonstrated utility of its Cymerus MSC technology in preclinical models of asthma, critical limb ischemia, diabetic wounds, heart attack and cytokine release syndrome, a life-threatening condition stemming from cancer immunotherapy.

[4] Based on (i) Fujifilm's estimate of the global market opportunity for CYP-001 and (ii) ClearView Healthcare Partner's estimate of the peak annual global sales opportunity for a CLI product

+Rule 4.7B

Appendix 4C

Quarterly report for entities subject to Listing Rule 4.7B

Introduced 31/03/00 Amended 30/09/01, 24/10/05, 17/12/10, 01/09/169

Name of entity

Cynata Therapeutics Limited

ABN	**Quarter ended ("current quarter")**
98 104 037 372	30 September 2018

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	(1,144)	(1,144)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	(144)	(144)
	(d) leased assets	-	-
	(e) staff costs	(189)	(189)
	(f) administration and corporate costs	(289)	(289)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	34	34
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**	**(1,732)**	**(1,732)**

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

Consolidated statement of cash flows		Current quarter $A'000	Year to date (3 months) $A'000
	(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	-	-
3.2	Proceeds from issue of convertible notes	-	-
3.3	Proceeds from exercise of share options	417	417
3.4	Transaction costs related to issues of shares, convertible notes or options	-	-
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)	(17)	(17)
3.10	**Net cash from / (used in) financing activities**	**400**	**400**

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	12,206	12,206
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(1,732)	(1,732)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	-	-
4.4	Net cash from / (used in) financing activities (item 3.10 above)	400	400

Consolidated statement of cash flows		**Current quarter** **$A'000**	**Year to date (3 months)** **$A'000**
4.5	Effect of movement in exchange rates on cash held	33	33
4.6	**Cash and cash equivalents at end of quarter**	**10,907**	**10,907**

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	3,907	8,706
5.2	Call deposits	7,000	3,500
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)**	**10,907**	**12,206**

6.	**Payments to directors of the entity and their associates**	**Current quarter $A'000**
6.1	Aggregate amount of payments to these parties included in item 1.2	255
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, bonus payment, salaries including superannuation benefits, and company secretarial fees.

7.	**Payments to related entities of the entity and their associates**	**Current quarter $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** *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	1,703
9.2	Product manufacturing and operating costs	-
9.3	Advertising and marketing	78
9.4	Leased assets	-
9.5	Staff costs	127
9.6	Administration and corporate costs	115
9.7	Other (provide details if material)	-
9.8	**Total estimated cash outflows**	**2,023**

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: 23 October 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.