ASX ANNOUNCEMENT 30 June 2021

Ethics Approval for Cynata's Clinical Trial in Diabetic Foot Ulcers

Key highlights

- **Ethics approval received for clinical trial in patients with diabetic foot ulcers**
- **First clinical trial to utilise the wound dressing technology recently licensed from TekCyte**
- **Patient recruitment expected to commence in 2H CY21**

Melbourne, Australia; 30 June 2021: Cynata Therapeutics Limited (ASX: "**CYP", "Cynata",** or the **"Company"**), a clinical-stage biotechnology company specialising in cell therapeutics, is pleased to announce that it has received approval by the Central Adelaide Local Health Network Human Research Ethics Committee to commence a clinical trial of Cynata's Cymerus™ mesenchymal stem cell (**MSC**) product in patients with diabetic foot ulcers.

The trial, entitled "*A Randomised, Controlled, Phase 1 Study to Investigate Safety, Tolerability and Efficacy of CYP-006TK in Adults with Diabetic Foot Ulcers*", aims to recruit 30 participants, who will be randomly assigned to receive either CYP-006TK or standard care treatment. This will be the first clinical trial to utilise CYP-006TK, a polymer-coated silicon dressing (seeded with Cymerus MSCs) that Cynata has licensed from TekCyte Pty Ltd (TekCyte). As announced on 28 June 2021, Cynata has engaged leading clinical research organisation, Datapharm Australia, to assist in the conduct and management of the trial.

The investigational treatment period is 4 weeks, and each patient will be evaluated for a total of 24 weeks. The primary endpoint of the trial is safety, while secondary efficacy endpoints include the following outcome measures after 12 and 24 weeks:

- Percentage ulcer area change
- Days to complete ulcer healing
- Days to 50% ulcer healing
- Percentage change in ulcer volume
- Ulcer pain

The trial will take place at Royal Adelaide Hospital and The Queen Elizabeth Hospital in Adelaide, under the leadership of Professor Robert Fitridge, who is Professor of Vascular Surgery at the University of Adelaide, Head of Vascular Surgery at The Queen Elizabeth Hospital, and Consultant Vascular Surgeon with the Central Adelaide Local Health Network. Patient recruitment is expected to commence in the second half of this year, subject to the completion of customary regulatory and administrative approvals, as well as other trial start up activities, which are currently underway.

A corporate presentation on the DFU clinical trial is attached to this announcement.

Dr Kilian Kelly, Cynata's Chief Operating Officer, said:
"Diabetic foot ulcers can severely impact quality of life, and often result in hospitalisation, amputation and even death. Existing treatment options often fail to heal diabetic ulcers in a timely manner, if at all, so new and more effective treatments are urgently needed. The estimated market value for diabetic foot ulcer treatments is already approaching US$10b,[1] and that figure is likely to grow significantly in the future, in

[1] Transparency Market Research, 2020 (Reflects global DFU treatment market by 2027).

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tandem with the growth in the incidence of diabetes worldwide. We are on target to commence the trial this year and look forward to working with Professor Fitridge and his team on this important study."

-ENDS-

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. Clinical trials of Cymerus MSC products in osteoarthritis (Phase 3) and in patients with respiratory failure are currently ongoing. Planning is also underway for further clinical trials of Cymerus MSC products in GvHD (through licensee Fujifilm), diabetic foot ulcers, critical limb ischemia, idiopathic pulmonary fibrosis, and renal transplantation. In addition, Cynata has demonstrated utility of its Cymerus MSC 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.

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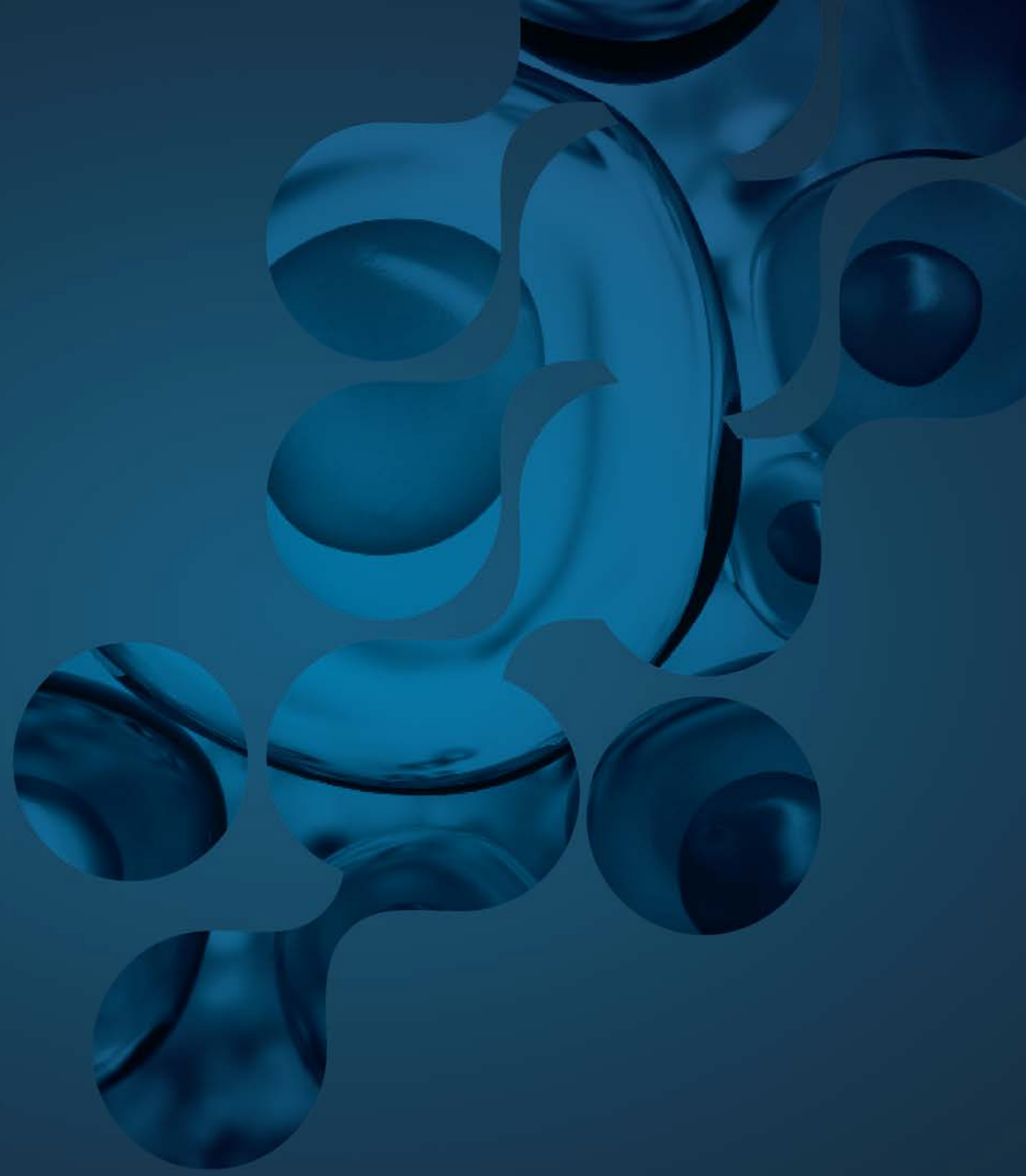
A Next Generation Stem Cell Therapeutics Company

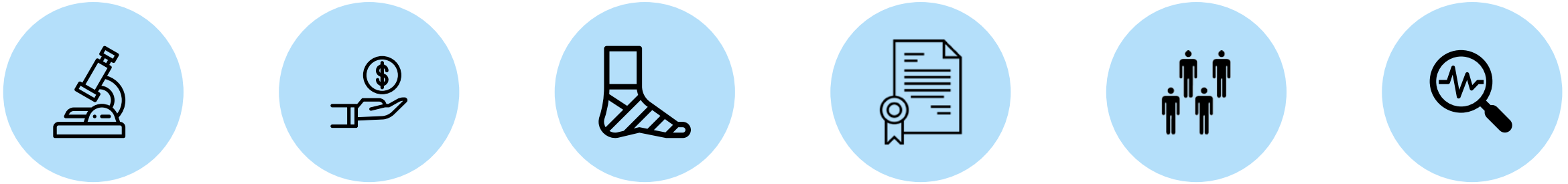
Overview of Diabetic Foot Ulcers Opportunity

30 June 2021



Key milestones achieved towards DFU clinical trial

Cynata is progressing toward a fully funded Diabetic Foot Ulcers (DFU) clinical trial[1]



Preclinical studies supporting further development ✓

Trial funding secured ✓

TekCyte license agreement secured ✓

Ethics approval for a Phase 1 clinical trial ✓

Trial commences[2] (expected to commence 2H FY21) ☐

Completion of trial: report top-line data and results ☐

1. Trial to be fully funded from available cash reserves.
2. Commencement of trial is subject to completion of customary regulatory and administrative approvals, as well as other trial start up activities – which are currently underway

DFU is an attractive indication to target

Head start in development

Clear safety results in Phase 1 GvHD trial and efficacy in a preclinical wound model provide a sound foundation

Large unmet medical need

DFU is a serious complication of diabetes, and has a global treatment market of ~$US10B[1]

Ethics approval received

Recruitment expected to commence in 2H CY21 (with trial start up activities currently underway)

Successful preclinical results

Positive data demonstrating the efficacy of Cymerus MSCs in a preclinical model of DFU[2]

Leverages TekCyte's technology

First clinical trial to utilise TekCyte's leading wound dressing technology

This trial will be fully funded by Cynata's current cash reserves

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1. Estimated DFU market (Source: Transparency Market Research, 2020 (Reflects global DFU treatment market by 2027))
2. Trial conducted independently by the Cooperative Research Centre for Cell Therapy Manufacturing (CTM-CRC). Results of preclinical model of Diabetic Wounds announced in May 2018. .

DFU is a serious disease and presents an unmet medical need

DFU is among the most common and serious complications of patients who have diabetes

Diabetic Foot Ulcers

- DFU are sores on the feet of patients with diabetes (also known as diabetic wounds)

Market opportunity

- **>400m diabetics globally,** with diabetic wounds estimated to **occur in ~15-25% of patients** sometime during their lifetime[1]
- In Australia alone diabetic foot disease is estimated to result in[2]:
  - **>27,000 hospitalisations annually**
  - **~4,400 amputations annually**
  - **~1,700 deaths annually**
- The global DFU treatment market is estimated to be **~US$10 billion[3]**

Next steps

- ✓ Central Adelaide Local Health Network Human Research Ethics Committee (HREC) approval
- ❑ Complete customary regulatory and administrative approvals, and trial start up activities
- ❑ Commence recruitment of patients: expected in 2H CY21

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1. Diabetics Australia (estimated ~415m adults with diabetes in 2015) ; Mutluoglu M, Uzun G, Turhan V, Gorenek L, Ay H, Lipsky BA. How reliable are cultures of specimens from superficial swabs compared with those of deep tissue in patients with diabetic foot ulcers? J Diabetes Complications. 2012 May-Jun;26(3):225-9
2. Van Netten JJ et al. Australian diabetes-related foot disease strategy 2028-2022: The first step towards ending avoidable amputations within a generation. Diabetic Foot Australia, 2017
3. Estimated DFU market (Source: Transparency Market Research, 2020 (Reflects global DFU treatment market by 2027)).

DFU | Phase 1 clinical trial design

Recruitment is expected to commence in 2H CY21

Target population

- 30 adult patients with Diabetic Foot Ulcers

Study design

- Patients will be randomly assigned to receive CYP-006TK (polymer-coated silicon dressing seeded with Cymerus MSCs) or standard care of treatment
- Treatment period will be 4 weeks
- Each patient is evaluated over a total of 24 weeks
- Cynata has engaged Datapharm Australia to assist in the conduct and management of the trial

Endpoints

- **Primary endpoint** will be *safety*
- **Secondary endpoints** will be *efficacy* endpoints consistent with previous pivotal trials[1] including;
  - Percentage ulcer area change
  - Days to complete ulcer healing
  - Days to 50% ulcer healing
  - Percentage change in ulcer volume
  - Ulcer pain

1. Conducted by other parties

Cymerus MSCs present a potential treatment for DFU

Cynata's Cymerus MSCs demonstrated promising efficacy results in a preclinical model of DFU

Preclinical trial design

- Positive efficacy data of Cymerus MSCs in a preclinical model of DFU[1]
- The preclinical trial was designed to compare MSCs and cells from various sources

Preclinical trial results

Primary outcome was speed of wound healing (measured as extent of skin restoration after three days)

- ✓ Cynata's Cymerus MSCs achieved **86% restoration**[2]
- ✓ Significantly faster wound healing that bone marrow-derived MSCs (which only achieved **51% restoration**)
- ✓ Significantly faster wound healing than dressings without MSCs (which only achieved **48% restoration**)

Cynata plans to undertake a clinical trial in DFU based on the solid preclinical foundation and utilise TekCyte's technology

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1. Trial conducted independently by the Cooperative Research Centre for Cell Therapy Manufacturing (CTM-CRC). Results of preclinical model of Diabetic Wounds announced in May 2018.
2. Measure of re-epithelialisation after three days

Cynata has partnered with TekCyte to optimise chance of success

This is the first clinical trial to utilise TekCyte's novel wound dressing technology

TekCyte has developed proprietary surface modification technologies to product polymer-coated dressings for the delivery of MSCs to wounds.

Cynata has **secured a worldwide exclusive licence agreement** with TekCyte Pty Ltd[1] – with the option to purchase the relevant technology outright.

The coating process provides **key benefits** in the delivery of MSCs[2]:

- ✓ Simple to apply
- ✓ Easily scalable
- ✓ Low capital costs
- ✓ Rapid translation from lab to the clinic
- ✓ Reproducible performance



TekCyte will manufacture and supply the active dressing to be utilised in Cynata's planned DFU clinical trial

1. Refer to announcement on 3 June 2021 "Cynata signs License Agreement with TekCyte"
2. Source: https://tekcyte.com/functionalised-coatings/

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