ASX ANNOUNCEMENT **9 August 2024**

Cynata to Present at ISCT Meeting

Melbourne, Australia; 9 August 2024: Cynata Therapeutics Limited (ASX: **"CYP", "Cynata",** or the **"Company"**), a clinical-stage biotechnology company specialising in cell therapeutics, announced that the Company will participate by invitation in the International Society of Cell and Gene Therapy (ISCT) ANZ 2024 Regional Meeting in Queenstown, New Zealand.

At 11:00am local time today, 9 August 2024, Dr Kilian Kelly, Cynata's Chief Executive Officer and Managing Director, will present on *Topical iPSC-derived MSC Therapy for Diabetic Foot Ulcers*. Dr Kelly's presentation will focus on the clinical development of CYP-006TK, Cynata's Cymerus™ iPSC[1]-derived MSC[2] topical wound dressing product candidate. A copy of the presentation is attached.

Established in 1992, the ISCT is a global society of clinicians, regulators, researchers, technologists, and industry partners with a shared vision to translate cell and gene therapy into safe and effective therapies to improve patients' lives worldwide.

-ENDS-

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

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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. A Phase 2 clinical trial in GvHD under a cleared US FDA IND, as well as trials of Cymerus products in osteoarthritis (Phase 3 – patient enrolment completed) and diabetic foot ulcers (DFU – patient enrolment completed) are currently ongoing, while a trial in renal transplant is expected to commence in the near future. 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

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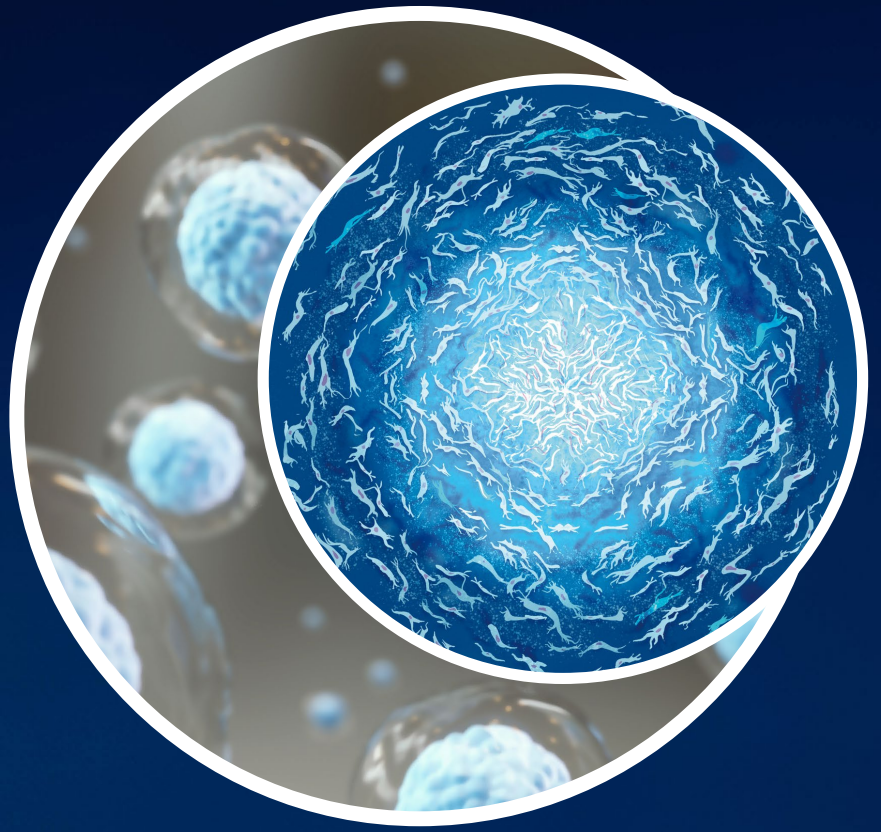

Topical iPSC-derived MSC Therapy for Diabetic Foot Ulcers

Kilian Kelly, PhD
CEO and Managing Director
Cynata Therapeutics Limited

Important information

Summary information

This Presentation contains summary information about Cynata Therapeutics Limited and its subsidiaries (**CYP**, or **Cynata**) which is current as at 2 August 2024. This Presentation should be read in conjunction with CYP's other periodic and continuous disclosure information lodged with the Australian Securities Exchange (**ASX**), which are available at www.asx.com.au.

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Company highlights

Revolutionary Cymerus™ iPSC-based manufacturing platform

- **Mesenchymal stem cells** (**MSCs**)[1] have shown potential to treat a wide range of illnesses,[2] but standard manufacturing methods require ongoing supply of new donors → challenges with consistency, potency and scalability
- The patented **induced pluripotent stem cell** (**iPSC**)-based **Cymerus™** platform overcomes major obstacle by enabling production of an **effectively limitless** quantity of **consistent**, **high-quality** MSC doses from a **single blood donation**
- Cynata is the **leader** of the burgeoning iPSC field: **first completed iPSC clinical trial** worldwide; **four** active clinical programs (including one in Phase 2 and one in Phase 3); US FDA **Orphan Drug Designation** and cleared **IND**[3]

Compelling clinical data

- **Steroid-resistant acute graft versus host disease (SR-aGvHD) Phase 1:**
  53% complete response; 87% overall response; 60% 2-year overall survival
- **Diabetic foot ulcer (DFU) Phase 1:**
  88% median wound surface area reduction vs 51% in controls[4]

Multiple significant near-term catalysts

- **Three** randomised controlled clinical trial readouts upcoming:
  DFU (Ph 1) – late 2024/early 2025; **aGvHD** (Ph 2) – 2H 2025; and **osteoarthritis** (Ph 3) – early 2026
- New trial in kidney transplantation to commence in Q3 2024

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1. Also known as mesenchymal stromal cells; 2. Zhou J, Shi Y. Cell Mol Immunol 20, 555–557 (2023); 3. IND = Investigational New Drug application, which is the clearance required from FDA to conduct clinical trials; 4. Initial data in first 16 patients (n=8 per group) after 10 weeks; final results in all 30 patients expected in late 2024/early 2025

Advanced and diverse clinical pipeline

	Indication	Trial phase	Upcoming catalysts*	Market opportunity
Cynata Sponsored	Acute Graft vs Host Disease (aGvHD) CYP-001 **FDA Orphan Designation**	**Phase 2 ongoing**	**Enrolment completion – Q4 2024** **Results – 2H 2025**	US$600m[1]
Cynata Sponsored	Diabetic Foot Ulcers (DFU) CYP-006TK	**Phase 1 ongoing** **(enrolment complete)**	**Results – Q4 2024/Q1 2025**	US$9.6bn[2]
Partnered	Osteoarthritis (OA) CYP-004 *(managed by USYD, funded by NHMRC)*	**Phase 3 ongoing** **(enrolment complete)**	**Results – 1H 2026**	US$11.6bn[3]
Partnered	Renal Transplantation (Renal) CYP-001 *(managed and funded by LUMC)*	**Phase 1 approved**	**Enrolment start – Q3 2024** **Cohort 1 results – Q4 2024**	US$5.9bn[4]

1. Global Graft versus Host Disease Market 2019-2029 (Reflects forecast market in 2026); 2. Zion Market Research, 2019 (represents global treatment market in 2025); 3. Persistence Market Research 2018 research report: "Osteoarthritis Treatment Market: Global Industry Analysis (2012-2016) and Forecast (2017-2025) (Reflect OA market by 2025); 4. Organ Transplant Immunosuppressant Drugs Market in 2026, Grand View Research, Inc.,2019

USYD = University of Sydney; NHMRC = National Health and Medical Research Council; LUMC = Leiden University Medical Center
* Timing of events is approximate, based on the Company's information as at the date of this presentation, and subject to change

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CYP-001: Two *Nature Medicine* publications

- CYP-001 has been granted **Orphan Drug Designation** by the US FDA for the treatment of GvHD
- Phase 1 trial of CYP-001 was the first completed clinical trial worldwide with **any iPSC-derived product**

nature medicine
LETTERS
https://doi.org/10.1038/s41591-020-1050-x
Nature Medicine **26**, 1720–1725 (2020)

Production, safety and efficacy of iPSC-derived mesenchymal stromal cells in acute steroid-resistant graft versus host disease: a phase I, multicenter, open-label, dose-escalation study

Adrian J. C. Bloor[1,2] ✉, Amit Patel[1], James E. Griffin[3], Maria H. Gilleece[4], Rohini Radia[5], David T. Yeung[6,7], Diana Drier[8], Laurie S. Larson[8], Gene I. Uenishi[9], Derek Hei[10], Kilian Kelly[11], Igor Slukvin[9] and John E. J. Rasko[12,13,14] ✉

nature medicine
Nature Medicine **30**, 1556–1558 (2024)
https://doi.org/10.1038/s41591-024-02990-z

Two-year safety outcomes of iPS cell-derived mesenchymal stromal cells in acute steroid-resistant graft-versus-host disease

Kilian Kelly[1], Adrian J. C. Bloor[2], James E. Griffin[3], Rohini Radia[4], David T. Yeung[5,6] & John E. J. Rasko[7,8,9] ✉

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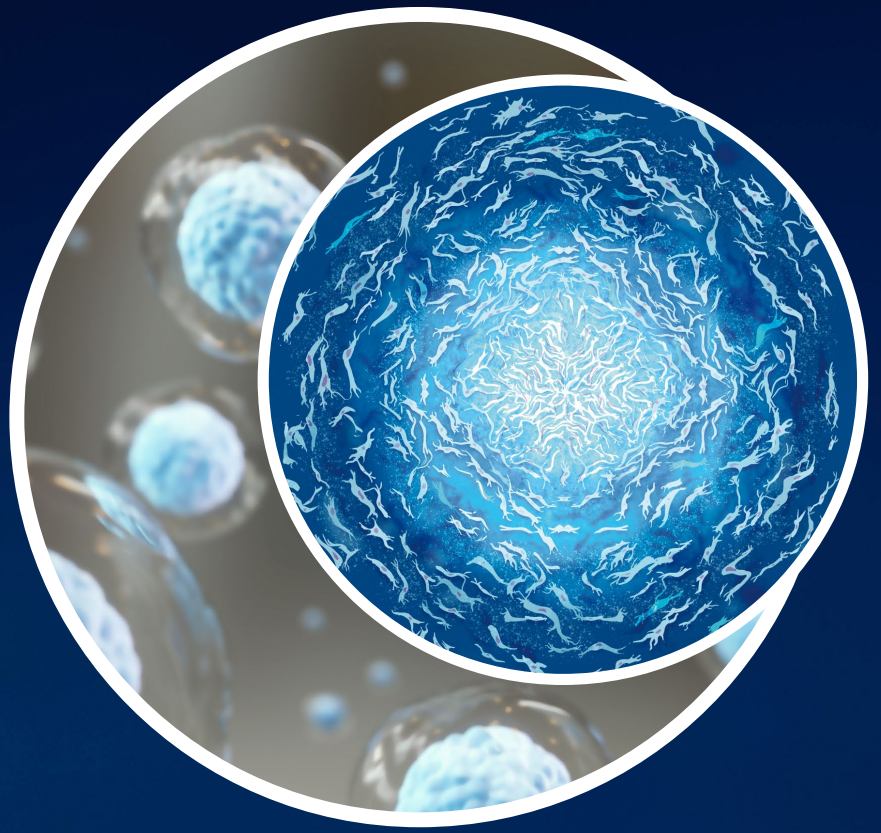
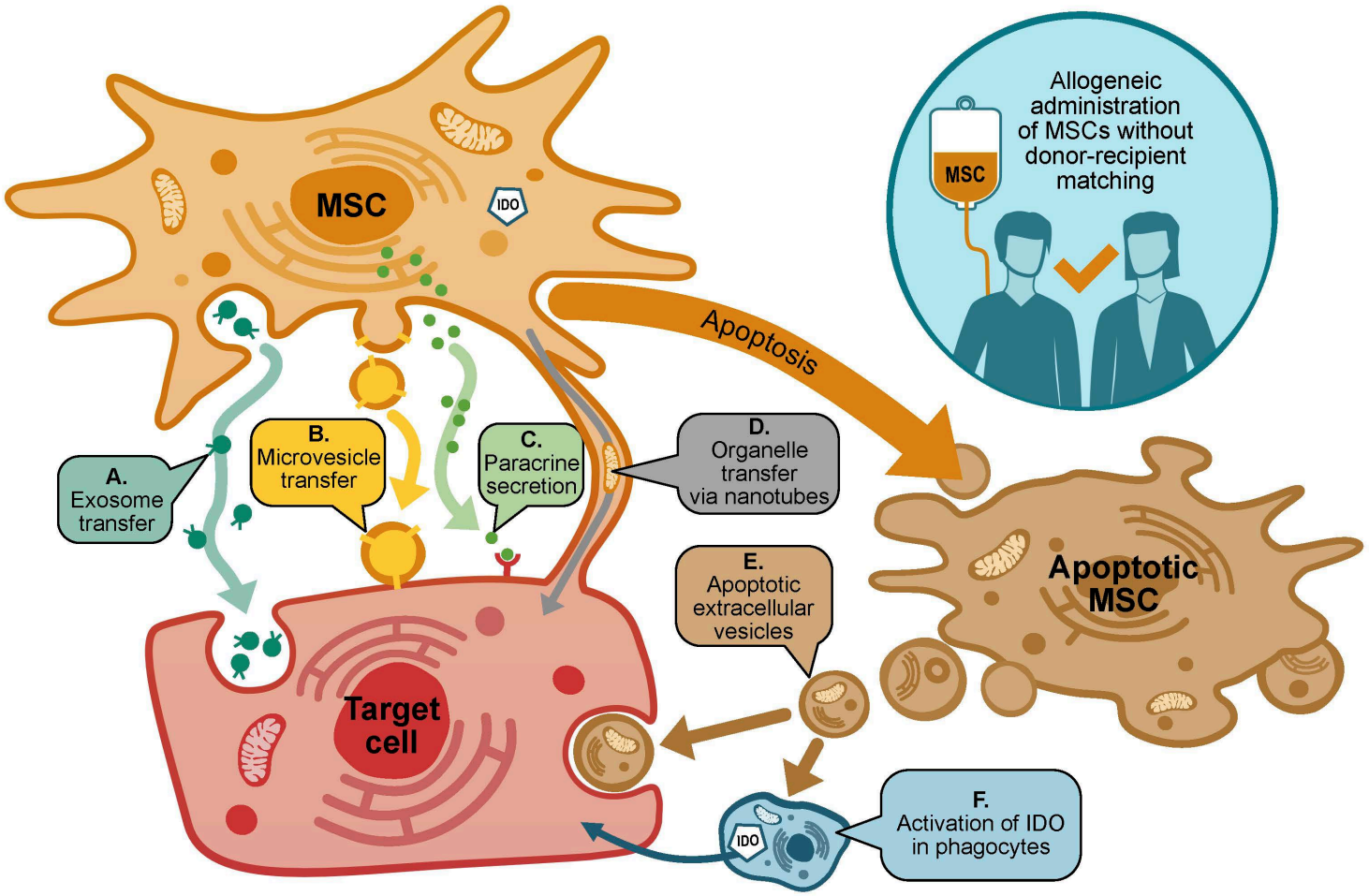
1. CYP-001 is Cynata's Cymerus iPSC-derived MSC product candidate for intravenous infusion

Revolutionary iPSC-based Cymerus™ Manufacturing Platform



Therapeutic potential of MSCs



Mesenchymal stem cells[1] (MSCs):

- Promote an **immunomodulatory** environment[2]
- The "sensor and switcher of the immune system"[3]
- Promote **tissue repair** and **regeneration**
- Can be used **without** matching donors to recipients
- Can be **engineered** to express other functional/therapeutic molecules
- However, with conventional manufacturing methods, there are consistency, potency and scalability challenges

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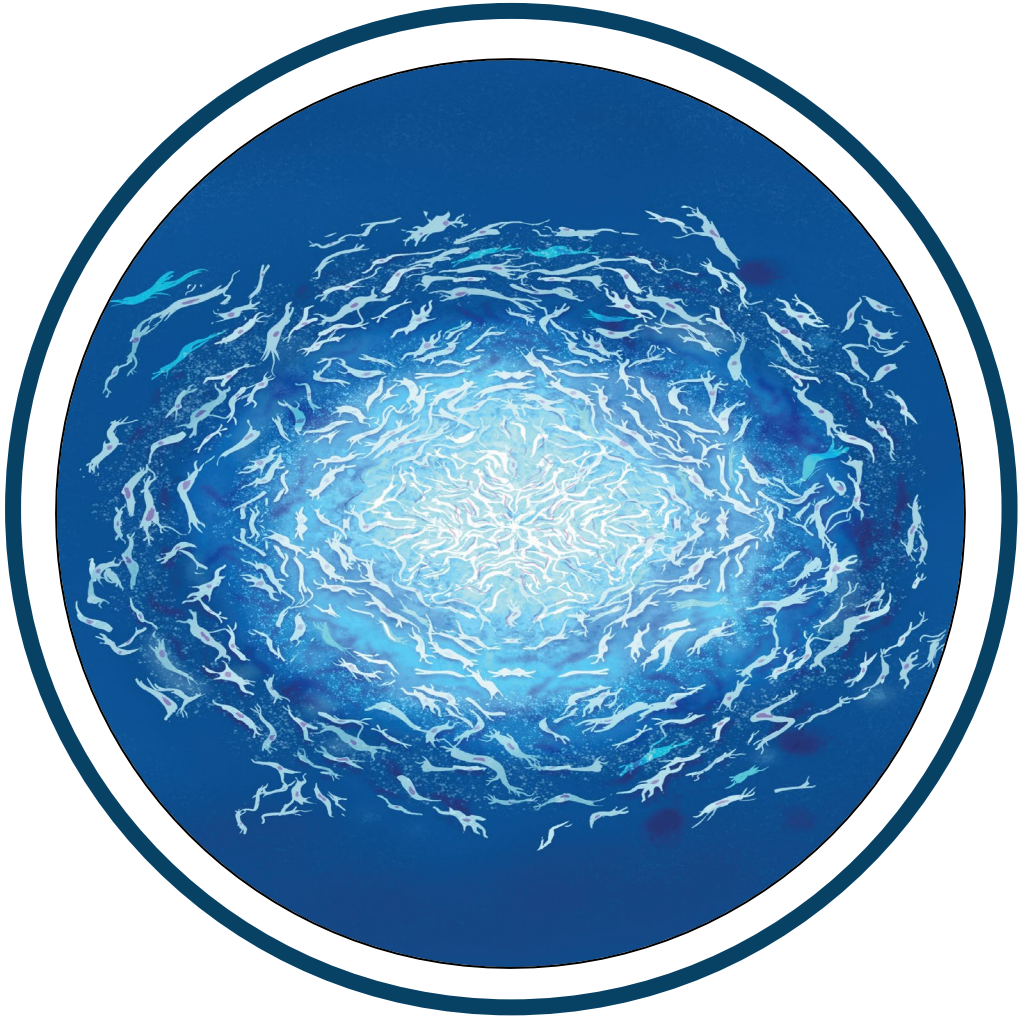
1. Also known as mesenchymal stromal cells
2. Kelly and Rasko, Front. Immunol. 12:761616 (2021)
3. Sarsenova et al, Front. Immunol.13:1010399 (2022)

Advantages of iPSC-based platform



Induced pluripotent stem cells (iPSCs):

- Mature **adult** cells **reprogrammed** to become **pluripotent**, which means:
  - Effectively **limitless** proliferation capacity
  - Potential to differentiate into any adult cell type (including MSCs)
- Similar properties to embryonic stem cells … but iPSCs are derived from **adult donors**, so they **avoid** ethical controversy associated with embryonic stem cells

→ iPSCs are **ideal** starting material for commercial production of cellular products

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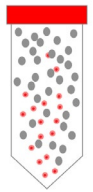
Conventional MSC process

Ongoing need for new donors

Substantial inter-donor **variability**

MSC isolation



Small number of MSCs per donation

Culture expansion

Extensive MSC culture expansion required

Major challenges:

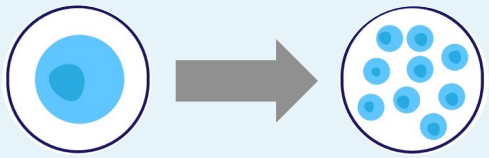
- Logistically challenging
- Inter-donor **variability** – **inconsistent** activity in MSCs from different donors
- MSCs undergo **functional changes** and **loss of potency** during extensive culture expansion

Cymerus™ iPSC-based process

One donor, one time

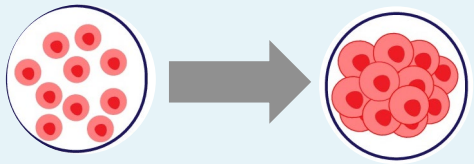
Avoids inter-donor variability

Reprogramming & iPSC expansion



Effectively **limitless** expansion potential

Differentiation into MSCs & culture expansion



Minimal MSC culture expansion

Robust patent protection

Advantages of **Cymerus™** platform:

- **Effectively limitless** iPSC expansion potential
- **Avoids** need for new donors
- **Avoids** inter-donor variability
- **Avoids** extensive MSC expansion
- High level **potency**, **consistency** and **scalability**

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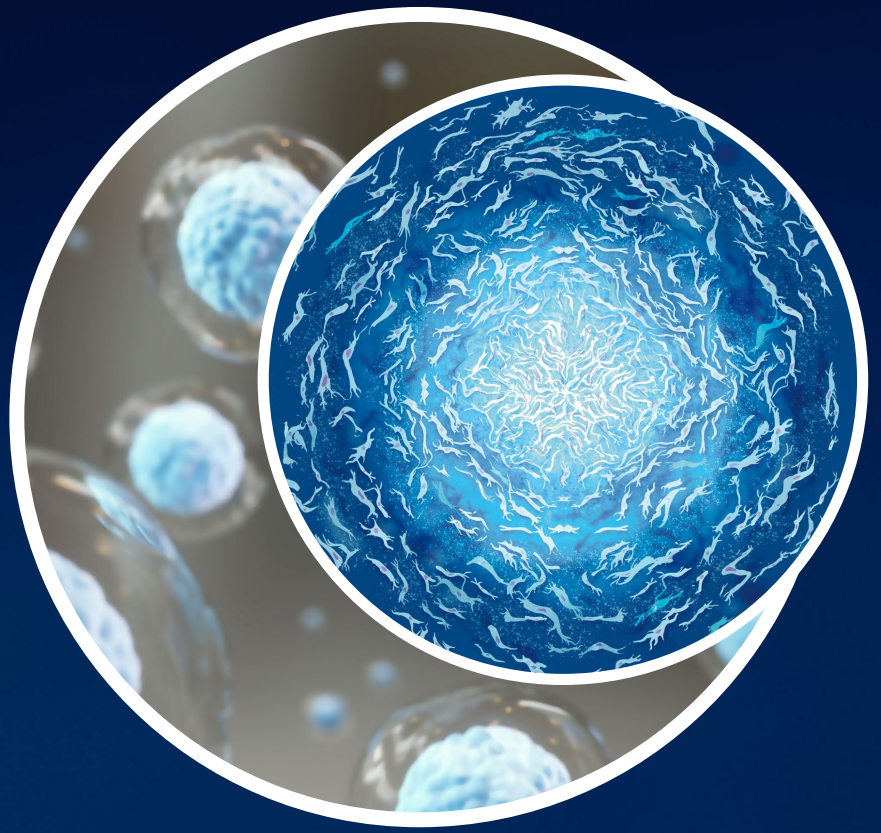
Diabetic Foot Ulcer (DFU)



Diabetic foot ulcer (DFU)

Diabetic Foot Ulcer

- Diabetes is fastest growing chronic disease worldwide[1] – affects **>400m** adults globally; forecast to affect **>600m** by 2045[2]
- Up to **34%** of those with diabetes will develop DFU[3]: very difficult to heal; painful; impair mobility; can lead to serious infections and/or amputation[3]
- Lower extremity complications of diabetes constitute a top ten condition in terms of years lived with disability[5,6]

Disease burden

- In Australia alone diabetic foot disease is estimated to result in[4]:
  - **>27,000 hospitalisations annually**
  - **~4,400 amputations annually**
  - **~1,700 deaths annually**
- The global DFU treatment market size is estimated at **US$8-10 billion** and is expected to exceed **US$14 billion by 2032[5,6]**

1. Zimmet P, Alberti KG, Shaw J. Global and societal implications of the diabetes epidemic. Nature. 2001;414(6865): 782-7
2. International Diabetes Federation. IDF Diabetes Atlas, 8th edn. Brussels, Belgium: International Diabetes Federation, 2017
3. Brem H, Tomic-Canic M. Cellular and molecular basis of wound healing in diabetes. J Clin Invest. 2007;117(5): 1219-22 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
4. Estimated DFU market (Source: Transparency Market Research, 2020 (Reflects global DFU treatment market by 2027))
5. Zhang Y et al Global Disability Burdens of Diabetes-Related Lower-Extremity Complications in 1990 and 2016
6. Lazzarini PA et al Diabetes-related lower-extremity complications are a leading cause of the global burden of disability.
7. Fortune Business Insights Market Research Report on Diabetic Foot Ulcer, published 2024. Data reproduced with permission.

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Unmet need

Existing treatment options often fail to heal diabetic ulcers in a timely manner, if at all

Current treatments

- Multifactorial disease → currently requires a multidisciplinary approach
- In addition to wound care, emphasis is on blood sugar control, infection management, offloading, vascular management and education/self care
- Wound care is anchored by debridement and the application of wound dressings comprised of a wide variety of materials (hydrogels, hydrocolloids, alginates etc)
- Clinical studies with a range of cytokines and growth factors have largely been unsuccessful, primarily because of their specificity to only single pathologic factors
- Thus, new and more effective treatments are urgently needed
- MSCs have been shown in multiple studies to have encouraging impact on angiogenesis and wound healing

Mechanisms of action: MSCs in DFU

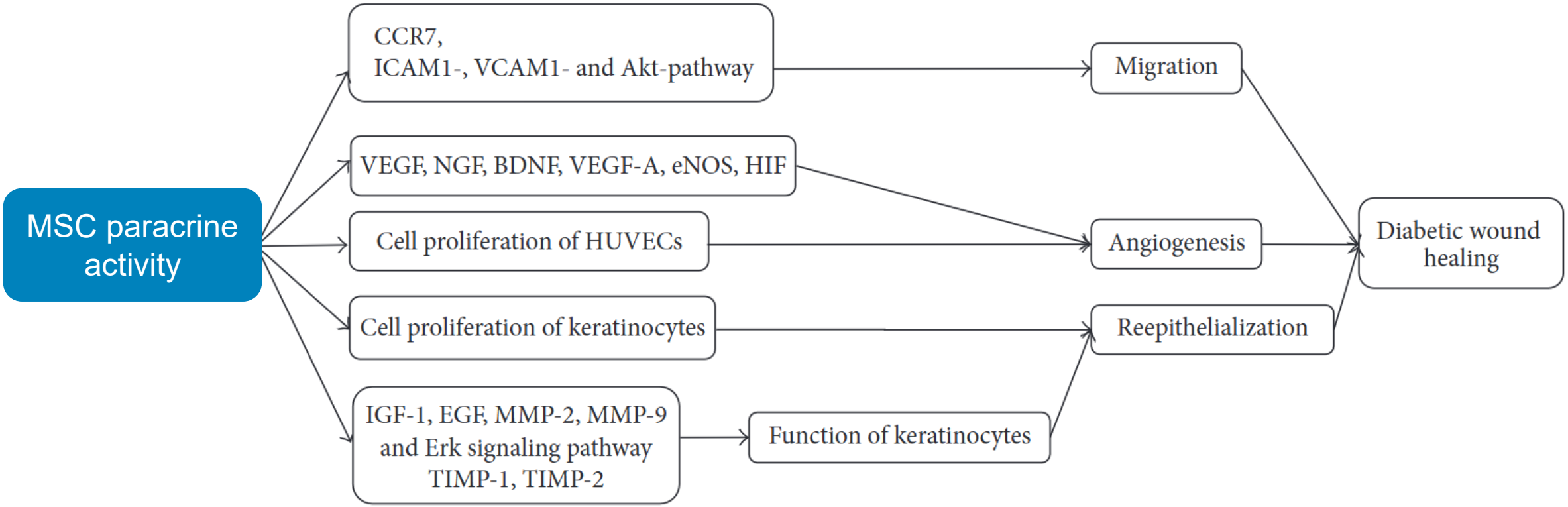
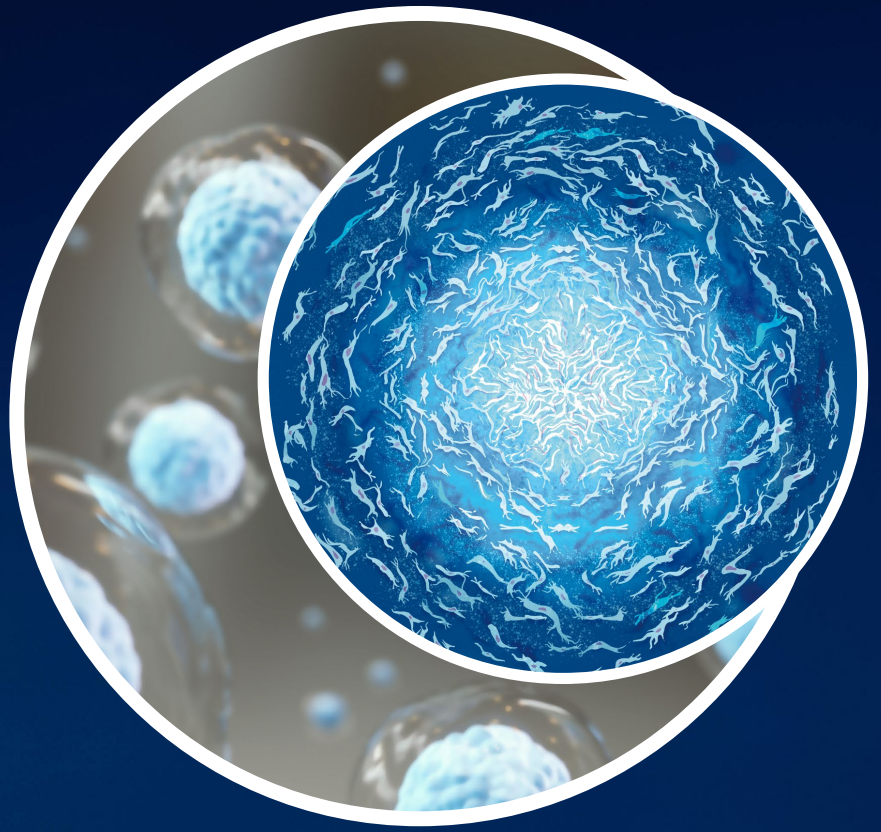


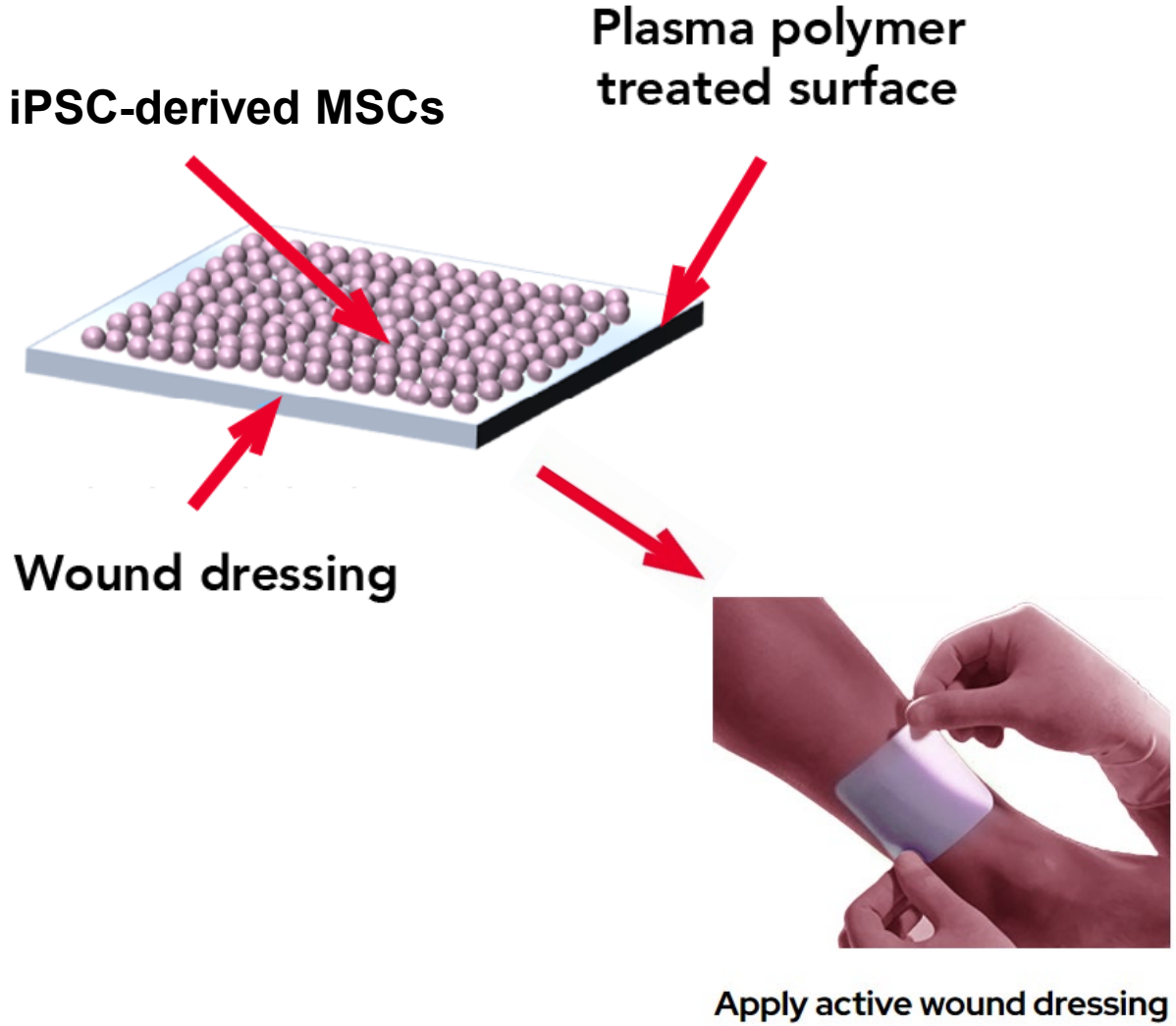
Image adapted from: Cao et al. J Diabetes Res. 2017:2017:9328347

CYP-006TK



CYP-006TK – a novel topical MSC product

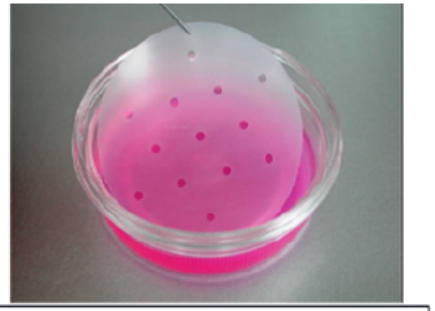
- CYP-006TK utilises a proprietary surface-coating, optimised for the delivery of MSCs directly to the wound bed
- Technology exclusively licenced to Cynata by Tekcyte Limited (agreement for Cynata to acquire this IP outright announced 1 July 2024)



Images provided by Tekcyte Limited

Transfer of cells to wound

In vitro cell transfer assay shows MSCs are transferred from dressing to wound



Chemically defined carrier

MSCs

Carrier dressing

Carrier + cells incubated at 37°C for 24 hours

Cells attached to carrier dressing

De-epidermised acellular human dermis (DED)

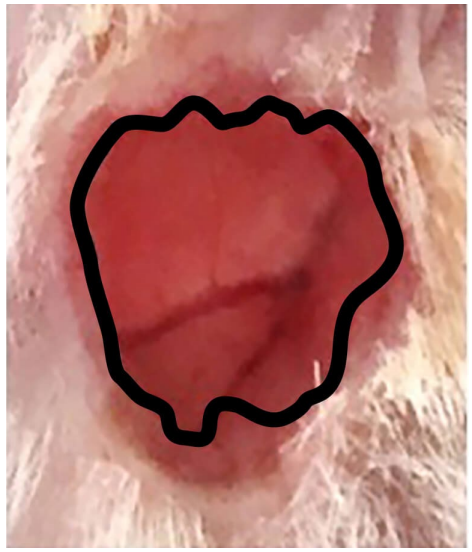
Carrier + cells transferred onto human DED and incubated for 24 hours at 37°C

Samples sacrificed in order to assess (using MTT-ESTA) transfer of cells from the carrier dressing to human DED

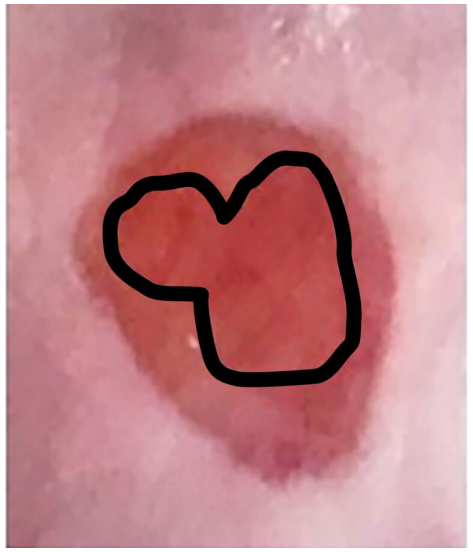
Images provided by Tekcyte Limited

Topical MSC delivery vs injection

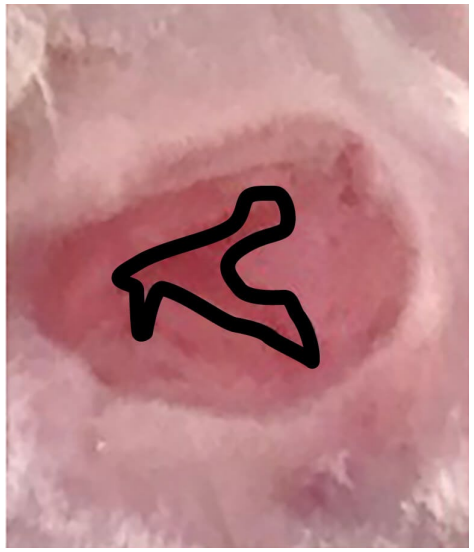
Diabetic mouse wound model showed that wounds healed faster when treated with the silicone patch seeded with MSCs, compared to injecting cells around the wound, or with the silicone patch alone



MSCs injected around wound



Silcone patch alone

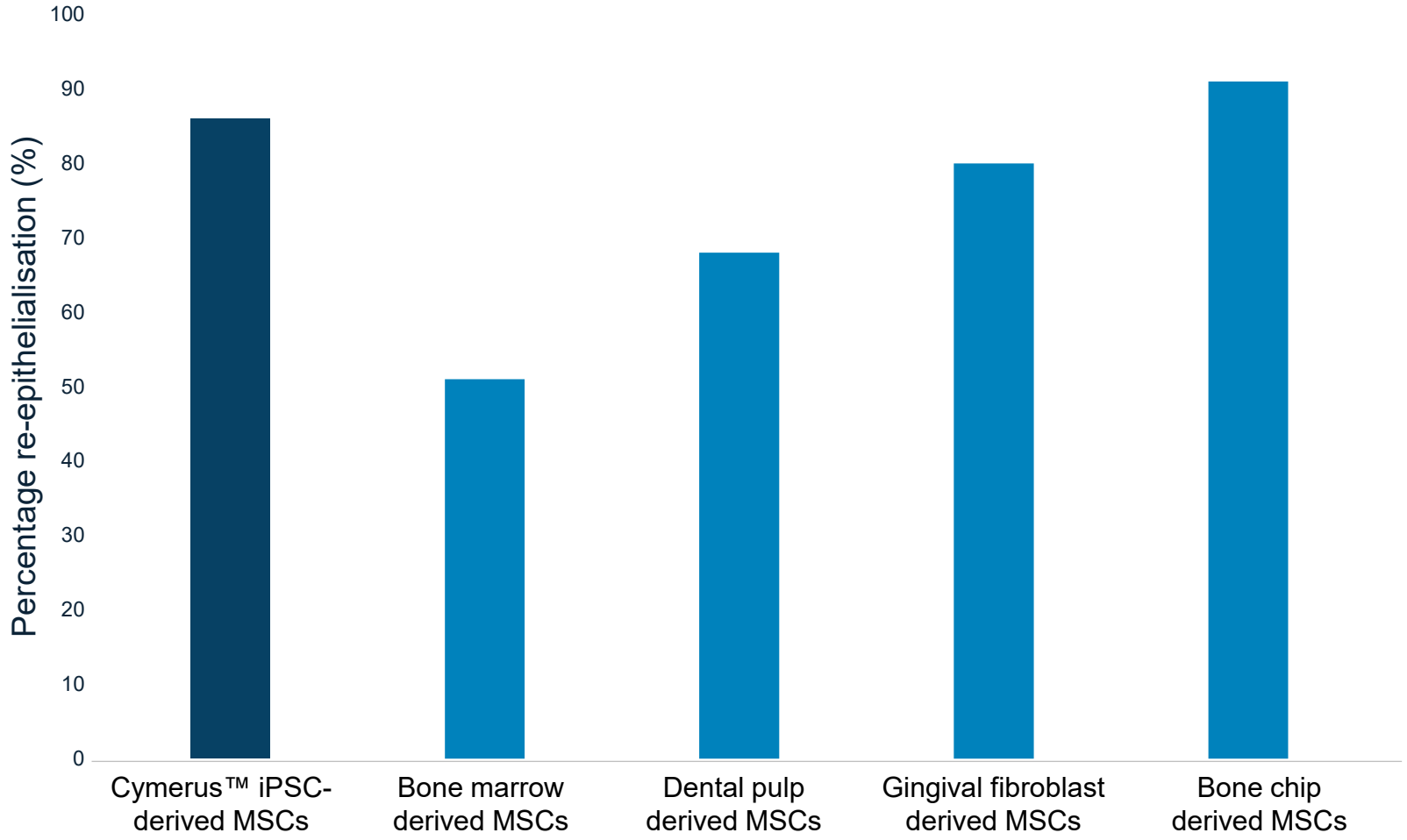


Silicone patch plus MSCs

Images provided by Tekcyte Limited

MSC source influences performance

Silicone patch seeded with MSCs from various sources, in preclinical model of diabetic wounds



Key findings

- Primary outcome measure was extent of wound surface re-epithelialisation after 3 days
- Cymerus MSCs resulted in significantly greater re-epithelialisation (86%) compared to bone marrow MSCs (51%)
- Although gingival fibroblasts and bone chip MSCs produced similar results, there are major challenges associated with producing clinical-grade cells from these sources at commercial scale

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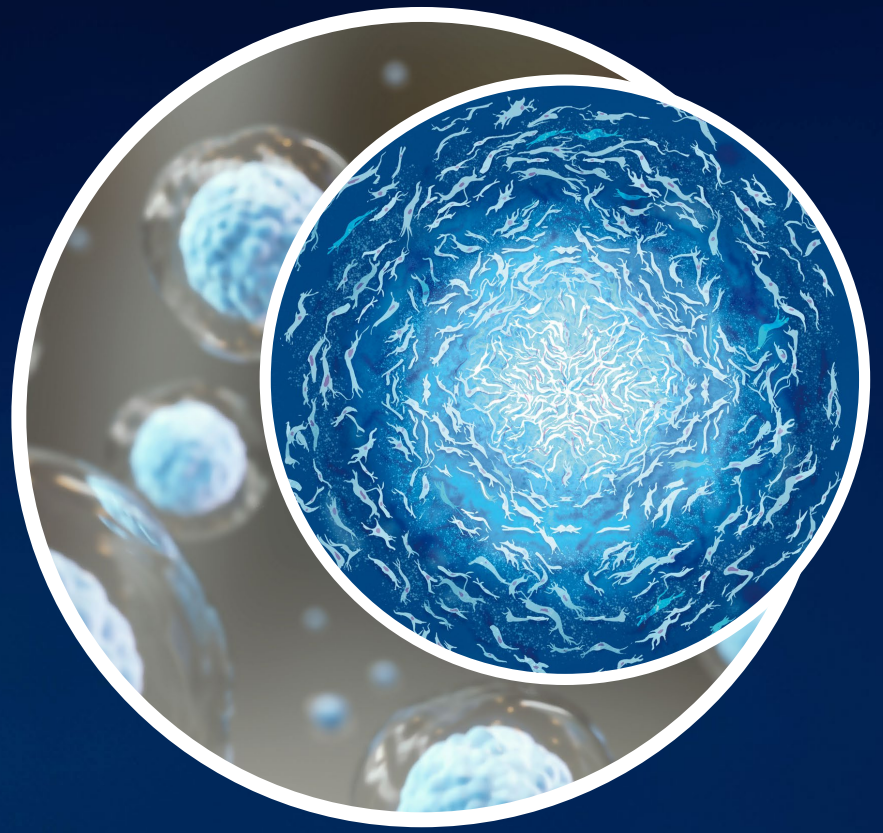
Phase 1 Clinical Trial



DFU | Phase 1 clinical trial (1)

Product

CYP-006TK (Novel silicone dressing seeded with Cymerus™ iPSC-derived MSCs)

Study design

- Multi-centre randomised controlled trial, conducted at clinical sites in Australia
- A total of 30 patients were randomised 1:1 to receive either:
  - Standard of care treatment (following best practice for the type, severity and stage of ulcer for each participant, at the investigator's discretion); OR
  - CYP-006TK treatment for 4 weeks (2 applications per week), followed by standard of care treatment
- Primary objective is safety; efficacy measures include wound healing, pain, quality of life

Study progress

- Patient enrolment complete (April 2024)
- Last patient visit expected ~September 2024
- Positive initial results released February 2024
- Final results anticipated in Q4 2024 or Q1 2025

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For further information: https://clinicaltrials.gov/study/NCT05165628

DFU | Phase 1 clinical trial (2)

Eligibility criteria

- Confirmed diagnosis of diabetes mellitus
- At least one cutaneous ulcer on foot or lower leg; area between 2 and 28 cm2; present for at least 6 weeks; classified as non-healing (<50% reduction in ulcer size after at least 4 weeks' treatment)
- Ankle-brachial index ≥ 0.4 and/or toe pressure >30 mmHg on affected limb
- Patients with active infection, planned surgery, osteomyelitis, malignancy etc excluded

Evaluation criteria

- Clinical assessment of ulcers
- Collection of 3-dimensional clinical photographs utilising a stereovision camera and image management software to conduct 3D surface area calculations followed by blinded, independent quantitative assessments of the data by a specialist service provider
- Monitoring of tolerability and adverse events

For further information: https://clinicaltrials.gov/study/NCT05165628

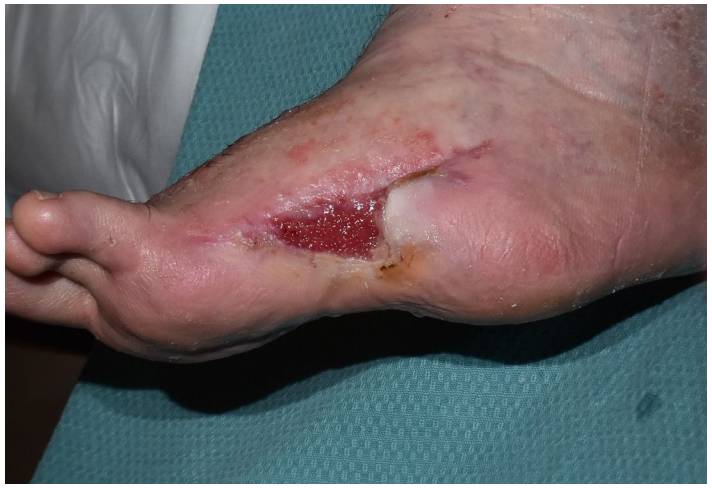
DFU | Phase 1 clinical trial – initial data

Product: CYP-006TK (topical Cymerus™ MSC wound dressing)

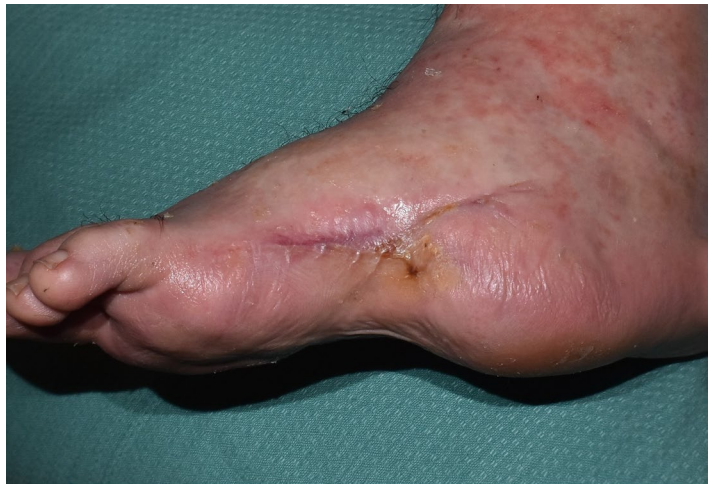
- Ongoing trial in non-healing diabetic foot ulcer (DFU)
- Patients randomised to receive standard of care (SoC) or CYP-006TK for 4 weeks, followed by SoC
- In the first 16 patients enrolled in the trial (8 per group), after 10 weeks' follow-up, the median reduction in wound surface area was:
  - **87.6%** in the active CYP-006TK group
  - compared to **51.1%** in SoC group

Example of ulcer healing in patient treated with CYP-006TK:

Day 0



Day 28



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For further information: https://clinicaltrials.gov/study/NCT05165628

Acknowledgements – DFU program

Manufacturing/Process Development/Preclinical Studies

Cell Therapy Manufacturing Cooperative Research Centre

TekCyte

Manufacturing/Process Development

WAISMAN BIOMANUFACTURING

Cell and Tissue Therapies WA

Clinical Trial

Royal Adelaide Hospital

Royal Perth Hospital

SIR CHARLES GAIRDNER HOSPITAL

FIONA STANLEY hospital

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Summary

Next generation stem cell company	• Leading platform technology in burgeoning stem cell sector • Diverse and highly credentialed leadership team with proven experience
Scalable manufacturing	• Cymerus™ manufacturing technology protected by robust patent portfolio • Enables scalable production of consistent MSCs from a single donation from a single donor, overcoming major challenges with conventional approaches
Compelling clinical data	• Very encouraging safety and efficacy results from aGvHD clinical trial (CYP-001) • Promising initial data from ongoing DFU clinical trial (CYP-006TK)
Rich clinical pipeline	• Broad pipeline with four active clinical programs • FDA cleared IND for Phase 2 aGvHD clinical trial; study underway • Patient enrolment complete in DFU & OA clinical trials • Commencement of renal transplantation clinical trial imminent
Significant growth potential	• Global estimated market opportunity across targeted indications of ~US$28bn[1] • Focus on indications with significant unmet need • Proactive B-2-B outreach to drive partnering strategy

cynata therapeutics

1. Refer to slide #4 for breakdown/sources

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