

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™ iPSC¹-derived MSC² 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

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 – 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

cynata

therapeutics

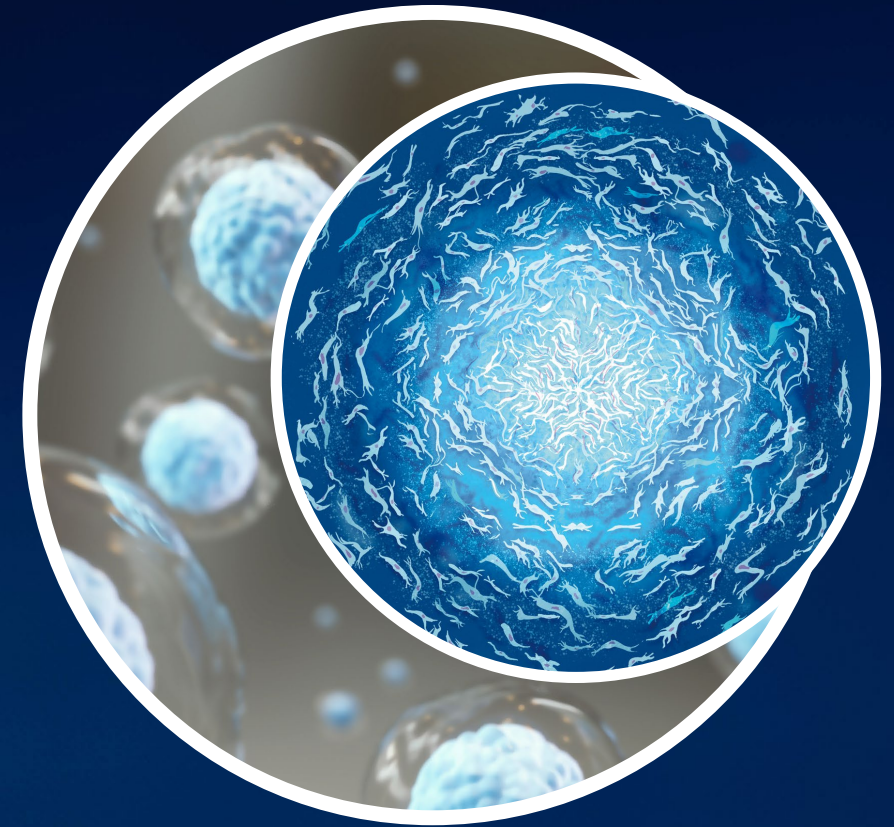


Topical iPSC-derived MSC Therapy for Diabetic Foot Ulcers

Kilian Kelly, PhD

CEO and Managing Director

Cynata Therapeutics Limited



International Society
ISCT
Cell & Gene Therapy®
AUSTRALIA AND NEW ZEALAND REGION

**ISCT ANZ 2024
REGIONAL MEETING**

Queenstown, New Zealand | 7–9 August, 2024

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.

Not an offer

This Presentation is not a prospectus, product disclosure statement or other offering document under Australian law (and will not be lodged with the ASIC) or any other law. This Presentation is for information purposes only and is not an invitation or offer of securities for subscription, purchase or sale in any jurisdiction. The release, publication or distribution of this Presentation (including an electronic copy) outside Australia may be restricted by law. If you come into possession of this Presentation, you should observe such restrictions. Any non-compliance with these restrictions may contravene applicable securities laws.

Not investment advice

This Presentation does not constitute investment or financial product advice (nor tax, accounting or legal advice) or any recommendation by CYP or its advisers to acquire CYP securities. This Presentation has been prepared without taking account of any person's individual investment objectives, financial situation or particular needs. Before making an investment decision, prospective investors should consider the appropriateness of the information having regard to their own investment objectives, financial situation and needs and seek legal, accounting and taxation advice appropriate to their jurisdiction. CYP is not licensed to provide financial product advice in respect of CYP securities.

Investment risk and past performance

An investment in CYP securities is subject to known and unknown risks, some of which are beyond the control of CYP and its directors. CYP does not guarantee any particular rate of return or performance of CYP. Past performance cannot be relied upon as an indicator of (and provides no guidance as to) future CYP performance including future share price performance.

Financial data

All financial information in this Presentation is in Australian currency (A\$) unless otherwise stated. This Presentation contains historical financial information based on financial information that has been disclosed to the ASX. Any discrepancies between totals and sums of components in tables and figures in this Presentation are due to rounding.

Forward-looking statements

This Presentation contains certain 'forward looking statements', which can generally be identified by the use of forward looking words such as 'expect', 'anticipate', 'likely', 'intend', 'should', 'could', 'may', 'predict', 'plan', 'propose', 'will', 'believe', 'forecast', 'estimate', 'target', 'outlook', 'guidance', 'potential' and other similar expressions. The forward looking statements contained in this Presentation are not guarantees or predictions of future performance and involve known and unknown risks and uncertainties and other factors, many of which are beyond the control of CYP, its directors and management, and may involve significant elements of subjective judgment and assumptions as to future events which may or may not be correct. There can be no assurance that actual outcomes will not differ materially from these forward looking statements. A number of important factors could cause actual results or performance to differ materially from the forward looking statements. No representation or warranty, express or implied, is made as to the accuracy, likelihood of achievement or reasonableness of any forecasts, prospects, returns or statements in relation to future matters contained in this Presentation. The forward looking statements are based on information available to CYP as at the date of this Presentation. Except as required by law or regulation (including the ASX Listing Rules), CYP and its directors, officers, employees, advisers, agents and intermediaries undertake no obligation to provide any additional or updated information whether as a result of new information, future events or results or otherwise. You are strongly cautioned not to place undue reliance on forward-looking statements.

Industry and Market data

Certain market and industry data used in connection with this Presentation may have been obtained from research, surveys or studies conducted by third parties, including industry or general publications. Neither CYP nor its representatives have independently verified any such market or industry data provided by third parties or industry or general publications.

Disclaimer

To the maximum extent permitted by law, CYP and its advisers, affiliates, related bodies corporate, directors, officers, partners, employees and agents (**Related Persons**) exclude and disclaim all liability, including without limitation for negligence, for any expenses, losses, damages or costs arising from this Presentation or reliance on anything contained in or omitted from it. To the maximum extent permitted by law, CYP and its Related Persons make no representation or warranty, express or implied, as to the currency, accuracy, reliability or completeness of information in this Presentation and disclaim any obligation or undertaking to release any update or revision to the information in this Presentation to reflect any change in expectations or assumptions. Statements made in this Presentation are made only as at the date of this Presentation. The information in this Presentation remains subject to change without notice.

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 controls⁴

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

Advanced and diverse clinical pipeline

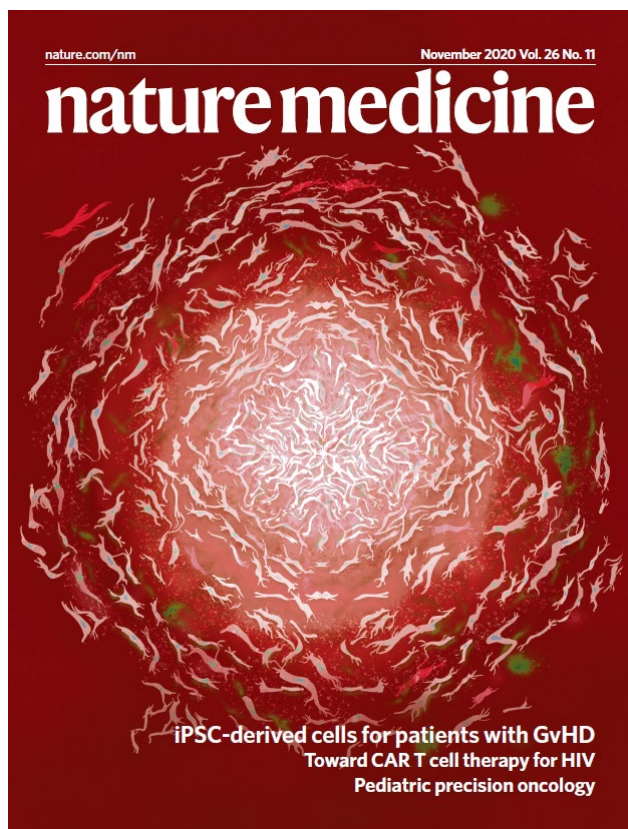
Indication	Trial phase	Upcoming catalysts*	Market opportunity
 Acute Graft vs Host Disease (aGvHD) CYP-001 FDA Orphan Designation	Phase 2 ongoing	Enrolment completion – Q4 2024 Results – 2H 2025	US\$600m ¹
 Diabetic Foot Ulcers (DFU) CYP-006TK	Phase 1 ongoing (enrolment complete)	Results – Q4 2024/Q1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

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 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 Patel¹, James E. Griffin³, Maria H. Gilleece⁴, Rohini Radia⁵, David T. Yeung^{6,7}, Diana Drier⁸, Laurie S. Larson⁸, Gene I. Uenishi⁹, Derek Hei¹⁰, Kilian Kelly¹¹, Igor Slukvin⁹ and John E. J. Rasko^{12,13,14}

nature medicine

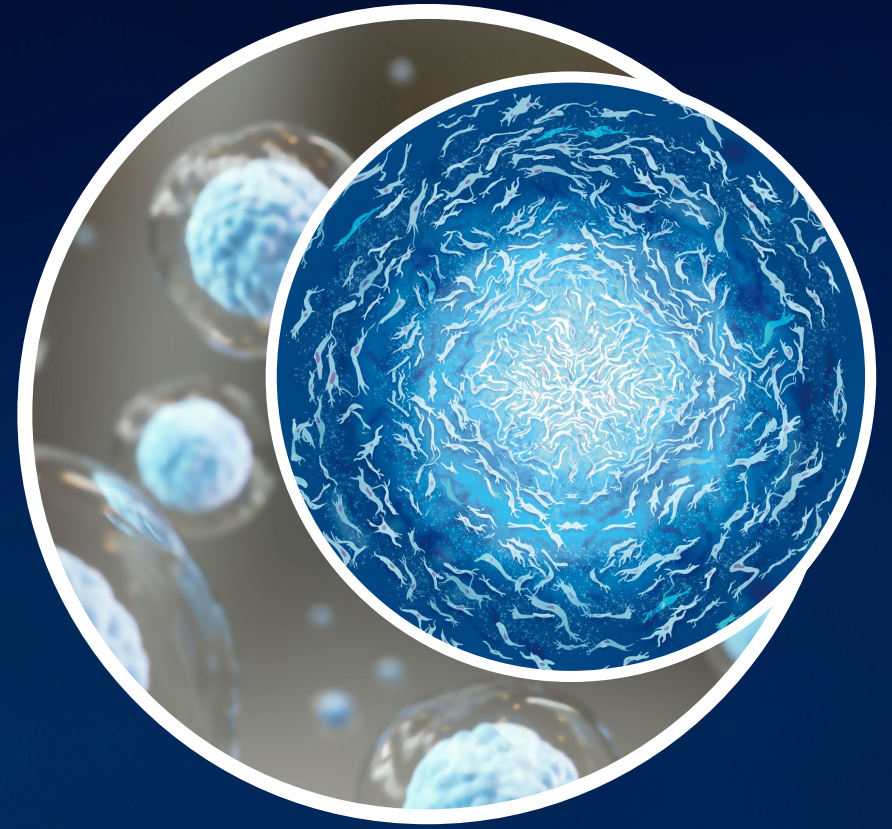
Nature Medicine 30, 1556–1558 (2024)

<https://doi.org/10.1038/s41591-024-02990-z>

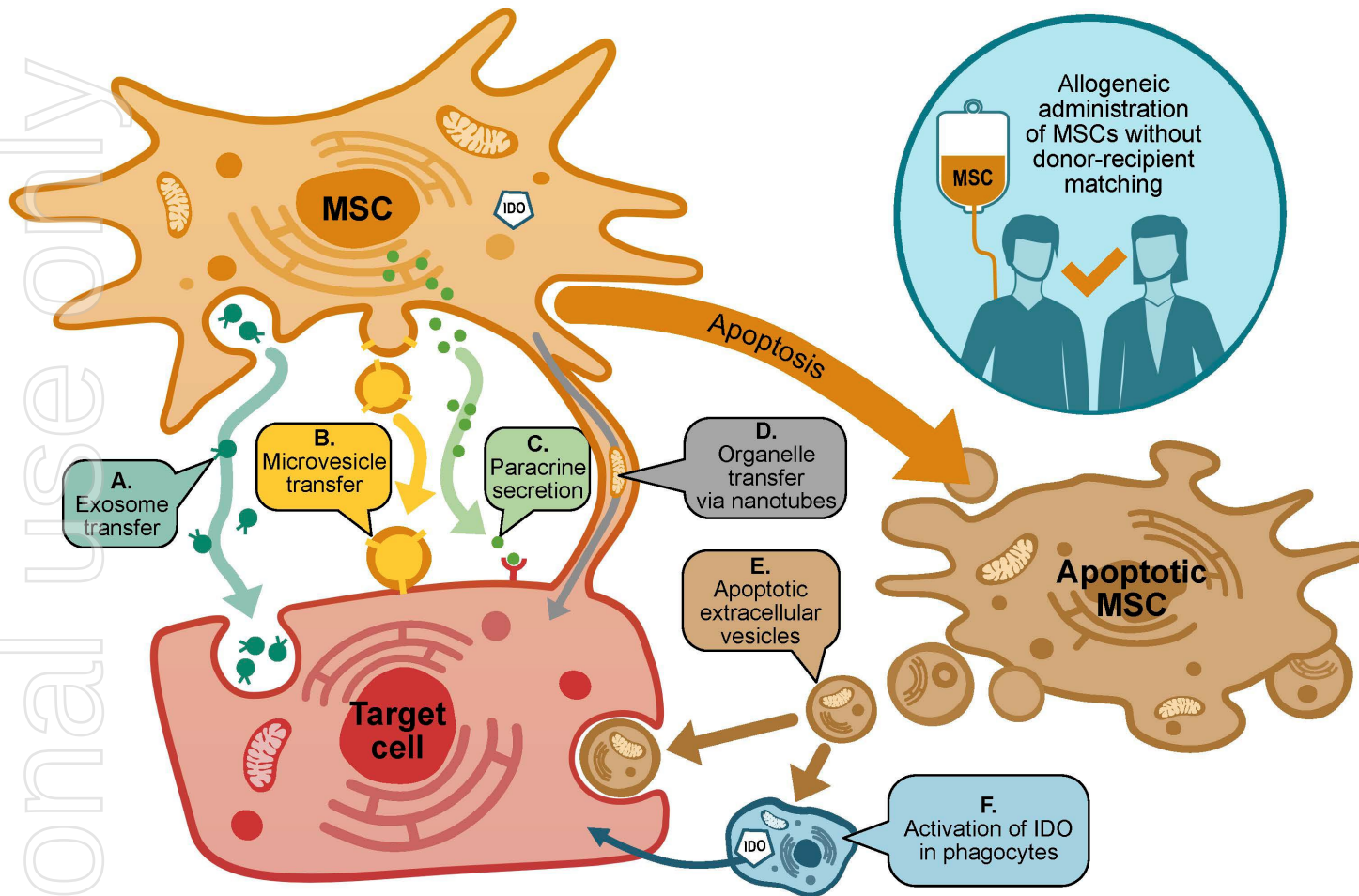
Two-year safety outcomes of iPS cell-derived mesenchymal stromal cells in acute steroid-resistant graft-versus-host disease

Kilian Kelly¹, Adrian J. C. Bloor², James E. Griffin³, Rohini Radia⁴, David T. Yeung^{5,6} & John E. J. Rasko^{7,8,9}

Revolutionary iPSC-based Cymerus™ Manufacturing Platform



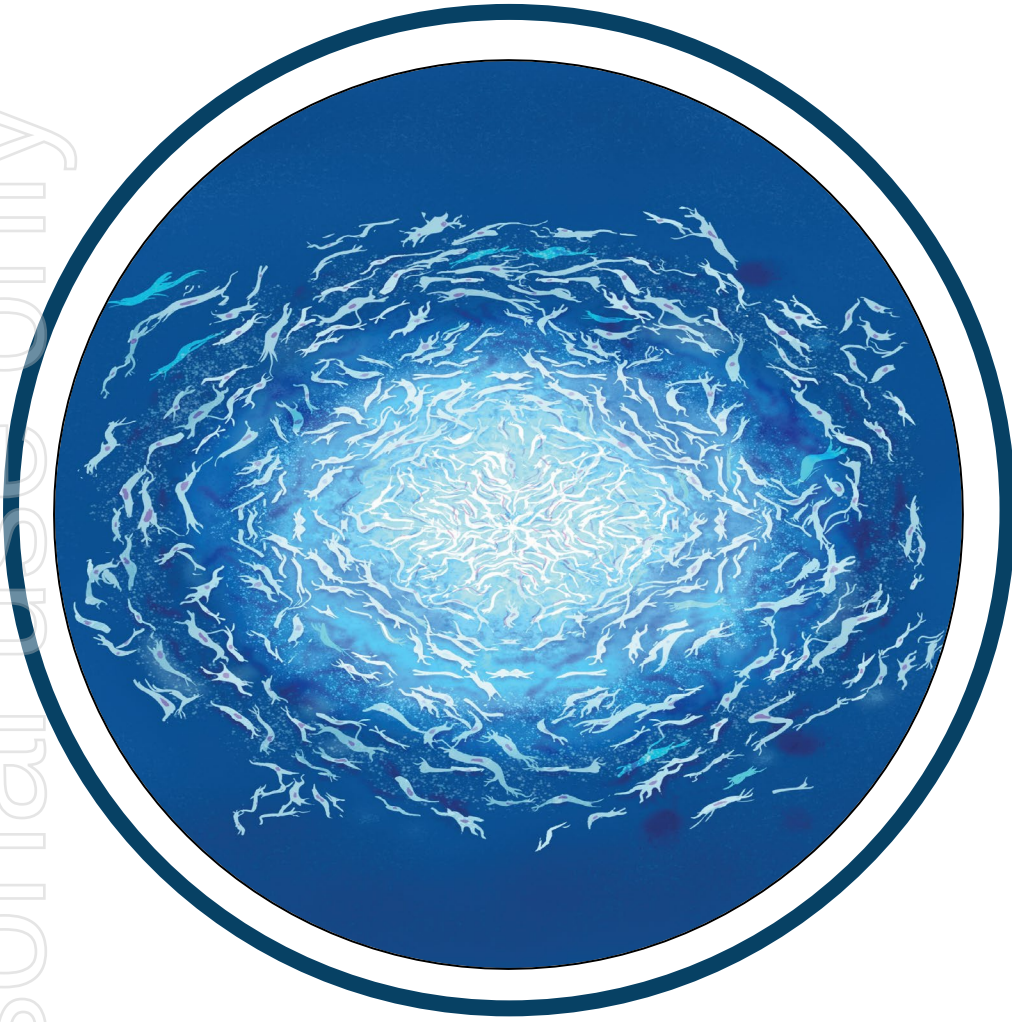
Therapeutic potential of MSCs



Mesenchymal stem cells¹ (MSCs):

- Promote an **immunomodulatory** environment²
- 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

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

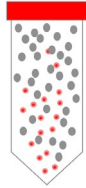
Conventional MSC process

Ongoing need
for new donors



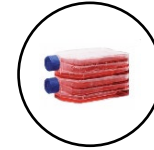
Substantial inter-donor **variability**

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**



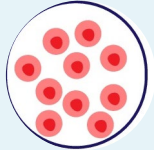
Avoids inter-donor
variability

Reprogramming &
iPSC expansion

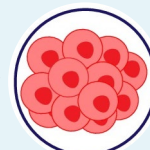


Effectively **limitless**
expansion potential

Differentiation into MSCs
& culture expansion



Minimal MSC
culture expansion

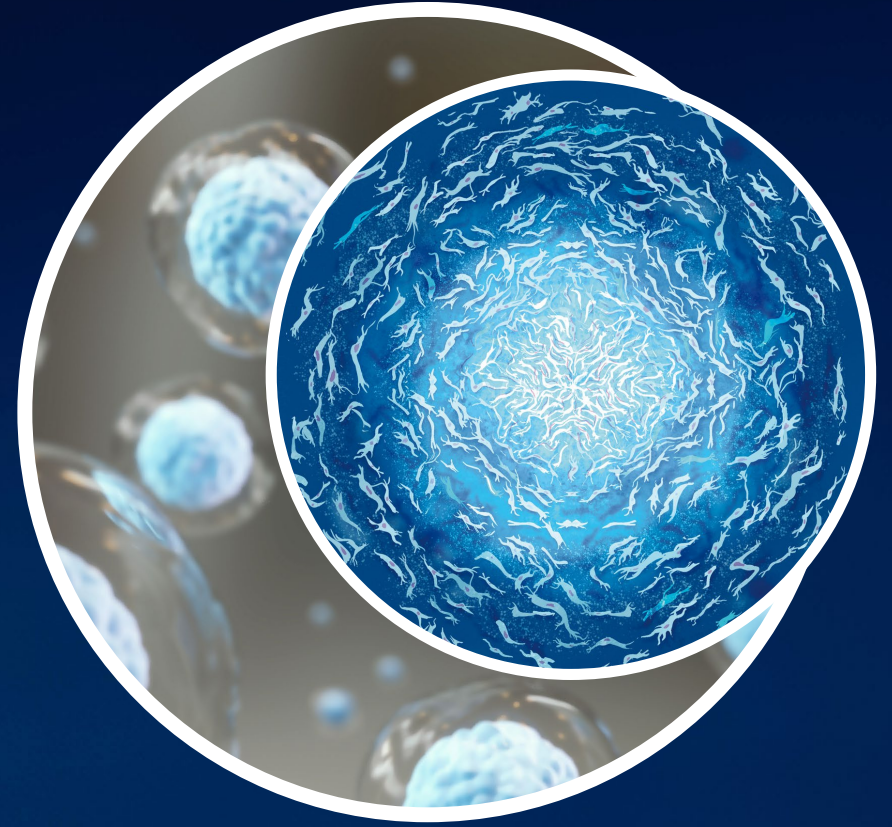


Robust patent protection

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**

Diabetic Foot Ulcer (DFU)



Diabetic foot ulcer (DFU)



Diabetic Foot Ulcer

- Diabetes is fastest growing chronic disease worldwide¹ – affects **>400m** adults globally; forecast to affect **>600m** by 2045²
- Up to **34%** of those with diabetes will develop DFU³: very difficult to heal; painful; impair mobility; can lead to serious infections and/or amputation³
- 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 in⁴:
 - **>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.

Unmet need

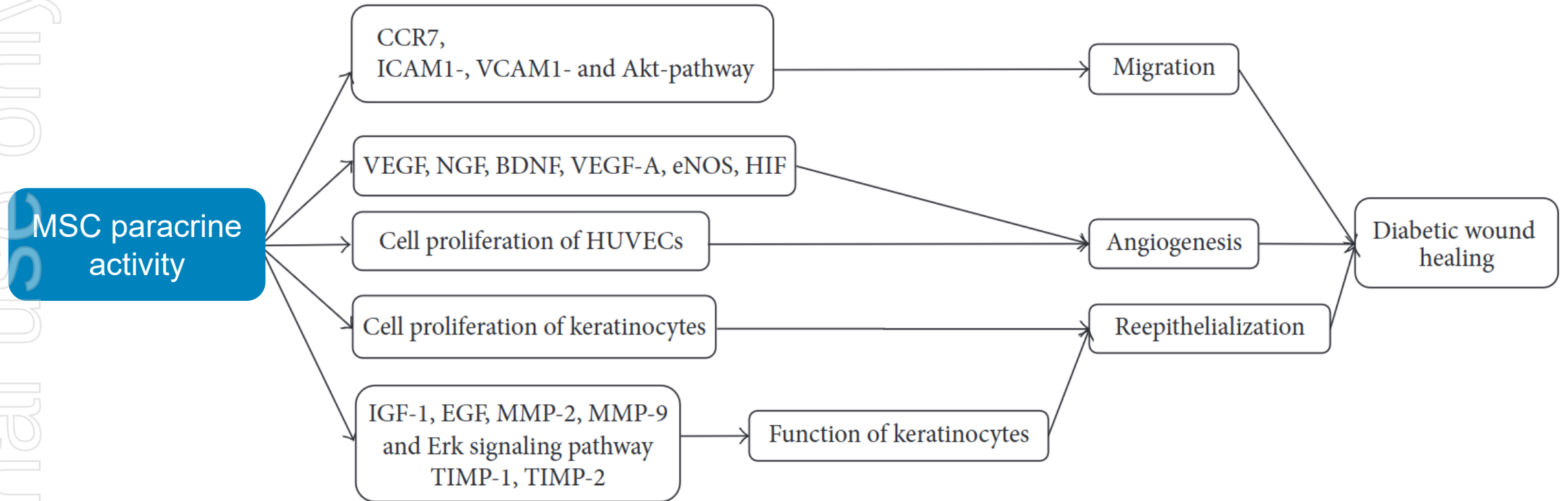
Existing treatment options often fail to heal diabetic ulcers in a timely manner, if at all



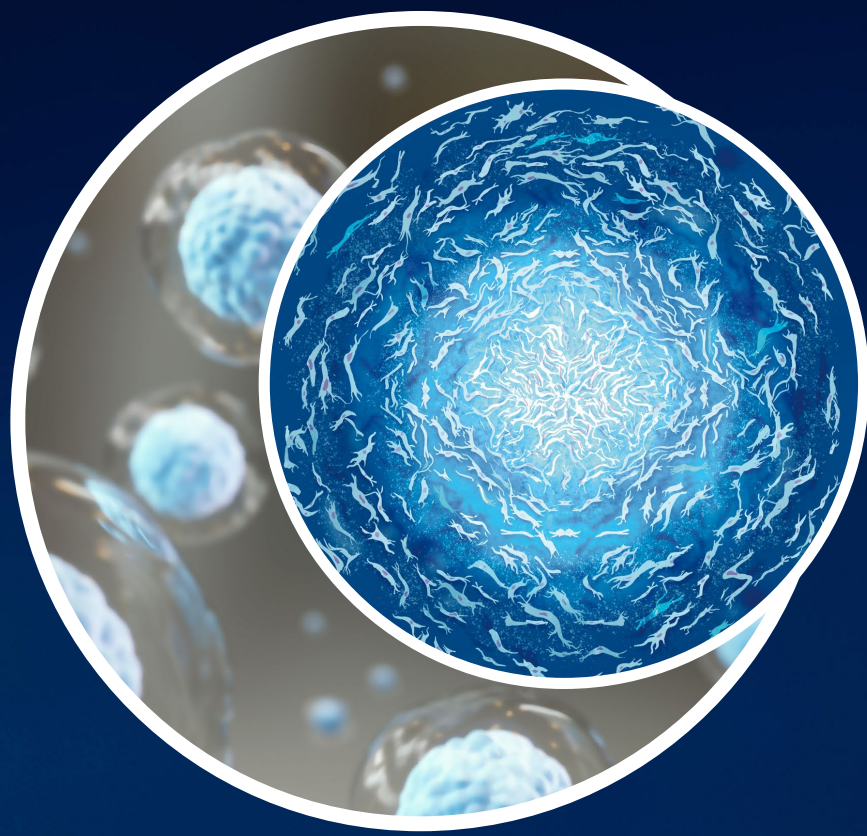
Current treatments

- 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

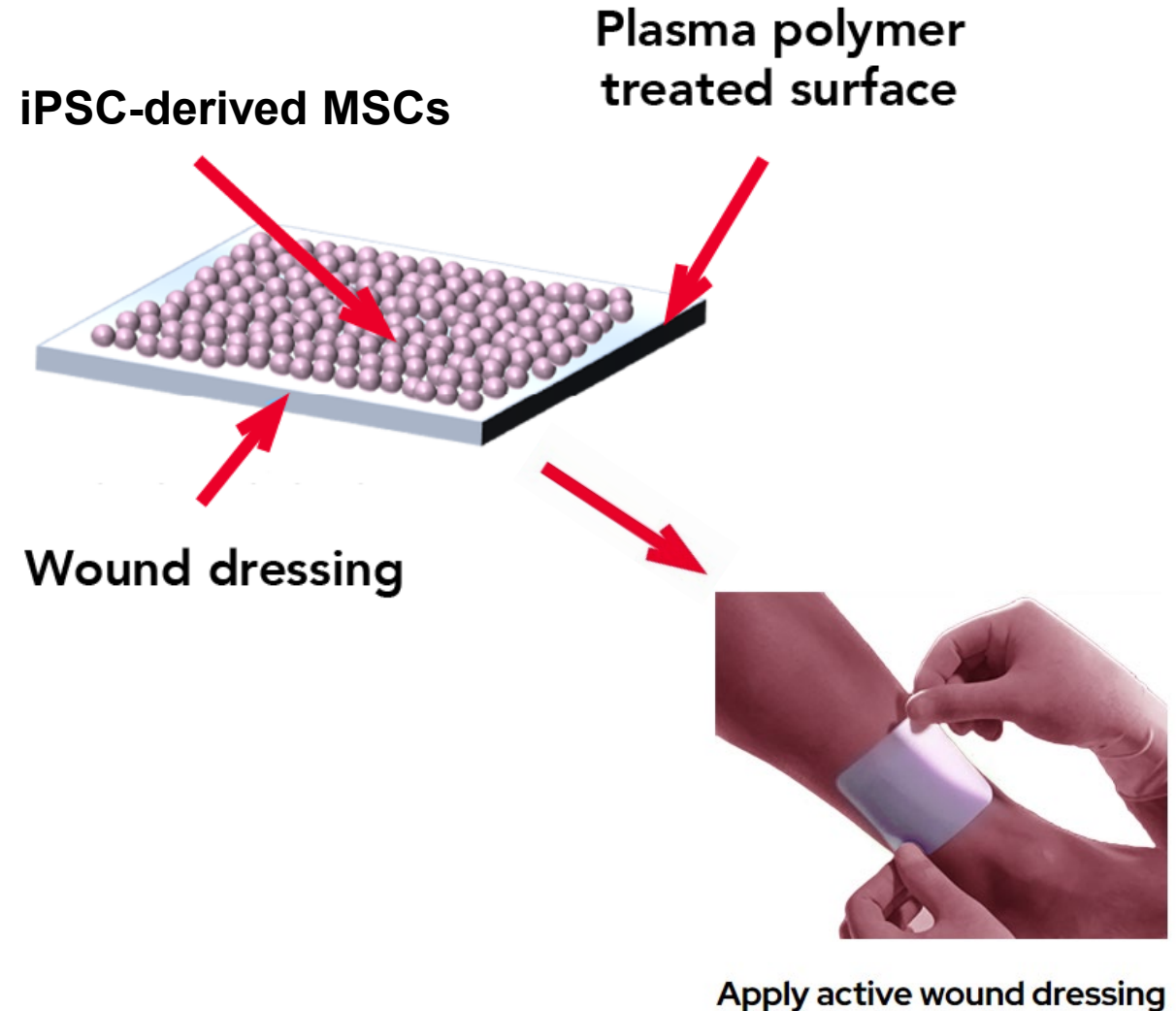


CYP-006TK



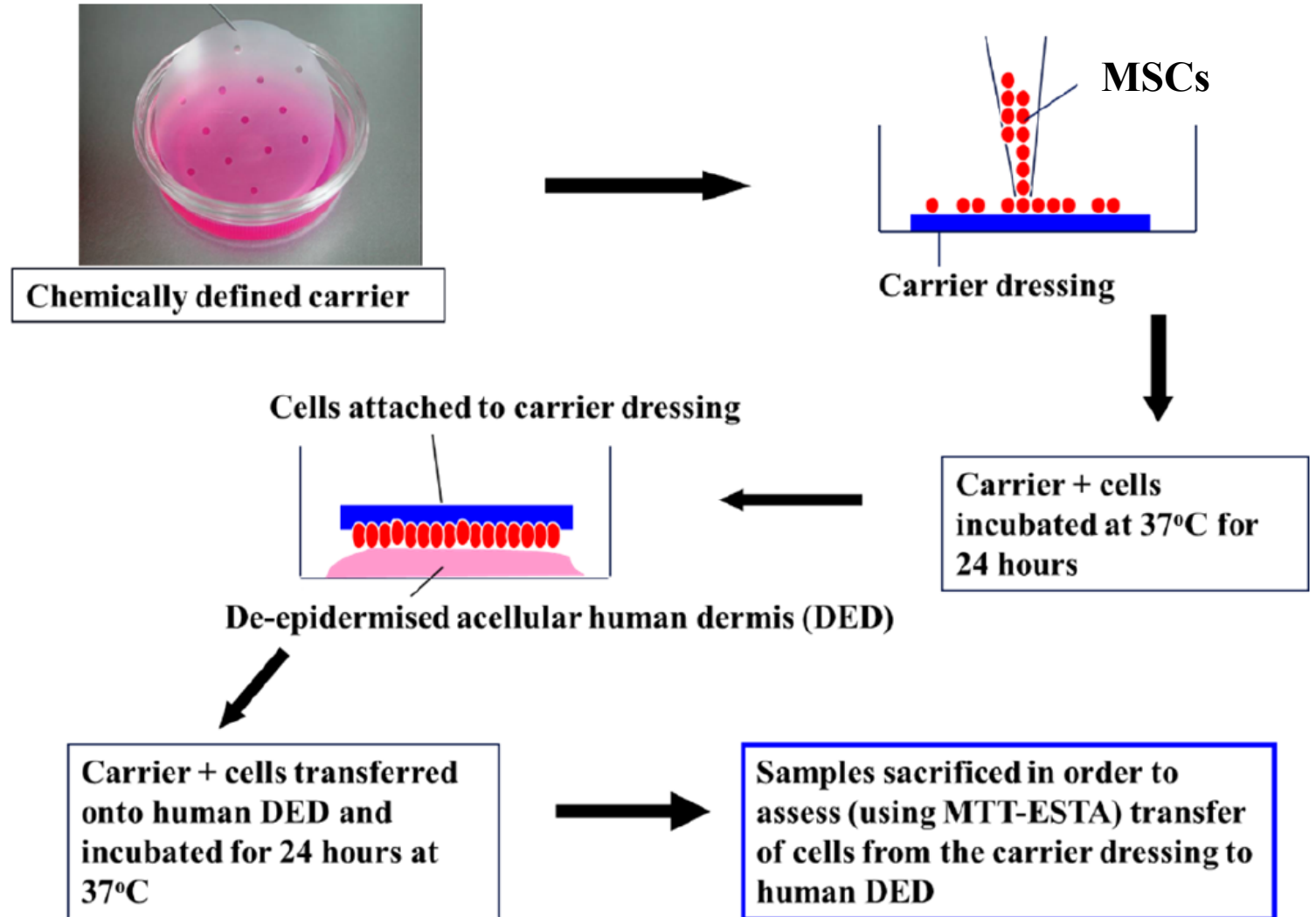
CYP-006TK – a novel topical MSC product

- 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)



Transfer of cells to wound

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



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



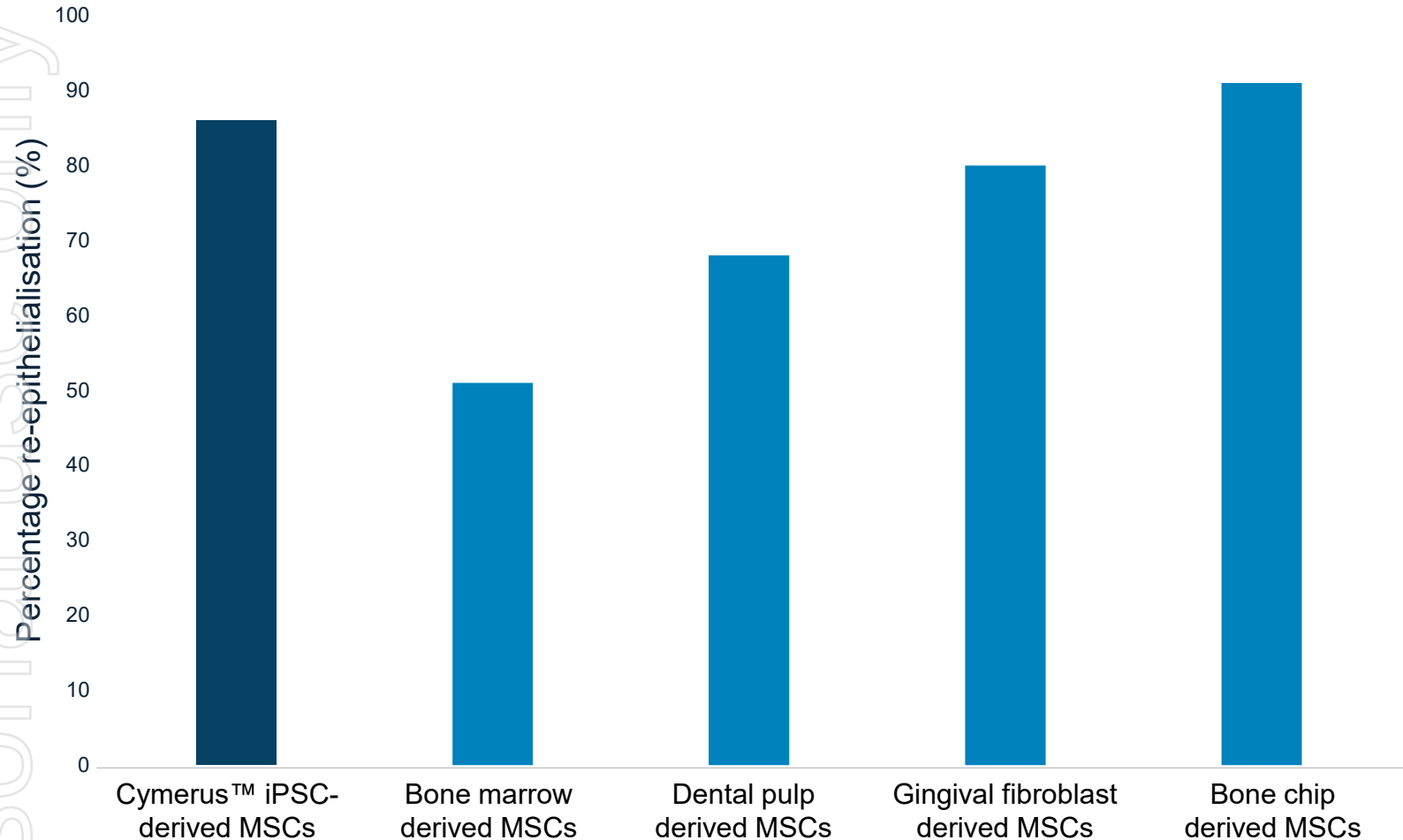
Silicone patch alone



Silicone patch plus
MSCs

MSC source influences performance

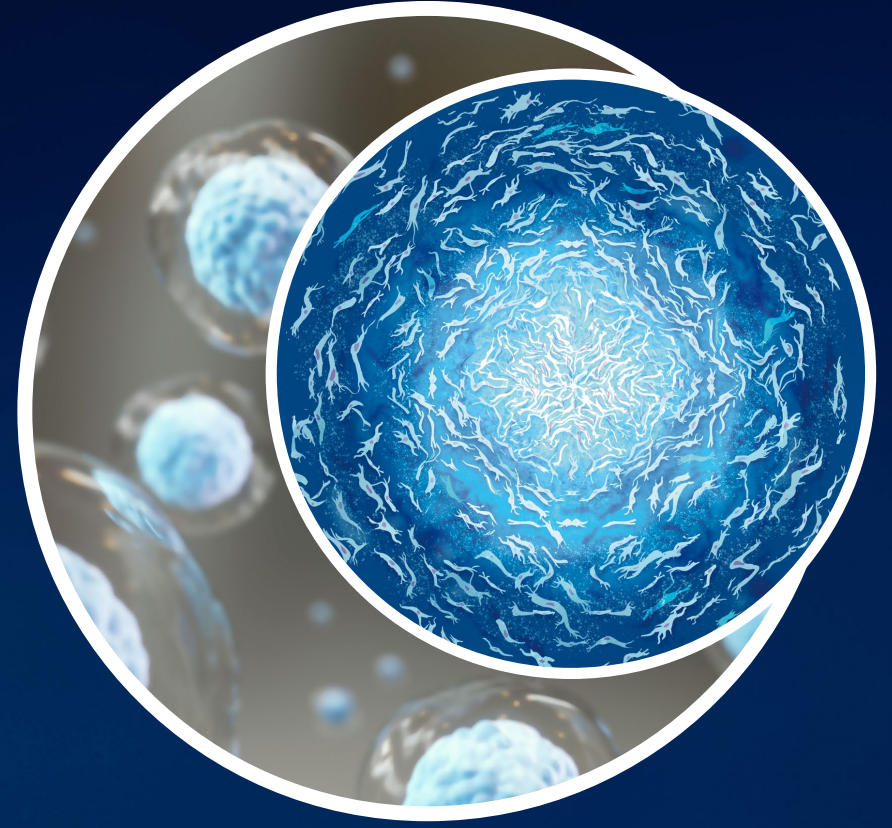
Silicone patch seeded with MSCs from various sources,
in preclinical model of diabetic wounds



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

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

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

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



Acknowledgements – DFU program

Manufacturing/Process Development/Preclinical Studies



Manufacturing/Process Development



Clinical Trial



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\$28bn¹
- Focus on indications with significant unmet need
- Proactive B-2-B outreach to drive partnering strategy



Contact Us

Cynata Therapeutics Limited

Level 3, 100 Cubitt Street
Cremorne
Victoria 3121
Australia



info@cynata.com



www.cynata.com



[cynatatherapeutics](https://www.facebook.com/cynatatherapeutics)



[@cynatastemcells](https://twitter.com/cynatastemcells)



[cynata-therapeutics](https://www.linkedin.com/company/cynata-therapeutics)