EVOLUTION CAPITAL

CYP | INITIATION REPORT | HEALTHCARE

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MSCs 2.0: Critical Bottlenecks Solved

Cynata Therapeutics Ltd

Evolution Capital initiates coverage on Cynata Therapeutics (ASX: CYP), a clinical-stage biotechnology company with differentiated, proprietary stem cell therapy manufacturing. While the regenerative medicine sector has long been hamstrung by the donor-dependency bottleneck – which results in inconsistent products and high-profile Phase 3 failures – Cynata has developed the world's first scalable, consistent, induced pluripotent stem cell (iPSC) platform, Cymerus™.

Solving the "Achilles' Heel" of MSCs

For decades, the promise of Mesenchymal Stem Cells (MSCs) has been undermined by a fatal flaw: reliance on multiple adult donors. This first-generation approach creates significant batch-to-batch variability and limited scalability, leading to regulatory setbacks (e.g., Mesoblast's initial BLA rejection) and commercial failures (e.g., Athersys). Cynata's Cymerus™ technology eliminates this variability entirely. By deriving all therapeutic cells from a single donor bank via iPSCs, Cynata produces an effectively infinite supply of uniform, pharmaceutical-grade MSCs. This is a fundamental de-risking event that transforms a biological craft into an industrial process.

Targeting Blockbuster Indications with Near-Term Catalysts

The platform is currently deployed across a diversified, late-stage pipeline targeting multi-billion-dollar unmet needs. The lead program, CYP-001, is in a pivotal Phase 2 trial for high-risk acute Graft-versus-Host Disease (aGvHD), an orphan condition with limited treatment options. Simultaneously, the company is advancing CYP-004 in a landmark Phase 3 trial for osteoarthritis (OA) – a holy grail indication with no approved disease-modifying therapies. With both major trials expected to read out in H1 2026, Cynata offers investors a catalyst-rich window with asymmetric upside potential. In addition, the Company is also undertaking a phase 1 clinical trial in Kidney Transplantation as well as strategic planning for further clinical development in Diabetic Foot Ulcers (DFU).

A Valuation Disconnect

The market currently prices Cynata as a generic, early-stage biotech, seemingly ignoring the strategic value of its manufacturing IP and the advanced stage of its assets. Our valuation is underpinned by a Sum-of-the-Parts (SOTP) DCF model, which ascribes value primarily to the high-probability aGvHD program (risked at a 30% PoS) and the massive commercial leverage of the OA asset (risked at a 45% PoS). Both assets are modelled only on US commercialisation, and therefore our fair valuation does not include revenues from other jurisdictions or from other pipeline assets. We view the recent validation of the MSC modality (via FDA approvals for paediatric aGvHD) as a rising tide that validates Cynata's mechanism of action while leaving the larger adult market wide open for its scalable solution. **Evolution initiates on CYP with a Speculative Buy Recommendation and a Price Target of $1.19.** Unlevered free cash flows are discounted using a 15% WACC.

Our analysis dives into the science of Cymerus™ and the three key debates that shape our assessment of Cynata's ability to deliver on its value proposition.

Recommendation	**SPEC BUY**
Price Target	**$1.19**
Share Price	**$0.335**
TSR	**255%**

Company Profile

Market Cap	~$79.5M
Enterprise Value	~$74.7M
SOI (diluted)	256M
Free Float	86.8%
ADV (3-month)	$109k
52-Week Range	$0.14 - $0.435

Price Performance

%	1M	3M	12M
Absolute	21.8%	17.5%	55.8%
ASX/S&P200	3.7%	-1.7%	6.5%

Company Overview

Cynata Therapeutics (ASX: CYP) is a clinical-stage Australian biotech developing Cymerus™, an iPSC-derived MSC platform designed to solve first-generation MSC constraints around donor variability, scalability, and CMC consistency. Its pipeline spans immunology, musculoskeletal, and wound care, led by CYP-001 in high-risk aGvHD (randomized Phase 2), CYP-004 in knee osteoarthritis (Phase 3), and CYP-006TK for diabetic foot ulcers (Phase 1 complete). The company follows a capital-efficient model with academic/strategic collaborators (e.g., University of Sydney, LUMC, Fujifilm).

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Contents

Investment Thesis

De-Risked Science Meets Near-Term Commercial Inflection

Evolution Capital views Cynata Therapeutics as a mispriced opportunity where the market has yet to fully appreciate the strategic divergence between biological efficacy and manufacturing feasibility. Historically, the MSC space (e.g., Athersys, Mesoblast) has faced challenges driven not necessarily by a lack of therapeutic potential, but by the inherent limitations of first-generation, donor-derived platforms in producing consistent, potent cells at scale. Cynata addresses this "CMC bottleneck" through its proprietary Cymerus™ iPSC platform, which ensures batch-to-batch uniformity that donor-dependent models struggle to match. We believe the technical risk is significantly reduced, underpinned by robust Phase 1 data in aGvHD (87% survival) and recent regulatory validation of the MSC modality via competitor approvals. Consequently, we view the upcoming Phase 3 osteoarthritis and Phase 2 aGvHD readouts as pivotal validation milestones for the platform. Positive data from these trials would likely catalyse a re-rating of the stock, narrowing the valuation gap between Cynata and its first-generation peers.

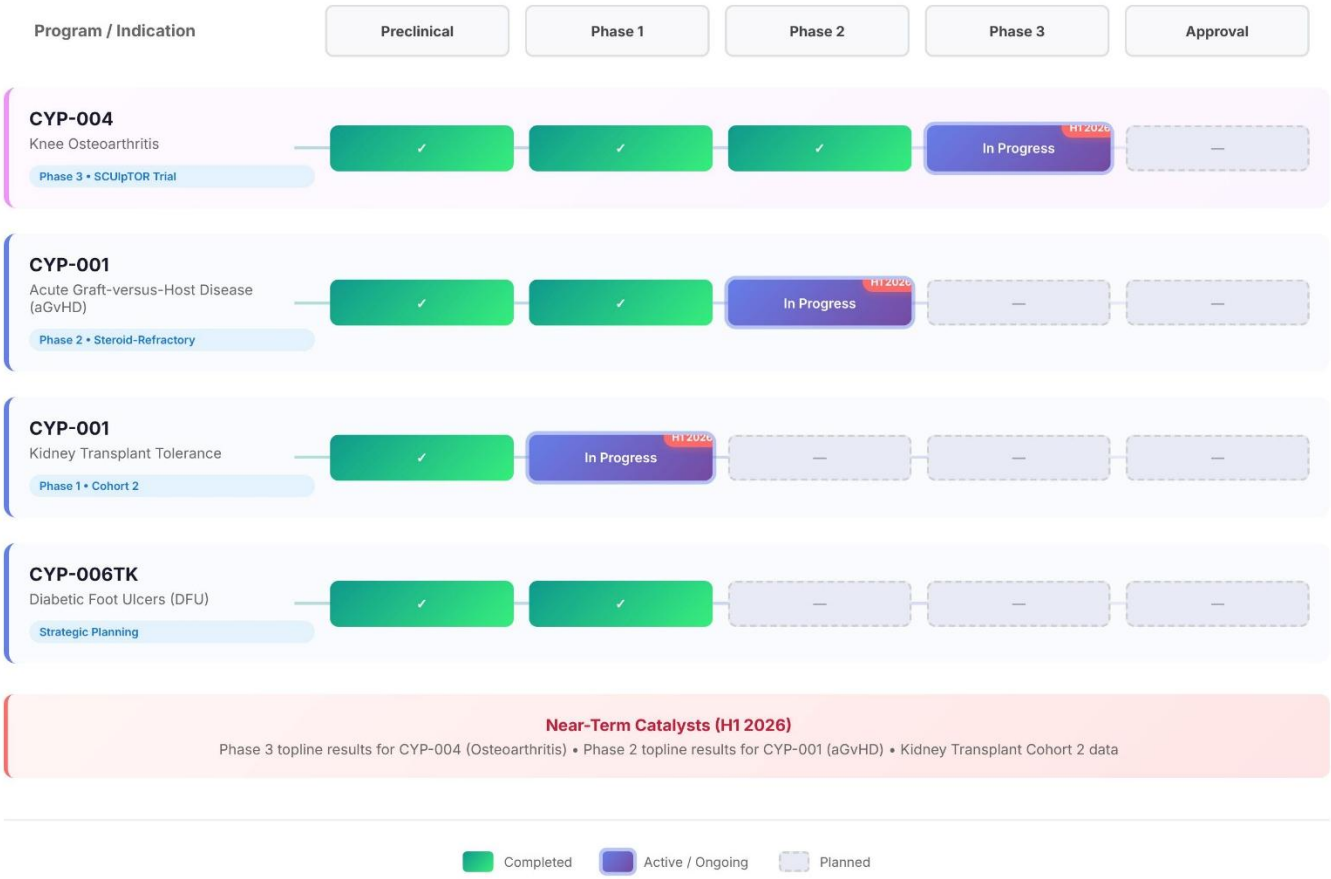
Asymmetric Upside: Pipeline Optionality for Free

Our valuation is anchored primarily in the risk-adjusted success of the aGvHD program and the commercial potential of the osteoarthritis asset. At current levels, the share price effectively ascribes negligible value to the remainder of the pipeline. We view the Diabetic Foot Ulcer (DFU) program – which demonstrated an 84% reduction in wound surface area in Phase 1 – and the kidney transplant tolerance program as significant "embedded options" for investors. Success in these indications, or the execution of a strategic partnership to advance them, represents upside to our base case. This structure creates an asymmetric risk-reward profile, where the downside is buffered by the intrinsic value of the manufacturing IP, while the upside provides exposure to multiple independent, high-value clinical opportunities.

Catalysts

Estimated Timing	Program	Event / Catalyst	Impact / Significance
Q2 CY26	CYP-004	Phase 3 Topline Results (OA)	Definitive efficacy readout for the world's first iPSC-derived cell therapy in osteoarthritis. Positive data on both pain and structural endpoints would likely trigger a repricing of the stock given the blockbuster TAM.
Q2 CY26	CYP-001	Phase 2 Topline Results (aGvHD)	Primary efficacy (ORR at Day 28) and safety data from the ~60-patient randomised trial. Validation here confirms the platform's utility in high-value immunology indications and supports a BLA filing strategy.
H1 CY26	CYP-001	Kidney Transplant Cohort 2 Data	Following positive DSMB review of Cohort 1 (Dec 2025), safety data from the second cohort will further validate the immune tolerance protocol, potentially opening a massive new chronic disease vertical.
H2 CY26	Corporate	FDA Regulatory Engagement	Anticipated End-of-Phase 2 meeting with the FDA to define the registrational path for CYP-001 in aGvHD, potentially clarifying the timeline to commercial launch.
Ongoing	CYP-006TK	Strategic Partnership / Licensing	Execution of a licensing deal for the diabetic foot ulcer (DFU) asset would provide non-dilutive capital and external validation of the wound care program, reducing burn rate.

Pipeline


Program / Indication
Preclinical
Phase 1
Phase 2
Phase 3
Approval
CYP-004
Knee Osteoarthritis
Phase 3 • SCUlpTOR Trial
In Progress
CYP-001
Acute Graft-versus-Host Disease (aGvHD)
Phase 2 • Steroid-Refractory
In Progress
CYP-001
Kidney Transplant Tolerance
Phase 1 • Cohort 2
In Progress
CYP-006TK
Diabetic Foot Ulcers (DFU)
Strategic Planning
Near-Term Catalysts (H1 2026)
Phase 3 topline results for CYP-004 (Osteoarthritis) • Phase 2 topline results for CYP-001 (aGvHD) • Kidney Transplant Cohort 2 data
Completed
Active / Ongoing
Planned

Financial Summary

VALUATION DETAILS	
Share Price (A$)	$0.335
Market Cap (A$m)	79.5
Enterprise Value (A$m)	74.7
Fair Value/Share (A$)	$1.19

STATEMENTS (A$m)	FY25	FY26E	FY27E	FY28E	FY29E
Income Statement					
Revenue	2.11	0.00	13.50	33.75	4.29
EBITDA	-9.11	-11.75	1.65	21.90	-9.78
EBIT	-9.39	-12.03	1.37	21.62	-10.06
Net Income	-9.39	-12.03	0.96	15.13	-10.06
Balance Sheet					
Cash & Cash Equivalents	5.05	2.06	15.09	26.62	21.65
Inventory	0.00	0.00	0.00	0.00	0.28
Receivables	0.10	0.00	2.22	5.55	0.71
Other Assets	2.04	1.82	1.89	2.41	2.27
Total Assets	7.20	3.88	19.19	34.58	24.92
Total Debt	0.00	0.00	0.00	0.00	0.00
Other Liabilities	1.22	0.28	0.29	0.29	0.44
Total Liabilities	1.22	0.28	0.29	0.29	0.44
Shareholders' Equity	5.98	3.60	18.91	34.29	24.48
Cash Flow Statement					
Net Income	-9.39	-12.03	0.96	15.13	-10.06
Add: D&A	0.28	0.28	0.28	0.28	0.28
Less: Change in NWC	0.13	-0.84	-2.21	-3.32	4.71
Cash Flow from Operations	-8.72	-12.34	-0.73	12.34	-4.82
Cash Flow from Investing	-0.05	-0.05	-0.35	-0.80	-0.15
Equity Raised (net)	7.61	9.40	14.10	0.00	0.00
Less: Dividends Paid	0.00	0.00	0.00	0.00	0.00
Cash Flow from Financing	7.61	9.40	14.10	0.00	0.00
Unlevered Free Cash Flow	-8.77	-12.39	-1.08	11.54	-4.97

PER SHARE DATA	FY25	FY26E	FY27E	FY28E	FY29E
Shares Out (dil., m)	226.0	257.7	305.3	305.3	305.3
Normalised EPS (A$)	-0.04	-0.05	0.00	0.05	-0.03
Dividends (A$/share)	0.00	0.00	0.00	0.00	0.00
Payout	0%	0%	0%	0%	0%
Franking	0%	0%	0%	0%	0%

RATIOS	FY25	FY26E	FY27E	FY28E	FY29E
Liquidity					
Current Ratio	4.4	8.0	61.2	110.9	52.0
Quick Ratio	4.2	7.3	60.5	110.2	50.9
Solvency					
Debt to Equity	0.00	0.00	0.00	0.00	0.00
Equity to Assets	0.83	0.93	0.99	0.98	0.98
Profitability					
ROA	-120.5%	-217.1%	8.3%	56.3%	-33.8%
ROE	-142.3%	-251.1%	8.5%	56.9%	-34.2%
EBITDA Margin	-431.1%	0.0%	12.2%	64.9%	-227.9%
NPAT Margin	-444.5%	0.0%	7.1%	44.8%	-234.5%
Growth					
Revenue	0.0%	0.0%	0.0%	150.0%	-87.3%
EBITDA	-3.8%	29.0%	114.0%	1231%	-144.7%
Underlying NPAT	-3.6%	28.1%	107.9%	1483%	-166.5%
EPS	0.0%	0.0%	0.0%	1408%	-163.3%
Valuation					
P/E	N/A	-22.3	317.1	23.5	-35.3
EV/Revenue	N/A	N/A	22.1	8.8	69.6
EV/EBITDA	N/A	N/A	181.6	13.6	N/A
Dividend Yield	0.0%	0.0%	0.0%	0.0%	0.0%

The Science Behind Cynata's MSC Platform

MSCs 101

Mesenchymal stem cells (Mesenchymal stromal cells (MSCs)) are adult stem cells first discovered in bone marrow and now known to reside in many tissues (fat, umbilical cord, etc.). They can mature into tissue like bone, cartilage and fat, but their real therapeutic promise lies in their ability to modulate the immune system and aid tissue repair. Unlike drugs that target a single molecule, MSCs act more broadly: they home to sites of inflammation or injury and secrete a cocktail of bioactive factors (cytokines, growth factors) that dampen harmful inflammation and stimulate healing. Because of these versatile properties, MSCs have been explored as treatments for a staggering range of conditions – from autoimmune disorders and graft-vs-host disease to heart failure and orthopaedic injuries. Over 1,000 clinical trials worldwide have tested MSC-based therapies in the past few decades. This makes MSCs one of the most widely studied cell therapy approaches, with a generally good safety profile established across thousands of patients.

Despite this promise and investment, MSC therapies have faced inconsistent results. Some trials showed encouraging outcomes (e.g. in severe inflammation), but many others fell short of expectations. A key reason is not that MSCs can't work, it's that early approaches to manufacturing and delivering these living cells had fundamental shortcomings. The science behind MSCs is sound; the challenge has been getting a consistent, potent dose of cells to patients at scale.

Limitations of First-Gen MSC Therapies

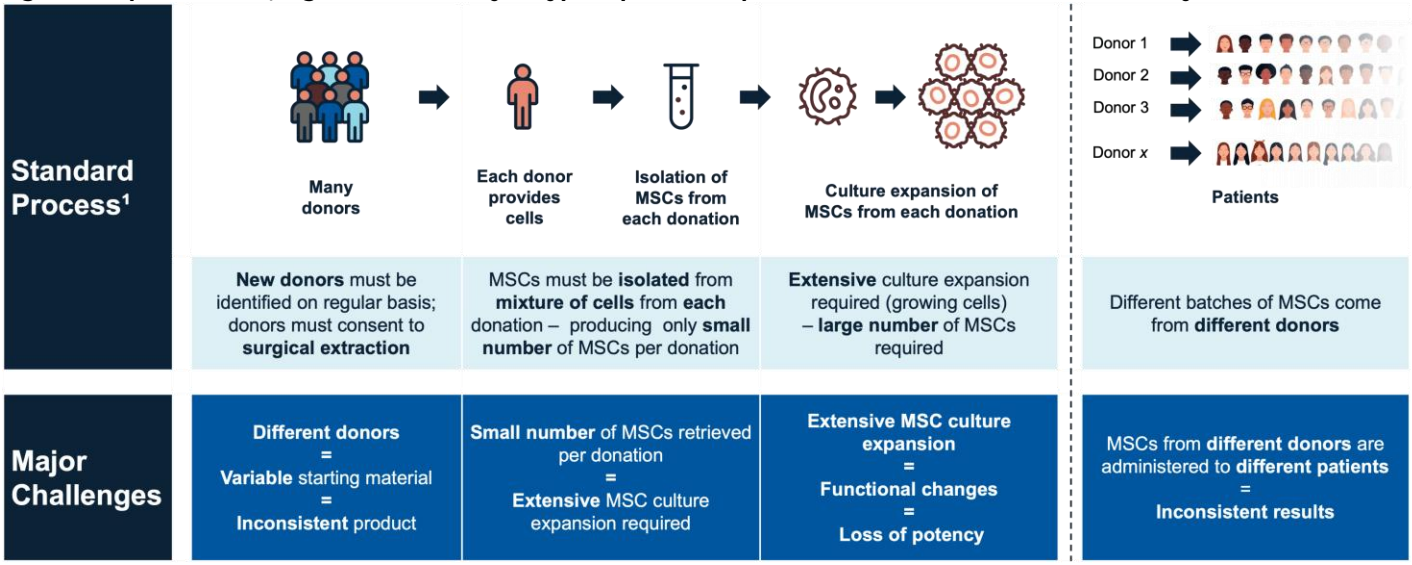
Traditional MSC therapies rely on harvesting cells from adult donors – for example, isolating MSCs from bone marrow or adipose tissue. While biologically feasible, this first-generation approach has critical limitations that became the "Achilles' heel" of MSC therapeutics:

- **Donor Variability and Inconsistency:** MSCs from different donors can behave very differently. Donors vary by age, genetics, and health status, meaning one donor's cells might be robust and effective while another's are less potent. This leads to an inconsistent final product and unpredictable clinical results. For regulators, such batch-to-batch variability is a major concern. Each manufactured batch could be a different therapy altogether.

- **Limited Scalability (Many Donors Needed):** A single donor provides tens of thousands of cells. Yet a single therapeutic dose might require hundreds of millions of cells. Closing that gap means repeat donor sourcing on a massive scale. Companies had to continuously recruit, screen, and collect tissue from numerous donors to have enough starting material. This is logistically complex, expensive, and ultimately unsustainable as a manufacturing model. It also exacerbates variability – every new donor is a new variable.

- **Potency Loss with Cell Expansion (Senescence):** To reach therapeutic cell numbers, MSCs must be grown through many lab culture cycles, often 25-40 population doublings. However, with each round of cell division the MSCs age and lose functionality. This process of cellular aging (senescence) means the final batch of cells may be a mix of aged, less effective cells. Over-expansion can reduce the cells' anti-inflammatory and regenerative capabilities – the very qualities they're supposed to deliver. Essentially, the more you grow them, the weaker they get. This attrition of potency likely contributed to the patchy outcomes observed in past MSC trials. The end-product often contained a heterogeneous mix of cells at varying stages of aging, making the therapy less reliable.

Figure 1: Representative, high-level summary of typical process to produce donor-derived MSCs. Source: Cynata website.



These manufacturing and quality-related challenges have hampered clinical development of MSC therapies. For example, Athersys – a once-prominent MSC company using adult bone marrow–derived cells – struggled with these issues. Their Phase 3 trial in stroke failed to meet its endpoint, and the company ultimately filed for bankruptcy in 2024. While many factors affect trial outcomes, the limitations of the first-gen manufacturing paradigm (multiple donors, extensive cell expansion) added significant risk and complexity.

Cymerus™: An iPSC-Based Solution

Cynata's answer to these challenges is its proprietary Cymerus™ platform, which effectively re-engineers the MSC production process from the ground up. The key innovation is starting with a renewable stem cell source – induced pluripotent stem cells (iPSCs).

iPSCs are created by taking an ordinary adult cell (like a blood or skin cell) and "reprogramming" it back into a stem cell state. In that state, it behaves a bit like an embryonic stem cell: it can self-renew indefinitely (unlimited growth) and can be directed to become virtually any cell type. In practical terms, an iPSC line is an infinite starting material: it can yield limitless batches of the target therapeutic cells.

The Cymerus process in three key steps:

1. **One Donor, One Time:** The company started with a single donation of cells from one healthy adult. That donor is used only once and there's no need for continuous donor recruitment.

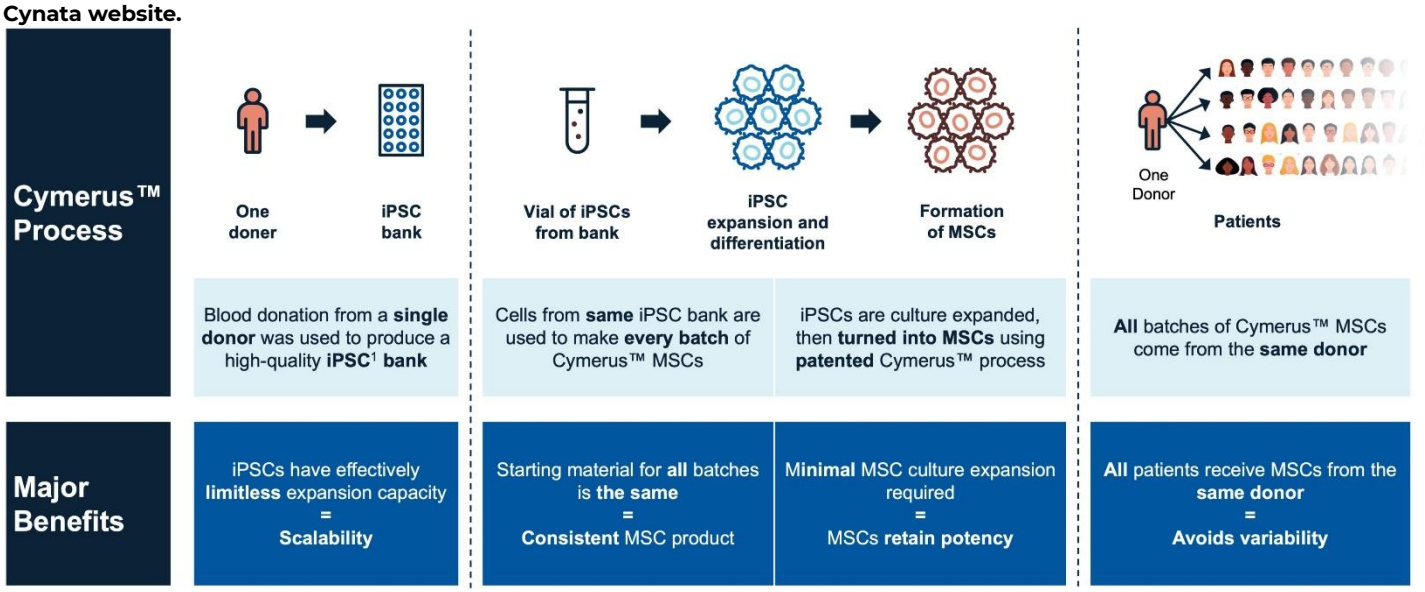
2. **Create a Master iPSC Bank:** Those donor cells are converted into iPSCs in the lab, and an iPSC master cell bank is established. This bank might contain millions of iPSC vials, all genetically identical and stored for long-term use. Importantly, this step is done once and never repeated. From here on, Cynata has a permanent, renewable source of starting material. All cells for therapy will originate from this uniform iPSC supply, eliminating donor-to-donor variability entirely – it's the same donor's genetics for every batch, and those cells are kept young and stable in the iPSC state.

3. **Differentiate iPSCs into MSCs (as needed):** Using its proprietary Cymerus differentiation method, Cynata directs the iPSCs to become mesenchymal stem/stromal cells in culture. Every batch will be consistent because it comes from the same starting cell line and a controlled process.

Crucially, the Cymerus approach breaks the old trade-off between scale and quality. Since the iPSC can propagate indefinitely, scale is achieved by expansion at the iPSC stage (when the cells are in a youthful, pluripotent state) rather than over-expanding the final MSCs. By the time MSCs are produced, they are needed only for that batch and are not forced through excessive divisions. This means the final MSC product is homogeneous, potent, and not senescent. All MSCs in a batch are essentially clones of one another, and the variability is dramatically reduced.

The other key benefit is ongoing donor sourcing is not required. By removing the need to constantly find new donors, Cymerus simplifies the supply chain and cuts cost. It also greatly reduces regulatory complexity. The entire process is more controllable, traceable, and reproducible.

Figure 2: Representative summary of how iPSCs are produced and turned into MSCs using the CymerusTM process. Source: Cynata website.



MOA: How Cynata's MSCs Work Across Diseases

MSCs function as signalling centres. They sense their environment and secrete therapeutic factors rather than permanently engrafting or replacing tissue. Cynata's MSCs work via this same fundamental mechanism of action, modulating biological processes in a dynamic way:

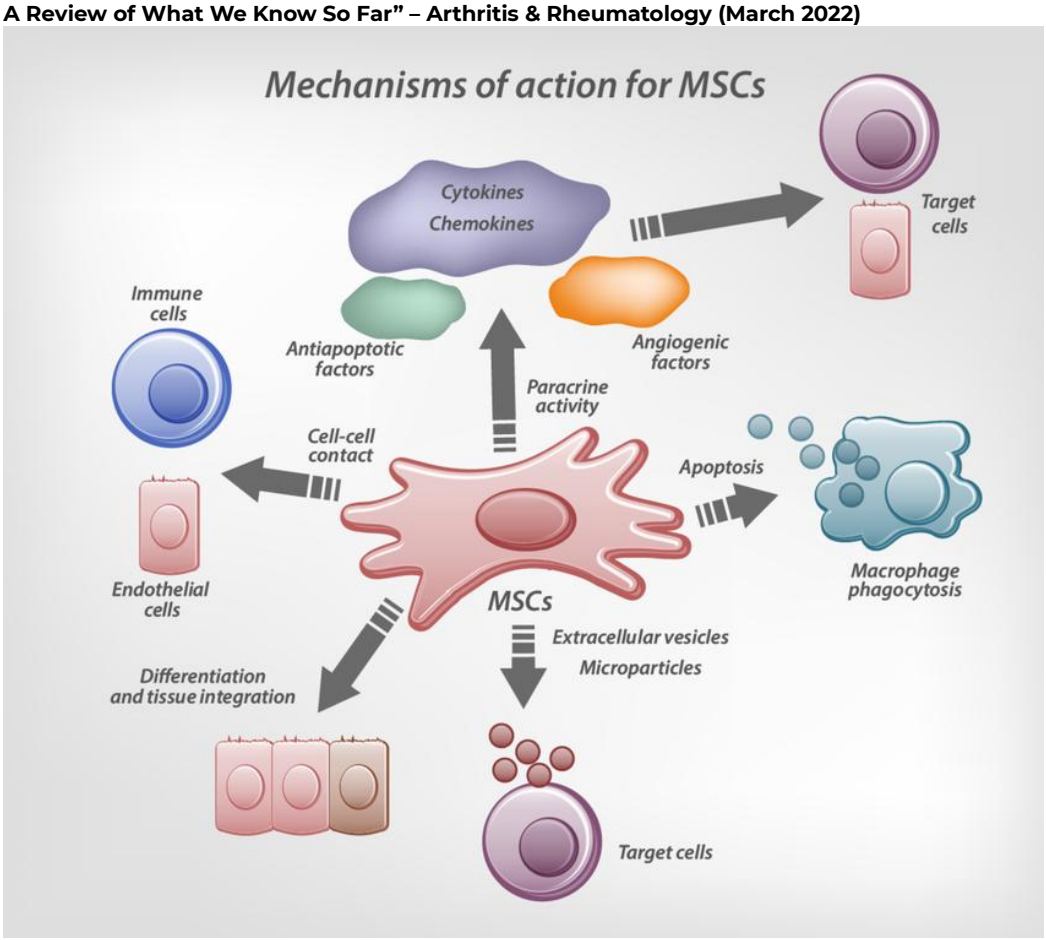
- **Immunomodulation:** In inflammatory conditions, MSCs can dial down an overactive immune response. They release anti-inflammatory cytokines and other signals that suppress hyperactive immune cells (like T-cells and macrophages). At the same time, they can promote a more regulatory, tolerant immune state (for instance, inducing regulatory T-cells). This is why MSCs have been used in diseases like graft-versus-host disease (GvHD), where the immune system is attacking the patient's own tissues. In acute GvHD, Cynata's CYP-001 product aims to tone down the donor immune attack on the patient's organs, potentially improving survival and reducing reliance on high-dose steroids. Similarly, in organ transplantation (e.g. Cynata's kidney transplant study), MSCs might help induce immune tolerance to the new organ, lowering the risk of rejection.

- **Tissue Repair and Regeneration:** MSCs also facilitate healing of damaged tissue. They secrete growth factors that promote the regeneration of blood vessels (angiogenesis) and support the survival and growth of local cells. In osteoarthritis (degenerative joint disease), MSC-derived factors may protect cartilage and reduce inflammation in the joint, potentially preserving tissue and alleviating pain. Cynata's CYP-004 (MSC product for knee osteoarthritis) is thought not to regrow new cartilage outright, but to create a more pro-healing environment in the joint – slowing cartilage breakdown and encouraging the body's own repair

mechanisms. Likewise, in difficult-to-heal wounds like diabetic foot ulcers (DFU), MSCs release pro-healing and pro-angiogenic factors (i.e. those that stimulate the formation of new blood vessels from existing vascular networks) that help tissue regenerate and close those chronic wounds. In Cynata's Phase 1 DFU trial, for example, the hope is that applying MSCs can kick-start proper healing in wounds that otherwise resist standard treatments.

- **Paracrine Signalling "Without Becoming New Tissue":** It's important to clarify that MSC therapy is not about the cells permanently engrafting or transforming into new organ tissue inside the patient. Studies show that MSCs typically survive only transiently in the body. Their impact comes from the paracrine signals (the bioactive molecules they release) that orchestrate other cells to repair damage. For instance, MSCs can facilitate the patient's own progenitor cells to proliferate or produce more matrix, thereby aiding repair indirectly. This paracrine MOA is broad, which is why the same MSC product can be tested in diverse diseases – the cells naturally adjust to the needs of the environment. Cynata's trials span immunological, cardiovascular and tissue repair indications, all leveraging this common mechanism of action in different contexts.

Figure 3: Schematic illustration of mechanisms of action of MSCs. Source: "Safety and Efficacy of Mesenchymal Stromal Cells and Other Cellular Therapeutics in Rheumatic Diseases in 2022: A Review of What We Know So Far" – Arthritis & Rheumatology (March 2022)



The Importance of Manufacturing Scalability

In biotech, a lot of attention goes to what a therapy does, but how it's made can be just as critical, especially for cell-based therapies. The term CMC (Chemistry, Manufacturing, and Controls) refers to the entire manufacturing and quality process for a therapy. Manufacturing living cells reliably is a far bigger challenge than mixing chemicals in a vat.

Cynata's Cymerus process is poised to solve the MSC manufacturing bottleneck, being the sole company to produce clinical-grade MSCs from iPSCs at scale. This translates into several advantages:

- **Larger Market Opportunities:** A scalable platform means Cynata's products, if efficacious, could be supplied to large patient populations (e.g. millions of osteoarthritis patients) without running into supply constraints. It makes therapies viable for mainstream indications, not just rare diseases.

- **Partnering and Licensing Potential:** Because the platform is product-agnostic (in theory, the same iPSC-derived MSC supply could be used for various diseases), Cynata could license or JV the technology for additional indications. Big pharma partners are often more willing to collaborate when manufacturing risk is low, and Cynata's IP in MSC production provides a strong negotiating asset.

- **Regulatory and Competitive Edge:** A well-controlled manufacturing process de-risks the regulatory review. With consistency built in, CMC questions from the FDA or EMA become easier to answer.

Debate #1 Do Cymerus MSCs Work Where Others Have Failed?

The skeptic's question is: do MSCs actually work? Indeed, first-generation MSC therapies have seen mixed results, hampered by donor-to-donor variability and manufacturing issues that led to inconsistent outcomes. This history has bred understandable skepticism toward any new MSC platform.

For Cynata, this debate is company-defining. The upcoming Phase 2 trial in acute graft-versus-host disease (aGvHD) and the Phase 3 SCUIpTOR trial in knee osteoarthritis (OA) are pivotal events. Success in these studies would validate Cynata's Cymerus™ platform and unlock large markets.

Past Failures of MSC Therapy Programs

Despite early promise, many first-generation mesenchymal stem/stromal cell (MSC) therapies failed to meet efficacy endpoints in late-stage trials. For example, Osiris Therapeutics' Prochymal (donor-derived MSCs) did not outperform placebo in two Phase 3 trials for graft-versus-host disease (GvHD) – in steroid-refractory GvHD, 45% of patients responded on Prochymal *vs.* 46% on placebo, and in first-line GvHD 35% improved on Prochymal *vs.* 30% on placebo. No overall survival benefit was seen, although post hoc analyses hinted at benefits in subgroups (e.g. GvHD affecting the liver/gut). Likewise, plans for a Crohn's disease trial of Prochymal were scaled back after disappointing early results. Another notable example is Athersys' MultiStem product: in a Japanese Phase 2/3 stroke trial (TREASURE), an IV allogeneic cell therapy given 18–36 hours post-stroke showed no significant difference in outcomes at 90 days compared to placebo (excellent recovery in ~11.5% of treated patients vs 9.8% placebo). In advanced COVID-19 ARDS, Mesoblast's remestemcel-L (an allogeneic MSC therapy) failed to achieve the targeted 30-day mortality reduction; a Phase 3 trial was halted at interim analysis when 30-day mortality was 37.5% in MSC-treated patients vs 42.7% in controls (not a statistically significant gap). These high-profile setbacks, along with others in cardiac disease and COPD, led to scepticism about MSC efficacy – one expert went so far as to say early trials "probably [show MSCs] don't work" broadly, except possibly in certain niches.

Why Did These Programs Fail?

A major factor is the biological and manufacturing limitations of first-generation MSC approaches. Traditional MSC products rely on isolating cells from adult donors (bone marrow, fat, etc.) and expanding them in culture. This process introduces high variability and often diminishes cell potency over time. A single donor tissue sample yields only ~10,000–80,000 MSCs, yet a typical adult dose requires ~100 million cells. Thus, companies had to massively expand cells *ex vivo*, which can drive MSCs into functional changes or senescence. As cells are passaged to reach required doses, they lose therapeutic potency.

Evidence from Lead Programs

aGvHD – High Response Rates & Survival

In a Phase 1 trial of Cynata's CYP-001 product for steroid-resistant aGvHD - the long-term results of which were published in *Nature Medicine* (Kelly et al., 2024) – patients achieved an 87% overall response rate and 53% complete response by Day 100. These are striking results in a condition where historically less than 20% of steroid-refractory patients survive two years. Notably, two-year overall survival in the CYP-001 trial was 60% (9 of 15 patients). For context, ruxolitinib (Jakafi®), a JAK inhibitor approved for steroid-refractory aGvHD, showed only ~38% survival at 18 months in its Phase 3 study.

Indication	Steroid-Refractory acute Graft-Versus-Host Disease (SR-aGvHD) after allogeneic HSCT, grades II-IV
Intervention	Two IV doses (day 0 and day 7) of CYP-001
Design	Phase I, open-label; primary evaluation at day 100
Key Efficacy Outcomes	
2yr OS	9/15 (60%)
6mth aGvHD	3/11 (27%); 2 grade I, 1 grade II
12mth aGvHD	0/11
24mth aGvHD	0/11
24mth chronic GvHD	3/9 (33%)

Over two years, CYP-001 achieved a 60% overall survival rate in a very high-risk steroid-refractory aGvHD population. At six months, only 3 of 11 surviving patients still had acute GvHD (two grade I, one grade II), all representing either partial response or stable disease from higher baseline grades, and by 12–24 months no patients had residual aGvHD, indicating durable control of the acute inflammatory process. However, 3 of 9 survivors (33%) had chronic GvHD at 24 months, consistent with the well-recognised longer-term complications of allogeneic transplant and managed with standard immunosuppressive regimens.

Cynata's MSCs also had a clean safety profile, with no treatment-related serious adverse events reported. This early evidence suggests Cymerus MSCs may deliver durable remissions where earlier approaches failed, potentially by providing consistent, potent cells that overcome the manufacturing shortcomings of first-gen MSC therapies. A global Phase 2 trial is now underway to confirm efficacy in aGvHD, and positive data would position Cynata as a front-runner for the adult market – especially after Mesoblast's MSC therapy was approved in children, validating the MSC modality but leaving adult aGvHD wide open.

Diabetic Foot Ulcer Phase 1 Trial

Cynata has also reported positive efficacy data in a Phase 1 trial for diabetic foot ulcers (DFU). DFU is an indication that tests MSCs' regenerative and anti-inflammatory capabilities: the trial found CYP-006TK improved wound healing compared to the standard-of-care control group.

Mean change from baseline in wound surface area:

- After 12 weeks, a decrease (improvement) of 181 mm^2 (64.6%) in the CYP-006TK group, and an increase (deterioration) of 355 mm^2 (22.0%) in the standard of care control group.

- After 24 weeks (end of study), a decrease (improvement) of 261 mm^2 (83.6%) in the CYP-006TK group, and an increase (deterioration) of 62 mm^2 (47.8%) in the standard of care control group.

Cynata also reported that larger wounds in particular healed to a greater extent in the CYP-006TK group compared to the standard of care control group. The mean change from baseline in wound surface area for larger wounds (>200mm^2) was:

- After 12 weeks, a decrease of 262mm^2 (68.4%) in the CYP-006TK group, and an increase of 540mm^2 (3.9%) in the standard of care control group.

- After 24 weeks (end of study), a decrease of 354mm^2 (84.2%) in the CYP-006TK group, and an increase of 135mm^2 (32.2%) in the standard of care control group.

Put simply, wounds treated with Cymerus MSCs almost entirely healed, whereas the standard-of-care treatment failed to decrease wound size.

Evidence from Peers

Mesoblast: FDA Approved for Paediatric aGvHD

Mesoblast, a pioneer in allogeneic MSCs, achieved a breakthrough in paediatric steroid-refractory GvHD with its product remestemcel-L (Ryoncil). In a Phase 3 trial of 54 children, remestemcel-L added to standard care achieved a Day 28 overall response rate of ~70%, significantly higher than the ~45% response in controls. This early response translated into improved survival: Day 100 survival was 74% on MSC therapy vs 57% with best available care. Long-term data showed durability, with remestemcel-L patients having around double the two-year survival rate of historical controls. These results led to remestemcel-L's approval (late 2024) as the first FDA-approved MSC therapy for paediatric SR-aGvHD. This affirms MSC's ability to deliver life-saving efficacy in GvHD. Notably, Cynata's target profile in GvHD is very similar, and the strong Mesoblast outcomes de-risk the concept: an allogeneic MSC therapy can substantially improve response and survival in GvHD patients who have no other options.

Takeda's Alofisel: Established MSC Therapy

Alofisel is an adipose-derived allogeneic MSC therapy approved in Europe for complex perianal fistulas in Crohn's disease. In its pivotal trial (ADMIRE-CD), Alofisel showed statistically significant efficacy where prior treatments often failed. At 24 weeks, 50% of patients receiving MSC injections achieved combined remission (closure of all fistula tracts with no abscess) vs 34% on placebo. By 52 weeks, the remission rate in the MSC group was ~56%, remaining significantly higher than placebo's ~39%. Many patients who would have otherwise required proctectomy or lifelong immunosuppression achieved sustained fistula healing. Alofisel's success (and subsequent EU approval) provides a precedent that MSCs can excel in treating inflammatory conditions with a reparative component, reinforcing the notion that the MSC modality is sound if product consistency and trial design are right.

MSC Efficacy in Other Late-Stage Trials

Mesoblast has also reported compelling efficacy signals in other difficult chronic diseases using optimized MSC products. In chronic heart failure, Mesoblast's Phase 3 DREAM-HF trial (537 patients) found that a single intracardiac injection of its MSC product (rexlemestrocel-L) significantly strengthened heart function and reduced major cardiac events in high-risk patients. Notably, patients receiving MSC therapy saw a 57% relative risk reduction in heart attacks or strokes compared to placebo over ~30 months, with an even larger 75% risk reduction in the subgroup with elevated inflammation. Although the trial's primary endpoint (reduction in heart failure hospitalizations) was not met, these outcomes, published in *JACC*, suggest MSCs' immunomodulatory effects can translate into tangible clinical benefits (fewer MIs and strokes) in a chronic inflammatory cardiac condition.

Similarly, in a Phase 3 trial for chronic low back pain due to degenerative disc disease, Mesoblast's MSC injections did not uniformly beat placebo on pain scores at 12 months, but showed remarkable impact on opioid usage: among patients on opioids at baseline, over three times as many MSC-treated patients were able to come off all opioids within 36 months compared to controls. This "opioid-sparing" effect, alongside significant pain reduction in an inflammatory subpopulation, earned the therapy an FDA RMAT designation for its potential in tackling pain without opioids.

Implications of Successful Trials for Cynata

The cumulative evidence indicates that Cymerus MSCs have a genuine opportunity to succeed. Cynata's upcoming readouts will be pivotal. A positive Phase 2 result in acute

GvHD would not only validate CYP-001's efficacy in a larger, controlled setting but could trigger substantial downstream benefits (e.g. resumption of advanced trials or commercialization by Fujifilm, and positioning Cynata at the forefront of iPSC-derived therapies). Meanwhile, success in the large Phase 3 osteoarthritis (OA) trial would be transformational as it would mark one of the first disease-modifying cell therapies for OA, opening the door to regulatory approval in a huge market. If Cynata can deliver clear efficacy in both an orphan immune disease (aGvHD) and a prevalent degenerative disease (knee OA), it will prove that the Cymerus platform consistently works across diverse conditions.

For the company and its investors, this would be a game-changer: Cynata would emerge with clinical validation that its MSC product is effective and scalable, likely attracting partners and accelerating paths to market. Re-rating of the stock is inevitable in this scenario.

Debate #2 Can Cynata Manufacture at Commercial Scale with Acceptable COGS and Lot-to-Lot Consistency?

Evidence of Consistency & Quality

Cynata has generated multiple independent data sets that speak directly to the consistency and quality of its Cymerus iPSC-derived MSCs. By utilizing advanced single-cell sequencing and functional stress-testing, the Company has demonstrated that its product avoids the variability inherent in donor-derived cells, supporting its viability as a scalable, off-the-shelf therapy.

Genomic Uniformity: Validated Large-Scale Transcriptomics
In a comprehensive study (Monash/Cynata poster), researchers profiled 72,709 individual MSCs across 13 different populations. This included multiple batches of clinical-grade Cymerus iMSCs alongside tissue-derived MSCs sourced from bone marrow, adipose tissue, and umbilical cords. With sequencing depth exceeding 100,000 reads per cell, the study provided a high-resolution view of cellular identity. Key findings included:

- **Source-Driven Identity:** Advanced clustering analysis (UMAP/hierarchical dendrograms) revealed that cells group primarily by their tissue of origin rather than by batch or vendor. Cymerus iMSCs formed tight, compact clusters that were distinct from bone marrow and adipose cells (which clustered together) and were most closely related to umbilical cord MSCs.

- **Superior Homogeneity:** Critical for manufacturing, the study quantified cell-to-cell variation using the 200 most variable genes. The mean transcriptomic variance was significantly lower in iMSCs compared to tissue-derived cells. Importantly, variance was comparable between different iMSC batches, whereas tissue-derived MSCs exhibited pronounced donor-to-donor variability.

Figure 4: Principal Component Analysis (PCA) of MSC Populations, which visualises the components responsible for the separation of MSCs based on their source of origin. Source: Hodgson-Garms et al., "A comparative analysis of the MSC transcriptome," Monash University & Cynata Therapeutics (2022).

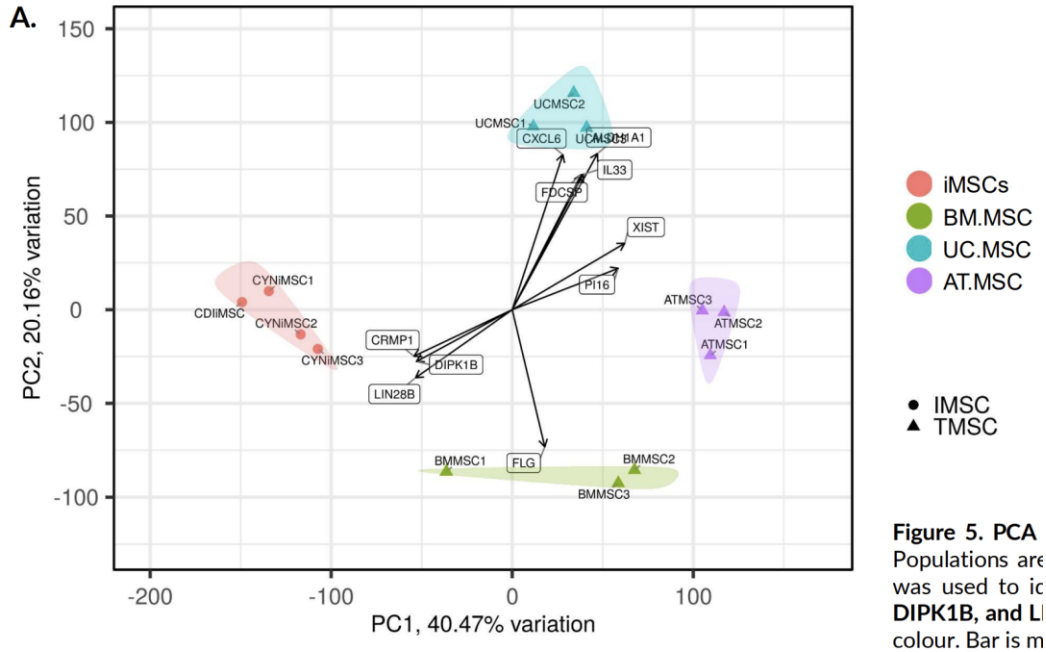


Figure 5. PCA
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- **Therapeutic Profile:** Differential expression analysis highlighted 5,491 genes upregulated in iMSCs (vs. 820 in tissue-derived MSCs). Gene ontology enrichment suggests iMSCs upregulate processes linked to telomere maintenance and RNA catabolism while downregulating pathways associated with humoral immune response and complement activation. This is consistent with a cell type that is more robust and proliferative, yet potentially less inflammatory.

The authors of the poster concluded that iMSCs "exhibit significantly less intrapopulation variation" and "less batch-to-batch heterogeneity," confirming the platform's ability to bypass the inconsistencies that plague conventional tissue-derived MSCs.

Functional Potency & Optimized Culture Conditions

Complementing the genomic data, Romanazzo et al. conducted a systematic evaluation of Cymerus iMSCs to determine if a therapeutically relevant state could be induced reproducibly and, crucially, maintained after freezing. Recognizing that clinical outcomes often vary due to starting population heterogeneity, the authors screened a matrix of culture conditions using polyacrylamide hydrogels of tuneable stiffness (1, 10, 40, 100 kPa) and defined extracellular matrix (ECM) coatings (collagen I, fibronectin, laminin).

The study identified specific environments – notably 1 kPa collagen and 10 kPa fibronectin-coated gels – that triggered a highly reproducible, pro-angiogenic (blood vessel forming) and immunomodulatory secretome (a set of proteins and signalling molecules released by a cell into the ECM). Media from iMSCs cultured on these optimized substrates drove significantly greater tube formation in human microvascular endothelial cells compared to standard tissue-culture plastic. In certain conditions (e.g., 10 kPa collagen), performance even exceeded positive controls supplemented with growth factors.

Why is this significant? Standard tissue-culture plastic (TCP) is the industry-standard method for growing MSCs. By proving that Cynata's "tuned" manufacturing process (using soft gels) yields cells that are biologically more potent than the industry baseline, it may be concluded that Cynata's product is engineered to be superior to generic MSCs.

Commercial Scalability: Stability Through Cryopreservation

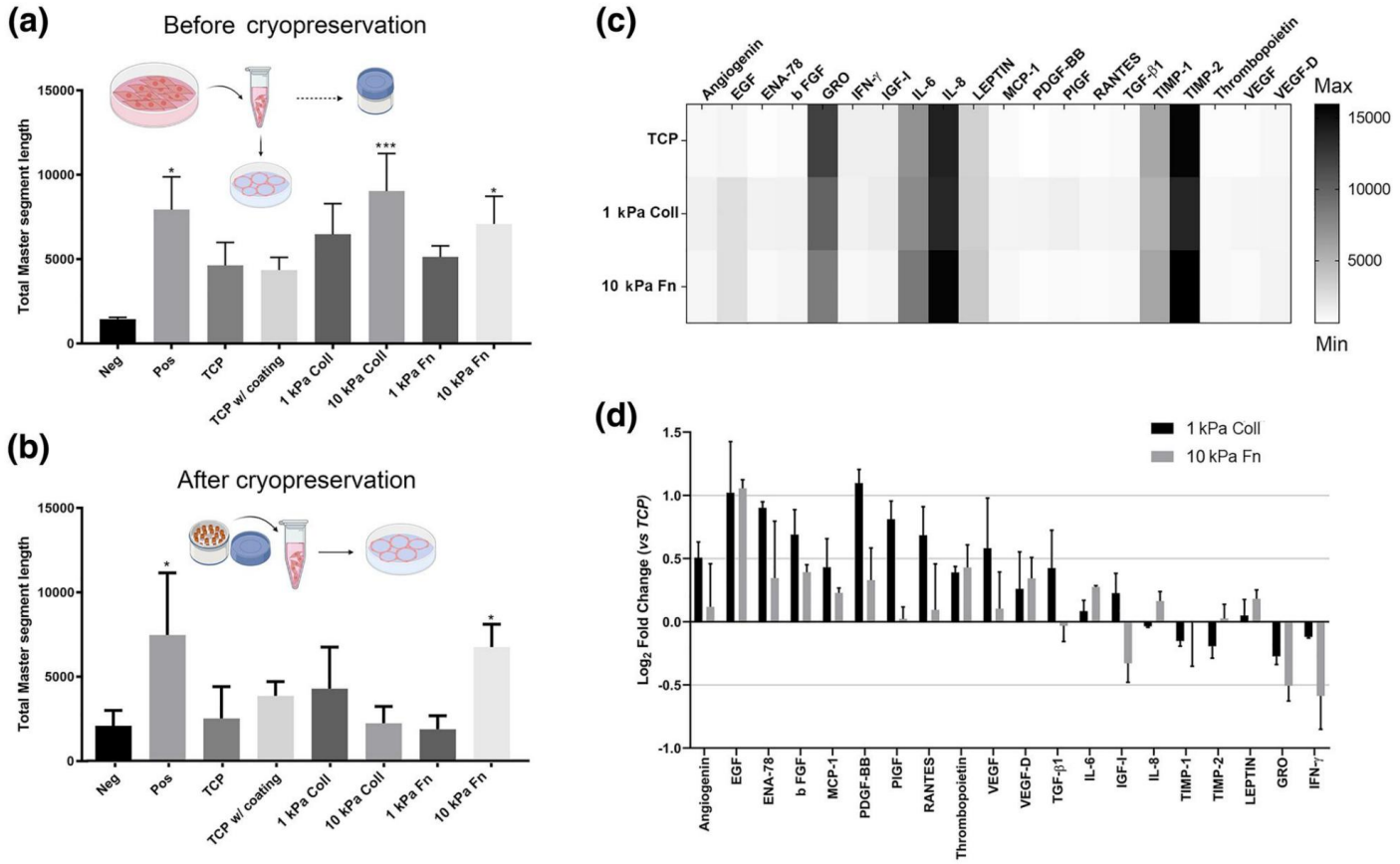
For an off-the-shelf therapy, cells must retain potency after the freeze-thaw cycle. The Romanazzo study provided critical validation of this commercial requirement:

- **Post-Thaw Potency:** iMSCs were cultured on optimized substrates, cryopreserved for up to 31 days, thawed, and re-assessed. The cells maintained the same rank-order of tubulogenesis before and after freezing, proving that the pro-angiogenic (i.e., facilitating of blood vessel formation) functional state persists through the supply chain cycle.

- **In Vivo Validation:** In the chick chorioallantoic membrane (CAM) assay, conditioned media from these cells produced significantly higher blood-vessel branching both before and after cryopreservation. A 1:1 mixed substrate of 10 kPa collagen/fibronectin yielded the strongest response.

- **Defined Biology:** Mechanistic studies linked this potency to integrin $\alpha V \beta 3$-mediated adhesion and actomyosin contractility. Blocking these pathways abolished efficacy, demonstrating that the cell behaviour is driven by controllable biophysical cues rather than random variation.

Figure 5: Functional Potency and Secretome Stability of Cymerus™ iPSC-MSCs Post-Cryopreservation. Source: Romanazzo et al., "Biomaterials directed activation of a cryostable therapeutic secretome in induced pluripotent stem cell derived mesenchymal stromal cells," *Journal of Tissue Engineering and Regenerative Medicine* (2022).



(a-b) Maintenance of Potency: These charts quantify the regenerative potency of Cynata's iPSC-MSCs, measured by their ability to stimulate blood vessel formation in vitro. The data demonstrates that iPSC-MSCs manufactured under optimized conditions (e.g., 10 kPa Fibronectin) exhibit significantly higher potency than cells grown on standard tissue culture plastic (TCP). Crucially, Panel (b) confirms that this therapeutic potency is preserved after cryopreservation (freezing and thawing), validating the stability of the Company's off-the-shelf commercial supply chain. **(c-d)** Defined Mechanism of Action: Cytokine array profiling reveals the biological drivers of this potency. The heat map (c) and fold-change quantification (d) show that these optimized iPSC-MSCs consistently upregulate a specific "therapeutic secretome," secreting significantly higher levels of key regenerative and immunomodulatory factors (such as VEGF, IL-8, and GRO) compared to standard controls.

Implications

These lines of evidence – genomic uniformity and functional stability – substantially de-risk the Cymerus platform from a CMC (Chemistry, Manufacturing, and Controls)

perspective. Cynata has demonstrated that it can manufacture highly uniform cell populations with stable, therapeutically relevant behaviours that withstand cryopreservation. This validates the platform's capacity to deliver a consistent, off-the-shelf product suitable for late-stage development and commercial supply.

Regulatory Validation of Cynata's Manufacturing

Cynata's manufacturing approach earned early acknowledgement from regulators. In 2017, the company engaged the FDA in a formal pre-IND meeting to discuss its Cymerus MSC product (CYP-001 for graft-versus-host disease). The FDA's feedback was resoundingly positive regarding manufacturing. Notably, regulators "confirmed that the scope and substance of Cynata's Chemistry, Manufacturing and Controls (CMC) dossier [for Cymerus] is commensurate with [FDA] expectations," indicating that Cynata's product was of suitable quality for clinical trial use in the US. In other words, even at that early stage, Cynata's data package on how they produce and test their cells met the FDA's standards – a clear green light to proceed with US development.

Debate #3: Where is the real value: OA vs aGvHD vs DFU? Which Indication should drive the SOTP?

The Allocation Dilemma

In the assessment of clinical-stage biotechnology equities, particularly those predicated on platform technologies like Cynata Therapeutics' Cymerus™, the allocation of valuation weight across diverse indications presents a complex strategic dilemma. The capital markets have struggled to efficiently price these disparate opportunities, often applying a blunt sum-of-the-parts (SOTP) discount that anchors enterprise value to the nearest-term catalyst while treating the larger, more complex indications as free, or even negative, optionality.

This section seeks to discern where the true, risk-adjusted value of the Cymerus platform resides.

Osteoarthritis (OA): Blue Sky Blockbuster

Osteoarthritis is the most prevalent chronic joint disease globally, yet it remains a therapeutic orphan, managed solely through symptom palliation rather than disease modification. The pharmaceutical industry has successfully developed disease-modifying anti-rheumatic drugs (DMARDs) for Rheumatoid Arthritis, Psoriatic Arthritis, and Ankylosing Spondylitis, creating multi-billion-dollar franchises such as Humira (adalimumab) and Enbrel (etanercept). Yet, for OA, the standard of care remains arrested in the 20th century: weight management, non-steroidal anti-inflammatory drugs (NSAIDs) with their attendant renal and gastrointestinal toxicity profiles, intra-articular corticosteroids that may paradoxically accelerate cartilage volume loss, and ultimately, Total Knee Replacement (TKR).

The "real value" of the OA indication lies in the potential for CYP-004 to breach this barrier and become the first true Disease-Modifying Osteoarthritis Drug (DMOAD) – an agent that not only provides symptomatic relief but structurally arrests or reverses the progressive degradation of articular cartilage.

The Scale of the Untreated Burden

OA is a disease driven by the inexorable forces of aging and biomechanics, and as the global population demographics shift older and obesity rates continue to rise, the incidence of OA is accelerating. According to data from the Centers for Disease Control (CDC) and recent epidemiological reviews, approximately 32.5 million adults in the United States currently suffer from OA. Specifically for knee OA, which is the primary target indication for CYP-004, the prevalence numbers are staggering. Analysis of the

NHANES III data and the longitudinal Johnston County Osteoarthritis Project suggests that the prevalence of symptomatic knee OA in adults over the age of 60 is approximately 13% for women and 10% for men. More recent estimates place the total number of symptomatic knee OA patients in the US at approximately 14 to 15 million.

However, for the purpose of valuation, it is critical to refine this TAM to the addressable patient population. Not every OA patient is a candidate for an advanced cell therapy. The target market generally excludes mild cases (Kellgren-Lawrence Grade 1) which are adequately managed with over-the-counter analgesics and lifestyle modifications. Conversely, it also excludes end-stage "bone-on-bone" disease (Kellgren-Lawrence Grade 4), where cartilage substrate is virtually nonexistent, and arthroplasty is the only viable solution. The commercial "sweet spot" for a DMOAD is the moderate to severe (KL Grade 2-3) population. These are patients who experience significant pain and functional limitation, have failed conservative therapy, but crucially, still possess sufficient cartilage volume to preserve or regenerate. Epidemiological data indicates that approximately 50-60% of symptomatic knee OA patients fall into this KL 2-3 category. This refinement filters the US addressable market to a highly robust 8 to 9 million patients.

Globally, the Global Burden of Disease study estimates nearly 595 million prevalent cases of OA. In major pharmaceutical markets such as the EU5 (Germany, France, Italy, Spain, UK) and Japan, the market dynamics mirror those of the US. In fact, Japan's super-aging society drives even higher per-capita rates of knee degeneration, creating a massive potential market for a non-surgical intervention. The forecast for the global knee OA market suggests growth to $9.1 billion by 2034.

Pricing & the DMOAD Premium

Currently, the OA market is characterized as volume-driven but value-poor. It is dominated by generic oral NSAIDs and relatively inexpensive intra-articular hyaluronic acid (HA) viscosupplements.

Hyaluronic acid injections (e.g., Synvisc, Euflexxa, Durolane) typically cost payers approximately $300 to $800 per treatment cycle. Extended-release corticosteroids, such as Zilretta, command a slight premium but generally remain priced under $1,000 per injection. These price points reflect their status as palliative devices or drugs with temporary efficacy.

A true DMOAD would not compete economically with ibuprofen or HA injections; it would compete with the economic burden of disability and surgical intervention. The average cost of a Total Knee Replacement (TKR) in the US ranges from $20,000 to $35,000, with revision surgeries costing significantly more. Furthermore, TKR is a major surgical procedure with significant rehabilitation time and risks of complications. A therapy that can delay the need for TKR by 5 to 10 years creates immense economic value for payers (insurance companies and Medicare) by deferring these high-cost events.

If CYP-004 demonstrates structural modification, it transitions the asset from a "pain management" valuation bucket to a "biologic therapy" bucket. Health economic models for DMOADs in development often assume a price point of $2,000 to $5,000 per year. Even assuming a conservative price of $1,500 per dose (with a potential regimen of one to two doses per year), capturing just 5% of the eligible US KL 2-3 population (approximately 400,000 patients) implies peak US sales of $600 million. A more optimistic penetration rate of 10-15%, not unreasonable for a first-in-class disease modifier, pushes this opportunity firmly into blockbuster territory (>$1.5 billion).

OA Competitive Landscape

The landscape of OA drug development is littered with failed programs, creating a winner-takes-all dynamic for the first entrant to successfully navigate the regulatory gauntlet. The challenge has been the regulatory requirement to demonstrate efficacy

in both symptomatic relief and structural modification. Competitors have historically succeeded in one while failing the other:

- **Lorecivivint (Biosplice):** This small-molecule CLK/DYRK inhibitor was long considered the frontrunner in the race for a DMOAD. However, its development has been marred by inconsistent results. While early phases showed promise, recent Phase 3 trials (OA-11) failed to meet primary endpoints for pain and function at 12 weeks, despite showing some structural signals in specific sub-groups. The failure to consistently demonstrate symptomatic benefit alongside structural maintenance has cast significant doubt on its approval path.

- **Sprifermin (Merck/TrialSpark):** This recombinant FGF-18 growth factor represents the inverse problem. In its Phase 2 FORWARD study, Sprifermin demonstrated statistically significant structural success, increasing cartilage thickness in a dose-dependent manner. However, it failed to translate this structural gain into significant symptomatic pain relief compared to placebo. Because regulatory agencies require a demonstrable clinical benefit (how the patient feels/functions) alongside the structural change, Sprifermin has faced a stalled development path.

- **Anti-NGF Antibodies (Pfizer/Eli Lilly - Tanezumab):** This class of potent analgesics was designed to treat pain, not structure. While highly effective at masking pain, they were halted due to safety concerns regarding rapidly progressive osteoarthritis (RPOA) – effectively, patients felt so little pain they overworked their joints to destruction. This failure effectively removed a major competitive class of biologics from the board.

- **Lutikizumab (AbbVie):** An anti-IL-1 alpha/beta dual variable domain immunoglobulin, Lutikizumab failed to show significant improvement in WOMAC pain scores or synovitis in Phase 2 trials, reinforcing the difficulty of targeting single inflammatory cytokines in a complex disease like OA.

Unlike small molecules or single-target growth factors, MSCs (like CYP-004) operate via a multimodal mechanism of action. They are immunomodulatory and act as paracrine signaling powerhouses. Upon injection into the joint, MSCs secrete a cocktail of bioactive factors (cytokines, chemokines, growth factors) that modulate the local microenvironment. This creates the potential to address both the inflammatory drivers of pain (symptom) and the catabolic processes driving cartilage degradation (structure) simultaneously. This dual-action capability addresses the specific failure points of previous candidates: unlike Tanezumab, MSCs do not mask pain at the expense of structure; unlike Sprifermin, their anti-inflammatory action may provide the symptomatic relief necessary to complement structural repair. Cynata's Phase 3 SCUlpTOR trial, with its robust 24-month follow-up and sophisticated MRI structural endpoints, is specifically designed to capture this DMOAD signal where others have failed.

The Verdict on OA Value

OA represents the highest-risk asset in the portfolio due to the historical difficulty of OA clinical trials (where the "placebo response" in pain endpoints is notoriously high). However, it unequivocally offers the highest reward. A successful Phase 3 readout would position CYP-004 as a prime acquisition target for Big Pharma majors (such as Pfizer, Novartis, or GSK) who are desperate to replace declining revenues with a first-in-class mass-market biologic. In the near term, the TAM is essentially uncapped due to the lack of approved competition.

aGvHD

CYP-001 in acute Graft-versus-Host Disease represents the foundational value of the company today. This asset addresses a high-mortality orphan condition with a clear regulatory pathway, a validated therapeutic modality, and a well-defined, accessible patient population.

Epidemiology: Niche but Critical Market

Acute GvHD is a catastrophic immunological complication that occurs when donor immune cells (the graft) attack the recipient's tissues (the host) following an allogeneic Hematopoietic Stem Cell Transplant (HSCT). The volume of allogeneic HSCTs is relatively stable but growing slowly. Approximately 30,000 to 40,000 allogeneic HSCTs are performed annually worldwide across major markets (US, Europe, Japan, China). The United States accounts for roughly 8,000 to 10,000 of these procedures annually. Despite prophylactic regimens, approximately 35-50% of transplant recipients develop acute GvHD.

The first line of defense for aGvHD is high-dose systemic corticosteroids. However, the critical commercial target for Cynata is the subset of patients who fail this therapy. Approximately 40-50% of patients become Steroid-Refractory (SR) or are classified as "High Risk" at diagnosis due to biomarker profiles or clinical severity. These patients face a dismal prognosis, with mortality rates historically exceeding 70-80% without effective salvage therapy.

This stratification filters the addressable market down to a target US population of approximately 1,500 to 2,000 patients per year, with a similar number in Europe. While numerically small compared to the millions of OA sufferers, these are patients in the intensive care unit, costing the healthcare system an inordinate amount. The value proposition here is life-saving intervention, which commands exceptional pricing power.

Competitive Landscape: Ruxolitinib Ceiling and the MSC Opportunity

The treatment landscape for SR-aGvHD has evolved significantly with the approval of Ruxolitinib (Jakafi), a JAK1/2 inhibitor marketed by Incyte. Jakafi is currently the standard of care for SR-aGvHD and generates substantial revenue as part of Incyte's multi-billion dollar franchise. However, it is a potent systemic immunosuppressant that carries significant risks, including cytopenias (low blood cell counts) and viral reactivation (CMV, EBV). Furthermore, clinical data indicates that roughly 40-50% of patients do not achieve a durable response to Ruxolitinib or eventually relapse. This creates a defined second-line or combination therapy market for agents with a better safety profile.

Mesoblast's Ryoncil (Remestemcel-L) recently received FDA approval specifically for paediatric SR a-GvHD. The approval explicitly validates that MSCs are an approvable therapeutic modality for GvHD. Importantly, Mesoblast's label is currently restricted to children. This leaves the adult market, which comprises the vast majority (>90%) of transplant patients, wide open for competition.

Cynata's CYP-001 competes directly with the therapeutic concept of Mesoblast's donor-derived MSCs but offers a superior manufacturing paradigm for the adult market. Treating an adult patient requires a dose 5 to 10 times larger than that for a child. Manufacturing this volume using donor-derived cells (Mesoblast's method) is expensive and logistically straining, requiring the recruitment and screening of thousands of donors to maintain supply. Cynata's iPSC-derived platform can produce infinite, consistent doses from a single donor. This ensures lot-to-lot consistency (a key regulatory requirement) and potentially significantly lower Cost of Goods Sold (COGS), making it the only truly scalable MSC solution for the larger adult market.

Pricing Power

Ruxolitinib treatment costs approximately $150,000 to $180,000 per course. Mesoblast has indicated that pricing for Ryoncil will reflect its value in saving young lives, with estimates potentially reaching $200,000 to $300,000 per course. Capturing 100% of the US adult SR-aGvHD market (~1,800 patients) at a conservative price point of $200,000 yields annual revenues of $360 million. Crucially, for a biotech company of Cynata's size, a reliable revenue stream would be transformative, sufficient to sustain the company's burn rate and self-fund the development of the broader pipeline without further equity dilution.

Verdict on aGvHD Value

Success in the ongoing Phase 2 trial essentially proves that the Cymerus platform works in humans. It validates the manufacturing consistency to the FDA and provides a commercial toehold in the US market. The approval of Mesoblast's product de-risks the regulatory path (the FDA accepts the endpoint and modality), while the limitations of Ruxolitinib preserve the commercial path. For a potential partner (such as Fujifilm or a mid-sized hematology player), CYP-001 represents a "plug-and-play" asset that fits seamlessly into existing commercial infrastructure.

Diabetic Foot Ulcers: Strategic Cash Flow

DFU is a high-volume, chronic indication, but one that exists within a fragmented, commoditized market dominated by medical devices and dressings rather than pharmaceuticals.

Epidemiology: Chronic Wound Epidemic

Diabetes is a global epidemic, and DFU is one of its most debilitating complications. Approximately 19-34% of diabetic patients will develop a foot ulcer in their lifetime. In the United States alone, DFU affects over 1.5 million people annually. Despite the standard of care – which involves offloading, debridement, and infection control – healing rates remain poor. Roughly 20% of DFUs remain unhealed after a year, leading to high rates of osteomyelitis and amputation. Indeed, DFU is the leading cause of non-traumatic lower limb amputation globally.

Competitive Landscape

Unlike the aGvHD market (dominated by a single pharmacotherapy) or the OA market (a graveyard of failed trials), the DFU market is fragmented across medical devices, advanced dressings, and bioactive skin substitutes. However, the market is currently bifurcated between passive scaffolds that offer structural support and active biological therapies that are hamstrung by manufacturing constraints.

Wound Care. The baseline treatment remains good wound care: sharp debridement, infection control, and mechanical offloading. However, clinical data consistently shows that ~50% of chronic DFUs fail to heal after 12 weeks of standard care alone. The only FDA-approved pharmaceutical therapy is Regranex (becaplermin), a recombinant PDGF gel marketed by Smith & Nephew. Despite being the sole approved drug, Regranex has historically seen limited market penetration due to high cost and a complex safety history (it carried a "Black Box" warning regarding malignancy risk for over a decade, which was only removed in 2018). This leaves a clear void for a safe, highly effective bioactive intervention.

Living Skin Substitutes. The current biological standard of care is dominated by first-generation bioengineered skin substitutes, primarily Apligraf (Organogenesis) and Dermagraft. These products – composed of living fibroblasts and keratinocytes derived from neonatal foreskin – have been on the market for decades. The limitation: while clinically effective, they suffer from profound logistical fragility. They typically require storage at tightly controlled temperatures, have short shelf-lives (often days to weeks), and are fragile to handle. Furthermore, as donor-derived "craft" products, they are expensive to manufacture, limiting their pricing flexibility.

Amniotic & Placental Allografts. A significant portion of the DFU market is held by dehydrated human amnion/chorion membrane (dHACM) products, such as Epifix (MiMedx) and Grafix (Smith & Nephew). These products rely on tissue donated from caesarean sections and are marketed for their growth factor content. This segment faces severe regulatory headwinds. The FDA has recently cracked down on tissue products claiming "regenerative" effects without a Biologics License Application (BLA), narrowing the commercial lane for "minimally manipulated" tissues (the "361" pathway) and forcing them towards the rigorous drug pathway where Cynata already operates.

Synthetic Matrices. Recent consolidation, such as Solventum's acquisition of Acera Surgical (Restrata), highlights the demand for synthetic scaffolds. These products (often electrospun matrices) provide a physical bridge for cells to migrate across but do not actively signal healing. They also don't actively modulate the immune environment or secrete factors to stimulate blood vessel growth. They rely entirely on the patient's own senescent cells to do the work, which, in diabetic patients, are often dysfunctional.

Cynata's Differentiation

CYP-006TK occupies a unique competitive niche. By seeding Cymerus™ iPSC-MSCs onto a novel polymer-coated silicone dressing, Cynata creates an active biological bandage. Unlike passive synthetics, CYP-006TK actively secretes potent angiogenic factors (VEGF, IL-8, ENA-78) to drive neovascularisation from the wound bed up (addressing the underlying ischemia). And unlike fragile living skins, CYP-006TK is cryopreserved and off-the-shelf, fitting seamlessly into the hospital pharmacy supply chain. On the regulatory front, as a standardized therapeutic pursuing a formal BLA pathway, Cynata avoids the regulatory uncertainty currently plaguing the amniotic tissue sector, offering a future-proof asset for potential partners.

Partnering and M&A Dynamics

For platform biotechs, value rarely waits for full commercial build-out. It is often crystallised at the moment an asset becomes financeable for someone else, either because the clinical risk has collapsed, or because the manufacturing story becomes credible at scale. That matters for Cynata because the three programs naturally map to three different monetisation paths: aGvHD as the validation wedge, OA as the prize asset, and DFU as a potential source of non-dilutive funding via partnering (rather than an internal sales-force build).

What Strategic Buyers Have Paid for And When

The clearest precedent for "platform + inflection point" M&A is Takeda/TiGenix. Takeda moved from partner to acquirer via a voluntary public takeover bid at €1.78/share, which was an ~82% premium, valuing TiGenix at ~€520m, with the timing anchored to the impending EU marketing authorisation for Alofisel and the logic of buying back future royalties/milestones embedded in the earlier licensing relationship. It's a useful reminder of two things: (1) acquirers will pay up when they can see a near-term regulatory path, and (2) they are often motivated by economics capture as much as science. Importantly, Takeda's later decision to withdraw Alofisel in 2024 after a confirmatory Phase 3 miss shows why buyers have become more disciplined on risk, even with approved regenerative assets.

A second, more relevant precedent for Cynata is Bayer/BlueRock: a ~$240m upfront plus ~$360m in milestones, with a total implied value of ~US$1b, explicitly framed around securing control of an iPSC platform that solves scalability/consistency constraints. This matters because Cymerus sits closer to that logic than to first-generation donor MSC narratives: strategic value can attach to the manufacturing architecture itself, not just a single indication.

Figure 6: Strategic Acquisition Precedent – Bayer & BlueRock Therapeutics (2019). Source: Bayer AG corporate announcements (August 2019) and subsequent BlueRock Therapeutics clinical and regulatory updates.

Deal Element	Key Details
Parties	Bayer AG to fully acquire BlueRock Therapeutics; announced 8 Aug 2019.
Asset	A pluripotent stem-cell platform positioned around iPSC-based engineered cell therapies (BlueRock "CELL+GENE"), with programs across neurology, cardiology, immunology.
Lead Product	Bemdaneprocel (BRT-DA01): an investigational cell replacement therapy designed to replace dopamine-producing neurons lost in Parkinson's; dopaminergic neuron precursors are derived from human embryonic pluripotent stem cells and surgically implanted into the brain.
Stage of Development	Was expected to enter the clinic sometime in 2019, therefore the stage was late-preclinical
Deal Structure	Bayer bought the remaining 59.2% (it already held 40.8%).
Economics	$240m cash upfront + $360m tied to pre-defined development milestones; implied total value of $1.0bn, inclusive of Bayer's existing stake.
Operating model post-acquisition	BlueRock to continue as an independent company/subsidiary.
Strategic Rationale	Bayer explicitly framed this as a "major milestone" toward a leading position in cell therapy, building its pipeline on BlueRock's platform.
Clinical Progression	Phase I signals: at 18 months, well tolerated with evidence of engraftment and increased F-DOPA signal after stopping immunosuppression at 12 months; "Good ON" time improved notably in the high-dose cohort.
Regulatory Accelerants	Fast Track (2021) and Regenerative Medicine Advanced Therapy Designation (RMAT) (2024) for bemdaneprocel.
Pivotal Step-up	Phase III (exPDite-2) launched: sham-surgery controlled, double-blind; ~102 participants; primary endpoint is ON-time without troublesome dyskinesia at week 78; first randomized patient treated 22 Sep 2025.
Manufacturing & Scale-up	Bayer is already building a manufacturing network; it spent ~$250m on a California cell-therapy facility (2023) and is planning for scale ahead of readouts.

Bayer's buyout of BlueRock is best read as a capability acquisition: once a pluripotent-cell platform is strategically relevant, owning the IP, process know-how and the manufacturing learning curve is worth more than carrying a minority stake and paying "partner economics" later. The lead Parkinson's program was still early when the deal was struck, which is why the price blended a meaningful upfront with back-end milestones – Bayer paid for platform scarcity, but kept exposure linked to development progress. Since then, value has been built the orthodox way: stepwise clinical de-risking, regulatory tailwinds, and escalation into a sham-controlled Phase III, while Bayer invests in industrial-scale manufacturing to make a complex therapy deployable. For Cynata, the lesson is that credible, scalable CMC plus a clear clinical anchor can shift the conversation from single-asset NPV to platform control – exactly the framing that tends to unlock partnering leverage and, in the right window, M&A interest.

How Deal Structures Signal Risk

The market has also become more explicit about risk-sharing. Mesoblast/Grünenthal is the textbook example: a >US$1b "headline" deal where the non-refundable upfront was only US$15m and the rest was contingent milestones/royalties, designed to help fund development while keeping the acquirer's cash exposure low until data settled the debate. Note this deal was not for aGvHD, rather it was for MPC-06-ID in chronic low back pain due to degenerative disc disease. The subsequent restructuring of milestone accounting after trial failure underlines the practical point: biobucks can evaporate if the clinical story breaks.

Figure 7: Strategic Partnership Precedent – Mesoblast & Grünenthal (2019). Source: Mesoblast Ltd and Grünenthal GmbH corporate announcements (September 2019) and subsequent company filings regarding the partnership amendment.

Deal Element	Key Details
Parties	Mesoblast & Grunenthal; September 2019.
Asset	MPC-06-ID, an allogeneic mesenchymal precursor cell (MPC) therapy.
Indication	Chronic low back pain due to degenerative disc disease (DDD).
Stage of Development	Described as phase III candidate; Mesoblast was completing a phase III US trial (readout expected 2020), and the parties planned a confirmatory phase III in Europe to meet EMA requirements.
Jurisdiction	Grunenthal received exclusive commercialisation rights for Europe and Latin America.
Upfront Cash	US$15m
Pre-launch Contingent Payments	Eligible for US$150m in upfront + milestone payments prior to product launch.
First-year Milestone Package	Commitments up to US$45m within the first year: $15m signing + $20m upon regulatory approval to begin a confirmatory Phase III trial in Europe + $10m tied to specific clinical and manufacturing outcomes.
Back-end Milestones	Cumulative milestones could exceed US$1b, depending on Phase III outcomes and adoption; also includes additional commercialisation milestone payments (not fully itemised in the press release).
Royalties	Tiered double-digit royalties on product sales.
Development plan	Parties agreed an overall development plan to satisfy European requirements and would collaborate on study design for the EU confirmatory Phase III; the two Phase III trials were intended to support FDA + EMA filings.
Post-deal Evolution	After MPC-06-ID's U.S. Phase III failure, the partnership was reworked; an amendment reclassified a US$2.5m milestone (received Dec 2019) as potentially repayable/deferrable, contingent on future recruitment/success.

DFU Precedents

DFU is the most natural partnering candidate, not because the market is small, but because the go-to-market is sales-force intensive and already owned by incumbents. The precedent set here is medtech consolidation in advanced wound care. Smith & Nephew's acquisition of Osiris was a bolt-on to accelerate its wound franchise. The consideration was US$660m all-cash, anchored to commercial-stage assets and at a ~4.6x LTM revenue multiple. More recently, Solventum paid US$725m upfront plus US$125m in milestones (US$850m total) for Acera's synthetic matrix, explicitly valuing products that avoid donor variability and supply constraints while still fitting established reimbursement dynamics. The throughline is clear: if DFU can be packaged as an off-the-shelf biological adjunct that slots into existing wound channels, strategic buyers can underwrite it even before it looks like a pharma-style franchise.

Figure 8: Strategic Acquisition Precedent – Solventum & Acera Surgical (2025). Solventum corporate announcements (November 2025) and deal presentation materials.

Deal Element	Key Details
Parties	Solventum (NYSE: SOLV) to acquire Acera Surgical; announced 20 Nov 2025.
Asset	Acera's Restrata® synthetic tissue matrix products, built on a proprietary electrospinning platform.
Modality	Fully resorbable, electrospun fiber matrix designed to support cell ingrowth; marketed as a synthetic alternative within regenerative wound care.
Indication	FDA 510(k) documentation lists wound management across multiple wound types including diabetic ulcers, venous ulcers, pressure ulcers, burns, surgical/trauma wounds (among others).
Stage of Development	Commercial-stage: Restrata products are currently available in the US and used for hard-to-heal, complex wounds in acute care settings; Solventum guided Acera to ~$90m 2025 sales.
Deal Structure	Acquisition (no royalty stack; full ownership), with a back-end contingent cash component.
Upfront Consideration	US$725m at closing
Contingent Payments	Up to $125m in contingent cash payments tied to achievement of future milestones (described as milestone- and performance-linked; specific thresholds not disclosed publicly in the announcement).
Expected Close	First half 2026.
Strategic Rationale	Solventum framed the deal as expanding MedSurg into synthetic tissue matrices (positioned as part of a ~$900m US market segment) and accelerating adoption by leveraging Solventum's global footprint and wound care sales force.
Commentary	Acera went into the deal having broadened Restrata's FDA-cleared footprint (notably, a 2025 clearance expanding into soft tissue reinforcement, i.e., moving beyond purely external wound settings), which can expand the revenue base that the earn-out is effectively betting on.

Why This Can Lead to Value for Cynata

In practical terms, the buyer is paying for three things: scalable CMC, one or two registrational shots on goal (OA/aGvHD), and a DFU asset that can be partnered rather than built in-house. Cynata's own "smart money" sequencing is consistent with how the sector has monetised risk: positive Phase 2 aGvHD data (H1 2026) could drive a licensing deal or an acquisition approach (and a platform re-rate), while positive Phase 3 OA data in 2026 is the type of catalyst that can force an auction for the asset or the company. The OA precedent for what de-risked can look like is stark: Sobi's Arthrosi deal carried US$950m upfront (US$1.45b total), signalling what happens when buyers believe the Phase 3 probability-of-success has moved decisively in their favour.

Forecasts & Model Assumptions

Our forecasts include Cynata's two most clinically advanced assets: CYP-001 in steroid-refractory acute GvHD and CYP-004 in knee osteoarthritis. Other programs (e.g., DFU and kidney transplant) are treated as unvalued option value in the base-case, consistent with the pipeline being led by these Phase 2/3 assets.

Across both programs, we take a deliberately conservative modelling stance by focusing on the US market only. This removes EU/ROW expansion upside from the base-case and anchors the valuation to the jurisdictions and pathways that we believe are most likely to drive near-term strategic interest. Within that US-only framing, we assume different commercialisation routes by asset: CYP-001 is directly commercialised (full revenue capture, but with a direct commercial build), while CYP-004 is monetised via a US-exclusive license (royalties plus supply economics).

CYP-001: US Only, Direct Commercialisation

For CYP-001, we assume Cynata retains US rights and launches directly into the transplant-centre ecosystem. In practical terms, this implies building a focused specialty footprint (medical affairs and a small sales team calling on key transplant centres), rather than a broad primary-care rollout. Because this is a direct model, the company captures the full product revenue in-market, but we explicitly incorporate the SG&A scaling required to support launch and ongoing commercial operations.

Market sizing is built from a straightforward patient-flow approach. We start with ~10,000 allogeneic transplants per year in the US (increasing with a 0.3% p.a. population increase rate), apply an aGvHD incidence rate of 42.5%, and then apply a 50% steroid-refractory/high-risk rate, resulting in a base-year addressable population of ~2,125 patients.

On pricing, we assume a A$0.5m net price per treatment course. Given the orphan, special care-level setting, we view this as a conservative anchor for a life-saving therapy, while still allowing for payer scrutiny and contracting dynamics. We model COGS at 10% of revenue, reflecting the view that Cymerus' iPSC-derived manufacturing architecture should be structurally advantaged versus first-generation donor-derived MSC approaches.

Development timing is phased as follows: Phase 3 completion in CY2028, FDA filing in CY2029, FDA approval in CY2030 (FY2031), with first commercial sales commencing in FY2031. Commercial uptake is intentionally conservative in the early years of launch: we assume penetration of 2.5% in Year 1 (FY2031), rising to 5% in Year 2, 7.5% in Year 3, 12.5% in Year 4, and 20% from Year 5 onward.

To reflect clinical-stage risk, we apply a 30% probability of success (PoS) factor to all CYP-001 cash flows. Our starting point is a ~26% cumulative PoS from Phase 2 to approval (40% Phase 2→3 × 65% Phase 3→approval), which we modestly adjust upward to reflect positive factors such as the strength of early response data, clean safety, and the regulatory tailwind of orphan positioning. The PoS is applied at the revenue line (i.e., we do not double-haircut the same risk elsewhere), with commercial execution risk embedded in conservative pricing and penetration assumptions.

Figure 9: CYP-001 (aGvHD) – US Market Revenue & Valuation Model (FY26–FY35E). Source: Evolution Capital's estimates.

Fiscal Year	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035
CYP-001 - ACUTE GVHD - US										
Market Size										
US allogeneic transplants	10,000	10,030	10,060	10,090	10,121	10,151	10,181	10,212	10,243	10,273
aGvHD incidence rate	42.5%	42.5%	42.5%	42.5%	42.5%	42.5%	42.5%	42.5%	42.5%	42.5%
SR-aGvHD rate	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%
Target patients (SR-aGvHD)	2,125	2,131	2,138	2,144	2,151	2,157	2,164	2,170	2,177	2,183
Pricing & Penetration										
Price per treatment	500,000	500,000	500,000	500,000	500,000	500,000	500,000	500,000	500,000	500,000
Market penetration rate	0.0%	0.0%	0.0%	0.0%	0.0%	2.5%	5.0%	7.5%	12.5%	20.0%
Patients treated	0	0	0	0	0	54	108	163	272	437
Revenue & Economics (000s)										
Product Revenue						26,963	54,088	81,376	136,034	218,307
COGS						2,696	5,409	8,138	13,603	21,831
Gross Profit						24,267	48,680	73,238	122,430	196,476
Gross Margin %						90.0%	90.0%	90.0%	90.0%	90.0%
Risk-Adjusted Revenue (000s)										
Probability of Success (PoS):	*30.0%*	*30.0%*	*30.0%*	*30.0%*	*30.0%*	*30.0%*	*30.0%*	*30.0%*	*30.0%*	*30.0%*
Risk-Adjusted Revenue						8,089	16,227	24,413	40,810	65,492
Risk-Adjusted COGS						809	1,623	2,441	4,081	6,549
Risk-Adjusted Gross Profit						7,280	14,604	21,972	36,729	58,943
Gross Margin %						90.0%	90.0%	90.0%	90.0%	90.0%

CYP-004: US Only, Licensed

For CYP-004, we assume Cynata does not build a large US commercial engine itself; instead, it licenses US rights to a partner with the scale to drive broad payer coverage and channel access. Under this structure, Cynata participates through upfront and milestone receipts, ongoing royalties on partner net sales, and supply economics via a manufacturing transfer fee (with associated COGS). Re the manufacturing transfer fee, the originator (Cynata) controls the manufacturing know-how or supply chain (Cymerus™ platform). Charging a transfer fee on top of COGS is standard practice and adds a layer of high-margin revenue that protects the licensor from manufacturing cost overruns.

Our addressable market is intentionally narrower than headline knee OA prevalence. We start with ~15m US adults with knee OA and assume 50% represent moderate disease suitable for a disease-modifying intervention. We then assume 70% of this cohort actively seeks treatment in a given year, producing a target population of ~5.25m patients.

Pricing is assumed at A$6,000 per treatment course, which is conservative versus the value proposition of a true DMOAD that can delay or avoid knee replacement. For simplicity, each patient is assumed to receive one treatment course per annum. Because we model a licensing route, the bulk of end-market economics sit with the partner; Cynata's economics are instead reflected through the royalty and supply stack.

License economics are modelled as follows (US$ terms converted in our model at an AUD/USD of 1.50):

- **Upfront & milestones:** US$20m upfront on filing (2027) and US$50m on FDA approval (2028).
- **Tiered royalties on net sales:** 10% on annual net sales up to US$250m, 12.5% on US$250–500m, and 15% above US$500m.
- **Supply economics:** 5% manufacturing transfer fee, with COGS assumed at 80% of manufacturing transfer revenue. In essence, this models Cynata selling to the partner at a 25% mark-up on the purchase price from FCDI.
- **Milestones excluded from base-case:** sales-based milestones including US$25m at $250m cumulative sales; US$50m at US$400m cumulative sales; and US$75m at US$1bn.

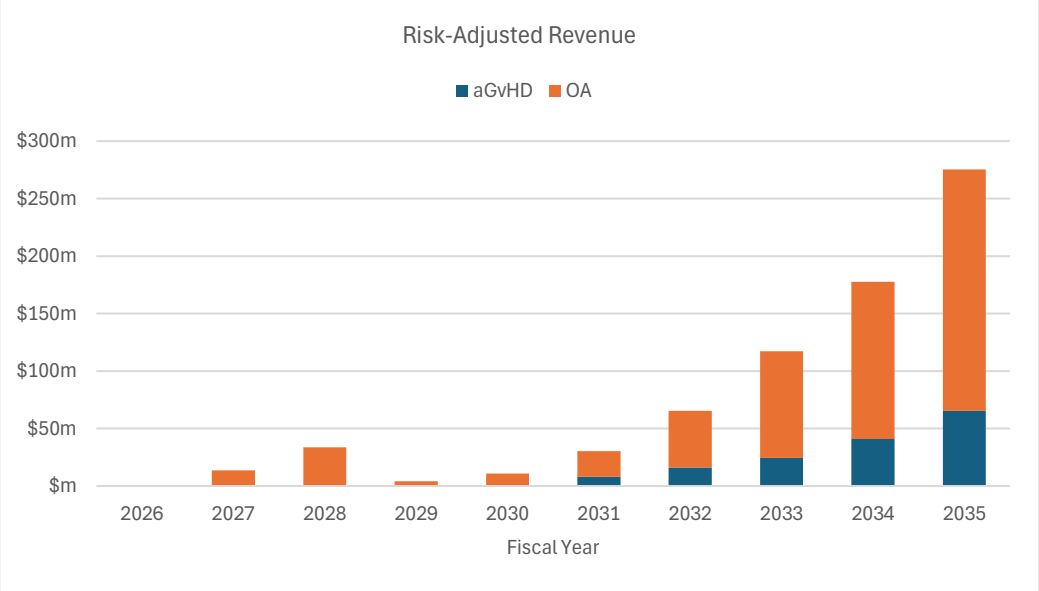
We assume Phase 3 results in 1H CY2026 (Feb-Apr 2026), a US filing in 2027, FDA approval in 2028, and first US commercial sales in 2029. Penetration is staged to reflect the historical difficulty of OA commercialisation (evidence thresholds, payer coverage, and physician behaviour).

We apply a 45% PoS factor to CYP-004 cash flows. This is a risk-adjusted view that starts with a Phase 3→approval industry benchmark of ~58% for chronic, non-oncology indications, but is moderated for the lack of DMOAD precedent, dual clinical/structural endpoints, competitive intensity and reimbursement uncertainty, partially offset by the size and design of the ongoing Phase 3 program.

Figure 10: CYP-004 (Osteoarthritis) – US Market Revenue & Valuation Model (FY26–FY35E). Source: Evolution Capital's estimates.

Fiscal Year	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035
CYP-004 - OSTEOARTHRITIS - US										
Market Size (000s)										
US Osteoarthritis	15,000	15,045	15,090	15,135	15,181	15,226	15,272	15,318	15,364	15,410
Moderate OA rate	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%	50.0%
Seeking treatment rate	70.0%	70.0%	70.0%	70.0%	70.0%	70.0%	70.0%	70.0%	70.0%	70.0%
Target patient population	5,250	5,266	5,282	5,297	5,313	5,329	5,345	5,361	5,377	5,393
Pricing & Penetration										
Price per treatment	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000
Market penetration rate				0.2%	0.5%	1.0%	2.0%	3.5%	5.0%	7.5%
Patients treated				10,595	26,566	53,292	106,904	187,644	268,867	404,510
Revenue & Economics (000s)										
Product Revenue				63,569	159,399	319,753	641,425	1,125,862	1,613,199	2,427,058
Cum Product Revenue				63,569	222,967	542,721	1,184,146	2,310,008	3,923,207	6,350,266
Licensing Payments		30,000	75,000							
Royalties				6,357	15,940	33,719	77,464	150,129	223,230	345,309
Manufacturing Transfer Revenue				3,178	7,970	15,988	32,071	56,293	80,660	121,353
Cost of goods supplied				2,543	6,376	12,790	25,657	45,034	64,528	97,082
Gross Profit		30,000	75,000	6,993	17,534	36,917	83,878	161,388	239,362	369,579
Gross Margin % (ex. Payments)				73.3%	73.3%	74.3%	76.6%	78.2%	78.8%	79.2%
Risk-Adj. Revenue (000s)										
Probability of Success (PoS):	*45.0%*	*45.0%*	*45.0%*	*45.0%*	*45.0%*	*45.0%*	*45.0%*	*45.0%*	*45.0%*	*45.0%*
Risk-Adjusted Revenue		13,500	33,750	4,291	10,759	22,368	49,291	92,890	136,750	209,998
Risk-Adjusted COGS				1,144	2,869	5,756	11,546	20,266	29,038	43,687
Risk-Adjusted Gross Profit		13,500	33,750	3,147	7,890	16,613	37,745	72,625	107,713	166,311
Gross Margin %	0.0%	100.0%	100.0%	73.3%	73.3%	74.3%	76.6%	78.2%	78.8%	79.2%

Figure 11: Forecast Risk-Adjusted Revenue Profile (FY26–FY35E) This chart illustrates our projected revenue composition, highlighting the shift from upfront licensing payments (OA) in the near term to recurring royalties (OA) and direct product sales (aGvHD) in the outer years.



Funding & Corporate

To ensure a fully funded path through the pivotal H1 2026 data readouts (Phase 3 Osteoarthritis and Phase 2 aGvHD), our financial model explicitly incorporates a material strengthening of the balance sheet via two assumed equity capital raises: A$10.0 million in FY26 to bridge the catalyst window, and a further A$15.0 million in FY27 to support regulatory progression. We have modelled these raises occurring at today's prevailing market price (A$0.32) rather than a success-based premium. While equity markets provide the necessary near-term liquidity, we view strategic business development – specifically the out-licensing of the Diabetic Foot Ulcer (DFU) asset for non-dilutive upfront cash, followed by a commercial partnership for the mass-market Osteoarthritis program – as the primary mechanism for mid-term cash security, ultimately replacing the reliance on shareholder funding.

Valuation

Operating Expenses & DCF Framework

We discount cash flows at a 15% all-equity WACC (4.5% risk-free rate; 7% market risk premium; 1.5 beta, reflecting high volatility of cell therapy company undertaking clinical trials), with a 4% terminal growth rate. Tax is modelled at 30%, with losses utilised post-profitability. Working capital assumptions are standardised at 60 days DSO, 90 days DIO, and 45 days DPO.

Operating expense assumptions are designed to reflect a capital-efficient biotech that only scales commercial infrastructure once an asset is approved. We model R&D spend of A$8.0m p.a. across FY26-FY29, stepping down to A$5.0m p.a. from FY30 onward, plus an ongoing R&D reinvestment rate of 10% of revenue post-launch. SG&A is modelled at a A$3.5m base (pre-revenue), then scales to 25% of revenue upon commercialisation, with a 3% annual escalation on the base component.

Regarding capital expenditure, under the turn-key manufacturing supply agreement Cynata has with FCDI, Fujifilm owns the facility and equipment. Cynata does not need to build a factory. As a result, only minor capex is incurred for computers, office fit outs, and perhaps specialised lab equipment for internal R&D. Therefore, Capex is calculated as 1% of risk-adjusted revenue, capped at $2.5m p.a.

DCF Output

On our assumptions, the DCF produces a materially higher intrinsic value than the current market capitalisation, reflecting (i) the scale of the osteoarthritis opportunity and the lucrativeness of even a conservatively estimated licensing deal, and (ii) the high-value, orphan pricing characteristics of acute GvHD under a direct US launch model. Importantly, this is a long-duration valuation – the majority of value is embedded in post-launch cash flows and the terminal value.

TERMINAL VALUE	
Terminal Year FCF	99,750,335
Terminal Growth Rate	4.0%
Terminal Value	943,094,075
PV of Terminal Value	233,118,432
VALUATION SUMMARY	
PV of Forecast FCF	65,568,748
PV of Terminal Value	233,118,432
Enterprise Value	298,687,180
EQUITY VALUE CALCULATION	
Enterprise Value	298,687,180
(+) Cash & Cash Equivalents	5,049,744
(-) Debt	0
(-) Minority Interest	0
Equity Value	303,736,924
PER SHARE ANALYSIS	
Current Shares Outstanding	237,454,400
Options & Warrants	18,518,333
Fully Diluted Shares	255,972,733
Value per Share (Basic)	1.28
Value per Share (Fully Diluted)	1.19
Current Share Price	0.34
Upside / (Downside) - Basic	**276.2%**
Upside / (Downside) - Diluted	**249.0%**

Relative to the prevailing share price of A$0.35 (market cap ~A$89m), our fully diluted valuation of A$1.19/sh implies ~249% upside (basic: ~276%). We would emphasise that the near-term path to closing this gap is catalyst-driven: the upcoming CYP-004 Phase 3 read-out (expected Feb-Apr 2026) and CYP-001 Phase 2 read-out (1H 2026) are the key de-risking events that can meaningfully shift investor-perceived PoS.

Sensitivity

Stress-testing our assumptions reveals the valuation is highly sensitive to the commercial success of the CYP-004 OA program, which serves as the primary driver of upside leverage. It remains relatively insensitive to GvHD pricing and upfront licensing cash.

CYP-001 - ACUTE GVHD (US MARKET ONLY)

Pricing & Economics

COGS as % of Revenue \ Price Per Treatment Course	$300,000	$400,000	$500,000	$600,000	$700,000
6%	1.07	1.14	1.21	1.28	1.34
8%	1.07	1.13	1.20	1.26	1.33
10%	1.06	1.12	1.19	1.25	1.31
12%	1.05	1.11	1.18	1.24	1.30
14%	1.05	1.11	1.17	1.22	1.28

CYP-004 - OSTEOARTHRITIS (US MARKET ONLY)

Pricing & Economics

COGS as % of Manufacturing Transfer Revenue: \ Price Per Treatment Course	$3,600	$4,800	$6,000	$7,200	$8,400
100%	0.76	0.93	1.10	1.27	1.44
90%	0.78	0.96	1.14	1.32	1.50
80%	0.81	1.00	1.19	1.37	1.56
70%	0.84	1.03	1.23	1.43	1.63
60%	0.86	1.07	1.28	1.48	1.69

License Economics

FDA Approval payment \ Up-front Payment	$12m	$16m	$20m	$24m	$28m
$30m	1.15	1.16	1.16	1.17	1.17
$40m	1.16	1.17	1.17	1.18	1.18
$50m	1.18	1.18	1.19	1.19	1.20
$60m	1.19	1.19	1.20	1.20	1.21
$70m	1.20	1.21	1.21	1.22	1.22

Tier 2 Royalty \ Tier 1 Royalty	6%	8%	10%	12%	14%
7.5%	1.11	1.13	1.15	1.17	1.19
10.0%	1.13	1.15	1.17	1.19	1.21
12.5%	1.15	1.17	1.19	1.21	1.22
15.0%	1.17	1.19	1.21	1.23	1.24
17.5%	1.19	1.21	1.23	1.24	1.26

OPERATING EXPENSE ASSUMPTIONS

R&D

Post-Launch R&D as % of Revenue \ Initial Annual R&D	$4.8m	$6.4m	$8.0m	$9.6m	$11.2m
6%	1.30	1.29	1.28	1.26	1.25
8%	1.26	1.24	1.23	1.22	1.21
10%	1.21	1.20	1.19	1.17	1.16
12%	1.17	1.15	1.14	1.13	1.12
14%	1.12	1.11	1.10	1.08	1.07

SG&A

Commercial SG&A \ Base Pre-Revenue SG&A	$2.1m	$2.8m	$3.5m	$4.2m	$4.9m
15%	1.45	1.43	1.42	1.40	1.39
20%	1.33	1.32	1.30	1.29	1.27
25%	1.22	1.20	1.19	1.17	1.16
30%	1.10	1.09	1.07	1.06	1.04
35%	0.98	0.97	0.96	0.94	0.93

COST OF CAPITAL

WACC

Market Risk Premium	Beta 1.19	0.9	1.2	1.5	1.8	2.1
	5%	3.86	2.68	1.98	1.51	1.19
	6%	3.08	2.09	1.51	1.13	0.88
	7%	2.52	1.68	1.19	0.88	0.67
	8%	2.09	1.37	0.95	0.69	0.52
	9%	1.77	1.13	0.78	0.55	0.41

OA Programme

The model is most sensitive to the assumed transfer price/royalty base for CYP-004. A ±20% variance in our base assumption of A$6,000 per treatment course results in a valuation swing of approximately ±15%. Osteoarthritis is a "volume game." Unlike the orphan GvHD indication, the OA market involves millions of patients. Even small changes in the unit price (or royalty rate) are multiplied across a massive patient population, creating exponential leverage in the terminal value. This confirms that CYP-004 is the true "blue sky" asset in the portfolio.

Cost of Capital

Given Cynata's pre-revenue status, the discount rate has a profound mechanical effect on the Net Present Value (NPV). We have used a conservative Beta of 1.5 (implied WACC ~15.0%). If we apply a highly punitive Beta of 1.8 (implied WACC ~17.1%), the valuation contracts to A$0.88/share. Crucially, even in this "distressed" scenario, the valuation remains >2x the current share price, offering a significant margin of safety.

aGvHD Programme

In contrast to OA, the model is remarkably resilient to changes in GvHD pricing. A ±20% shift in the price of CYP-001 (Base: A$500k) moves the needle by only 6-7c per share. GvHD is a low-volume, high-value orphan indication. While it provides high-margin revenue, the absolute number of units sold is capped by the small patient population (~2,000 addressable patients/year). Consequently, CYP-001 acts as a stable "valuation floor" that underpins the company's worth but does not drive the same leverage as the mass-market OA program.

Licensing Terms

Varying the upfront license fee for CYP-004 has virtually no impact on the long-term valuation. In a DCF model spanning 10+ years, a one-off cash payment in Year 1 or 2 is mathematically insignificant compared to the recurring, high-margin royalty streams in the terminal years.

Key Risks

Clinical Risk

The most immediate binary risk to our valuation is the outcome of the Phase 3 SCUlpTOR trial in Osteoarthritis (CYP-004). Pain trials in this indication are notoriously difficult to de-risk due to the "placebo effect," which often leads to high response rates in control arms and obscures the treatment benefit. A failure to meet the primary endpoints for pain and function would fundamentally break the investment thesis, effectively eliminating the majority of the valuation upside derived from the mass-market OA program.

Commercial Risk

Our valuation model heavily relies on the assumption that Cynata will secure a strategic licensing partner to fund late-stage development and commercialization for CYP-004. As a small-cap biotech, the company lacks the balance sheet to independently commercialize a mass-market drug in the US or EU, making a partnership essential for value realization. If Cynata fails to secure a partner or is forced to accept unfavourable terms – such as royalty rates below our 10% base case – the intrinsic value of the asset would be significantly impaired.

Regulatory & Manufacturing Risk

While Cynata's iPSC-based Cymerus™ platform theoretically solves the batch consistency issues that plague donor-derived cell therapies, the FDA has not yet approved an iPSC-derived therapeutic. This places Cynata in the position of a regulatory pioneer, facing the "first-mover disadvantage" of navigating an unproven approval pathway. Additionally, the FDA has historically been cautious with cell therapies, often issuing Complete Response Letters (CRLs) regarding potency assays and manufacturing controls, which could lead to material delays.

Funding & Dilution Risk

Cynata remains a pre-revenue, loss-making enterprise with a finite cash runway relative to its clinical ambitions. Without a licensing deal that provides substantial non-dilutive capital (upfront payments), the company will likely be required to raise equity capital to fund ongoing operations. If such capital is raised at a discount to the prevailing share price, it would permanently dilute existing shareholders and lower our per-share fair value target.

Reimbursement & Pricing Risk

The commercial success of CYP-004 is contingent upon US payers (insurers and Medicare) agreeing to reimburse the therapy at a premium price point (modelled at ~A$6,000 per course). The osteoarthritis market is currently dominated by low-cost generics and palliative treatments, meaning payers may resist covering a novel cell therapy without robust evidence of disease modification (cartilage regeneration). If the product is relegated to a "last-line" salvage therapy, peak market penetration would likely fall well below our conservative estimates.

Competitive Risk

The landscape for disease-modifying osteoarthritis drugs (DMOADs) is highly competitive, with major pharmaceutical players like Merck KGaA and Biosplice advancing their own late-stage candidates. If a competitor reaches the market first with a more effective or lower-cost alternative, Cynata could face significant barriers to adoption and eroded market share. Furthermore, the broader regenerative medicine sector continues to evolve, and new modalities could displace cell therapy as the standard of care for joint preservation.

Appendix

Major Shareholders

Ranking	Shareholder	Last Update Shareholding	31/12/2025 Percentage Held
1	Bioscience Managers Pty Ltd	23,588,040	9.93
2	Fidelity International Ltd	20,967,806	8.83
3	Acuity Capital Investment Management Pty Ltd	11,500,000	4.84
4	FUJIFILM Holdings Corporation	8,088,403	3.41
5	Craig Darby	4,213,853	1.77
6	Kenneth Wilson	3,549,905	1.49
7	AGATI PTY LTD	2,803,862	1.18
8	Ross MacDonald	2,000,000	0.84
9	Aily Lamb	1,950,000	0.82
10	David Prodrick	1,700,138	0.72
11	Patrick Walsh	1,594,610	0.67
12	Malcolm Washer	1,559,534	0.66
13	Kilian Kelly	797,428	0.34
14	Miroslawa Rej	771,518	0.32
15	Pawel Rej	771,518	0.32
16	Paul Wotton	585,076	0.25
17	Geoffrey Edward Brooke	312,898	0.13
18	Janine Rolfe	255,167	0.11
19	Darryl Maher	116,666	0.05

Board & Management

Dr Kilian Kelly – CEO & MD

Dr Kilian Kelly has over 20 years' experience in biopharmaceutical research and development, including almost 15 years focussed on the development of mesenchymal stem cell (MSC) based therapies. He joined Cynata in March 2014, initially as Vice President, Product Development, then Chief Operating Officer from May 2019, and since July 2023 has been CEO & MD. At Cynata, he has overseen all stages of the development of the Cymerus™ induced pluripotent stem cell (iPSC)-derived MSC technology, including the first completed clinical trial of any iPSC-derived product worldwide.

Dr Kelly previously held positions at Biota Pharmaceuticals, Mesoblast Limited, Kendle International, Amgen and AstraZeneca. He holds a Masters in Pharmacy degree from the Robert Gordon University, Aberdeen, a PhD in Pharmaceutical Sciences from Strathclyde University, Glasgow, and he is a Graduate of the Australian Institute of Company Directors (AICD), Melbourne. He is a member of the International Society for Cell and Gene Therapy (ISCT), the International Society for Stem Cell Research (ISSCR), the Royal Pharmaceutical Society and the AICD. Dr Kelly also serves on the ISCT Asia-Pacific Industry Committee, the ISSCR Best Practices Working Group for the Development of PSC-Derived Therapies and the Industry Interface Committee of the Center for Commercialisation of Regenerative Medicine (CCRM) Australia.

Dr Geoff Brooke – Independent Non-Executive Chairman

Dr Brooke joined the Cynata Board in May 2019 as Non-Executive Director, and was subsequently appointed Chair in August 2020. He has more than 30 years' venture capital experience, including co-founding GBS Venture Partners in 1996 and serving as President of Medvest Inc., a US-based early-stage venture capital group he founded with Johnson & Johnson. Dr Brooke's experience includes company formation and acquisitions, as well as public listings on the NYSE, NASDAQ and ASX. Additionally, from 2009 until 2015, he was an Independent Director of the Victoria Workcover Authority. Dr

Brooke currently serves on the Boards of two other public companies, as Chair of Actinogen Medical Limited (ASX: ACW), and Non-Executive Director of Acrux Limited (ASX:ACR). He also works with a number of other entities, including as a consultant to BioScience Managers. Dr Brooke holds a Bachelor of Medicine/Surgery from Melbourne University and a Masters of Business Administration from IMEDE (now IMD) in Switzerland.

Janine Rolfe – Independent Director

Ms Rolfe joined the Cynata Board in September 2022 and brings over two decades' of legal, governance and management experience across multiple sectors, including highly regulated industries and complex global businesses. Before recently transitioning as a professional non-executive director, Janine's last executive position was General Counsel & Company Secretary of Link Administration Holdings Limited (Link Group). Prior to that, Janine founded Company Matters Pty Limited and worked both in-house (Qantas Airways Limited) and in private practice (Mallesons Stephen Jaques, now King & Wood Mallesons), across a diverse and distinguished career. Janine is an Independent Non-Executive Director of Cloudwerx Holdings Pty Limited and a Board Member of the Independent Liquor & Gaming Authority, NSW Government. Janine has held a number of Board positions in the past including with Property Exchange Australia Limited (PEXA), the Qantas Foundation Trustee, and Bothar Boring Pty Limited. Janine is a member of the Australian Institute of Company Directors (AICD) and received a Bachelor of Economics and Bachelor of Laws (Honours) from the University of Sydney.

Dr Paul Wotton – Independent Director

Dr. Wotton joined Cynata's Board of Directors in June, 2016. He is Executive Chairman of the Biotech LaunchPad at Rice University, Houston. He was President and CEO of Obsidian Therapeutics, Founding CEO of Sigilon Therapeutics (Acquired by Lilly) and President and CEO Ocata Therapeutics, Inc. (NASDAQ: OCAT) which was acquired by Astellas in 2016. Prior to Ocata, Dr. Wotton had served as President and CEO of Antares Pharma Inc. (NASDAQ: ATRS). Prior to joining Antares, Dr. Wotton was the CEO of Topigen Pharmaceuticals. Earlier in his career he held senior level executive positions at SkyePharma plc, Eurand International BV, Penwest Pharmaceuticals, Abbott Laboratories and Merck, Sharp and Dohme. Dr. Wotton is a member of the board of Vericel Corporation (NASDAQ:VCEL), Chairman of Dimension Inx., and Chairman of Kytopen Inc. Dr. Wotton received his Ph.D. in pharmaceutical sciences from the University of Nottingham. In 2014 he was named EY Entrepreneur of the Year (NJ) in Life Sciences.

Dr Darryl Maher – Independent Director

Dr Maher joined the Cynata Board in June 2020 following over 20 years in the pharmaceutical industry as a senior R&D Executive at CSL Limited. His most recent position was Vice President of R&D and Medical Affairs at CSL Behring Australia where he was responsible for the development of multiple successful drug products from initiation through clinical development and ultimately to commercialisation. Dr Maher undertook medical training, qualified as a specialist haematologist and completed a PhD before commencing his career in the pharmaceutical industry. He was a former President of the Australian Pharmaceutical Physicians Association and a director of Vaccine Solutions. He earned his Bachelor of Medicine/Surgery from the University of Melbourne, Australia and undertook his PhD at The Walter and Eliza Hall Institute of Medical Research. He is a retired Fellow of both the Royal Australian College of Physicians and the Royal College of Pathologists of Australia.

Evolution Capital Ratings System

Recommendation Structure	• **Buy:** The stock is expected to generate a total return of >10% over a 12-month horizon. For stocks classified as 'Speculative', a total return of >30% is expected. • **Hold:** The stock is expected to generate a total return between -10% and +10% over a 12-month horizon. • **Sell:** The stock is expected to generate a total return of <-10% over a 12-month horizon.
Risk Qualifier	• **Speculative ('Spec'):** This qualifier is applied to stocks that bear significantly above-average risk. These can be pre-cash flow companies with nil or prospective operations, companies with only forecast cash flows, and/or those with a stressed balance sheet. Investments in these stocks may carry a high level of capital risk and the potential for material loss.
Other Ratings	• **Under Review (UR):** The rating and price target have been temporarily suppressed due to market events or other short-term reasons to allow the analyst to more fully consider their view. • **Suspended (S):** Coverage of the stock has been suspended due to market events or other reasons that make coverage impracticable. The previous rating and price target should no longer be relied upon. • **Not Covered (NC):** Evolution Capital does not cover this company and provides no investment view.

Expected total return represents the upside or downside differential between the current share price and the price target, plus the expected next 12-month dividend yield for the company. Price targets are based on a 12-month time frame.

Disclaimer & Disclosures

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