ShawandPartners

Cynata Therapeutics (CYP)

Rating: Buy | Risk: High | Price Target: $1.20

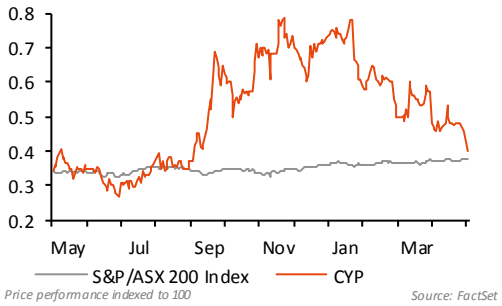
Solving the Stem Cell Production Problem. Initiation of Coverage with a BUY and $1.20 TP

Key Information	
Current Price ($ps)	0.42
12m Target Price ($ps)	1.20
52 Week Range ($ps)	0.27 - 0.79
Target Price Upside (%)	185.7%
TSR (%)	185.7%
Reporting Currency	AUD
Market Cap ($m)	37.8
Sector	Health Care
Avg Daily Volume (m)	0.1
ASX 200 Weight (%)	0%

Fundamentals				
YE 30 Jun (AUD)	FY16A	FY17E	FY18E	FY19E
Sales ($m)	0.1	0.0	20.6	21.0
NPAT ($m)	(4.9)	(3.8)	14.4	15.2
EPS (cps)	(6.8)	(4.8)	16.0	16.9
EPS Growth (%)	(12.7%)	29.5%	433.6%	5.6%
DPS (cps) (AUD)	0.0	0.0	0.0	0.0
Franking (%)	0%	0%	0%	0%

Ratios				
YE 30 Jun	FY16A	FY17E	FY18E	FY19E
P/E (x)	(4.6)	(8.8)	2.6	2.5
EV/EBITDA (x)	(3.7)	(10.6)	2.6	1.5
Div Yield (%)	0.0%	0.0%	0.0%	0.0%
Payout Ratio (%)	0.0%	0.0%	0.0%	0.0%

Price Performance				
YE 30 Jun	1 Mth	2 Mth	3 Mth	1 Yr
Relative (%)	(9.0%)	(19.1%)	(35.8%)	12.4%
Absolute (%)	(7.7%)	(15.2%)	(30.0%)	23.5%
Benchmark (%)	1.3%	3.9%	5.8%	11.1%



Price performance indexed to 100 *Source: FactSet*

Major Shareholders	
FUJIFILM Corporation	8.9%
Phillip Capital	4.0%
Slukvin, Igor	2.6%
Dixon, Ian	2.5%
Celtic Capital	2.4%

Disclaimer

Shaw and Partners acted for CYP in a corporate capacity within the past 12 months for which it received a fee. See the back page of this report for the full disclaimer.

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Event

Shaw and Partners initiates coverage of Cynata Therapeutics (CYP) with a BUY rating and a $1.20 target price.

Highlights

- **A unique production method.** CYP's Cymerus™ technology is the only likely viable production method for generating medicinal mesenchymal stem cells (MSC) for large scale clinical applications. We are not aware of any competing technology under development that is a scalable method of growing MSCs which don't lose potency as successive generations of cells are produced and do not rely on multiple cell donors. Trial data and third party validation of CYP's MSCs and the opportunity for them continues to build. Fujifilm has taken an 8.9% equity position in CYP and optioned the global rights for use in graft-versus-host disease (GvHD). apceth Biopharma GmbH has conducted due diligence on the production method and found the characteristics of the cells produced using Cymerus were highly satisfactory. The UK regulator has approved a first trial in humans validating safety and manufacturing procedure. CYPs pre-clinical trials have shown the MSCs produced performed very favourably and independent studies have provided further verification.

- **MSCs are the most prospective of the different stem cells in development, but there is a largely unrecognised production problem.** The MSC opportunity, to repair damaged or diseased tissues such as heart, bone and cartilage, and or, treat diseases such as diabetes and heart disease is the biggest and most prospective field of stem cell endeavour. More than 600 trials of MSCs are underway globally reflecting their acceptance and wide utility. Mesoblast Ltd. (MSB:ASX, $1.2bn) and TiGenix N.V. (TIG:BE, $200mn), are examples of some of the global companies investing billions developing MSC therapeutics. Despite this investment there remains a key problem - potent MSCs cannot be produced consistently at commercial scale using first generation production methods. This flaw in the business model of MSC companies is not well recognised by investors, but CYP provides a unique solution which may be required by all MSC based therapeutics targeting indications with large patient numbers.

- **Final validation of the safety and efficacy of CYP's MSCs is likely with its GvHD trial.** The key risk, that we expect to be substantially overcome in 2017, is showing that CYP's MSCs are at least as safe and effective as MSCs manufactured using first generation processes. Positive results from CYP's GvHD trial in 2017 should provide the confirmatory evidence. This will open the Cymerus production method to commercial uses for multiple indications across therapeutic markets worth billions. Other risks we consider to be less significant include: i) delays in clinical trial enrolment; ii) an inability to negotiate additional strategic partnerships; and iii) poor results from clinical trials.

Recommendation - BUY

The data around CYP's MSCs - both its own and that developed by external groups - and the partnering deals it is putting in place increasingly point towards validation and industry acceptance of its process for producing MSCs. CYP still needs to show that its MSCs are at least therapeutically equivalent to harvested cells, however it has made significant steps forward towards being the only likely viable MSC solution for large scale clinical applications. Thanks to Japan's relatively quick approval framework for stem cell therapeutics, time to market (~2020) is also potentially quite soon. In addition the company has sufficient cash to meet major milestones in the coming 18-24 months. We believe these factors aren't recognised by CYP's market capitalisation of $38m. Our valuation, based on a discounted cash flow, determines a value of A$1.20 per share which values the company well below recent relevant acquisition prices. BUY

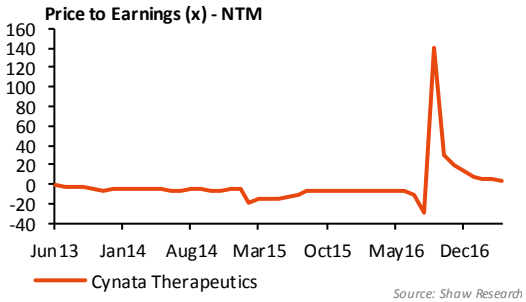
Cynata Therapeutics
Health Care
Pharmaceuticals, Biotechnology & Life Sciences
FactSet: CYP-AU / Bloomberg: CYP AU

Key Items	Data
Recommendation	BUY
Risk	HIGH
Price ($ps)	0.42
Target Price ($ps)	1.20
52 Week Range ($ps)	0.27 - 0.79
Shares on Issue (m)	90.1
Market Cap ($m)	37.8
Enterprise Value ($m)	38.2
TSR (%)	185.7%

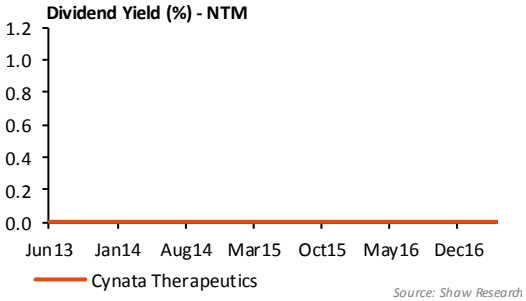
Valuation NPV	Data
Beta	1.85
Cost of Equity (%)	14.3%
Cost of Debt (net) (%)	7.5%
Risk Free Rate (%)	5.0%
Terminal Growth (%)	3.0%
WACC (%)	18.9%

Company Description

Cynata Therapeutics Ltd. is an stem cell and regenerative medicine company, which develops a therapeutic stem cell platform technology, Cymerus™, using discoveries made at the University of Wisconsin-Madison. The company was founded on March 12, 2003 and is headquartered in Armadale, Australia.



Source: Shaw Research



Source: Shaw Research

Financial Year End: 30 June

Investment Summary (AUD)	FY15A	FY16A	FY17E	FY18E	FY19E
EPS (Reported) (cps)	**(6.0)**	**(6.8)**	**(4.8)**	**16.0**	**16.9**
EPS (Underlying) (cps)	**(6.0)**	**(6.8)**	**(4.8)**	**16.0**	**16.9**
EPS (Underlying) Growth (%)	49.8%	(12.7%)	29.5%	433.6%	5.6%
PE (Underlying) (x)	**(15.4)**	**(4.6)**	**(8.8)**	**2.6**	**2.5**
EV / EBIT (x)	**(16.5)**	**(3.5)**	**(10.0)**	**2.8**	**1.5**
EV / EBITDA (x)	**(18.7)**	**(3.7)**	**(10.6)**	**2.6**	**1.5**
DPS (cps) (AUD)	0.0	0.0	0.0	0.0	0.0
Dividend Yield (%)	0.0%	0.0%	0.0%	0.0%	0.0%
Franking (%)	0%	0%	0%	0%	0%
Payout Ratio (%)	0.0%	0.0%	0.0%	0.0%	0.0%
Free Cash Flow Yield (%)	(3.9%)	(19.2%)	(13.9%)	(3.9%)	46.5%

Profit and Loss (AUD) (m)	FY15A	FY16A	FY17E	FY18E	FY19E
Sales	0.0	0.1	0.0	20.6	21.0
Sales Growth (%)			*(79.7%)*	*81,087.5%*	*1.8%*
Other Operating Income	0.3	1.0	1.7	0.0	0.0
EBITDA	**(3.4)**	**(4.8)**	**(3.6)**	**15.0**	**15.2**
EBITDA Margin (%)	*nm*	*nm*	*nm*	*72.9%*	*72.3%*
Depreciation & Amortisation	(0.4)	(0.3)	(0.2)	(0.7)	0.0
EBIT	**(3.8)**	**(5.1)**	**(3.8)**	**14.4**	**15.2**
EBIT Margin (%)	*nm*	*nm*	*nm*	*69.8%*	*72.3%*
Net Interest	0.1	0.1	0.0	0.0	0.0
Pretax Profit	(3.7)	(4.9)	(3.8)	14.4	15.2
Tax	0.0	0.0	0.0	0.0	0.0
Tax Rate (%)	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*
Minorities	0.0	0.0	0.0	0.0	0.0
NPAT Underlying	**(3.7)**	**(4.9)**	**(3.8)**	**14.4**	**15.2**
Significant Items	0.0	0.0	0.0	0.0	0.0
NPAT Reported	**(3.7)**	**(4.9)**	**(3.8)**	**14.4**	**15.2**

Cashflow (AUD) (m)	FY15A	FY16A	FY17E	FY18E	FY19E
EBIT	(3.8)	(5.1)	(3.8)	14.4	15.2
Tax Paid	0.0	0.0	0.0	0.0	0.0
Net Interest	0.1	0.1	0.0	0.0	0.0
Other	1.1	0.6	(1.5)	(15.9)	2.4
Operating Cashflow	**(2.6)**	**(4.3)**	**(5.3)**	**(1.5)**	**17.6**
Capex	0.0	0.0	0.0	0.0	0.0
Acquisitions and Investments	0.0	0.0	0.0	0.0	0.0
Disposal of Fixed Assets/Investments	0.0	0.0	0.0	0.0	0.0
Other	0.0	0.0	0.0	0.0	0.0
Investing Cashflow	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Free Cashflow	**(2.6)**	**(4.3)**	**(5.3)**	**(1.5)**	**17.6**
Equity Raised / Bought Back	2.2	5.0	0.0	0.0	0.0
Dividends Paid	0.0	0.0	0.0	0.0	0.0
Change in Debt	0.0	0.0	0.0	0.0	0.0
Other	0.0	(0.5)	0.0	0.0	0.0
Financing Cashflow	**2.2**	**4.5**	**0.0**	**0.0**	**0.0**
Net Change in Cash	**(0.4)**	**0.2**	**(5.2)**	**(1.5)**	**17.6**

Balance Sheet (AUD) (m)	FY15A	FY16A	FY17E	FY18E	FY19E
Cash	4.7	4.9	(0.4)	(1.8)	15.7
Accounts Receivable	0.0	0.1	0.0	16.4	14.0
Inventory	0.0	0.0	0.0	0.0	0.0
Other Current Assets	0.0	0.0	0.0	0.0	0.0
PPE	0.0	0.0			
Goodwill & Intangibles	4.4	4.1	3.9	3.2	3.2
Investments	0.0	0.0	0.0	0.0	0.0
Other Non Current Assets	0.0	0.0			
Total Assets	**9.1**	**9.0**			
Accounts Payable	0.3	0.4	0.3	0.3	0.3
Short Term Debt	0.0	0.0	0.0	0.0	0.0
Long Term Debt	0.0	0.0	0.0	0.0	0.0
Income Taxes Payable	0.0	0.0	0.0	0.0	0.0
Other	0.0	0.1	0.0	0.0	0.0
Total Liabilities	**0.4**	**0.5**	**0.3**	**0.3**	**0.3**

Ratios	FY15A	FY16A	FY17E	FY18E	FY19E
ROE (%)	(35.1%)	(53.8%)			
Net Debt / Book Equity (x)	(0.5)	(0.6)			
Net Debt / EBITDA (x)	1.4	1.0	(0.1)	0.1	(1.0)

Investment view - BUY

Since CYP acquired its Cymerus™ technology in 2013, significant clinical and pre-clinical developments - both its own and by external groups - have propelled the technology forward as the only likely viable MSC production technology for large scale clinical applications.

Our confidence that CYP's technology will be disruptive to the global stem cell market, estimated to be worth US$100b p.a. in eight years (see page 6), is based on:

1. 600 + ongoing trials of stem cells and more specifically 493 trials of MSCs which have concluded MSC are efficacious in a wide range of diseases and conditions,
2. The substantial industry evidence now available highlighting loss of potency from traditional MSC manufacturing methods once cells have been expanded beyond thirteen population doublings (see page 5), which represents a production problem that is preventing stem cells realising their commercial potential.
3. CYP's pre-clinical program in vitro and in animal models has demonstrated the sterility, purity, potency, stability, safety and indicative efficacy of Cymerus™ MSCs.
4. In 2016 apceth[1] and Regience[2], both conducted independent due diligence on CYP's MSCs and concluded that the key characteristics of cells produced using Cymerus, was highly satisfactory,
5. In 2017 Fujifilm, one of the largest global investors in stem cell technology, invested $US3mn in CYP at a 35% premium to CYP's 6 month VWAP and partnered CYP's CYP-001 MSC product for prevention and treatment of GvHD worldwide,
6. The UK Medicines and Healthcare products Regulatory Agency trial approval validates CYP's manufacturing and safety. The trial approval provides validation from one of the most highly regarded regulatory authorities in the world that CYP's manufacturing process and preclinical development programs have established what it considers to be a product safe enough to be trialled in humans, and,
7. Waisman Biomanufacturing, CYP's contract manufacturer, has established indicative efficacy using a range of assays[3].

Safety and efficacy is key

The one outstanding point that regulators require CYP to demonstrate is that its Cymerus produced MSCs, when administered into humans, show safety and efficacy and that benefits clearly outweigh any remaining small risks, which is the way regulators typically consider applications for follow on trials.

This is the key expected outcome from CYP's GvHD trial. Risks associated with the trial are the usual risks associated with moving into human trials including: i) delays in clinical trial enrolment; ii); poor results from clinical studies with CYP's candidates, and iii) inability of CYP to negotiate additional strategic partnerships, and iv) emerging evidence that possibly not all MSCs are the same. However, as outlined above and in more detail through this report CYP's existing data pack is very supportive of a positive result.

Positive GvHD data will be transformational for the entire stem cell industry

A substantial amount of research and clinical success has already been achieved with therapies based on MSC derived from donor derived tissues such as bone marrow and adipose tissue, so positive data will enable: i) other parties to confidently use CYP's MSCs in developing their own therapies. This includes Fujifilm which will take forward CYP's GvHD program, and ii) CYP to develop its own programs to commercialise.

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[1] apceth GMbh co, a German biotech owned by the Struengman brothers who sold generic pharmaceutical company Hexal to Novartis for US$7.5Bn, entered into a licensing option with CYP in 2016 for the exclusive use of Cymerus in the treatment of cancer and certain other targets. In 2017 apceth withdrew from developing cancer therapeutics; however it did announce that its trials of Cymerus MSCs showed the rate of growth and health of cells was highly satisfactory and that interest in the other targets remained.

[2] Regience, a Japanese company developing MSC therapies with Fuji Micra, was negotiating to license Cymerus for use in Japan, South Korea and other markets in Asia across a wide group of indications. However CYP chose Fujifilm (the owner of Cellular Dynamics a manufacturer of induced pluripotent stem cells) as its GvHD partner.

[3] A US firm, Waisman Biomanufacturing has established process development, scale-up and clinical-grade production of CYPs MSCs. Scale-up has demonstrated indicative commercial viability.

The key risks associated with CYP will then be different to a typical biotech because: i) Cymerus will fore mostly be a production technology, as such it won't suffer from discovery risk it will be more akin to repurposing risk, and 2) because of Fujifilm's interest in CYP and other stem cell technologies and companies, takeover by Fujifilm at a low valuation (see page 7) will become a key concern.

Commersialisation (thanks Japan) could be quite soon

With changes to the Japanese approval process for stem cell therapeutics[4] we expect the opportunity to have a commercial product by 2020 and partnering of other programs by 2018 is realistic.

Valuation

For valuation purposes we have used a DCF methodology and looked at recent acquisitions, neither of which are completely adequate, primarily because the utility of Cymerus is so wide that it is not fully captured by our DCF valuation or in the opportunities before the acquisitions tabled. However, both DCF and recent acquisitions suggest significantly more value than is reflected in CYPs current capitalisation.

Relevant recent acquisitions, predominantly in Japan[4], include:

i) In 20015 Fujifilm paid US$307m for Cellular Dynamics International (CDI), a manufacturer of induced pluripotent stem cells (iPSCs) which we believe has significantly less commercial potential than CYP. Notably CYP sourced its iPSC's from CDI and the two companies were spun out of the same institution; and,

ii) In November 2015 Astellas (Japan) acquired Ocata Inc for USD380m which we believe has limited therapeutic applicability primarily in ophthalmic applications.

We believe CYP should have a value in excess of CDI and Ocata once it has confirmation of the effectiveness of its MSCs in humans suggesting a value of greater $3.00 ps.

Prior to this confirmation a risked adjusted DCF is the way we have valued CYP. We have focused on the three indications we expect to be progressed relatively quickly based on the strong body of third party evidence supporting the potential for MSCs in these indications. They include; GvHD, Asthma, and Crohn's Disease all of which could be generating partnering payments over the next couple of years. This does however, leave a large number of big indications such as oncology, heart disease and diabetes outside our valuation, which represents risk to the upside.

Figure 1: DCF assumptions

Tax Rate	30%	Shares on issue - dil	90.1
Risk Free Rate	5.0%	Share price	A$0.42
Debt Premium	2.5%	Market Value of Equity	A$38m
After-tax Market Risk Premium	5.0%	Fair Value of Net Debt	-A$5m
Equity Beta	1.9	Required Equity Return	14.3%
Adj. Terminal Nominal Growth	3.0%	Net Debt/Enterprise Value	-51.2%

Source: Shaw and Partners

Our un-risked DCF value for these three programs is $12.00 ps. This un-risked valuation sheds light on the prize at the end of successfully commercializing the three programs identified above. Risk adjusting this valuation, based on Biostrategic's risk data, suggests a current valuation of $1.20. We will re-weight the risk adjustment upon successful completion of the Phase I GvHD clinical trial and add indications to our forecasts as programs or partnering deals are announced. At that point we believe the upside risk to CYPs share price will be multiples of its current share price and the down side risk becomes negligible.

[4] Since Japan put in place a favourable regulatory framework in 2014, easing approval rules for stem cell development, Japan has become one of the fastest places in the world to get a regenerative medical product to market and regenerative medicine acquisitions have accelerated.

Not all stem cells are equal!

There are a number of different types of stem cells, each of which have different characteristics that are very significant to their commercial potential. The main difference is whether they are undifferentiated stem cells (cells which can still turn into any other type of stem cell) such as Embryonic Stem Cells (ESC), more mature partially differentiated stem cells such as MSCs or later stage (ie mature) differentiated cells such as somatic cells which are essentially body cells, such as skin cells, that don't differentiate further.

Somatic cells have markers on them which enable a host's immune systems to identify them as foreign and kill them. Consequently they cannot be used in allogenic[8] applications unless the donor and recipient are matched. Ethical issues around the use of ESCs in therapeutics have hampered their use. This has left MSCs and particularly iPS derived MSCs (see page 6) as the key focus for potential therapeutic use.

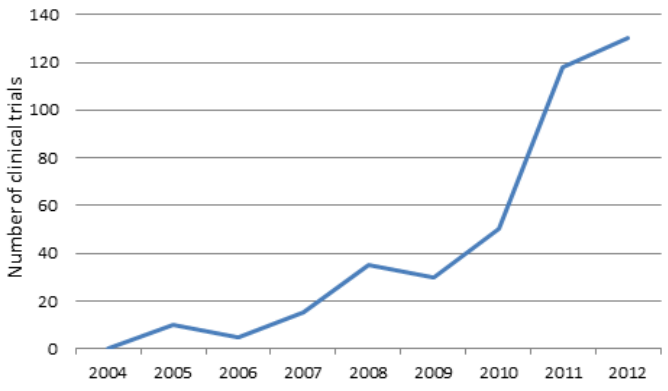
MSC generate growth factors that have the potential to treat multiple conditions.

In the early 2000's stem cell companies and research organisations flocked to extract donor MSCs typically from bone marrow because of their ability to: i) replicate themselves; one cell becomes two, two become four, four become eight, indefinitely, ii) generate Somatic cells[5] including: cardiomyocytes (heart cells), adipocytes (fat cells), osteocytes (bone cells), chondrocytes (cartilage cells), and smooth muscle cells, and iii) more significant to the therapeutic setting MSCs also produce a large amount and number of different growth factors (e.g. cytokines) that perform multiple functions associated with tissue regeneration, inflammation management and immunomodulation. Many of these factors are critical mediators in angiogenesis and the prevention of cell apoptosis, such as vascular endothelial growth factor (VEGF), insulin-like growth factor 1 (IGF-1), fibroblast and hepatocyte growth factor (IL-6 , CCL-26).

MSC research makes up the bulk of the world wide stem cell research effort accounting for ~40% of stem cell IND submissions to the FDA between 2006 and 2013. 600+ clinical trials have been completed or are currently underway investigating not only treating symptoms, but also addressing underlying causes of disease. MSCs have shown efficacy in clinical trials up to and including phase 3.

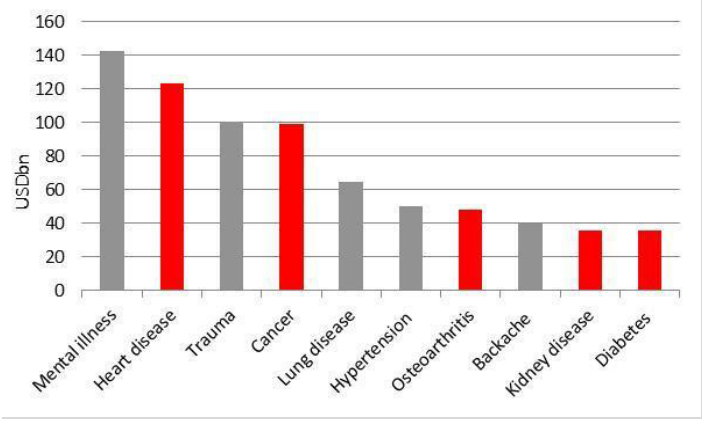
Key diseases that MSCs are expected to have a role in treating include: Stroke, heart disease, diabetes, lupus, Crohn's disease, osteoarthritis, MS, and cancer which are currently generating sales of more than $340b pa from drugs that are often ineffective.

Figure 2: Stem cell trials



Source: iPScell.com, Shaw and Partners

Figure 3: Top 10 diseases and US$bn value



Source: Forbes, Shaw and Partners

[5] In therapeutic uses the MSCs being developed by CYP and others are not turning into somatic cells, rather once administered into a human body they are generating a cocktail of cytokines (growth factors), specific to different situations and controlled by the MSC, which in turn attract immune cells to a disease site and help the body to generate its own somatic cells. – If MSC differentiated into a somatic cell (eg chondrocyte) they would develop markers on the cell that show it to be foreign and the immune system would destroy it. MSCs don't have these markers.

The MSC industry's flaw - production and potency problems

MSCs have worked well in early trials and an autologous industry has gained some commercial traction, however there is now solid evidence (corporate disclosures[6], academic literature[7] and our conversations with numerous independent academics and executives involved in MSC development) that harvested MSCs lose potency as they are expanded. Without the capability to produce potent cells at scale the entire allogenic industry does not have a commercial path forward.

Potency is a problem facing the stem cell industry which iPS derived MSCs appear to have the unique capability to solve

The loss of potency associated with first generation methods of manufacturing therapeutic MSC products is a flaw in the business model of all MSC based companies. It is an issue for: 1) later stage MSC clinical trials which are not producing results equivalent to early stage trials because of the increased number of cells required (typically hundreds of millions of cells are needed for each treatment), 2) regulators which have indicated that follow up donor cells, which are not necessarily identical, will require their own testing and approval, and therefore 3) costs for treating any disease with large populations.

iPS cells – a break through that delivered part of the solution

In 2007 scientists first manufactured what they called Induced Pluripotent stem cells (iPS cells) which have subsequently been shown to have effectively the same properties and capabilities as ESC, and the ability to differentiate into all cell types found in the body without losing potency. The science of reprogramming adult somatic cells using re-programming genes is complex, but now well established.

With substantial improvements over the original process, multiple different technologies for generating iPS cells now exist. There is relatively little risk in this technology, it is well understood and increasingly widely used for research and drug development, but iPS cells themselves are not used therapeutically because they are undifferentiated. Rather, they serve as an essentially unlimited resource for manufacturing the eventual differentiated therapeutic product, such as an MSC in CYP's case.

CYP's patented Cymerus™ technology is the only technology for deriving MSCs from iPS cells and the only commercially scalable technology we are aware of

There are a number of autologous processes for generating differentiated cells from iPS cells, however it is very clear that autologous cells are not going to provide a cost effective commercial solution for large indications[8,9].

CYP has the only known viable allogenic solution

CYP has licensed the key patents[10] to make MSCs from the iPS cells. CYP's Cymerus is consequently the only commercially scalable technology that can make off the shelf MSCs from iPS cells that can be used for therapeutic purposes.

The one outstanding point that regulators require CYP to demonstrate is that it's Cymerus produced MSCs when administered into humans are safe and effective and that benefits clearly outweigh any remaining small risks, which is the way regulators typically consider applications for follow on trials.

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[6] Kimbrel, Lanza, (Ocata Therapeutics) Mesenchymal Stem Cell Population Derived from Human Pluripotent Stem Cells Displays Potent Immunomodulatory and Therapeutic Properties, March 20, 2014 'MSCs are being tested in a wide range of human diseases; however, loss of potency and inconsistent quality severely limit their use.'; The Alliance for Regenerative Medicine survey of Big Pharma found "the most significant challenge is product consistency and standards, the second most significant challenge is manufacturing/scale up."

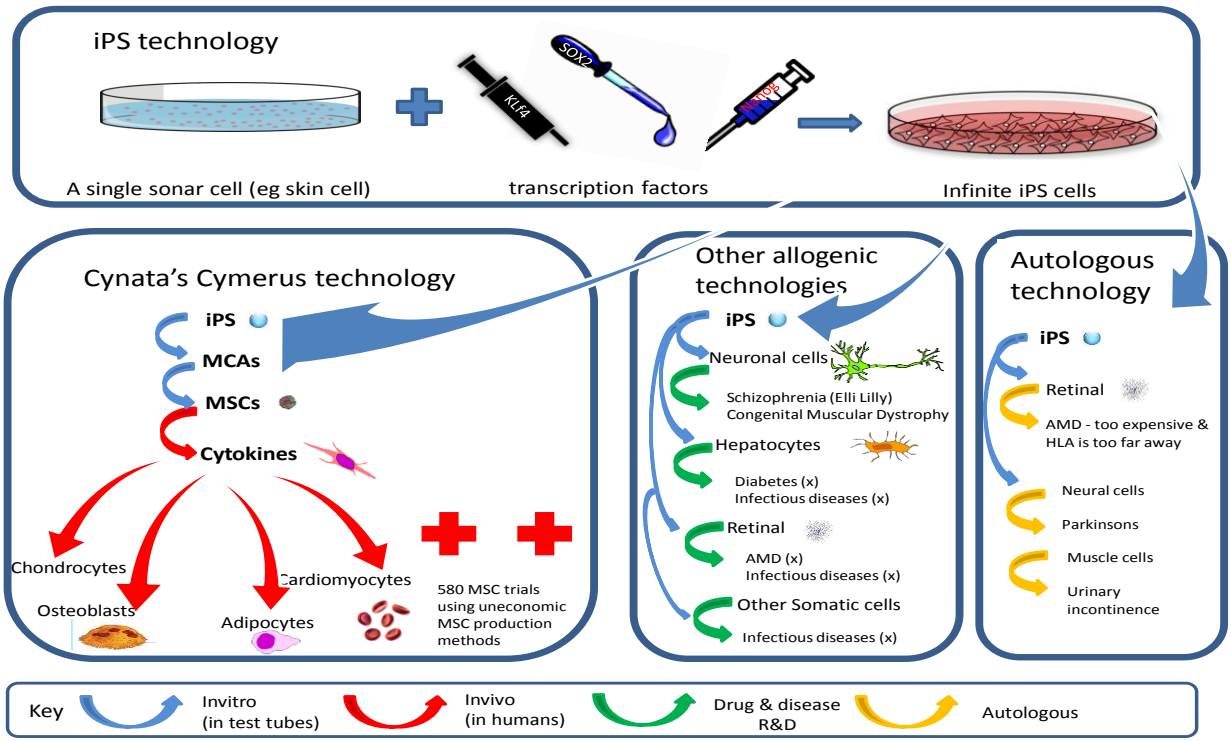
[7] Jacques Galipeau, ISCT, Why Prochymal failed. Cytotherapy, 2013; LeBlanc etal, Expansion of MSCs.

[8] Autologous cells are cells derived from the recipient. Allogenic cells are cells derived from a donor which enables scalable manufacturing of an "off-the-shelf" product.

[9] There are a number of groups using technologies downstream of iPS to generate somatic cells from autologous procedures. None are currently in the clinic or have resulted in approved products. Riken was the most advanced, it did a single Retinal transplant but halted its trial for unspecified reasons, and later stated autologous iPS is not a commercial proposition and that it now hopes to progress from autologous iPS cells to allogeneic iPS cells. Somatic cells derived from allogenic iPS cells used for therapeutic purposes will have to be matched to the recipient because they carry markers (MHC class 2 antigens) that attract the hosts immune system. Notably MSCs do not carry these markers.

[10] CYP's licensed patents cover MSCs, MCAs and other similar cells to MSCs giving it broad coverage across the field – which is significant given there is a debate over what constitutes a MSC. The patents are licensed from The Wisconsin Alumni Research Foundation (WARF), which holds the rights to all the intellectual property created at the University of Wisconsin. The key patent application was granted in the US in November2009 as No. 7,615,374. CYP has also licensed two other WARF patent families – Primate embryonic stem cells, WO/1996/022362 (priority date 20/1/1995), and Serum-free cultivation of primate embryonic stem cells, WO/2001/066697 (priority date 9/3/2000). These two patent families cover the embryonic stem cell line from which MCAs were first derived, and a technique of expanding these cells without foetal bovine serum.

Figure 4: iPS commercialisation opportunities



Source: Shaw and Partners

Takeover is likely - Without Cymerus Fujifilm is unlikely to realise its potential

Fujifilm invested in iPS cell technology in 2015 acquiring CYP's sister company out of the University of Wisconsin – Cellular Dynamics International[11,12] - but, there are shortcomings to its position [13] which the company wants to address. The shortcomings include: 1) its iPS technology is not unique, 2) there is limited opportunity to leverage iPS technology, and 3) returns from supplying iPS technology or iPS cells are low margin.

Fujifilm has stated: i) 'We want our cells to be used for cell therapy', ii) an intention to spend more than 400 billion yen on acquisitions, and, iii) that it will make a more aggressive push into regenerative medicine doubling its health-care revenue to 1 trillion yen by 2018. Leveraging its position in iPS is its intention but, without CYPs Cymerus™ Fujifilm's iPS technology has limited therapeutic potential.

With Cymerus™ Fujifilm would move into a much stronger position with exclusive rights to an end to end production capability (iPS manufacture through to MSC production) locking up a large part of the global therapeutic stem cell market.

Other companies with iPS technology that could achieve similar ends include: Healios, Astellas, Takeda, Celgene and Reprocell. They all have iPS technology which could be leveraged owning Cymerus. Regience, a Japanese regenerative medicine company, offered to take equity in CYP and Dr Paul Wotton, from Ocata (acquired by Astellas), joined the CYP board in 2016 and recently became chairman. Takeda has invested US$250m in a joint program with Japanese interests and is now in a similar position as Fujifilm.

[11] Fujifilm acquired Cellular Dynamics I (CDI), a manufacturer of induced pluripotent stem cells in 2015 for $307mn. Essentially Fuji bought technology, scientists, and staff of an established business servicing invitro research. The rationale was to change pharmaceutical industry practice away from testing with animal cells towards human iPS cells. However, drug development is a small market with low margins and Fuji has stated it will leverage other technologies to scale the business.

[12] CYP has a non-exclusive license from CDI/Fujifilm to manufacture iPS cells using its technology for the life of the patents. Royalties payable to Fujifilm have not been publicly disclosed, we expect the technology would command royalties reflecting a low single digit percentage of net sales.

[13] Fujifilm does own another stem cell business, Japan Tissue Engineering Co. which has autologous cartilage and skin products on the market, used by burn victims and others. It currently has three cell therapies: 1) aged related MD. Which had treated 10 people as at October 2014, 2) Parkinson's, and, 3) a cell therapy for the replacement of scarred heart muscle following heart attack. These indications could potentially be developed as allogenic solutions using CDIs iPS technology, however it won't happen quickly or with current technology given the markers iPS derived somatic cells carry. doubling its health-care revenue to 1 trillion yen by 2018.

Forecasts and Valuation

The potential utility of MSCs, as identified above and as evidenced by the 600+ stem cell trials that have been conducted, is across a wide range of indications. For valuation purposes we have focused on three indications; GvHD, Asthma, and Crohn's Disease. This leaves a large number of big indications such as oncology, osteoarthritis, heart disease and diabetes outside our valuation.

Graft versus Host Disease

Graft-versus-host disease (GvHD) is a complication that can occur after a bone marrow or stem cell transplant, if transplanted cells regard the recipient's body as foreign and attack the recipient's body. After a transplant, the recipient is usually treated with drugs that suppress the immune response. This helps reduce the chances (or severity) of GvHD, however up to 30% of HLA-identical marrow graft recipients and up to 90% of patients receiving marrow from unrelated donors still develop significant acute GVHD.

MSCs are believed to have immune modulatory effects [14] in patients with GvHD. MSCs are generally given in escalating doses by intravenous transfusion. No severe reactions have been documented even when MSCs from unrelated donors were transplanted.

CYP has received approval from the UK Medicines and Healthcare products Regulatory Agency (MHRA), the principal healthcare regulatory body in the United Kingdom, to proceed with a Phase 1 clinical trial of CYP-001 in patients with steroid-resistant GvHD.

CYP's study will be the first time that an allogeneic, iPSC-derived MSC cell product has been used in humans. The trial cements CYP's global leadership in iPSC MSC therapeutics. CYP expects the trial to be completed by the end of 2017.

The global market for a MSC solution to GvHD is believed to be worth $200m which Fuji estimate could peak at US$300m in 2024. We expect Japan with its new regulatory framework for stem cell products is likely to be the first country to approve the use of CYP's MSCs in GvHD. This could be achieved with phase 2 results by 2020, with a phase 3 trial done alongside commercial sales. High level market penetration is likely for a successful product given the poor prognosis for patients receiving current standard of care.

CYP has a deal with Fujifilm to market its MSC product for prevention and treatment of GvHD worldwide and possibly other diseases, in return for as yet undisclosed upfront and milestone payments and a US$3mn investment in CYP at a 35% premium to CYP's 6 month VWAP. The total deal size was $60m with an upfront of US$3m on taking up its option and additional milestone payments. In addition, a double digit royalty on sales make this an attractive deal for CYP which we estimate could generate $30m pa at its peak all of which would drop through to CYP's EBIT line.

Asthma

Asthma is a chronic (long-term) lung disease that inflames and narrows the airways. Asthma causes recurring periods of wheezing, chest tightness, shortness of breath, and coughing. The coughing often occurs at night or early in the morning. Treatments for severe cases are largely inadequate at resolving the sufferer's conditions so new ones are needed for therapy-resistant asthma.

Asthma affects more than 300 million people worldwide (34m in the US) and although asthma-related deaths are currently uncommon they are increasing, approximately 5,000 people a year die from asthma in the US and there is believed to be 100,000 to 250,000 fatalities throughout the world each year.

MSCs have the capacity to modify immune responses to asthma leading to a reduction in asthma symptoms, including the production of factors that trigger airway constriction.

[14] MSCs have immunomodulatory effects. Patients with post-transplant complications based on deregulated immune effector cells may benefit from an immunomodulatory effect of MSCs by its homostatic role of T-cell subsets. MSCs reduce the secretion of IFN-γ by IL-2-stimulated NK cells, but do not inhibit their K562 lysis.28 Several factors have been suggested to induce T-cell suppression by MSCs in vitro, including among those hepatocyte growth factor and transforming growth factor-β1, IL-2, indoleamine 2,3-dioxygenase, prostaglandin E2, and IL-10. http://www.nature.com/bmt/journal/v42/n2s/full/bmt2008294a.html

This has been shown by numerous University studies[15,16] and CYP's own preclinical bench work in conjunction with Monash University which suggests CYP's iPS-derived MSCs may have potential clinical use as a treatment for asthma[17], and there are also numerous unapproved autologous stem cell treatments for asthma offered in the USA.

A well-managed asthma patient is not likely to be a candidate for MSC treatment, however, patients with more serious lung disease (be that poorly managed asthma or even more severe lung disease like ARDS) will be.

We expect with the safety of CYPs MSCs determined with its GvHD trial, CYP could be in a position to partner in 2018 and take its MSCs into a phase 1 asthma trial in 2019 with a commercial product possible in Japan by 2023 and 2-3 years later in other countries.

We believe with phase I/II data which shows some indication of efficacy CYP should expect an upfront $20m, milestones $80m, and a high single digit royalty.

Crohn's disease

Crohn's disease is a type of inflammatory bowel disease that occurs in half a million people in North America. It may affect any part of the gastrointestinal tract from mouth to anus, causing a wide variety of symptoms, including abdominal pain, bloating, diarrhea (which may be bloody if inflammation is at its worst), vomiting (can be continuous), or weight loss. Skin rashes and arthritis can also occur.

Crohn's disease has a genetic component, but it is an auto-immune disease in which the person's own immune system attacks the gastrointestinal tract possibly directed at microbial antigens. The terminal ileum is the part of the bowel most often affected in this disease. Treatment often includes immune-suppressant therapy with steroids. Antibiotics and anti-inflammatories are also used extensively to maintain symptomatic control, improve health-related quality-of-life measures, and minimize complications from the disease. Key vendors in the space are: AbbVie, Astra Zeneca, Biogen, J&J, Takeda, UCB.

Research is ongoing to evaluate the effects of stem cells on a range of auto-immune condition including Crohn's. MSCs derived from bone marrow and adipose tissue have been investigated as possible treatments for Crohn's disease in multiple clinical studies. An MSC product is in marketing registration in the EU for Crohn's related fistula[18].

We expect with the safety of CYPs MSCs determined with its GvHD trial, CYP could be in a position to partner in 2018 and move into a phase 1 Crohn's disease trial in 2019 with a commercial product possible in Japan by 2023 and 2-3 years later in other countries.

Industry forecasts suggest the market is worth ~USD3.6b and the global market is forecast by TechNavio to grow at a CAGR of 2.84% from 2014 to 2019.

In 2009 Athersys sold the rights to its autologous cell treatment for inflammatory bowel disease to Pfizer for an upfront of $6m, with additional payments of up to $105 million at certain milestones. This transaction supports our view that CYP should expect a total deal size of USD100m with royalty of 10 to 12%.

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[15] This effect was long lasting, even after the human stem cells were no longer detected in the lungs. This was because these cells triggered a significant increase in alveolar macrophages, cells crucial to maintaining healthy lungs. http://www.med.monash.edu.au/sobs/news/2014/using-stem-cells-to-treat-asthma.html

[16] Weizmann Institute scientists conducted a series of experiments in which they cleared the lung's stem cell compartments with a method they had developed, then injected the new stem cells into mouse models of lung damage. The embryonic lung stem cells managed to find their way through the blood to the lungs and settle into the proper compartment. By six weeks, these cells were differentiating and creating normal lung tissue. The damaged lungs healed in the mice, and their breathing improved significantly. - the National Institutes of Health in Maryland, UK, injected asthmatic mice with the cells and found they stopped symptoms.

[17] Monash Biomedicine Discovery Institute has demonstrated Significant Efficacy with CYP's MSC Technology in Preclinical Asthma Study. The study, conducted under the supervision of Associate Professor Chrishan Samuel and Dr Simon Royce at Monash University, in the Department of Pharmacology and the Monash Biomedicine Discovery Institute, Melbourne, in mice closely resembles the clinical manifestations of asthma in humans using the well-established chronic allergic airways disease model. In this study mice were induced by sensitising and challenging them with a protein called ovalbumin which caused them to exhibit significantly increased airway hyper-responsiveness (AHR); ($p<0.001$ vs saline-treated control group), which is the key characteristic of asthma. Intravenous administration of Cynata's MSCs in these animals caused a statistically significant (60-70%) decrease in AHR ($p<0.01$) relative to untreated sensitised animals. Moreover, intranasal administration of Cynata's MSCs completely normalised AHR, to a level that was no longer different to healthy animals, in which the asthma model had not been induced. No adverse safety findings were observed during the study.

[18] Tigenix: Cx601is injected locally and therefore does not require as many cells.

An Experienced Board and Management

CYP has a relatively small, albeit experienced board and management team as detailed below

Dr Wotton – Chairman. Dr Wotton joined the Board in June 2016 and was appointed Chairman in 2017. Dr Wotton is currently the President and CEO (since May 2016) of Sigilon Inc. and was previously President and CEO of Ocata Therapeutics Inc. (NASDAQ: OCAT) taking the company through a take-over by Atellas Pharma Inc., in a US$379 million all cash transaction. Prior to Ocata, Dr Wotton had served as President and CEO of Anteres Pharma Inc. (NASDAQ: ATRS), since October 2008. Prior to joining Antares, Dr Wotton was the CEO of Topigen Pharmaceuticals and prior to Topigen, he was the Global Head of Business Development of SkyePharma PLC. Dr Wotton has held senior level positions at Eurand International BV, Penwest Pharmaceuticals, Abbott Laboratories and Merck, Sharp and Dohme. Dr Wotton is a member of the board of Vericel Corporation, a US company developing autologous cellular therapies and also past Chairman of the Emerging Companies Advisory Board of BIOTEC Canada.

Dr Macdonald - Chief Executive Officer. Dr Macdonald has over 22 years' experience and a track record of success in pharmaceutical and biotechnology businesses. His career history includes positions as Vice President of Business Development for Sinclair Pharmaceuticals Ltd (now Sinclair IS Pharma), a UK-based specialty pharmaceuticals company and Vice President, Corporate Development for Stiefel Laboratories Inc, the largest independent dermatology company in the world and acquired by GlaxoSmithKline in 2009 for £2.25b. Dr Macdonald has also served as CEO of Living Cell Technologies Ltd, Vice President of Business Development of Connetics Corporation and Vice President of Research and Development of F H Faulding & Co Ltd. His other positions have included non-executive director roles at Telesso Technologies Ltd, iSonea Ltd, Hatchtech Pty Ltd and Relevare Pharmaceuticals Ltd. Dr Macdonald currently serves as a member of the Investment Committee of UniSeed Management Pty Ltd.

Dr Washer – Non-Executive Director. Dr Washer was CYPs Chairman for a period of four years, he has over 20 years of CEO and Board experience in medical technology, biotech and agrifood companies. He is currently the Chairman of Orthocell Ltd (ASX: OCC) and Minomic International Ltd. He was previously the CEO of Calzada Ltd (ASX: CZD), the founding CEO of Phylogica Ltd (ASX: PYC) and CEO of Celentis and managed the commercialisation of intellectual property from AgResearch in New Zealand with 650 scientists and $130m revenues. He was also a founder of a NZ$120m New Zealand based life science fund and Venture Partner with the Swiss based Inventages Nestlé Fund. He is currently the Investment Director with Bioscience Managers and has held a number of Board positions in the past as the Chairman of iSonea Ltd, Resonance Health Ltd (ASX: RHT) and Hatchtech Pty Ltd, and as a Director of iCeutica Pty Ltd, Immuron Ltd (ASX: IMC) and AusBiotech Ltd. He was also a Senator with Murdoch University and is currently a Director of Zelda Therapeutics.

Dr. Chiplin - Non-Executive Director. Dr. Chiplin joined the Board in November 2014. Dr. Chiplin is Managing Director, Newstar Ventures Ltd and has significant international experience in the life science and technology industries. Recent transactions that Dr. Chiplin has been instrumental in include US stemcell company Medistem (acquired by Intrexon), Arana Therapeutics (acquired by Cephalon) and Domantis (acquired by GSK). Cynata Therapeutics Limited Dr Chiplin is also a director of Adalta Pty Ltd, Benitec Biopharma Ltd (ASX: BLT), Batu Biologics Inc., The Coma Research Institute, Prophecy Inc (Chairman), ScienceMedia Inc and Scancell Holdings plc (SCLP.L, Executive Chairman). Dr Chiplin's Pharmacy and Doctoral degrees are from the University of Nottingham, UK.

Mr Webse - Non-Executive Director. Mr Webse joined the Board in May 2012. Mr Webse has over 25 years' company secretarial experience and is the managing director of Platinum Corporate Secretariat Pty Ltd, a company specialising in providing company secretarial, corporate governance and corporate advisory services. Mr Webse was a non-executive director of 4DS Memory Limited (ASX: 4DS).

Dr Killian Kelly – Vice President, Product Development. Dr Kilian Kelly joined Cynata in 2014 he has a PhD in Pharmaceutical Sciences and is a trained pharmacist. He has a long and successful history working with major pharmaceutical companies in Europe, predominantly in areas of regulatory and clinical affairs and in project management. In particular in a former position he had responsibility for clinical development and regulatory activities at a major therapeutic stem cell company so he has direct experience in the development of stem cell-based medical products.

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