EDISON

Mesoblast

Development update

Novartis licenses ARDS program

Pharma & biotech

Mesoblast announced that Novartis has signed a partnership with the company to develop remestemcel-L for acute respiratory distress syndrome (ARDS), whether or not the ARDS was caused by COVID-19. This is an important validation of both the platform as well as its application in the treatment of respiratory disease. Novartis will make a US$25m upfront payment and an additional US$25m equity investment. Mesoblast may receive a total of US$505m in development milestones, an additional US$750m in sales milestones and tiered double-digit royalties. Additionally, Novartis will fully fund global clinical development for all-cause ARDS and potentially other respiratory indications.

Year end	Revenue (US$m)	PBT* (US$m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
06/19	16.0	(86.5)	(15.69)	0.0	N/A	N/A
06/20	31.6	(79.6)	(13.28)	0.0	N/A	N/A
06/21e	72.9	(60.4)	(10.29)	0.0	N/A	N/A
06/22e	8.6	(92.8)	(15.83)	0.0	N/A	N/A

Note: *PBT and EPS are normalized, excluding amortization of acquired intangibles, exceptional items and share-based payments.

COVID-19 ARDS Phase III ongoing

Mesoblast has an ongoing 300-patient randomized, controlled Phase III trial of remestemcel-L in COVID-19 related moderate/severe ARDS patients. Enrolment has surpassed 180 patients and is expected to complete in calendar Q121, with one interim analysis remaining (two have already been conducted). At the interim analysis, the trial can be stopped early for efficacy or futility.

Update on Ryoncil in SR-aGVHD

On 30 September the FDA issued a complete response letter (CRL) for Ryoncil in pediatric SR-aGVHD patients, stating that at least one additional randomized controlled trial (in either pediatric or adult patients) would be necessary for approval. Mesoblast is likely to appeal this decision through the FDA dispute resolution pathway though the timing is unclear. If Mesoblast's appeal is unsuccessful, we think approval is unlikely before FY23 at the earliest.

Key Phase III data in HF and back pain coming soon

There are currently two Phase III readouts expected in Q4 CY20. These are the DREAM HF-1 Phase III trial of Revascor in 566 advanced heart failure patients and the MPC-06-ID trial in 404 chronic lower back pain patients.

Valuation: A$4.9bn or A$8.41 per share

We have increased our valuation to A$4.9bn or A$8.41 per share (A$7.88 per diluted share) from A$4.6bn or A$7.89 per share (A$7.53 per diluted share). The increase is mainly due to adding the ARDS program into our valuation now that it has been licensed by Novartis. We also rolled forward our NPV. These were offset in part by shifting Ryoncil approval to 2023, lowering the probability of success to 60% from 80% as well as lower net cash.

30 November 2020

Price	**A$4.07**
Market cap	**A$2,388m**
	US$0.73/A$
Net cash (US$m) at September 2020	17.1
Shares in issue	586.6m
Free float	78.5%
Code	MSB
Primary exchange	ASX
Secondary exchange	Nasdaq

Share price performance

%	1m	3m	12m
Abs	33.9	(21.7)	121.8
Rel (local)	22.7	(27.5)	126.2
52-week high/low	A$5.50		A$1.10

Business description

Mesoblast is an Australia-based biotechnology company developing adult stem-cell therapies based on its proprietary MPC and MSC platforms. Its lead programs are in pediatric aGvHD, heart failure, ARDS and lower back pain, all of which are in Phase III or later.

Next events

Heart failure and back pain Phase III data	Q4 CY20
Remestemcel-L COVID-19 related ARDS Phase III completion	Q1 CY21

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Edison profile page

A significant validation

Mesoblast announced that Novartis has signed a partnership with the company to develop remestemcel-L for ARDS, whether or not the ARDS was caused by COVID-19, as well as potentially other conditions. This is an important validation of both the platform as well as its application in the treatment of respiratory disease, an area of intense focus for Novartis. Novartis will make a US$25m upfront payment and an additional US$25m equity investment. Mesoblast may receive a total of US$505m in development milestones, an additional US$750m in sales milestones and tiered double-digit royalties. Additionally, Novartis will fully fund global clinical development for all-cause ARDS and potentially other respiratory indications once the all-cause ARDS Phase III is initiated (though this is dependent upon the successful completion and outcome of the COVID-19 related ARDS study). Mesoblast will be responsible for both clinical and commercial manufacturing and Novartis will purchase commercial product from the company. There are also US$50m in manufacturing milestones related to the successful implementation of a next-generation manufacturing process. Novartis will be responsible for any capital expenditure related to increasing capacity requirements for the manufacture of remestemcel-L.

Outside of respiratory indications, Novartis also has an option to become the commercial distributor of Ryoncil (the brand name of remestemcel-L in graft versus host diseases). For most non-respiratory indications, Novartis and Mesoblast may fund development and commercialization on a 50/50 profit share basis.

With regard to the market opportunity in COVID-19-related ARDS, this is a little difficult to quantify given the recent excellent vaccine data, which may dramatically affect the size of that market. However, ARDS outside of COVID-19 is a well-documented unmet medical need. US incidence rates are approximately 36 cases per 100,000 population (indicating approximately 120,000 patients per year), while EU incidence rates range from 3.0 in Germany[1] to 7.2 in Spain.[2]

Mesoblast is currently conducting a 300-patient randomized, controlled US Phase III trial of remestemcel-L in COVID-19 patients with moderate/severe ARDS who are on ventilator support. The primary endpoint is all-cause mortality up to 30 days post randomization. The first patient was dosed in early May and recruitment is expected to complete in the first calendar quarter of 2021. Interim analyses were conducted after 30% and 45% enrolment was achieved and the trial was recommended to continue as planned. An additional interim analysis is expected after 30 days of follow-up once 60% enrolment is achieved. As the company announced that it has over 180 patients enrolled, we would expect the final interim analysis in mid-late December. At the interim analysis, the trial can be stopped early for efficacy or futility.

Ryoncil

Mesoblast has announced that the FDA has issued a CRL on 30 September for Ryoncil in pediatric SR-aGVHD patients, stating that at least one additional randomized controlled trial (in either pediatric or adult patients) would be necessary for approval. This has occurred even though the FDA's Oncologic Drugs Advisory Committee (ODAC) voted nine to one in August that the available data support the efficacy of Ryoncil in pediatric SR-aGVHD patients. The company had a Type A meeting with the FDA on 17 November to discuss a potential accelerated approval with a post-approval requirement for an additional study, but at present it appears the FDA will not agree to this.

1 Lewandowski et al., Incidence, severity, and mortality of acute respiratory failure in Berlin, Germany. *American Journal of Respiratory and Critical Care Medicine. 1995;151:1121-5.*

2 Villar et al., The ALIEN study: incidence and outcome of acute respiratory distress syndrome in the era of lung protective ventilation. *Intensive Care Medicine* (2011) 37:1932–1941

If the formal minutes of the meeting (expected within 30 days of the event) confirm this, Mesoblast will request a further Type A meeting to initiate the FDA dispute resolution pathway. If this also proves unsuccessful, we estimate approval could then occur in FY23 at the earliest.

While the FDA decision is disappointing, the US pediatric indication represents only US$103m of the US$574m in peak sales we model for the product in the US and EU. The adult market was always going to require its own randomized controlled trial and we believe the US adult market represents almost triple the opportunity as the pediatric market in the US (US$300m in peak sales).

Heart failure and back pain

For Revascor, the necessary number of primary endpoint events has occurred in the DREAM HF-1 Phase III trial in 566 advanced heart failure patients and final study visits have been completed. A quality review of all data is ongoing at all sites. Study data are expected by the end of the calendar year. The primary endpoint is a reduction in recurrent heart failure-related major adverse cardiac events such as heart failure-related hospitalization and cardiac death.

The MPC-06-ID Phase III trial is also expected to provide data by the end of this year. It enrolled 404 patients with chronic lower back pain due to degenerative disc disease and has a composite primary endpoint that includes measures of pain and disability/function at 12 and 24 months. As with the DREAM HF-1 trial, final study visits have been completed with a quality review of all data ongoing. Two Phase III trials will likely be necessary for approval in this indication and a confirmatory European Phase III is being planned with partner Grünenthal.

Valuation

We have increased our valuation to A$4.9bn or A$8.41 per share (A$7.88 per diluted share) from A$4.6bn or A$7.89 per share (A$7.53 per diluted share). The increase is mainly due to adding the ARDS program into our valuation now that it has been licensed by Novartis. However due to the lack of significant data we are currently only assuming a 30% chance of success, though that will change as we learn more about the efficacy profile. We forecast US$1.7bn in potential peak sales, the vast majority of which comes from the US market due to the higher incidence in the country as well as the greater propensity to prescribe higher priced medicines. It is important to note that our valuation for this program does not include any value of the COVID-19 related ARDS indication (due mainly to the difficulty in forecasting that number going forward) and does not include any milestone payments as their details are unknown.

In addition to adding ARDS, we also rolled forward our NPV. These changes were offset in part by shifting Ryoncil approval to 2023, lowering the probability of success to 60% from 80% as well as lower net cash. The impact from the delay on our valuation was relatively minimal as the US pediatric market is a relatively small portion (<20% of peak sales) of the total Ryoncil opportunity, and as stated previously, we had already anticipated that the adult market was going to require its own randomized controlled trial.

Exhibit 1: Mesoblast valuation table

Product	Indication	Prob. of success (%)	Launch (FY)	Peak sales (US$m)	rNPV (A$m)
Active projects					
MSC-100-IV	Acute graft versus host disease (GvHD)	Range 50%-60%	2023	574	1,058.6
MSC-100-IV	ARDS	30%	2024	1,736	335.7
Revascor (MPC-150-IM)	Congestive heart failure (CHF) (includes use with LVAD)	50%	2023	3,208	2,225.2
MPC-06-ID	Intervertebral disc repair	50%	2022	3,302	1,886.8
On-hold projects					
MPC-300-IV	Diabetic nephropathy	5.0%	On hold	2,186	56.7
MPC-300-IV	Rheumatoid arthritis	5.0%	On hold	1,350	32.2
MPC-25-IC	Acute myocardial infarction (AMI)	5.0%	On hold	1,057	50.3
MPC-25-Osteo	Lumber fusion	5.0%	On hold	662	21.3
Total value					**5,666.7**
R&D expenses					(345.4)
Manufacturing expenses					(113.7)
G&A expenses					(138.0)
Net cash (A$m at 30 September, 2020)					23.5
Non-dilutive funding interest and repayments					(161.7)
Total (A$m)					**4,931**
Shares (m)					586.6
Value per share (A$)					**8.41**
Options outstanding (2020 onwards) (m)					38.91
Fully diluted shares in issue (m)					625.50
Fully diluted value per share (A$)					7.88

Source: Edison Investment Research

Financials

Mesoblast reported total revenue for the first quarter of FY21 (the period ending 30 September 2020) of US$1.3m, down from US$17.0m in the same period in the prior year. Most of this difference was due to the inclusion of US$15m in payments that were part of the Grünenthal licensing agreement in Q1 FY20 revenues. Also, royalties on sales of Temcell in Japan fell from US$1.9m to US$1.3m as JCR had a temporary shutdown in production in order to expand facility capacity due to increasing demand beyond the initial forecast. R&D increased to US$19.3m from US$12.4m mainly due to the expense of the Phase III trial in COVID-19 patients with moderate/severe ARDS and pre-commercial activities for remestemcel-L. Manufacturing expenses increased from US$2.7m to US$11.9m due to the production of supply for the COVID-19 Phase III and building up inventory for the Ryoncil launch. Management and administration expenses also increased to US$7.7m from US$5.5m due to higher share-based payments to employees and consultants and increased overheads.

We have increased our FY21 revenue estimate to US$72.9m from US$50.9m due to the addition of the Novartis upfront payment as well as the shift of US$30m in Grünenthal milestone payments we previously forecast for FY20 into FY21. This was partially offset by the removal of Ryoncil revenues from our model for the year. Our FY21 R&D estimate has increased by US$13.6m (due to the costs associated with the COVID-19 related ARDS Phase III), our manufacturing expense estimate by US$16.8m and our SG&A estimate by US$12.0m. We are introducing FY22 estimates, which feature US$8.6m in revenues and do not assume any additional milestone payments (the vast majority of our estimate is comprised of Temcell royalties).

For the period ending 30 September 2020, Mesoblast reported cash and equivalents of US$108m, with US$34.9m in short-term debt and an additional US$56.1m in long-term debt. Our forecasts for Mesoblast's financing needs in part depend on whether Ryoncil sales start sooner than anticipated, potential future partnership royalties/milestones, as well as the company's aggressiveness in investing in the business. Additionally, we have not yet included the US$25m equity investment

from Novartis and will do so once the transaction closes. That said, we had not been forecasting a need to raise additional capital (as we previously assumed US approval of Ryoncil in CY20) but with this apparent Ryoncil approval delay, we are now forecasting a need to raise US$140m by the end of FY23 (modelled as illustrative debt).

Exhibit 2: Financial summary

US$'000s	2019	2020	2021e	2022e
Year end 30 June	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS				
Revenue	16,003	31,614	72,850	8,600
Cost of Sales	0	0	0	0
Gross Profit	16,003	31,614	72,850	8,600
R&D Expenses	(57,531)	(52,993)	(63,592)	(57,233)
Manufacturing & Commercialization Expenses	(14,466)	(22,782)	(27,338)	(13,669)
SG&A Expenses	(18,293)	(20,142)	(30,214)	(21,149)
EBITDA	(75,373)	(64,758)	(46,275)	(83,197)
Operating Profit (before amort. and except.)	(75,935)	(66,851)	(48,368)	(85,290)
Intangible Amortization	(1,577)	(1,574)	(1,750)	(1,750)
Exceptionals	(6,264)	1,380	15,107	0
Share-based payments	(4,368)	(7,522)	(5,434)	(5,434)
Operating Profit	(88,145)	(74,567)	(40,446)	(92,474)
Net Interest	(10,609)	(12,788)	(11,991)	(7,552)
Profit Before Tax (norm)	(86,544)	(79,639)	(60,359)	(92,841)
Profit Before Tax (FRS 3)	(98,754)	(87,355)	(52,437)	(100,026)
Tax	8,955	9,415	0	0
Profit After Tax (norm)	(77,589)	(70,224)	(60,359)	(92,841)
Profit After Tax (FRS 3)	(89,799)	(77,940)	(52,437)	(100,026)
Average Number of Shares Outstanding (m)	494.4	528.8	586.6	586.6
EPS - normalized fully diluted (c)	(15.69)	(13.28)	(10.29)	(15.83)
EPS - normalized (c)	(15.69)	(13.28)	(10.29)	(15.83)
EPS - (IFRS) (c)	(18.16)	(14.74)	(8.94)	(17.05)
Dividend per share (c)	0.0	0.0	0.0	0.0
Gross Margin (%)	100.0	100.0	100.0	100.0
EBITDA Margin (%)	N/A	N/A	N/A	N/A
Operating Margin (before GW and except) (%)	N/A	N/A	N/A	N/A
BALANCE SHEET				
Fixed Assets	589,593	597,054	596,835	597,259
Intangible Assets	583,126	581,601	581,217	583,310
Tangible Assets	826	10,271	10,332	8,663
Investments	5,641	5,182	5,286	5,286
Current Assets	62,522	136,548	73,879	45,576
Stocks	0	0	0	0
Debtors	4,060	1,574	2,446	2,446
Cash	50,426	129,328	66,265	37,962
Other	8,036	5,646	5,168	5,168
Current Liabilities	(44,331)	(90,143)	(87,697)	(77,372)
Creditors	(13,060)	(28,491)	(30,586)	(30,586)
Deferred revenue	(17,264)	(29,197)	(22,218)	(22,218)
Short term borrowings	(14,007)	(32,455)	(34,893)	(24,568)
Long Term Liabilities	(126,732)	(94,133)	(54,839)	(130,271)
Long term borrowings	(67,279)	(57,023)	(24,568)	(100,000)
Deferred revenue	0	0	0	0
Other long term liabilities	(59,453)	(37,110)	(30,271)	(30,271)
Net Assets	481,052	549,326	528,178	435,192
CASH FLOW				
Operating Cash Flow	(54,572)	(43,911)	(21,817)	(88,473)
Net Interest	(3,217)	(12,454)	(11,390)	(6,951)
Tax	0	0	0	0
Capex	(279)	(2,096)	(424)	(424)
Acquisitions/disposals	0	0	0	0
Financing	30,258	144,946	0	0
Dividends	0	0	0	0
Other	21,203	0	0	0
Net Cash Flow	(6,608)	86,485	(33,631)	(95,848)
Opening net debt/(cash)	21,634	30,860	(39,850)	(6,804)
Loan movements	0	0	0	0
Other	(2,619)	(15,775)	585	2,438
Closing net debt/(cash)	30,860	(39,850)	(6,804)	86,606

Source: Company reports, Edison Investment Research

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