Phase 3 Roll-Out

US trial sites start dosing patients

PAR's Phase 3 pivotal trial in knee osteoarthritis (KOA) is underway in the US, with 21 of the planned 56 US trial sites activated and patient dosing commenced. All eight of the Australian sites have been dosing participants since January CY22. Site initiation is planned to start in the UK/ EU over CY22.

The news starts the clock for its next key milestone - topline results of the PAR-002 trial expected in Q4CY24.

CEO & funding to be confirmed

There has been no update on the company's search for a new CEO. Funding to complete its clinical program is still to be secured.

Potential support from PAR-008

The topline data from PAR-008 Disease Modifying OA (DMOA) Trial are expected in Q3CY22. The data will be used to inform discussions with regulators regarding a path to DMOA designation. They are no approved DMOA drugs. Current treatments only provide symptomatic relief. A therapy that halted disease progression or reduced pathological changes would be likely to see clinician and patient support.

Valuation, Risks and Sensitivities

MST's valuation of $3.97ps. is unchanged. However, we note cash at 30.03.22 of ~$40m, as the company embarks on its multi-trial program. The valuation assumes that PAR can deliver its trial program timelines. In MST's view, uncertainty around the stock will continue until there is confirmation of a CEO and funding.

The valuation is subject to the usual drug development risks including confirmation of drug efficacy and safety, regulatory approval, competing therapies, funding and market uptake.

ASX-listed biotechnology company, Paradigm Biopharma's (PAR.AX) strategy is to take already approved medicines that have shown safety and efficacy in one condition and repurpose them for new indications. The aim is to reduce time, cost and risk. Its first candidate is injectable pentosan polysulphate sodium (iPPS), Zilosul®, for use in osteoarthritis of the knee (KOA) and hip (HOA) and mucopolysaccharidosis (MPS), a genetic enzyme disease. Zilosul®'s mechanism of action offers potential application use in a number of other diseases. Clinical data to date have demonstrated benefit with minimal adverse effects.

Stock	PAR.ASX
Price	A$1.13
Market cap	A$275m
Valuation	A$3.97

Next news

- H2CY22 - 1st 002 Trial patient enters PAR-006 treatment durability trial
- Q3CY22 – PAR-008 Trial primary readout
- H1CY23 – Dose Selection for PAR-002 and PAR-003
- H1CY23 – 1st Patient to enter PAR-003 Confirmatory trial

PAR.AX Share Price (A$)

Source: Factset

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Financial Summary

Paradigm Biopharmaceuticals Ltd — **PAR-AU**

Year end 30 June

MARKET DATA		
Share Price	**A$/share**	**1.13**
52 week high / low	A$	2.69 - 0.925
Valuation (12 month forward)	**A$**	**3.97**
Market capitalisation	**A$m**	**263**
Shares on issue	m	232
Options	m	4
Other equity	m	-
Potential shares on issue (diluted)		236

12 month performance

INVESTMENT FUNDAMENTALS		FY20	FY21	FY22E	FY23E	FY24E
EPS Reported (undiluted)	¢	(6.0)	(16.7)	(20.5)	(5.7)	1.5
EPS Underlying (undiluted)	**¢**	**(6.0)**	**(16.7)**	**(20.5)**	**(5.7)**	**1.5**
Underlying EPS growth	%	n/m	n/m	n/m	n/m	n/m
P/E Reported (undiluted)	**x**	**n/m**	**n/m**	**n/m**	**n/m**	**n/m**
P/E at Valuation	x	n/m	n/m	n/m	n/m	n/m
Dividend	**¢**	**-**	**-**	**-**	**-**	**-**
Payout ratio	%	0%	0%	0%	0%	0%
Yield	**%**	**-**	**-**	**-**	**-**	**-**

KEY RATIOS (A$)		FY20	FY21	FY22E	FY23E	FY24E
Forecast year end shares	m	225	230	232	232	232
Market cap (Y/E / Spot)	**$m**	**254.0**	**259.8**	**262.5**	**262.5**	**262.5**
Net debt /(cash)	$m	(103.9)	(71.0)	(25.4)	(12.3)	(15.8)
Enterprise value	**$m**	**150.0**	**188.8**	**237.1**	**250.2**	**246.7**
EV/Sales	x	40.6	21.6	54.8	6.2	16.7
EV/EBITDA	**x**	**(11.3)**	**(5.5)**	**(4.9)**	**(18.4)**	**51.3**
EV/EBIT	x	(11.3)	(5.5)	(4.9)	(18.4)	51.3
Net debt / Enterpprise Value	x	(0.7)	(0.4)	(0.1)	(0.0)	(0.1)
Gearing (net debt / EBITDA)	**x**	**7.8**	**2.1**	**0.5**	**0.9**	**(3.3)**
Operating cash flow per share	$	(0.0)	(0.2)	(0.2)	(0.1)	0.0
Price to operating cash flow	**x**	**(25.2)**	**(7.4)**	**(5.7)**	**(20.0)**	**74.0**
Free cash flow	**$m**	**(4.5)**	**(34.3)**	**(46.3)**	**(13.2)**	**3.5**
Free cash flow per share	$	(0.02)	(0.15)	(0.20)	(0.06)	0.02
Price to free cash flow	**x**	**(56.9)**	**(7.6)**	**(5.7)**	**(20.0)**	**74.0**
Free cash flow yield	**%**	**-1.8%**	**-13.2%**	**-17.6%**	**-5.0%**	**1.4%**
Book value / share	$	0.48	0.34	0.13	0.07	0.09
Price to book (NAV)	**x**	**2.3**	**3.3**	**8.8**	**15.1**	**12.9**
NTA / share	$	0.47	0.33	0.12	0.06	0.07
Price to NTA	**x**	**2.4**	**3.4**	**9.8**	**18.2**	**15.1**
EBITDA margin	%	n/m	n/m	n/m	n/m	32%
ROE (Average Equity)	%	n/m	n/m	n/m	n/m	n/m
ROA (EBIT)	%	n/m	n/m	n/m	n/m	n/m
Interest cover (EBIT / net interest)	x	n/m	n/m	n/m	n/m	18.3

PROFIT AND LOSS (A$)		FY20	FY21	FY22E	FY23E	FY24E
Revenue & Other Income	A$m	3.7	8.7	4.3	40.4	14.8
COGS	A$m	-	(0.1)	(0.1)	-	-
Gross margin	**A$m**	**3.7**	**8.6**	**4.3**	**40.4**	**14.8**
Corporate costs	A$m	(17.0)	(43.1)	(52.3)	(54.0)	(10.0)
EBITDA	**A$m**	**(13.3)**	**(34.5)**	**(48.1)**	**(13.6)**	**4.8**
D&A	A$m	-	-	-	-	-
EBIT	**A$m**	**(13.3)**	**(34.5)**	**(48.1)**	**(13.6)**	**4.8**
Interest (Net)	A$m	1.0	0.2	0.5	0.4	0.3
Non-operating income	A$m	-	-	-	-	-
Pre-tax Profit	**A$m**	**(12.3)**	**(34.3)**	**(47.5)**	**(13.2)**	**5.1**
Tax	A$m	-	-	-	-	(1.5)
Minorities	A$m	-	-	-	-	-
Underlying NPAT	**A$m**	**(12.3)**	**(34.3)**	**(47.5)**	**(13.2)**	**3.5**

BALANCE SHEET (A$)		FY20	FY21	FY22E	FY23E	FY24E
Cash	A$m	103.9	71.0	25.4	12.3	15.8
Receivables	A$m	3.5	8.5	0.3	1.7	0.6
Inventory	A$m	-	-	0.2	1.0	0.4
PPE	A$m	0.1	0.1	0.1	0.1	0.1
Intangibles	A$m	2.9	2.9	2.9	2.9	2.9
Other	A$m	1.9	2.2	2.3	2.3	2.3
Total Assets	**A$m**	**112.4**	**84.8**	**31.2**	**20.3**	**22.1**
Accounts Payable	A$m	2.8	5.0	0.3	1.7	0.6
Borrowings	A$m	-	-	-	-	-
Leases	A$m	0.9	0.8	0.6	0.6	0.6
Provisions	A$m	0.5	0.8	0.6	0.6	0.6
Other	A$m	-	-	0.1	0.1	0.1
Total Liabilities	**A$m**	**4.2**	**6.5**	**1.5**	**2.9**	**1.9**
Shareholder's equity	**A$m**	**108.2**	**78.3**	**29.7**	**17.4**	**20.3**

CASH FLOW (A$)		FY20	FY21	FY22E	FY23E	FY24E
Receipts from customers & R&D incentive	A$m	3.6	3.4	4.9	7.1	8.1
Payments to suppliers and employees	A$m	(14.8)	(38.6)	(51.8)	(54.0)	(10.0)
Milestones	A$m	-	-	-	33.3	6.7
Interest	A$m	1.1	0.3	0.6	0.4	0.3
Tax	A$m	-	-	-	-	(1.5)
Operating cash flow	**A$m**	**(10.1)**	**(34.9)**	**(46.3)**	**(13.2)**	**3.5**
Capex	A$m	(0.1)	(0.0)	-	-	-
Acquisitions	A$m	-	-	-	-	-
Other	A$m	5.8	0.7	-	-	-
Investing cash flow	**A$m**	**5.6**	**0.7**	**-**	**-**	**-**
Borrowings	A$m	1.8	(0.0)	0.0	-	-
Equity	A$m	34.3	1.0	-	-	-
Dividend	A$m	-	-	-	-	-
Financing cash flow	**A$m**	**36.1**	**1.0**	**0.0**	**-**	**-**
Change in Cash / FX	A$m	31.6	(33.3)	(46.3)	(13.2)	3.5
Year end cash	**A$m**	**103.9**	**71.0**	**25.4**	**12.3**	**15.8**

Source: Company, MST Access

Investment Thesis

Snapshot of Paradigm Biopharma (PAR.AX)

- As a repurposed drug, polysulphate pentosan (Zilosul®), for knee & hip OA presents a lower safety risk.
- Zilosul® Phase 2b trial data support a potential superior advantage to current drug therapies.
- Positive results in Phase 3 trials would be expected to support application for US, EU and Australian approval.
- The readout of Phase 3 trial arm, PAR-002, is planned for Q4CY24. The results may act as guide to final Phase 3 results.
- PAR is seeking non-dilutive funding to complete the Phase 3 trial program.
- A new CEO is to be appointed.

Investment thesis

- Zilosul® carries lower risk as a repurposed drug from a safety perspective and as a later stage asset as it commences Phase 3 trials.
- Higher-than-average probability of approval**:** The similarity of the Phase 2b and 3 trials supports a higher probability that the Phase 3 trial will repeat a statistically significant Phase 2b result.
- Large market with current drugs offering only short-term relief and significant adverse effects: Market opportunity is significant if the Phase 3 data confirm the data to date of meaningful pain relief and limited adverse effects. If PAR can demonstrate a potential disease-modifying role, there is also likely to be very strong interest from clinicians and patients.
- To be confirmed – there is some stock uncertainty from funding and management perspectives. PAR will require further funding to complete the planned pivotal and confirmatory trials to support regulatory approval. MST model assumes that a licensing agreement will be negotiated following topline results of DMOA trial PAR-008 in Q3CY22. The new CEO is yet to be appointed and will need to demonstrate the experience and ability to take the company through the next stages.

Valuation, Risks, Sensitivities

MST's valuation of $3.97ps. is unchanged. We note cash at 30.03.22 of ~$40m, as the company embarks on its multi-trial program. The valuation assumes that PAR can deliver its trial program timeline and secure funding. In MST's view, some uncertainty will continue until there is confirmation of a CEO and funding.

The valuation is subject to the usual drug development risks including confirmation of drug efficacy and safety, regulatory approval, market uptake, competing therapies and funding. COVID outbreaks may impact trial timelines.

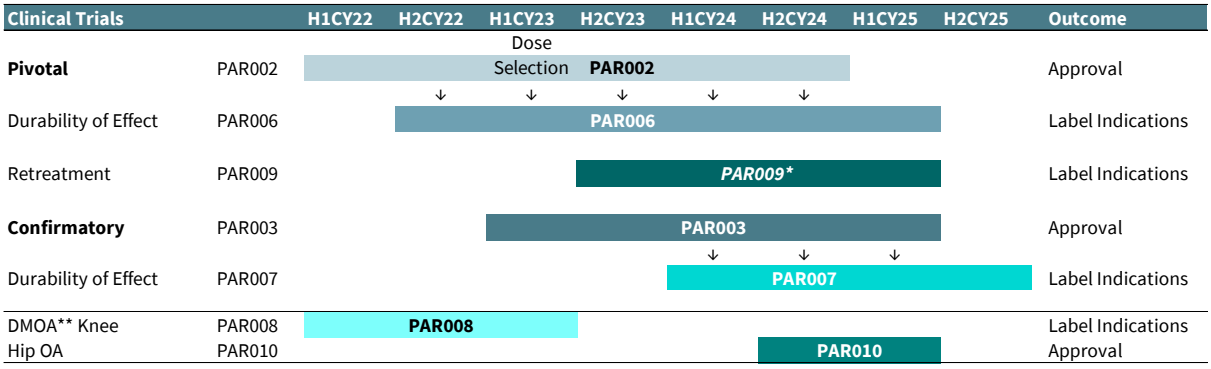
Expected CY21 News flow

- H2CY22 - 1st 002 Trial patient enters PAR-006 treatment durability trial
- Q3CY22 – PAR-008 Trial primary readout
- H1CY23 – Dose Selection for PAR-002 and PAR-003
- H1CY23 – 1st Patient enters PAR-003 Confirmatory trial

Trial program underway, next - CEO and funding confirmation

PAR's Phase 3 pivotal trial in knee osteoarthritis (KOA) is underway, with 21 of the planned 56 US trial sites activated and patient dosing commenced. All eight of the planned clinical trial sites in Australia have started screening and enrolling patients. Site initiation will commence in the UK and EU over CY22.

We review the Phase 3 trial program to highlight the expected news flow and potential impact.



* PAR 009 Timelines to be determined

** Disease Modifying OA

The Phase 3 trial will enrol 900 KOA patients in the pivotal clinical trial, PAR-002, and 735 in the confirmatory trial, PAR-003. PAR-002 is an adaptive, 2-stage, randomised, double-blind, placebo-controlled, multi-center (US/AUS/UK/EU) study. In addition to demonstrating safety and efficacy, the trial program will examine the durability of the treatment effect and safety/timing of re-treatment.

Pivotal PAR-002

Adaptive Stage 1

Dosing – the primary objective of Stage 1 is to confirm the optimal dose. Participants will be randomly assigned to a 6-week period of once weekly 2mg/kg dose or twice weekly 1.5mg/kg or a fixed dose weekly with a fourth cohort to receive placebo. The selected dose will be based on an optimal balance of efficacy and safety.

Adaptive Stage 2

On confirmation of the optimal dose, participants will be randomised 1:1 to receive the selected Zilosul® dose regimen or placebo for 6 weeks.

Confirmatory PAR-003

A confirmatory Phase 3 trial will commence in H1CY23 using the dose selected by the Stage 1 PAR-002 trial. The topline data read out of PAR-002 is expected in Q4CY24 and with PAR-003 to follow in Q1CY25. Positive trial outcomes are expected to support regulatory approval in US, EU and other countries.

Phase 3 Endpoints

The primary endpoint in the Phase 3 trials is a change from baseline at Day 56 in WOMAC® [i]pain scale. Secondary outcomes include change from baseline at multiple time points out to day 168 in WOMAC® Pain and Function and Patient Global Impression of Change and Quality of Life.

PAR-006, -007, -009 Trials

Durability of treatment effect and re-treatment

PAR is undertaking further trials, PAR- 006 and 007, to examine the durability of Zilosul® treatment effect with PAR-009 to confirm the safety of re dosing. As PAR-002 and PAR -003 participants complete their treatment

regimen, they will be enrolled in PAR-006 and PAR-007 clinical trials respectively to monitor the durability of treatment effect.

The PAR-009 study comprising some 270 patients will be undertaken to assess retreatment at various intervals, in order to support the use of Zilosul® over multiple cycles. The timeline is yet to be determined.

From a competitive view, in addition to the ability of PAR-002 and -003 to demonstrate superiority of safety and efficacy, extended durability of the treatment effect would be expected to support market uptake and pricing negotiations. The re-treatment study will be important in demonstrating that repeated dosing is safe for ongoing treatment.

PAR-008 Disease Modifying OA trial (DMOA)

PAR is also conducting a clinical trial in KOA patients to determine if Zilosul® offers a Disease Modifying role in OA (DMOA). It will need to demonstrate the ability of Zilosul® to inhibit the progression of the disease and/or improve the condition. There are no approved DMOA drugs. PAR-008 is a 60 patient Phase 2b trial that is measuring the change in a number of synovial fluid biomarkers associated with pain, inflammation and OA disease progression following treatment with Zilosul®. Topline results are expected to be announced in Q3CY22. Results of the trial are expected to inform discussions with the regulators regarding the path DMOA designation.

OA Canine trial

PAR is also conducting a canine trial in OA. Pain and function will be assessed as well as changes in blood biomarkers, structural and bone marrow lesions by MRI. The 20 week follow up study equates to the equivalent of three human years in terms of OA changes. The aim of the trial is to support the results of PAR-008 with confirmatory data over an implied extended period.

FDA Fast Track Designation

Over Q4FY22, PAR received FDA Fast Track designation. The shorter FDA review process includes:

- A 'Rolling Review' by the FDA – documentation to support approval may be submitted to the FDA for review as it is completed. Usually, all data must be collated before submission, potentially slowing the approval process.
- More frequent consultations with the FDA, to better guide and streamline the process.
- Potentially leading to other FDA designations if PAR meets the appropriate criteria, including:
  - Accelerated Approval under which the FDA may grant approval on a surrogate endpoint.
  - Priority Review – which aims to make a decision about an application for approval within 6 months of submission as compared to 10 months under standard review.

The designation is based on investigation of PPS in the treatment of OA.

CEO and funding to be confirmed

In MST's view, the uncertainty regarding the new CEO and funding continue to dampen the stock's performance.

CEO appointment

In November 2021, the company announced that former CEO and founder, Dr Paul Rennie, was to assume the role of non-executive Chair with the company to appoint a new CEO. The Board prefers the CEO to be US-based, as the company looks to turn its focus on commercialisation. The delay in an appointment brings uncertainty and in MST's view is weighing on the stock's performance.

Funding

PAR's Q3FY22 4C reported cash at A$39.9m (prev. A$55.03m). R&D comprised A$14m of expenditure, which included US$5m a milestone payment relating to the US Phase 3 Knee Osteoarthritis (KOA) trial and R&D

relating to PAR-008, PAR-006 and Mucopolysaccharidoses Syndrome (MPS) clinical trials. The company is expecting to receive its R&D tax rebate over the next quarter.

PAR will require additional funding to complete the Phase 3 trial and commercialise Zilosul® for the KOA markets. The company has stated it will seek non-dilutive funding to complete its Phase 3 program. PAR has participated in ~30 meetings at EU partnering conference and will attend further conferences as it seeks nondilutive funding for its extensive R&D program.

Valuation, Risks, Sensitivities

MST's valuation of $3.97ps. is unchanged. We note cash at 30.03.22 of ~$40m, as the company embarks on its multi-trial program. PAR does not have the cash to complete its planned trial program. The valuation assumes that PAR can secure funding and deliver its trial program. PAR plans to announce the results of its PAR-008 trial in Q3CY22. Strong data may support licensing discussions. In MST's view, investor reservation will continue until there is confirmation of a CEO and funding.

The valuation is subject to the usual drug development risks including confirmation of drug efficacy and safety, regulatory approval, market uptake, competing therapies and funding. They present upside and downside risk to our valuation assumptions. COVID outbreaks may impact trial timelines.

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