Strong newsflow over CY23

Phase 3 off to good start

CY23 looks to be a busy year for PAR with a number of key milestones in both its Knee Osteoarthritis (KOA) and Mucopolysaccharidosis (MPS) trial programs. In late CY22, PAR announced that its pivotal Phase 3 trial program for KOA had passed its first safety review - a significant milestone. The review is conducted by an external Data Monitoring Committee (DMC). It assesses the safety and efficacy of the trial study, as well as ensuring the validity and scientific merit of the trial. It is an important tick for PAR's management as the team co-ordinates a global trial program which plans to include 120 clinical trial sites. The first Canadian trial site was activated in late 2022.

Busy Year ahead

The key expected milestones include:

- Confirmation of dosing for the KOA trials which will signal the start of PAR-003, the Phase 3 confirmatory trial. PAR-002 and 003 trial participants 'roll over' into the PAR-006 and 007 for six-month observational follow-up studies.
- 6 and 12 month data from the PAR-008 trial to help inform discussions with the US and EU regulatory agencies regarding the requirements for classification as a Disease Modifying Osteoarthritis (DMOA) drug. Canine study data also to be reported.
- Topline data from PAR's VI trial and complete data from the MPS-I trial.

One area to watch over the coming year will be how PAR plans to fully exploit the commercial potential of both its KOA and MPS programs. In mid CY22, the company appointed Mr Marco Polizzi as CEO to boost the commercial experience within PAR. His unexpected departure leaves a gap within the company's management skill set. Mr Rennie, founder of PAR, has transitioned to Executive Chair.

Valuation, Risks and Sensitivities

MST's valuation of $3.27ps. is unchanged. The valuation assumes that PAR can deliver its trial program timelines. The valuation is subject to the usual drug development risks, commercial uptake – regulatory approval market entry, market size, market share, pricing, drug supply, competitor products, timelines and potential licensing metrics – all may differ to MST assumptions. Cash balance as of 31 December 2022 was $83.92m (Q1: $92.375m). During the December quarter PAR received an R&D Tax Incentive Rebate of $7.4m.

PARADIGM BIOPHARMA

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	$1.48
Market cap	$415m
Valuation	$3.27 (unchanged)

Next news

- Q1CY23 H1CY23 – 6 month data PAR-008 DMOA trial
- H1CY23 – Dose selection for ongoing KOA phase 3 trials
- H1CY23 – 1st patient enters PAR-003 confirmatory trial
- H1CY23 - 8 & 26 week canine study data

PAR.AX Share Price (A$)

Source: Factset

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Figure 1 – MST Financial Summary

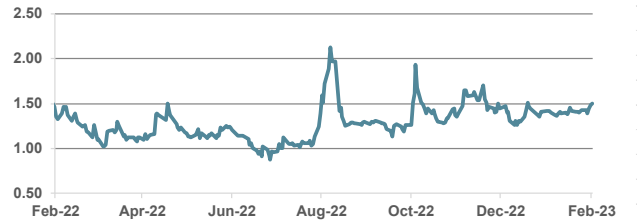
Paradigm Biopharmaceuticals Ltd — PAR-AU

Year end 30 June

MARKET DATA

Share Price	**A$/share**	**1.48**
52 week high / low	A$	2.16 - 0.86
Valuation (12 month forward)	**A$**	**3.27**
Market capitalisation	**A$m**	**415**
Shares on issue	m	285
Options	m	4
Other equity	m	47
Potential shares on issue (diluted)	m	336

12 month performance



INVESTMENT FUNDAMENTALS		FY20	FY21	FY22	FY23E	FY24E
EPS Reported (undiluted)	¢	(6.0)	(16.7)	(16.8)	(15.2)	(11.2)
EPS Underlying (undiluted)	**¢**	**(6.0)**	**(16.7)**	**(16.8)**	**(15.2)**	**(11.2)**
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$)		FY20	FY21	FY22	FY23E	FY24E
Forecast year end shares	m	225	230	233	283	330
Market cap (Y/E / Spot)	**$m**	**332.6**	**340.3**	**344.4**	**419.5**	**488.6**
Net debt /(cash)	$m	(103.9)	(71.0)	(39.7)	(59.2)	(92.2)
Enterprise value	**$m**	**228.7**	**269.2**	**304.7**	**360.4**	**396.4**
EV/Sales	x	61.8	30.8	34.9	22.2	12.6
EV/EBITDA	**x**	**n/m**	**n/m**	**n/m**	**n/m**	**n/m**
EV/EBIT	x	n/m	n/m	n/m	n/m	n/m
Net debt / Enterpprise Value	x	n/m	n/m	n/m	n/m	n/m
Gearing (net debt / EBITDA)	**x**	**7.8**	**2.1**	**1.0**	**1.3**	**2.4**
Operating cash flow per share	$	(0.0)	(0.2)	(0.1)	(0.2)	(0.1)
Price to operating cash flow	**x**	**(33.0)**	**(9.7)**	**(10.7)**	**(9.7)**	**(13.2)**
Free cash flow	**$m**	**(4.5)**	**(34.3)**	**(32.2)**	**(43.2)**	**(36.9)**
Free cash flow per share	$	(0.02)	(0.15)	(0.14)	(0.15)	(0.11)
Price to free cash flow	**x**	**(74.5)**	**(9.9)**	**(10.7)**	**(9.7)**	**(13.2)**
Free cash flow yield	**%**	**n/m**	**n/m**	**n/m**	**n/m**	**n/m**
Book value / share	$	0.48	0.34	0.18	0.22	0.29
Price to book (NAV)	**x**	**3.1**	**4.3**	**8.1**	**6.7**	**5.1**
NTA / share	$	0.47	0.33	0.17	0.21	0.28
Price to NTA	**x**	**3.2**	**4.5**	**8.7**	**7.0**	**5.2**
EBITDA margin	%	n/m	n/m	n/m	n/m	n/m
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	n/m

PROFIT AND LOSS (A$)		FY20	FY21	FY22	FY23E	FY24E
Revenue & Other Income	A$m	3.7	8.7	8.7	16.2	31.4
Expenses	A$m	(17.0)	(43.2)	(48.0)	(60.7)	(70.0)
EBITDA	**A$m**	**(13.3)**	**(34.5)**	**(39.3)**	**(44.4)**	**(38.6)**
D&A	A$m	-	-	-	-	-
EBIT	**A$m**	**(13.3)**	**(34.5)**	**(39.3)**	**(44.4)**	**(38.6)**
Interest	A$m	1.0	0.2	0.0	1.2	1.7
Non-operating income	A$m	-	-	-	-	-
Pre-tax Profit	**A$m**	**(12.3)**	**(34.3)**	**(39.2)**	**(43.2)**	**(36.9)**
Tax	A$m	-	-	-	-	-
Minorities	A$m	-	-	-	-	-
Underlying NPAT	**A$m**	**(12.3)**	**(34.3)**	**(39.2)**	**(43.2)**	**(36.9)**

BALANCE SHEET (A$)		FY20	FY21	FY22	FY23E	FY24E
Cash	A$m	103.9	71.0	39.7	59.2	92.2
Receivables	A$m	3.5	8.5	6.7	0.7	1.3
Inventory	A$m	-	-	-	0.4	0.8
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$m	1.9	2.2	1.3	1.3	1.3
Total Assets	**A$m**	**112.4**	**84.8**	**50.7**	**64.5**	**98.6**
Accounts Payable	A$m	2.8	5.0	7.1	0.7	1.3
Borrowings	A$m	-	-	-	-	-
Leases	A$m	0.9	0.8	0.6	0.6	0.6
Provisions	A$m	0.5	0.8	0.7	0.7	0.7
Other	A$m	-	-	-	-	-
Total Liabilities	**A$m**	**4.2**	**6.5**	**8.4**	**2.0**	**2.6**
Shareholder's equity	**A$m**	**108.2**	**78.3**	**42.3**	**62.6**	**96.0**

CASH FLOW (A$)		FY20	FY21	FY22	FY23E	FY24E
Receipts from customers	A$m	-	-	0.1	16.2	22.0
Payments to suppliers and employees	A$m	(14.8)	(38.6)	(41.8)	(60.7)	(70.0)
Milestones, R&D Rebates, Grants	A$m	3.6	3.4	9.5	-	9.3
Interest	A$m	1.1	0.3	0.0	1.2	1.7
Tax	A$m	-	-	-	-	-
Operating cash flow	**A$m**	**(10.1)**	**(34.9)**	**(32.2)**	**(43.2)**	**(36.9)**
Capex	A$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)	0.1	-	-
Equity	A$m	34.3	1.0	-	62.7	70.0
Dividend	A$m	-	-	-	-	-
Financing cash flow	**A$m**	**36.1**	**1.0**	**0.1**	**62.7**	**70.0**
Change in Cash / FX	A$m	31.6	(33.3)	(32.1)	19.5	33.1
Year end cash	**A$m**	**103.9**	**71.1**	**39.7**	**59.2**	**92.2**

Key milestones expected over CY23

PAR.AX is repurposing pentosan polysulphate sodium (PPS) as an injectable formulation (Zilosul®) for a number of inflammatory related conditions. Its first targets include osteoarthritis (OA) and mucopolysaccharidoses (MPS). PPS has been approved for >50 years for use in haemorrhagic cystitis.

CY23 looks to bring strong newsflow as PAR's two clinical programs progress. Positive data from the PAR-008 trial and canine studies are expected to trigger discussions with the FDA regarding an ongoing program to demonstrate a disease modifying role for Zilosul®. Confirmation of the most effective Zilosul® dose will trigger the start if the confirmatory KOA trial, PAR-003.

Figure 2 – Newsflow over CY23

Timing	Milestone	Newsflow
Q1CY23	PAR–008	6-month DMOA data
Q1CY23	MPS I	Presentation at the XVII International Conference on Lysosomal Disease
Q1CY23	MPS VI	Poster presentation at World Symposium in Lysosomal Disease
Q1CY23	DMOA	Presentations at Osteoarthritis Research Society International World Congress (OARSI) -Poster, Clinical Trial Update, Oral presentattions
H1CY23	PAR-002, 003,007	Dose confirmation from Stage 1 of PAR-002. PAR-003 & PAR-007 to commence
H1CY23	Canine Data	Complete 8 & 26 week data report
H1CY23	MPS VI	Phase 2 - full trial recruitment
H2CY23	PAR-008	12-month DMOA data
H2CY23	MPS VI, I	Topline data from MPS-VI trial and full data from the MPS-I trial

Source: Company Reports, MST Assumptions

KOA PAR-002 trial progress and commencement of PAR-003, PAR-006 trial

√ 1st Data Monitoring Committee (DMC) review in Phase 3 KOA trial

The first safety review by the Data Monitoring Committee (DMC) of its pivotal PAR-002 clinical trial concluded that the clinical trial should proceed without modification. The DMC is responsible for assessing safety and efficacy during the conduct of Paradigm's PAR-002 study, as well as ensuring the validity and scientific merit of the trial. The 'tick of approval' brings confidence on the execution of large clinical trial of >900 patients with ~120 planned trial sites over the US, Australia, UK, EU and Canada.

Dose Confirmation to trigger start of PAR-003

PAR's pivotal PAR-002 adaptive staged design includes a dose confirmatory stage. Stage 1 aims to determine the optimal dose. Participants in the PAR-002 trial are being 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. The completion of the Stage 1 is not planned to include release of any efficacy data.

The selected dose will be used in the continuing PAR-002 and PAR-006 trials. PAR-003, the confirmatory trial and PAR-007, the observational follow-up trial will commence with the selected dose. Data from PAR-006 and PAR-007 aim to establish the duration of the treatment effect.

Further data on potential Disease Modifying Role in Osteoarthritis (DMOA)

Currently approved OA drug therapies offer only short to medium term relief of symptoms including pain and swelling. None to date has been approved as a disease modifying therapy – able to halt the progress of the disease and/or reduce the symptoms over the longer term. PAR's Phase 2b clinical trial reported reduction in volume in Bone Marrow

Oedema (BME) lesions and a number of changes in blood serum biomarkers. The trial results support a potential DMOA role.

PAR-008 is being undertaken to further explore the potential DMOA effect of Zilolsul®. In October 2022, PAR reported that PAR-008's Day 56 data were supportive in a number of 'DMOA' endpoints including joint biomarkers, pain and knee function. 6-month data are expected over Q1CY23, with 12-month data to follow in H2CY23. PAR plans to use the data to support discussions with the FDA regarding the potential path to seeking a DMOA approval.

Results in canine study

PAR also plans to announce 26-week data from its canine DMOA studies in H1CY23. Dogs age more quickly than humans with 20 weeks of dog's life being the equivalent of 3 'human' years. The aim of the study is to expedite 'long term' data. 21 dogs with OA of the stifle joint (equivalent of the ankle joint in humans) are being treated with PPS for 6 weeks. Trial endpoints are similar to the PAR-008 study including synovial biomarkers and X-ray changes of the joint cartilage. Early data announced in October 2022 were supportive. The 20 weeks of ongoing monitoring will provide data the equivalent of 3 years in human.

MPS Clinical trials

PAR is also conducting clinical trial programs in MPS-I and MPS-VI. Topline data from MPS-VI trial and full data from the MPS-I trial are expected by CY23 end. Positive data may support a licensing agreement with associated payments to assist in the funding of the KOA trials.

In summary, PAR is expecting news flow over CY23 regarding its KOA Phase 3 and MPS Phase 2 trial programs as well as further evidence of Zilosul®'s DMOA potential. In MST's view, clearly positive news is likely to support funding/ potential licensing activities.

Investment Thesis

Snapshot of Paradigm Biopharma (PAR.AX)

PAR.AX is repurposing pentosan polysulphate sodium (PPS) as an injectable formulation (Zilosul®) for a number of inflammatory related conditions. Its first targets include osteoarthritis (OA) and mucopolysaccharidoses (MPS). PPS has been approved for >50 years for use in haemorrhagic cystitis.

- Zilosul® Phase 2b trial data support a potential superior advantage to current drug therapies.
- Positive results in Phase 3 trials are expected to support application for US, EU and Australian approval.
- The readout of Phase 3 trial arm, PAR-002, is planned for Q4CY24.
- With cash at ~A$83.29m at Dec 2022. MST estimates that PAR has funding to Q1CY24.

Investment thesis

- Zilosul® carries lower development risk: Firstly as a repurposed drug, it has strong supporting safety data and secondly, 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 higher market penetration, pricing advantages and potentially longer term use.

Valuation, Risks, Sensitivities

MST's valuation of $3.27ps. is unchanged. Cash balance as of 31 December 2022 was $83.92m (on 30 September 2022 it was $92.375m). During the December quarter Paradigm received a R&D Tax Incentive Rebate of $7.4m. Planned newsflow over FY23, particularly the DMOA studies, should help support the company's licensing raise plans.

MST valuation carries a number of assumptions with respect to regulatory approval, commercial uptake – timing around trials and market entry, market size, market share, pricing, drug supply, competitor products, timeline and potential licensing metrics. The MST model assumes these assumptions may not be realised, posing risk to the valuation.

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