Positive Early Disease Modifying Data

PAR.AX has announced interim data from both its PARA_OA_008 Phase 2 clinical trial and canine study. The studies are exploring its drug, injectable pentosan polysulphate sodium (iPPS) in a potential disease modifying (DMOA) role. The data provide:

1. early evidence of a potential DMOA role

The 008 Day 56 data were supportive in a number of 'DMOA' endpoints including joint biomarkers, pain and knee function. PAR will continue monitoring the effects of the treatment to 6 months before seeking discussions with the FDA on the next steps. They are no approved DMOA drugs to provide a guide to the FDA requirements. MST notes Merck KGaA's sprifermin DMOA trial continues with data to 5years+.

2. positive results in canine study

PAR has also reported early data from its canine study. 21 dogs with OA of either the hind or front limb joint were treated with iPPS at a 3 mg/kg (1.7mg/kg human equivalent) or placebo for 6 weeks. The dog trial program has provided early data including 7/9 dogs showing a clinically meaningful improvement in weight bearing as measured by Total Pressure Index (TPI).

3. additional support of KOA trials 002,003

The 008 trial also reported statistically significant improvements in pain, function and stiffness in the twice-weekly treatment group compared to placebo. In MST's view, the data provide support of the Knee OA (KOA) Phase 3 trials, PAR_OA_002 and 003.

Valuation, Risks and Sensitivities

MST's valuation is unchanged at $3.27ps. The data are positive however, too early at two weeks post dosing to confirm a DMOA effect. We also await further clarity on the regulatory processes to establish DMOA status to be provided.

The valuation is subject to the usual drug development risks, commercial uptake – funding, regulatory approval market entry, market size, market share, pricing, drug supply, competitor products, timelines and potential licensing metrics – all may differ to MST assumptions.

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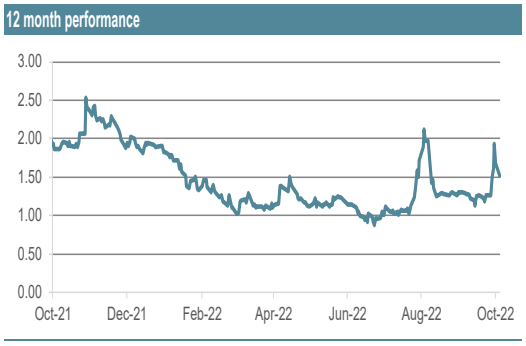
ASX-listed biotechnology company, Paradigm Biopharma's (PAR.AX) strategy is to take already approved medicines that have shown safety and efficacy in one condition and repurpose them for new indications. The aim is to reduce time, cost and risk. Its first candidate is injectable pentosan polysulphate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

Stock	PAR.AX
Price	A$1.52
Market cap	A$432m
Valuation	A$3.27 (Unchanged)

Next news

- H2CY22 – 1st 002 Trial patient enters PAR-006 treatment durability trial
- H2CY22 - First Data Safety Monitoring Board Review for PAR-002 study
- 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

Financial Summary

Paradigm Biopharmaceuticals Ltd — PAR-AU

Year end 30 June

MARKET DATA

Share Price	**A$/share**	**1.52**
52 week high / low	A$	2.69 - 0.86
Valuation (12 month forward)	**A$**	**3.27**
Market capitalisation	**A$m**	**432**
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**	**340.5**	**348.3**	**352.5**	**429.4**	**500.1**
Net debt /(cash)	$m	(103.9)	(71.0)	(39.7)	(59.2)	(92.2)
Enterprise value	**$m**	**236.6**	**277.3**	**312.8**	**370.3**	**407.9**
EV/Sales	x	64.0	31.8	35.8	22.8	13.0
EV/EBITDA	**x**	**(17.8)**	**(8.0)**	**(8.0)**	**(8.3)**	**(10.6)**
EV/EBIT	x	(17.8)	(8.0)	(8.0)	(8.3)	(10.6)
Net debt / Enterpprise Value	x	(0.4)	(0.3)	(0.1)	(0.2)	(0.2)
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**	**(33.7)**	**(10.0)**	**(10.9)**	**(9.9)**	**(13.5)**
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**	**(76.2)**	**(10.2)**	**(10.9)**	**(9.9)**	**(13.5)**
Free cash flow yield	**%**	**-1.3%**	**-9.8%**	**-9.1%**	**-10.1%**	**-7.4%**
Book value / share	$	0.48	0.34	0.18	0.22	0.29
Price to book (NAV)	**x**	**3.1**	**4.4**	**8.3**	**6.9**	**5.2**
NTA / share	$	0.47	0.33	0.17	0.21	0.28
Price to NTA	**x**	**3.2**	**4.6**	**9.0**	**7.2**	**5.4**
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**

Source: Company, MST Access

Investment Thesis

Snapshot of Paradigm Biopharma (PAR.AX)

- As a repurposed drug, injectable pentosan polysulphate sodium (Zilosul®), presents a lower safety risk.
- Zilosul®'s 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.
- Early data emerging from its DMOA studies are supportive of a wider role for Zilosul® with the potential ability to slow or halt the disease process.

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 confirms 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.
- Pricing premium: There are no approved DMOA drugs. Confirmation of a DMOA role would also support a pricing premium in comparison to current therapies.

Valuation, Risks, Sensitivities

MST's valuation of $3.27ps. is unchanged. Further data that confirm a DMOA role are likely to see an increase in valuation, given the unmet medical need and progressive debilitating nature of OA.

The valuation is subject to the usual drug development risks, commercial uptake, funding, regulatory approval market entry, market size, market share, pricing, drug supply, competitor products, timelines and potential licensing metrics – all may differ to MST assumptions.

Expected CY21 News flow

- H2CY22 - 1st 002 Trial patient enters PAR-006 treatment durability trial
- H2CY22 - First Data Safety Monitoring Board Review for PAR-002 study
- H1CY23 – Dose Selection for PAR-002 and PAR-003
- H1CY23 – 1st Patient enters PAR-003 Confirmatory trial

PAR 008 shows positive trends in potential DMOA biomarkers

PAR.AX has announced interim data from its PARA_OA_008 Phase 2 clinical trial. The 60 patient trial aims to explore a potential DMOA role through changes in key synovial fluid (joint) biomarkers that are associated with pain, inflammation and OA disease progression. Participants have been randomised into three treatment groups according to a 1:1:1 ratio (19 randomised to iPPS twice-weekly, 20 randomised to iPPS once-weekly plus a placebo injection once-weekly, 22 randomised to placebo twice-weekly).

The trial is an exploratory study and not intended to be powered to obtain statistical significance. The primary endpoint was change from baseline at Day 56, in one or more synovial fluid biomarkers. The trial endpoints also included pain and knee function. Further data will be taken at various assessment timepoints out to one year. Results of the trial are expected to inform discussions with the regulators regarding a Phase 3 trial to confirm DMOA designation.

Positive PAR_OA_008 Results

1. Primary endpoint - The trial showed a trend in reduction of a number of OA associated synovial fluid biomarkers. They included:
   ↓ Nerve growth factor (NGF) - associated with pain reduction.
   ↓Tumour necrosis factor (TNF)-α, Interleukin-1β (IL-1β), and Interleukin-6 (IL-6) associated with inflammatory pathways.
   ↓ Cartilage oligomeric matrix protein (COMP) and ↓ Alanine–Arginine–Glycine–Serine (ARGS) and ↑ Tissue inhibitor of MMP (TIMP-1) associated with cartilage and potential disease modification.

   In all cases, the synovial biomarker changes in iPPS-treated subjects at day 56 were favourable compared to placebo controls. The results were supportive in developing a greater understanding iPPS's method of action (MOA) which is important in the regulatory processes and supportive of potential disease modification.

2. The trial also included assessment of pain, function and stiffness. The mean percentage reduction in pain (WOMAC assessment) was 50% in 2X weekly iPPS versus 30% in placebo (p=0.05) and 50% to 25% in WOMAC function in the twice weekly iPPS compared to placebo (p=0.017). The data showed statistically significant improvements in all three measurements in the twice-weekly treatment group compared to placebo. The results were in keeping with PAR's Phase 2b trial in KOA. We note that in H1CY23, PAR plans to confirm the dose for its PAR_OA_002 trial. Currently it is exploring both weekly and twice-weekly dosing. The 008 data may also inform the dosing confirmation.

3. In keeping with iPPS trials to date, no serious adverse events were reported. The most common side effects were injection site reactions, all of which were mild in intensity and self-limiting.

4. The study also evaluated the effect of iPPS on the biomarkers in the blood and urine and possible correlations with the synovial joint biomarker levels. PAR's Phase 2b clinical trial showed serum and urine changes in biomarkers COMP, a disintegrin and metalloproteinase with thrombospondin motifs (ADAMTS-5) and C-telopeptide fragments of type II collagen (CTX-II). The data may assist in understanding the MOA and the importance of relevant markers.

Supportive canine data

PAR is also conducting an OA trial in a 21-dog cohort over 20 weeks. Pain and function are being assessed as well as changes in blood biomarkers. Changes in structural and bone marrow lesions are being measured by MRI. A 20 week follow up equates to the equivalent of 3 human years in terms of OA changes and thereby the trial aims to provide insight to iPPS treatment outcomes and potential DMOA effect over an extended period. Data to date have been supportive in improved joint function, synovial and serum biomarkers and OA structural changes. Functional improvement as measured by Total Pressure Index (TPI) has shown early positive effect.

Sprifermin -DMOA

MST notes that Merck KGaA's Sprifermin continues its DMOA clinical trial program. Sprifermin is a recombinant human fibroblast growth factor 18 (rhFGF18) analog that increases cartilage production. The trials' timelines are long, in part reflecting the primary endpoint. Sprifermin aims to increase the articular cartilage in the knee joint and thereby reduce the effects of cartilage destruction and restore normal joint function and reduce the associated pain and limited movement. The poor blood supply in the articular cartilage presents challenges in terms of long timelines. The trial continues with data of > five years.

iPPs may offer a faster trial program. iPPS's method of action (MOA) is yet to be confirmed. The current DMOA studies aim to help elucidate the pathways. PAR plans to present data from 008 trial and canine study in discussions with the regulatory bodies to find acceptable endpoints for a trial to confirm a DMOA role. FDA acceptance of biomarkers and changes in bone marrow lesions that have been shown to correlate with changes in pain, movement and the joint structure potentially promise shorter timelines.

Figure 1: Sprifermin Phase 1 Trial

Timeframe	Participants	Primary Endpts	Secondary Endpts	Results
2009-2014	192	6-12mths change in cartilage thickness via MRI	Cartilage volume and thickness, joint space width, pain WOMAC	No stat significant difference in primary endpts; but stat significant secondary endpts

Source: MST, Merck

Figure 2: Sprifermin Phase 2 Trial

Timeframe	Participants	Primary Endpts	Secondary Endpts	Results
2012-2020	549 (494 participants evaluated)	24-36 mths change in cartilage thickness via MRI	Pain WOMAC	Stat significant primary endpts; secondary endpts met but not stat significant

Source: MST, Merck KGaA

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