FDA raises another query

PAR has received a further query from the FDA regarding its Investigational New Drug (IND) application to start its pivotal Phase 3 trial, PAR_002, in the US.

The query relates to a finding in one of 26 preclinical studies that PAR 'repeated' following its pre-IND meeting with the FDA in CY20. The FDA's request arose as Zilosul® is a repurposed injectable drug and the original studies related to an oral formulation and were not conducted under the current Good Laboratory Practice standards.

PAR does not consider the finding will impact the trial as;

- It was not deemed clinically significant.
- It was only noted in one animal out of hundreds examined.
- It is not an uncommon finding in rat model studies.

There were no deaths in the animal groups and there have been no reports of the related finding in any of the 400+ patients treated to date.

PAR has been requested to submit a report from a 'clinical study expert' to review the finding and note any mitigation strategies to monitor for it over the trials. PAR has already presented a non-clinical expert report.

PAR plans to submit its responses over the next month, which will trigger another 30 day FDA review period. The start of the US Phase is now expected to be in October versus the original date of June.

Impact of delay

- Timing – The query adds another ~2 months to the IND process and potentially ~3 months to the completion of OA_002 trial in the US. PAR is undertaking measures to reduce the effect including expansion of the Australian and EU trials.
- Cost/Funding – PAR has stated its current $71m will support its planned trials program in OA and MPS. It believes that the finalisation of the IND will trigger further partnership interest. MST valuation assumes a licensing deal over FY23.

Valuation, Risks and Sensitivities

MST values PAR at A$974m, $4.25ps. We flag risk of further delay to the trial timetable with potential impact on the MST valuation. It also is subject to the usual drug development risks including drug efficacy and safety, regulatory approval, new competing therapies, funding and market uptake. The model is based on positive results triggering a licensing agreement with milestone payments and royalties to follow.

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 in the knee (KOA) and hip (HOA) and mucopolysaccharidosis (MPS), a genetic enzyme disease. Management presents a strong background in drug development.

Stock	ASX: PAR
Price	A$1.97
Market cap	A$444m
Valuation	A$4.25

Company data	
Net cash (30/06/21)	$71.1m
Shares on issue	226m
Options/ Rights	1.5m
Primary exchange	ASX

Next steps

Q3C621: Phase 2b/3 OA_002 to start
Q4CY21: OA_006 trial in treatment extension to start

PAR share price (12 months)

Source: FactSet

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Financial Summary

Paradigm Biopharma

PROFIT AND LOSS $A	2019A	2020A	2021F	2022F	2023F
Income	3,245,628	4,695,494			43,500,000
R&D Tax Rebate Incentive			43,500	10,000,000	
Research and development expenses	-7,896,708	-12,793,576	-30,000,000	-40,000,000	-45,000,000
Employee expenses	-2,575,983	-1,226,649	-5,000,000	-5,000,000	-5,000,000
General and administration expenses	-1,471,497	-2,939,988	-5,000,000	-5,000,000	-5,000,000
Impairment loss	-6,928,984				
Operating Profit/ Loss	-15,627,544	-12,264,719	-39,956,500	-40,000,000	-11,500,000
Interest Income/Expense	261,710	-34,168	840,875	448,188	195,847
Profit/Loss before income tax	-15,365,834	-12,298,887	-49,669,418	-39,551,812	-11,304,153
Income tax expense / (benefit)					
Net Operating Profit/Loss	-15,627,544	-12,298,887	-49,669,418	-39,551,812	-11,304,153
Other comprehensive Income					

BALANCE SHEET	2019A	2020A	2021F	2022F	2023F
ASSETS					
Current assets					
Cash and cash equivalents	78,836,173	103,922,241	64,806,616	25,254,804	13,950,651
Trade and other receivables	3,532,227	3,509,777	3,553,277	3,553,277	3,553,277
Prepaid expense	137,113	192,380	100,000	100,000	100,000
Financial assets held at amortized cost	6,500,000	746,200		-	
Total current assets	82,505,513	108,370,598	68,459,893	28,908,081	17,603,928
Non-current assets					
Intangible assets	2,981,359	2,947,588	3,000,000	3,000,000	3,000,000
Right-of-use assets		832,917			
Security Deposits Receivable		102,616			
Other	24,029	109,913	24,000	24,000	24,000
Total non-current assets	3,005,388	3,993,034	3,024,000	3,024,000	3,024,000
LIABILITIES					
Current liabilities					
Trade and other payables	2,315,992	2,784,324	1,797,355	1,797,355	1,797,355
Employee benefits	388,591	455,510	400,000	400,000	400,000
Lease Liabilities		124,731			
Total current liabilities	2,704,583	3,364,565	2,197,355	2,197,355	2,197,355
Non Current Liabilities		817,348	220,444	220,444	220,444
Net assets	82,806,318	108,181,719	69,066,094	29,514,282	18,210,129
EQUITY					
Issued capital	109,468,292	145,865,076	145,865,076	145,865,076	145,865,076
Share based payments reserve	4,072,844	3,585,189	3,585,189	3,585,189	3,585,189
Accumulated losses	-30,734,818	-41,268,546	-80,384,171	-119,935,983	-131,240,136
TOTAL EQUITY	82,806,318	108,181,719	69,066,094	29,514,282	18,210,129

CASHFLOW	2019A	2020A	2021F	2022F	2023F
Cash flows from operating activities					
Operational Income					43,500,000
Research and development tax incentive received	2,318,718	3,621,355	43,500	10,000,000	
Payments for Phase III and II/III Trials			-30,000,000	-40,000,000	-45,000,000
Payments to suppliers and employees (Inclusive of GST)	-8,773,072	-14,797,407	-10,000,000	-10,000,000	-10,000,000
Interest received	89,259	1,120,163	840,875	448,188	195,847
Net cash outflow from operating activities	-6,365,095	-10,090,057	-39,115,625	-39,551,812	-11,304,153
Cash flows from investing activities					
Payments for intangible assets	-4,198	-3,353			
Payments for plant and equipment	-17,781	-127,537			
Payments for financial assets held at amortized cost	-6,500,000	5,753,800			
Net cash outflow from investing activities	-6,521,979	5,622,910			
Cash flows from financing activities					
Proceeds from the issue of share capital	86,962,482	35,000,000			
Proceeds from exercise of share options	1,084,854	1,839,328			
Payments of share issue costs	-5,269,719				
Net cash inflow from financing activities	82,777,617	36,053,215			
Net increase/ (decrease) in cash and cash equivalents	69,890,543	31,586,068	-39,115,625	-39,551,812	-11,304,153
Cash at the beginning of the financial period	2,445,630	72,336,173	103,922,241	64,806,616	25,254,804
Cash at the end of the financial period	72,336,173	103,922,241	64,806,616	25,254,804	13,950,651

Source: PAR reports, MST estimates

Snapshot of Paradigm Biopharma (PAR.AX)

- Repurposing polysulphate pentosan (Zilosul®) for knee & hip osteoarthritis, presenting a lower safety risk.
- Zilosul® trial data have demonstrated more effective relief and lower side effects to current therapies.
- Positive results in Phase 3 trials will support application for US, EU and Australian approval.
- Pivotal Phase 3 Trial, PAR_002 readout is planned for Q1/Q2CY23.
- PAR is exploring potential licensing opportunities.

Investment thesis

- **Zilosul® carries lower risk** as a repurposed drug and a later stage asset as it enters Phase 3 trial.
- **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 the data from the OA_008 trial support Zilosul®'s disease-modifying ability, potentially the first approved OA drug to do so, there is also likely to be very strong interest from licensing partners as well as from clinicians and patients.
- **Funding**: MST model assumes that a licensing agreement before or on the news of positive results of the KOA pivotal trial in Q1/Q2CY23 will help fund the expanded trial program.
- **Revenues**: First revenues started from post Ross River Virus arthralgia patients under the Australian SAS. The model assumes revenue from a KOA licensing deal on release of Phase 3 data over CY23, with sales revenues in late CY24/early CY25. TGA provisional approval sales for KOA are expected from CY24. We note risk from potential further trial delay.

Valuation

MST risk-adjusted discounted cash flow valuation of $974m or $4.25 per share compares to $444m market capitalisation, $1.97ps.

The valuation includes assumptions of probability of approval, commercial performance and is subject to the usual sensitivities/risks regarding trial delay, competitor activity, market size, pricing, patient usage, product supply, timing of regulatory approval and reimbursement. They present upside and downside risk to our valuation assumptions. The ongoing COVID pandemic presents risk of delay and potential further costs.

The model assumes sufficient funding for OA_002 and OA_003 with further funding to complete the total trial program.

MST believes that the target indication and novel aspects of Zilosul® are likely to attract corporate and investor interest. The valuation based on the use of iPPS as Zilosul® in both knee and hip OA and in mucopolysaccharidosis (MPS). It does not ascribe any value to other potential clinical applications.

Expected CY21 News flow

- √ Q1CY21 – Commence clinical trial OA_008
- *√ Q1CY21 – Investigational New Drug (IND) submission to FDA* - ***in progress***
- Q3CY21 – Commence Phase 2b/3 OA 002
- Q4CY21 – Commence OA_006 trial in treatment extension

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