BELL POTTER

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Speculative

See key risks on Page 4 and Biotechnology Risk Warning on Page 7. Speculative securities may not be suitable for Retail Clients.

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Paradigm Biopharmaceuticals (PAR)

Edging Toward IND

Recommendation
Buy (unchanged)
Price
$1.97
Valuation
$3.00 (previously $3.15)
Risk
Speculative

GICS Sector

Pharmaceuticals & Biotechnology

Expected Return	
Capital growth	**52.3%**
Dividend yield	**0.0%**
Total expected return	**52.3%**

Company Data & Ratios	
Enterprise value	**$376.5m**
Market cap	**$447.6m**
Issued capital	**227.2m**
Free float	**91%**
Avg. daily val. (52wk)	**$2.2m**
12 month price range	**$1.87 - $3.19**

Price Performance

	(1m)	(3m)	(12m)
Price (A$)	1.94	2.26	3.40
Absolute (%)	14.43	-1.77	-34.71
Rel market (%)	11.79	-8.23	-59.72

Absolute Price

SOURCE: IRESS

Further confirmation on toxicology data

PAR provided an update on its Investigative New Drug (IND) application for Zilosul earlier today. The IND was lodged in March 2021 and following its initial review the FDA had come back to the company with six questions. Today's update indicates the Agency accepted PAR's responses to five of the six questions. The Agency requires further explanation on one final point relating to the non clinical toxicology data.

The key points are: 1) The FDA is placing emphasis on mechanism of action and safety as evidenced by these ongoing enquiries. This drug will potentially be available to millions of users in need of a non-opioid pain relief for osteoarthritis, hence the need for an outstanding safety record; and 2) PAR does not believe it will be required to generate further pre-clinical toxicology data in order to satisfy the FDA's enquiries. The exact nature of the toxicology issue was not discussed, however, we understand the risk can be mitigated with a small adjustment to the clinical protocol. Zilosul has been administered to several hundred patients across the phase 2 clinical program in Australia and the Special Access Scheme with no significant safety matters to note.

Investment View: Maintain Buy (Spec)

We now expect the opening of the IND will be delayed until at least October 2021 and accordingly, this pushes back approval by 6 months compared to our previous expectation. First commercial revenues expected in late CY24. The timing of spend on the clinical program has been amended in the forecast to reflect the change in start date. In our view, the opening of the IND will represent a significant milestone for PAR with recruitment of clinical trials to begin shortly thereafter. Once recruitment begins it is likely there will further interest from marketing partners. Closing cash at 30 June 2021 was $71.1m which we estimate represents maximum of 2 years working capital prior to any deal income. Valuation is lowered to $3.00 and we maintain our Buy (Speculative) rating.

Earnings Forecast

June Year End	FY20	FY21e	FY22e	FY23e
Revenues	4.7	3.4	3.0	5.2
EBITDA $m	-12.3	-34.3	-42.6	-26.4
NPAT (underlying) $m	-12.3	-33.8	-42.1	-25.9
NPAT (reported) $m	-12.3	-33.8	-42.1	-25.9
EPS underlying (cps)	-6.1	-14.7	-18.4	-11.3
EPS growth %	na	na	na	-39%
PER (x)	nm	nm	nm	nm
FCF yield (%)	nm	nm	nm	nm
EV/EBITDA (x)	nm	nm	nm	nm
Dividend (cps)	-	-	-	-
Franking	0%	0%	0%	0%
Yield %	0.0%	0.0%	0.0%	0.0%
ROE %	-11.4%	-45.5%	-129.1%	-373.0%

SOURCE: BELL POTTER SECURITIES ESTIMATES

IND Edges Closer

Key Points:

The Investigative New Drug (IND) application for Zilosul was lodged in March 2021. While the IND has not yet been opened, the pathway towards that goal is now clear with just one matter to be resolved.

During a review of the non-clinical toxicology data (toxicology data collected from rat studies) the FDA identified a marker which caused it some safety concern. This safety matter was raised with the company earlier this year in the original set of 6 questions following the first review of the dossier for the IND.

PAR responded to the original questions, however, the FDA now requires a further explanation of this one question on toxicology. The exact nature of the FDA's concern was not discussed.

The company believes it has sufficient data to respond to the FDA's questions and is highly unlikely to be required to generate further pre-clinical data. The toxicology data was prepared by the company in 2020 following a request from the FDA.

The way forward is for the company to prepare a further response to the FDA including input from a clinical expert. PAR will also modify the clinical protocol for the phase 3 trial to include an additional monitoring step during the dose escalation phase.

TIMING

The company intends to respond to this latest question from the FDA by the end of August 2021. It is likely the FDA will take a further 30 days to respond. Assuming there a no further questions the IND may open. Our best estimate is that the IND may open by mid-October, 2021.

LESSON LEARNT

While the IND process has been drawn out, in our view there is nothing that could have been done to abbreviate the process. No doubt COVID has slowed down all communication with the FDA and was also responsible for slowing down the preparation of the toxicology studies. Nevertheless the company is now on the cusp of a major value creating event – being the opening of the IND.

At the completion of the Phase 3 trial, the result should be a very clean data package supported by excellent safety data – both pre-clinical and clinical.

In the interim, the company intends to commence recruitment of the phase 2b dose escalation study in Australia, ahead of the IND opening in the US. Screening for patients in Australia will begin in 4Q21. PAR is unlikely to commence recruitment in Europe until the final dose escalation work is completed in the US and Australia.

Figure 1 - Changes to earnings

	2021			2022			2023		
	New	Old	% change	New	Old	% change	New	Old	% change
Revenues	3.4	3.0	13%	3.0	3.0	0%	5.2	5.2	0%
EBITDA	-34.3	-41.4	21%	-42.6	-42.6	0%	-26.4	-21.4	23%
NPAT	-33.8	-40.9	21%	-42.1	-42.1	0%	-25.9	-20.9	24%
EPS	-14.7	-17.8	21%	-18.4	-18.4	0%	-11.3	-9.1	24%

SOURCE: BELL POTTER SECURITIES

Earlier this year we had expected enrolment of the phase 2b/3 clinical program to commence in June. This is now pushed back until at least November/December 2021. There will be approximately 1,600 patients across the phase 2b/3 program inclusive of the confirmatory study being conducted in Europe.

The adjustment to earnings reflect the expected delay to commencement of revenues from product sales. FY21 revenue and costs have been adjusted to reflect our best estimate of income and costs and closing cash based on the recent quarterly cash flow statement. There are no changes to FY22 and costs are increased in FY23. The DCF valuation is risk weighted to allow for the risk associated with the phase 3 clinical program.

Following adjustment to earnings our valuation is amended to $3.00 from $3.15 and we maintain our Buy (speculative) rating.

Paradigm Biopharmaceuticals

Paradigm Biopharmaceuticals is an Australia biotechnology company focused on repurposing Pentosan Polysulfate Sodium (PPS) for the treatment of Osteoarthritis (OA) in the knee. If approved the drug will have the brand name Zilosul.

The global market for a safe, effective treatment that provides superior patient outcomes compared to the standard of care is a multiple blockbuster. The recently completed phase II study produced some highly encouraging results that are worthy of further clinical trials.

In the US along the incidence of moderate to severe osteoarthritis is estimated at 30m persons. The pricing of the drug will ultimately be determined by the economic benefit associated with its use as well as the cost of other therapies. The conservative estimate is US$2,500 per year which places the addressable market in the tens of billions of US$.

PROGRESS IN THE CLINIC

December 2018 - PAR announced headline results from its phase 2b randomised, double blind, placebo controlled multicentre trial, investigating subjects with Osteoarthritis and concurrent Bone Marrow Edema (BME) lesions (n=112). The trial met the clinical endpoint of change in Knee Injury and Osteoarthritis Outcome Score (KOOS) pain achieving both clinically meaningful and statistically significant results between placebo and PPS.

The headline results were followed up with strong signals of efficacy in the secondary endpoints (including KOOS function). This phase II trial was conducted at 6 sites in Australia.

PATHWAY TO APPROVAL

The company is pursuing a 505(b)2 registration pathway in the US. PAR is now awaiting the opening of the IND in order to commence an approval study.

ADJACENT INDICATIONS

Paradigm recently executed an Exclusive In-License Agreement for the use of iPPS in the treatment of mucopolysaccharidoses (MPS), a group of inherited lysosomal storage disorders. A key unmet medical need in this class of inherited disease is the lack of treatment of joint pain and dysfunction akin to osteoarthritis, hence the applicability of iPPS in treating these rare joint diseases. MPS is classified as an Orphan Indication/Designation in the US/EU and provides Paradigm the opportunity to serve a US$1.4bn p.a. market that is in desperate need of new cost-effective treatments.

KEY RISK AREAS

Regulatory Pathway - PAR is seeking registration for iPPS under the 505(b)2 regulatory pathway. The pathway is designed specifically for repurposed drugs including changes in dose form, strength, route of administration, formulation, dosing regimen or indication. This proposed repurposing of PPS has some rare characteristics.

- While the drug has been approved for years as an oral format and there is ample safety data, the proposed format, the dose and the indication (being OA) are all new.
- There is also the issue of the opioid crisis. PPS is a non steroid, non opioid, non addictive substance that has been shown to have a significant impact of pain levels associated with OA. It may help to reduce the accidental deaths from opioid overdose.
- PAR intends to conduct two phase 3 studies, one pivotal study of 750 subjects and a confirmatory phase 3 study of ~400 subjects.
- PAR will present a comprehensive set of safety data from the recent Phase II trial together with data from subjects treated in the compassionate use program and two phase 3 trials, thus representing a safety set of nearly 1,400 subjects. The evidence of

treatment will be established from two adequate and well controlled studies and further supported by the phases 2 data set.

Intellectual Property

- The company has several patents over the formulation and dosing on iPPS for the treatment of OA. The validity of these patents is highly likely to be challenged at some point, especially if the drug is a commercial success.
- The company has an exclusive supply contract with Bene Pharmaceuticals (Bene). We understand the exclusivity applies to human use only (excludes veterinary use). Bene holds the only drug Masterfile with the FDA to manufacture PPS. This supply contract represents a crucial piece of the company's value as it effectively prevents or delays the creation of generics.
- We are not aware of the contractual conditions that may lead to a termination of this contract (if any).
- We understand there are some other manufacturers of PPS, however, these products are not registered for human use and may not be referenced in any application for registration for human use. We understand the primary use of these products is veterinary.

Clinical Risk

- The efficacy of iPPS has not been validated in a large, multicentre, randomised, controlled clinical trial. There is no guarantee that the results from earlier studies will be repeated in a larger phase III study.

Commercial Validation

- Our valuation makes assumptions regarding selling price and volume in relation to future revenues from the sale of iPPS. In order for physicians to prescribe the drug and for payers to offer reimbursement, the clinical trials will need to demonstrate clinically significant improvement over the standard of care i.e. meaningful improvement in patient quality of life for pain reduction, side effect management and mobility amongst others. Early indicators based on the data from the phase II study are encouraging.

Paradigm Biopharmaceuticals

as at 3 August 2021

Recommendation	Buy, Speculative
Price	$1.97
Valuation	$3.00

Table 1 - Financial summary

Profit & Loss (A$m)	FY19	FY20	FY21e	FY22e	FY23e
Year Ending June					
Gross royalties	-	-	-	-	-
Gross milestones	-	-	-	-	-
Gross revenues	-	-	-	-	0.4
Risk adjusted revenues	-	-	-	-	0.2
COGS (Bene Royalty expense)	-	-	-	-	- 0
Gross profit	-	-	-	-	0
GP margin	na	na	na	na	na
R&D incentive/Upfront receipts	3.2	4.7	3.4	3.0	5.0
Total revenues	**3.2**	**4.7**	**3.4**	**3.0**	**5.2**
Other expenses	**-11.9**	**-17.0**	**-37.7**	**-45.6**	**-31.6**
EBITDA	**-8.7**	**-12.3**	**-34.3**	**-42.6**	**-26.4**
Depreciation	-	-	-	-	-
Amortisation	- 6.9	-	-	-	-
EBIT	-15.6	-12.3	-34.3	-42.6	-26.4
Sundry income	-	-	0.5	0.5	0.5
Pre tax profit	-15.6	-12.3	-33.8	-42.1	-25.9
Tax expense	-	-	-	-	-
NPAT- normalised	-15.6	-12.3	-33.8	-42.1	-25.9
Net abnormal items	-	-	-	-	-
Reported NPAT	-15.6	-12.3	-33.8	-42.1	-25.9

Cashflow (A$m)	FY19	FY20	FY21e	FY22e	FY23e
Gross cashflow	-6.5	-11.2	-34.1	-42.2	-26.3
Net interest	0.1	1.1	0.5	0.5	0.5
Tax paid	0.0	0.0	0.0	0.0	0.0
Operating cash flow	-6.4	-10.1	-33.6	-41.7	-25.8
Maintenance capex	0.0	-0.1	0.0	0.0	0.0
Capitalised clinical trial spend	0.0	0.0	0.0	0.0	0.0
Free cash flow	-6.4	-10.2	-33.6	-41.7	-25.8
Business acquistions	0.0	0.0	0.0	0.0	0.0
Proceeds from issuance	82.8	34.2	0.7	0.0	0.0
Movement in investments	0.0	0.0	0.0	0.0	0.0
Dividends paid	0.0	0.0	0.0	0.0	0.0
Change in cash held	76.4	24.0	(32.9)	(41.7)	(25.8)
Cash at beginning of period	2.5	72.4	104.0	71.1	29.4
Cash at year end	72.4	104.0	71.1	29.4	3.6

Balance Sheet (A$m)	FY19	FY20	FY21e	FY22e	FY23e
Cash	72.4	104.0	71.1	29.4	3.6
Receivables	3.5	3.5	3.4	3.0	3.0
Other current assets	6.6	0.9	0.9	0.9	0.9
Intangibles	-	0.1	0.1	0.1	-
Intangibles	3.0	3.0	3.0	3.0	3.0
Other	-	1.0	1.0	1.0	1.0
Total assets	85.5	112.4	79.5	37.4	11.5
Trade payables	2.3	2.8	2.8	2.8	2.8
Other liabilities	-	0.9	0.9	1.0	1.0
Other provisions	0.4	0.5	0.4	0.6	0.6
Total Liabilities	2.7	4.2	4.2	4.3	4.4
Net Assets	82.8	108.2	75.3	33.0	7.1
Share capital	109.5	145.9	146.6	146.6	146.6
Retained earnings	(30.7)	(41.3)	(75.1)	(117.2)	(143.1)
Reserves	4.1	3.7	3.8	3.7	3.6
Shareholders Equity	82.8	108.2	75.3	33.0	7.1

Last sale 03/08/2021	1.97
Recommendation	Buy (Spec)
Issued Capital	227.2
Market Cap	447.6

Valuation Ratios (A$m)	FY19	FY20	FY21e	FY22e	FY23e
Reported EPS (cps)	-10.5	-6.1	-14.7	-18.4	-11.3
Normalised EPS (cps)	-10.5	-6.1	-14.7	-18.4	-11.3
EPS growth (%)	na	na	na	na	-39%
PE(x)	**nm**	**nm**	**nm**	**nm**	**nm**
EV/EBITDA (x)	nm	nm	nm	nm	nm
EV/EBIT (x)	nm	nm	nm	nm	nm
NTA (cps)	41.5	46.8	31.6	13.1	1.8
P/NTA (x)	0.0	0.0	0.1	0.2	1.1
Book Value (cps)	43.1	48.2	32.9	14.4	3.1
Price/Book (x)	0.0	0.0	0.1	0.1	0.6
DPS (cps)	-	-	-	-	-
Payout ratio %	0%	0%	0%	0%	0%
Dividend Yield %	0.0%	0.0%	0.0%	0.0%	0.0%
Franking %	0%	0%	0%	0%	0%
FCF yield %	-168%	-230%	-744%	-923%	-572%
Net debt/Equity	0%	0%	0%	0%	0%
Net debt/Assets	0%	0%	0%	0%	0%
Gearing	net cash	net cash	net cash	net cash	net cash
Net debt/EBITDA (x)	n/a	n/a	n/a	n/a	n/a
Interest cover (x)	n/a	n/a	n/a	n/a	n/a

SOURCE: BELL POTTER SECURITIES ESTIMATES

Recommendation structure

Buy: Expect >15% total return on a 12 month view. For stocks regarded as 'Speculative' a return of >30% is expected.

Hold: Expect total return between -5% and 15% on a 12 month view

Sell: Expect <-5% total return on a 12 month view

Speculative Investments are either start-up enterprises with nil or only prospective operations or recently commenced operations with only forecast cash flows, or companies that have commenced operations or have been in operation for some time but have only forecast cash flows and/or a stressed balance sheet.

Such investments may carry an exceptionally high level of capital risk and volatility of returns.

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