BELL POTTER

3 December 2020

Speculative

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

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Imugene (IMU)

HER-2 VAXX shows 5.4m OS benefit

Recommendation
Buy (unchanged)
Price
$0.125
Valuation
$0.17 (previously $0.05)
Risk
Speculative

GICS Sector

Pharmaceuticals & Biotechnology

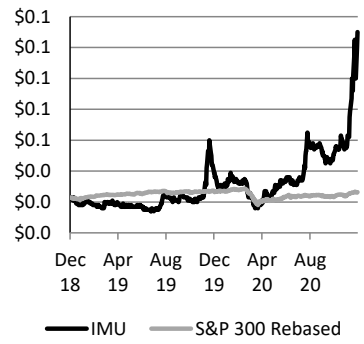
Expected Return	
Capital growth	**36.0%**
Dividend yield	**0.0%**
Total expected return	**36.0%**

Company Data & Ratios	
Enterprise value	**$579.1m**
Market cap	**$553.1m**
Issued capital	**4,597.8m**
Free float	**95%**
Avg. daily val. (52wk)	**$1.2m**
12 month price range	**$0.02 - $0.14**

Price Performance

	(1m)	(3m)	(12m)
Price (A$)	0.06	0.06	0.04
Absolute (%)	128.07	132.14	195.45
Rel market (%)	119.27	124.24	198.89

Absolute Price



SOURCE: IRESS

B Cell Immunotherapy – new kid on the block

Imugene recently announced further interim data from the first 27 patients to reach the first evaluation point in its randomised controlled phase 2 gastric cancer trial investigating the efficacy and safety of its HER-Vaxx (IMU-131) therapy in combination with standard of care chemotherapy. HER-Vaxx is a new class of immunotherapy drug designed to invoke a B cell response in cancers expressing high levels of the HER-2 protein. In the active arm of the study, median overall survival is 14.2 months compared to 8.8 months in the control group with the hazard ratio of 41.2%. Not surprisingly there have been fewer deaths in the active arm of the study with the longest HER-Vaxx treated patient remaining on therapy and progression free 16.3 months after dosing.

HER-2 is a well known and validated cancer target particularly in breast cancer where the Roche Genentech drugs Herceptin and Perjeta in conjunction with chemotherapy are the standard of care. Nevertheless bio-similars for Herceptin are now available in both the US and Europe, hence the timing of this new data is favourable. The data will allow IMU to conduct meaningful discussions with potential development partners in a range of new combinations across a range of cancer indications.

The phase 2 trial is not yet completed with a further 5 patients required, however, based on the efficacy data to date, the independent data monitoring committee has seen fit to recommend a reduction in patient numbers from 68 to 34. In other words the IDMC deems it unethical to continue to treat patients on the standard of care.

Investment View: Retain Buy (Speculative)

The stock has provided a 300% TSR since our initiation in May 2020. The data from this phase II trial is highly encouraging, however, a great deal more clinical trial work is required. The company now has two clinical stage assets with a third to follow shortly. Further clinical updates and news flow are likely in 2021. The company is well funded with $26m in cash and additional funding likely from options now deep in the money. Valuation is raised to $0.17 and we maintain our Buy (Speculative) recommendation.

Earnings Forecast

June Year End	FY20	FY21e	FY22e	FY23e
Revenues	4.2	4.2	4.5	4.5
EBIT $m	-10.8	-11.8	-11.5	-7.5
NPAT (underlying) $m	-10.5	-11.3	-11.0	-7.0
NPAT (reported) $m	-10.5	-11.3	-11.0	-7.0
EPS underlying (cps)	-0.3	-0.3	-0.2	-0.2
EPS growth %	nm	nm	nm	-36%
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%
ROE %	-18%	-23%	-29%	-23%

SOURCE: BELL POTTER SECURITIES ESTIMATES

Very Encouraging Data In Phase 2

Imugene's HER-Vaxx (IMU-131) is a B-cell peptide cancer immunotherapy designed to treat tumours that over-express the HER-2 receptor. HER-2 positive cancers are not uncommon in gastric, breast, ovarian, lung and pancreatic cancers. The immunotherapy is constructed from several B cell epitopes derived from the extracellular domain of HER-2. The drug has been shown in pre-clinical studies, Phase I and now Phase 2 studies to stimulate a potent polyclonal antibody response to the HER-2 protein, a well-known and validated cancer target.

The seminal research piece on the prognostic value of HER-2 in the gastric cancer setting is the ToGA study and the follow up sub group analysis. The analysis showed that those tumours expressing high levels of the HER-2 protein had the highest immunogenic response to Herceptin (Trastuzumab)[1]. The screening process covered nearly 4,000 patients with the hit rate for HER-2 positive cancers (ICH 2 or 3) at ~22%.

Herceptin was the breakthrough monoclonal antibody therapy first approved for the treatment of HER-2 positive breast cancers in 1998 and later approved for the treatment of HER-2 positive gastric cancers in the US. The drug is similarly approved by the EMA, however, we understand is not readily available in numerous other countries.

The current trial is being conducted at sites across Eastern Europe and India targeting HER-2 positive gastric cancer – being jurisdictions where Herceptin is not readily available.

HER-Vaxx is a polyclonal antibody (rather than either Herceptin or Perteta which are both monoclonal antibodies). Being polyclonal the drug binds to multiple sites on the HER-2 receptor, hence it aims to mimic the mechanism of action of both Herceptin and Perjeta in a single drug.

Patients in the study were dosed at 50µg of IMU-131 plus the chemotherapy regime. The MTD had previously been established in the earlier phase I trial.

KEY INCLUSION CRITERIA

All patients were screened for HER-2 expression prior to inclusion in the study and only HER-2 positive cases were included. In this randomised study, following screening patients were allocated one to one between the control arm receiving standard of care chemotherapy vs the active arm of the trial where patients received standard of care chemotherapy plus HER-Vaxx (NCT 02795988).

We summarise the key efficacy data as follows:

Figure 1 - Summary clinical data

	Chemotherapy	Chemotherapy plus HER-Vaxx
Patients	13	14
Median overall survival (months)	8.8	14.2
Events (deaths)	8	4
Hazard ratio	0.418	
80% confidence interval	0.186, 0.942	
1 sided p-value	0.083	

SOURCE: COMPANY DATA

The key efficacy point is the 5.4 month extension in overall survival.

[1] Gastric Cancer 2015 Jul 18(3); 476 - 84

Following the release of the data the Independent Data Monitoring Committee (IDMC) provided guidance that it was appropriate to reduce the size of the study from 68 to 34. This is primarily because of the effect size (i.e. very strong efficacy signal).

The interim data only reported the primary end point of overall survival and did not include progression free survival or time to progression free survival. There were 8 deaths in the control arm vs 4 in the active arm of the study.

In regard to safety, the IDMC confirmed no added toxicity for HER Vaxx combined with chemotherapy. There was no difference in safety between the two arms of the trial.

The hazard ratio of 41.8% is another standout result. Patients in the active arm of the trial were 58.2% less likely to die than patients in the control arm. This is considered a highly meaningful outcome, nevertheless, new drugs are approved on the basis of survival rather than hazard ratios. The hazard ratio is an outcome of the survival data.

The hazard ratio of 41.2% compares to 65% in the sub group analysis in ToGA[2]. This analysis provided further encouragement for investigators.

The p value of 0.083 is less than the pre specified alpha of 10% (i.e. the investigators believed coming into the study that the probability of a chance outcome was less than 10%). As this is a one sided p value (designed only to test whether the drug is more effective than the control), the 10% threshold is normal for this statistical analysis and provides an adequate signal of efficacy.

In this proof of concept study, twice as many patients in the HER-Vaxx arm of the study remained alive at the time of the interim analysis compared to the SOC chemotherapy. The longest HER-Vaxx treated patient in the study remains on therapy and progression free at 16.3 months.

WHERE TO FROM HERE

The current phase 2 trial has an additional 5 patients to recruit, hence we anticipate it still has at least 18 months to run. Imugene is yet to conduct the full analysis of the data from the current trial and this will only be completed once sufficient events (deaths) are recorded. In particular we look forward to further analysis concerning the duration of response and the ability of the drug to invoke a native B cell response.

The strong efficacy data together with an acceptable safety profile from this study provides the company with numerous options to consider for the development of IMU-131. The drug is almost certain to have a place in the treatment landscape for HER-2 positive cancers as a combination with chemotherapy, however we expect this will take several more years of development work in the clinic.

Ideally we would like to see efficacy as a monotherapy, however, ethical standards prevent this where there is a standard of care in place. We agree that the five month median overall survival benefit is unlikely to be co-incidental and can be reasonably confident the drug has efficacy.

In the US and Europe Herceptin and Perjeta (Roche Genentech) remain the dominant drugs for the treatment of HER2 positive cancers, however, bio-similars for Herceptin have recently been introduced making this drug more affordable.

As the patents on the leading HER2 immunotherapy drugs expire, the appeal of a new chemical entity like IMU-131 potentially increases. We theorise that a three way combination of IMU-131 with an immune check point inhibitor (Keytruda, Opdivo) and chemotherapy is a future combination the investigators may consider.

Note that in order to become a first line therapy any new combination must prove a survival benefit (in a large randomised controlled study) in excess of the current standard of care.

[2] Being those patients who were either IHC2+ or IHC3+

PD-1 VAXX (IMU-201)

Imugene also announced the recruitment of its first patient in the phase 1 clinical study of the new chemical entity PD1-Vaxx.

The drug has been in licenced from Ohio State University in the US. In short, it is a B Cell immunotherapy designed to disrupt PD-1/PD-L1 interaction. The drug invokes a B cell response to produce polyclonal antibodies targeting the PD1 receptor on the surface of T cells.

The study consists of two parts. Part 1, monotherapy dose-escalation of IMU-201 (PD1-Vaxx) to establish an optimal biological dose as monotherapy (Part 1a) followed by a combination dose escalation with standard of care treatment to establish a combination optimal biological dose of IMU-201(Part 1b). Part 2 dose expansion, will further characterize the safety, tolerability, and immunogenicity of IMU-201 in combination with SOC treatment for NSCLC at the defined expansion dose-level from Part 1b.

The trial is being run across 6 sites in Australia and the United States. We expect interim data in early 2022.

Figure 2 - Clinical Trials Summary

	Current Status	Indication	Stage	N	Estimated Total $m	FY21 2H20	1H21	2H21	FY22 1H22	2H22	FY23 1H23	2H23
B Cell Immunotherapy												
HER Vaxx	Recruiting	Gastric Cancer	Phase 2	34	5.0				★			
PD1 Vaxx	Recruiting	NSCLC	Phase 1	32	5.5							
Oncolytic Virus												
Vaxinia MAST study	Not yet recruiting	Solid Cancers	Phase 1	~60	15.0							
Check Vacc	Not yet recruiting	Triple Neg BC	Phase `	32	5.0							
Estimated clinical spend			Phase 1		**30.5**							

★ Expected Reporting

SOURCE: COMPANY DATA AND BELL POTTER SECURITIES ESTIMATES

VALUATION

In relative valuation terms, as always there is a large discrepancy between companies in the biotech sector across Australia and the rest of the world.

IMU now has both its B cell immunotherapy drugs in the clinic. In our view IMU is most likely to sell or partner these assets as the clinical data matures. The path to market for either drug remains unclear at the this time. For IMU-131 the future is almost certainly an approval as a combination with one or more agents. The first indication is yet to be decided.

The first of the company's oncolytic virus drug candidates is also due to enter the clinic in 2021. The Vaxinia virus produced excellent data in pre-clinical studies where it had a potent oncolytic impact in cancer cell lines. We understand the company will be submitting an IND enabling dossier in early 2021 ready to start trials later in the year.

Figure 3 - Relative Valuations

	Currency	Market Cap	Enterprise Value	FY19 Revenues	FY20 Revenues	FY21 Revenues (estimates)	FY19 EBITDA	FY20 EBITDA (estimates)	FY21 EBITDA (estimates)
Pharma Peers		$m	$m	$m	$m	$m	$m	$m	$m
Immugene	AUD	602	572	-	3.7	-	(8.3)	(10.8)	(11.8)
Immutep	AUD	173	155	0.1	13.0	-	(13.0)	(12.4)	36.1
Starpharma	AUD	542	514	1.7	10.9	-	(15.0)	(13.7)	(10.0)
Oncosil	AUD	126	105	-	3.6	-	(8.7)	(6.9)	(6.5)
Paradigm	AUD	670	567	-	2.7	-	(15.9)	(15.5)	(33.6)
Replimmune	USD	2,420	2,219	-	-	-	(30.8)	(58.0)	(78.0)

SOURCE: BLOOMBERG AND BELL POTTER SECURITIES ESTIMATES

The IMU valuation is supported by a DCF, however, the assumptions for deal revenues remain several years into the future and there is a relatively large risk adjustment on these

future cash flows pertaining to risk. There is no guarantee the company will be able to secure an appropriate development partner.

Of the company's in the peer list, Replimmune is the standout. REPL is a US biotech with several clinical programs under way with its oncolytic virus (OV) candidates. The largest of these is a 240 patient randomised controlled phase 2 study combining its OV with Libtayo (being an immune checkpoint inhibitor) for the treatment of advanced cutaneous squamous cell carcinoma. This CERPASS trial is potentially a registration study. REPL's valuation of US$2.42bn (A$3.5bn) is encouraging. IMU's Vaxinia assets are perhaps two to three years behind the lead OV at REPL (in terms of clinical data output).

Elsewhere, Starpharma has three phase II trials under way in its oncology program across a range of cancers and is due to commence reporting interim data in 2021. Oncosil has recently commenced its commercialisation of Oncosil therapy for the treatment of pancreatic cancer. Its therapy is approved in the EU. Immutep is in phase II studies with its lead oncology agent. Paradigm Biopharmaceuticals is about to commence an approval study in the US for its iPPS therapy in the treatment of osteoarthritis.

Funding - IMU had $26.6m of cash as at 30 September 2020. In addition there are 461m listed options with an average exercise price of ~4.5 cents with expiry in November 2021 and November 2022. There are also a further 245m unlisted options with an average exercise price of ~4.2cents. All the options are deep in the money with a combined capacity to raise ~$30m. If all options are exercise the dilution is approximately 15%.

Based on our forecast which assumes zero ($nil) deal revenues in the three year forecast period, the company has sufficient cash for up to three years, however, the forecast allows for only $10m in R&D expense over FY21 and FY22. The available funds are unlikely to be sufficient to fund the full R&D program hence further dilution from the exercise of options is likely. The company may also take on a development partner at some point which could involve non dilutive funding. We have not allowed for the dilution from a further capital raise at this time.

The implied market capitalisation at our revised target price of $0.17 is $~780m, hence remaining at a large discount to REPL. IMU has the advantage of 4 different assets (2 of which are clinical stage).

Figure 4 - Summary of earnings changes

	2021			2022		
	New	Old	% change	New	Old	% change
Revenues	4.2	3.7	14%	4.5	3.2	41%
EBIT	-11.8	-9.4	-25%	-11.5	-12.8	10%
NPAT	-11.3	-8.9	-27%	-11.0	-12.3	11%
EPS	-0.3	-0.2	-27%	-0.2	-0.3	17%

SOURCE: BELL POTTER SECURITIES ESTIMATES

Changes to earnings are not material. We estimate the company has up to three years cash runway.

Imugene
as at 3 December 2020

Recommendation	Buy, Speculative
Price	$0.125
Target (12 months)	$0.17

Table 1 - Financial summary

`	FY19	FY20	FY21e	FY22e	FY23e
Year Ending June					
R&D incentive	4.1	4.2	4.2	4.5	4.5
Total Revenue	**4.1**	**4.2**	**4.2**	**4.5**	**4.5**
COGS	-	-	-	-	-
Gross profit	4.1	4.2	4.2	4.5	4.5
R&D Expense	-7.6	-9.4	-10.0	-10.0	-6.0
Other expenses	-4.8	-5.6	-6.0	-6.0	-6.0
Total Expenses	-12.4	-15.0	-16.0	-16.0	-12.0
EBIT	-8.3	-10.8	-11.8	-11.5	-7.5
Interest income	0.4	0.3	0.5	0.5	0.5
Pre tax profit	(7.9)	(10.5)	(11.3)	(11.0)	(7.0)
Tax expense	-	-	-	-	-
NPAT- normalised	**(7.9)**	**(10.5)**	**(11.3)**	**(11.0)**	**(7.0)**
Reported NPAT	(7.9)	(10.5)	(11.3)	(11.0)	(7.0)

Cashflow (A$m)	FY19	FY20	FY21e	FY22e	FY23e
Gross cashflow	-7.9	-10.4	-11.8	-11.5	-7.5
Net interest	0.4	0.3	0.5	0.5	0.5
Operating cash flow	-7.5	-10.1	-11.3	-11.0	-7.0
Proceeds from asset sales	0.0	0.0	0.0	0.0	0.0
Free cash flow	-7.5	-10.1	-11.3	-11.0	-7.0
Business acquistions	0.0	-1.5	0.0	0.0	0.0
Proceeds from issuance	20.3	22.7	0.0	0.0	0.0
Movement in borrowings	0.0	0.0	0.0	0.0	0.0
Other	-1.5	0.0	0.0	0.0	0.0
Change in cash held	11.3	11.1	-11.3	-11.0	-7.0
Cash at beginning of period	7.8	19.0	30.1	18.8	7.8
FX adjustment	0.0	0.0	0.0	0.0	0.0
Cash at year end	**19.0**	**30.1**	**18.8**	**7.8**	**0.8**

Balance Sheet (A$m)	FY19	FY20	FY21e	FY22e	FY23e
Cash	19.0	30.1	18.8	7.8	0.8
Receivables	-	4.2	4.2	4.2	4.2
Other current assets	4.4	0.2	0.2	0.2	0.2
Property, Plant and Equipment	0.3	0.2	0.2	0.2	0.2
Intangibles	7.1	30.5	30.5	30.5	30.5
Other non current assets	-	-	-	-	-
Total assets	30.8	65.2	53.9	42.9	35.9
Trade payables	2.4	1.4	1.4	1.4	1.4
Debt - inerest bearing	-	-	-	-	-
Vendor payable	-	-	-	-	-
Other provisions	1.1	4.0	4.0	4.0	4.0
Total Liabilities	3.5	5.4	5.4	5.4	5.4
Net Assets	27.3	59.8	48.5	37.5	30.5
Share capital	63.1	92.8	92.8	92.8	92.8
Other equity	-	12.1	12.1	12.1	12.1
Retained earnings	(36.8)	(47.3)	(58.6)	(69.6)	(76.6)
Reserves	0.2	2.2	2.2	2.2	2.2
Shareholders Equity	26.5	59.8	48.5	37.5	30.5

Valuation Ratios (A$m)	FY19	FY20	FY21e	FY22e
Reported EPS (cps)	-0.2	-0.3	-0.3	-0.2
Normalised EPS (cps)	-0.2	-0.3	-0.3	-0.2
EPS growth (%)	nm	nm	nm	nm
PE(x)	**nm**	**nm**	**nm**	**nm**
EV/EBIT (x)	nm	nm	nm	nm
P/NTA (x)	23.3	18.9	30.7	79.0
Book Value Per Share (cps)	0.7	1.4	1.1	0.8
Price/Book (x)	17.0	9.3	11.4	14.8
DPS (cps)	-	-	-	-
Payout ratio %	0%	0%	0%	0%
Dividend Yield %	0.0%	0.0%	0.0%	0.0%
Franking %	0%	0%	0%	0%
FCF yield %	nm	nm	nm	nm
Net debt/Equity	0%	0%	0%	0%
Net debt/Assets	0%	0%	0%	0%
Gearing	net cash	net cash	net cash	net cash
Net debt/EBITDA (x)	n/a	n/a	n/a	n/a
Interest cover (x)	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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