EDISON

Imugene

On track for Phase Ib

On track for anti-tumour vaccine trial in H215

Pharma & biotech

Imugene is on track to initiate a Phase Ib/II trial of its gastric (stomach) cancer therapeutic vaccine, HER-Vaxx, in H215. HER-Vaxx aims to replicate and improve on the combination of two proven therapeutic antibodies, Herceptin and Perjeta (Roche), which significantly improves survival in breast cancer and may do so in gastric cancer. Global gastric cancer incidence is 934,000 cases with few current therapeutic options and low survival. Imugene raised A$3.6m in H214, which gives it sufficient funds to initiate the Phase Ib/II trial, with the aim of gaining a major pharma deal following Phase II data in the buoyant cancer immunotherapy area.

Year end	Revenue (A$m)	PBT* (A$m)	EPS* (c)	DPS (c)	P/E (x)	Yield (%)
06/14	0.5	(0.4)	(0.1)	0.0	N/A	N/A
06/15e	0.3	(2.3)	(0.2)	0.0	N/A	N/A
06/16e	0.0	(2.8)	(0.2)	0.0	N/A	N/A
06/17e	0.0	(3.1)	(0.2)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding intangible amortisation, exceptional items and share-based payments.

Antibodies that target HER2 boost cancer survival

HER-Vaxx comprises three linked HER2 peptides (protein fragments) delivered in a flu-based virosome. In the Phase I in 10 breast cancer patients, 8 developed antibodies against HER2, a proven cancer target. The marketed anti-HER2 therapeutic antibodies Herceptin and Perjeta improve overall survival by 34% (hazard ratio 0.66) in breast cancer. HER2 is overexpressed in up to 20% of gastric cancers and Herceptin improves survival by 2.5 months (13.5 months vs 11.0 months chemotherapy control). A potent vaccine would be a major advance in gastric cancer therapy, as the disease is poorly served by other therapeutic options.

Preparations well advanced for Gastric cancer trial

Since we initiated coverage in November 2014, Imugene has made good progress in preparing for the 18-patient Phase Ib trial due to commence in H215: preclinical testing confirmed in December that HER-Vaxx fusion peptide antigens are highly immunogenic, generating high levels of HER-2-specific antibodies, and that the generated antibodies recognise native HER-2 proteins; the trial protocol was finalised in December; and a CRO will be appointed shortly. Results are imminent from preclinical trials that aim to identify new insights into the HER-Vaxx technology and to generate data to support an IND application to the US FDA. The Phase Ib will be followed by a randomised Phase II trial in 68 gastric cancer patients.

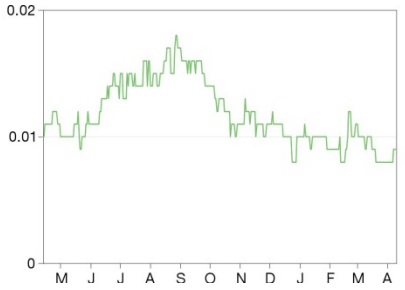
Weaker Australian dollar boosts valuation

Due to the continued weakness of the A$ we lower our long-term exchange rate assumption to A$0.80/US$ (previously A$0.88/US$), which increases our risk-adjusted NPV to A$52.6 (previously A$49.3m), equivalent to 4.1c/share. Our valuation assumes a 20% likelihood of success and includes a A$25m deal upfront after Phase II (at a 30% probability) and a A$50m Phase III success milestone at a 20% probability. The immunotherapy area has recently seen sizeable overall deal values including large milestones. Cash was A$3.0m on 31 December 2014.

13 April 2015

Price	**A$0.01**
Market cap	**A$13m**
	A$0.80/US$
Cash (A$m) at 31 December 2014	A$3.0m
Shares in issue	1,329.9m
Free float	58%
Code	IMU
Primary exchange	ASX
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	0.0	(10.0)	(18.2)
Rel (local)	(2.4)	(17.5)	(24.5)
52-week high/low		A$0.02	A$0.01

Business description

Imugene restructured into a cancer vaccine business with the acquisition of HER-Vaxx, a proprietary HER2 +ve cancer vaccine, in December 2013. A Phase Ib dose study is planned in gastric cancer starting in H215 with a randomised Phase II follow-on study in 68 patients.

Next events

File IND application	Q215
Phase Ib start	H215
FY15 results	Q315

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Valuation

We have calculated a discounted, risk-adjusted cash flow valuation using the key assumptions in Exhibit 1. These are then applied to the market data in Exhibit 2 to give potential peak sales of about US$725m.

Exhibit 1: Valuation parameters

Key model assumptions	Value
HER2+ percentage of diagnosed patients[1]	20%
Percentage eligible for therapy	75%
US price (US$) per year	75,000
Royalty percentage from partner	12%
Share of IMU revenue payable to BSFE until 2030 (based on royalties and milestones received from partners)	18%
Upfront payment in 2019 (A$m)	25

Source: Edison Investment Research

Exhibit 2: Market data and non-adjusted cash flow in 2030

Market (US$ unless otherwise stated)	Cases	Eligible	Uptake	Number treated	Price (US$'000)	Value ($m)
US	22,200	3,330	25%	833	75.0	62
Western EU	62,240	9,336	40%	3,734	60.0	224
Eastern EU	18,360	2,754	25%	689	37.5	26
Eastern Europe and Russia	59,000	8,850	25%	2,213	37.5	83
Japan	102,740	15,411	15%	2,312	112.5	260
China	382,940	57,441	5%	2,872	18.8	54
E Asia	37,360	5,604	2%	112	18.8	2
other	249,160	37,374	2%	747	18.8	14
Total	**934,000**	**140,100**				**725**
Sales in A$	Rate	US$0.80/A$				A$907
Royalty from partner to Imugene	Rate	12%				A$109
Share of Imugene income paid to BSFE (18%)						(A$20)
Potential Imugene profit after A$2m admin costs and 30% tax in 2030						A$61

Source: Market data references,[2,3] Edison Investment Research

Pricing and market share will vary according to patent strength, competition and the level of healthcare funding and infrastructure at that time. A US price of $75,000 per year is assumed, with patients taking therapy for a year on average. Prices are usually lower in Europe, higher in Japan and reduced elsewhere. There seems to be no Japanese patent, so a lower share is used there.

Our standard practice is to assume a probability of success between 10% and 20% for Phase I trials. We apply a 20% probability for HER-Vaxx, at the top of this range, in view of the safety and tolerability shown in the Phase I trial, and the fact that the HER-2 epitopes included in the vaccine have been validated as targets by the efficacy of the approved monoclonal therapeutics Herceptin (trastuzumab, Roche) and Perjeta (pertuzumab, Roche).

Exhibit 3: Valuation table (based on Exhibits 1 and 2)

Discounted cash flow stream	Probability	Present value (A$m)
Value of net cash flow until 2032 (excluding upfront payments)	20%	46.5
Value of 2019 upfront and 2023 milestone (net of royalties)	30%	6.1
Total value		52.6

Source: Edison Investment Research

The assumed upfront of A$25m is generally comparable with Phase II deals, although no specific antibody-based vaccine benchmarks can be ascertained. An approval milestone of A$50m is assumed at the technical probability of 20%. We assume that 18% of HER-Vaxx revenue received

1 Jørgensen, J. T. Role of human EGFR 2 in gastric cancer. World J. Gastroenterol. 20, 4526–35 (2014).
2 Jemal, A. et al. Global cancer statistics. CA. Cancer J. Clin. 61, 69–90.
3 Ferlay, J. et al. Cancer incidence and mortality patterns in Europe. Eur. J. Cancer 49, 1374–403 (2013).

by Imugene (including upfront, milestone and royalty payments) is paid to BSFE,[4] the original owners of the HER-Vaxx IP. A 30% Australian tax rate is applied from 2026. This gives an indicative value (Exhibit 3) of A$53m (4.1c/share); this is not a price target.

Financials: Cash to fund Phase II

Imugene obtained the main HER-Vaxx intellectual property in December 2013 through the acquisition of Biolife Science Qld for A$4.5m in equity (300m shares at A$0.015 each). Imugene is currently seeking to divest its previous focus, a drug delivery technology (Linguet), which has a carrying value of A$0.3m. The other intangible asset on the balance sheet as of 31 December was HER-Vaxx, which is valued at A$6.6m.

The operating loss in H115 was A$1.1m, compared with our previous forecast of a loss of A$1.4m for the full year. We have increased our forecast spend on both R&D and administrative costs, and now forecast operating losses of A$2.4m in FY15 and A$2.8m in FY16.

Imugene raised A$2.6m in FY14 (to 30 June 2014) to fund initial HER-Vaxx development and preparation for the clinical trial. Revenue in FY14 comprised an R&D tax rebate of A$0.5m and some interest income; an R&D rebate payment of A$0.23m was received in February 2015. As most Phase Ib/II costs will be outside Australia, no further R&D tax rebates have been assumed. In November and December 2014, the company raised a further A$3.6m (A$3.3m after costs) in a placement and share purchase plan (358m shares issued at A$0.01/share). Cash was A$3.0m on 31 December 2014. The current funding is sufficient to initiate the Phase Ib/II trial, but further funding will be needed. Illustrative long-term debt of A$1m in 2016e and A$4m in 2017e is included to represent this. Financial projections are shown in Exhibit 4.

Sensitivities

The major potential value inflection point for investors is that the Phase II produces strong data to enable a big pharma licensing deal (with an upfront fee) that covers Phase III costs. Prior to then, potential partners may also take notice if the Phase Ib shows evidence of potential efficacy (cellular plus humoral immune response, generation of anti-HER2 antibodies). In October 2014 BMS paid US$50M for an option to acquire Austrian biotech F-star Alpha, and its Phase I-ready bi-specific antibody drug targeting HER2-positive cancers; total deal value could reach US$475m if the drug is approved in the US and Europe. The double antibody action that HER-Vaxx aims to replicate, and perhaps improve on, is proven in breast cancer. In Phase I, in a non-target population, HER-Vaxx generated antibody responses against all three peptides. These are strong positive indicators.

Uncertainties arise as it is unclear how effectively HER-Vaxx can be combined with chemotherapy in Phase II as vaccine responses take time to develop and chemotherapy could potentially inhibit the immune response. On the other hand, some chemotherapy agents, including cisplatin, have been shown to stimulate the immune system.[5] The Phase I trial showed that patients treated with HER-Vaxx produced antibodies against HER2, but we do not yet know how the concentration of antibodies compares with the levels seen in patients treated with Herceptin or Perjeta. As the vaccine aims to stimulate an immune response against the normal HER2 protein that the immune system usually tolerates as “self”, the amount, potency and duration of anti-HER2 antibody production will be an important indicator of likely efficacy.

Royalties are hard to forecast since most gastric cancer patients are in Asia and therapeutic options may broaden over the next eight years as other candidate trials report data.

4 Biolife Science Forschungs und Entwicklungsges mbHH (BSFE, a company incorporated in Austria).

5 Biasi et al. Cisplatin induced antitumor immunomodulation. Clin Cancer Res; 20(21); 5384–91 (2014).

Exhibit 4: Financial summary

A$'000s	2014	2015e	2016e	2017e
Year end 31 June	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS				
Revenue	511	343	0	0
Cost of Sales	0	0	0	0
Gross Profit	511	343	0	0
EBITDA	(386)	(2,382)	(2,825)	(3,125)
Operating Profit (before GW and except.)	(386)	(2,382)	(2,825)	(3,125)
Intangible Amortisation	(1,691)	0	0	0
Exceptionals, share based payments	(66)	(75)	(75)	(75)
Other	0	0	0	0
Operating Profit	(2,143)	(2,457)	(2,900)	(3,200)
Net Interest	27	50	0	0
Profit Before Tax (norm)	(359)	(2,332)	(2,825)	(3,125)
Profit Before Tax (FRS 3)	(2,116)	(2,407)	(2,900)	(3,200)
Tax	0	0	0	0
Profit After Tax (norm)	(359)	(2,332)	(2,825)	(3,125)
Profit After Tax (FRS 3)	(2,116)	(2,407)	(2,900)	(3,200)
Average Number of Shares Outstanding (m)	689.2	1,126.6	1,329.9	1,329.9
EPS - normalised (c)	(0.05)	(0.21)	(0.21)	(0.23)
EPS - FRS 3 (c)	(0.31)	(0.21)	(0.22)	(0.24)
Dividend per share (c)	0.0	0.0	0.0	0.0
Gross Margin (%)	N/A	N/A	N/A	N/A
EBITDA Margin (%)	N/A	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	N/A	N/A	N/A	N/A
BALANCE SHEET				
Fixed Assets	6,874	6,874	6,874	6,874
Intangible Assets	6,874	6,874	6,874	6,874
Tangible Assets	0	0	0	0
Other	0	0	0	0
Current Assets	1,758	2,306	406	281
Stocks	0	0	0	0
Debtors	15	15	15	15
Cash	1,223	2,280	380	255
Other	520	11	11	11
Current Liabilities	(697)	(322)	(247)	(247)
Creditors	(247)	(247)	(247)	(247)
Current loans	0	0	0	0
Other inc HER-Vaxx IP creditor	(450)	(75)	0	0
Long Term Liabilities	(1,202)	(1,127)	(3,127)	(5,127)
Long term debt	0	0	(1,000)	(4,000)
HER-Vaxx IP Creditor	(75)	0	0	0
Other long term liabilities	(1,127)	(1,127)	(2,127)	(1,127)
Net Assets	6,732	7,730	3,905	1,780
CASH FLOW				
Operating Cash Flow	(1,171)	(2,323)	(2,900)	(3,125)
Net Interest	27	50	0	0
Tax	0	0	0	0
Capex	(600)	0	0	0
Acquisitions/disposals	6	0	0	0
Financing	2,396	3,600	0	0
Dividends	0	0	0	0
Other funding	0	(270)	0	0
Net Cash Flow (ex-debt movements)	657	1,057	(2,900)	(3,125)
Opening net debt/(cash)	(566)	(1,223)	(2,280)	620
HP finance leases initiated	0	0	0	0
Other	0	(0)	0	0
Closing net debt/(cash)	(1,223)	(2,280)	620	3,745

Source: Imugene reports, Edison Investment Research. Note: FY13 is omitted as it is not relevant to the current business.

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