EDISON

Prima BioMed

ASCO update

Preliminary LAG-3 combo data in breast cancer

Pharma & biotech

Preliminary efficacy data, which Prima BioMed presented at ASCO from the 15-patient, safety run-in phase of its AIPAC study, showed sustained immune activation and an encouraging 47% tumour response rate in breast cancer following IMP321 plus paclitaxel combination therapy. Recruitment in the randomised Phase IIb component of AIPAC is ongoing, with top-line data likely by mid-2019. Efficacy data from the final two cohorts in the TACTI-mel trial of IMP321 plus Keytruda in melanoma are expected in H217 and H118 respectively. The 47% AIPAC response rate is in line with Phase I studies and consistent with our expectations, so we leave our valuation unchanged at A$252m (12c per share).

Year end	Revenue (A$m)	PBT* (A$m)	EPS* (c)	DPS* (c)	P/E (x)	Yield (%)
06/15	1.3	(12.9)	(0.9)	0.0	N/A	N/A
06/16	1.9	(13.7)	(0.6)	0.0	N/A	N/A
06/17e	1.3	(12.7)	(0.6)	0.0	N/A	N/A
06/18e	10.6	(4.0)	(0.2)	0.0	N/A	N/A

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

Encouraging response rate in AIPAC run-in

The 47% response rate in 15 metastatic breast cancer patients treated with IMP321 in combination with paclitaxel during the safety run-in study was similar to the 50% response rate reported in a previous Phase I trial, and higher than the c 30% response rate seen in published studies of weekly paclitaxel in breast cancer. Top-line PFS data from the ongoing 226-patient, randomised Phase IIb component of AIPAC could mature sometime between late 2018 and mid-2019; patients receive either 30mg of IMP321 or placebo, in combination with weekly paclitaxel. IMP321 is a LAG-3-based, antigen-presenting cell activator that enhances immune responses.

Efficacy data from final TACTI-mel cohort likely H118

Prima's TACTI-mel trial is using IMP321 to enhance efficacy in melanoma patients who have had a suboptimal initial response to the PD-1 immune checkpoint inhibitor Keytruda. As we previously reported, one of the six patients (17%) in the first cohort (1mg) experienced a complete response (CR). Recruitment in the third and highest (30mg) dose cohort is expected to complete in Q317. We expect to see efficacy data from the second cohort in H217 and from the final cohort in H118.

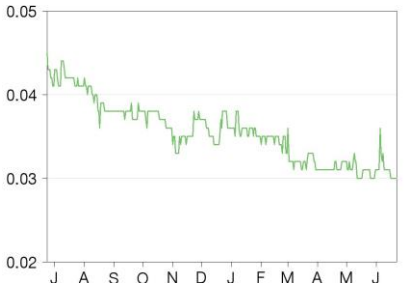
Valuation: Unchanged at A$252m, 12c per share

Our valuation is unchanged at A$252m, which is equal to 12c per share on an undiluted basis or 8c per share after accounting for dilution from options, warrants and convertible notes. Guidance is that the cash balance of A$13.9m at 31 March will be sufficient to fund operations through Q1 CY18, excluding any milestone payments from partners Novartis and GlaxoSmithKline (GSK). Milestone revenue (we model ~A$9m in FY18) would extend the cash runway.

23 June 2017

Price	**A$0.03**
Market cap	**A$62m**
	US$0.76/A$
Gross cash (A$m) at 31 March 2017	13.9
Shares in issue	2,073.1m
Free float	93%
Code	PRR
Primary exchange	ASX
Secondary exchange	NASDAQ

Share price performance



%	1m	3m	12m
Abs	(3.2)	(9.1)	(33.3)
Rel (local)	(2.1)	(9.3)	(37.9)
52-week high/low	A$0.05		A$0.03

Business description

Prima BioMed is an ASX-listed biotechnology company focused on cancer immunotherapy. Its pipeline is based on three products using a LAG-3 immune control system: IMP321 for cancer chemo-immunotherapy and partnered products IMP731 (GSK) and IMP701 (Novartis).

Next events

TACTI-mel cohort 2 safety and activity data	H217
TACTI-mel cohort 3 safety and activity data	H118
IMP761 preclinical data	2017

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Initial AIPAC response data presented at ASCO

Prima presented encouraging data from the safety run-in phase of its AIPAC Phase IIb breast cancer trial at the American Society of Clinical Oncology (ASCO) meeting held in Chicago on 2-6 June 2017. The trial is testing the effect of combining the IMP321 soluble LAG-3 fusion protein with paclitaxel in women with hormone receptor positive metastatic breast cancer (mBC) who have not previously received chemotherapy for metastatic disease. Women with HER2 positive tumours who are eligible for treatment with trastuzumab (Herceptin) are excluded from the trial.

In the safety-run-in phase 15 women were treated with either 6mg or 30mg of IMP321 in combination with weekly paclitaxel chemotherapy (80mg/m^2 in three weeks out of every four). Both doses of IMP321 were found to be safe and well tolerated when used in combination with paclitaxel, with no dose-limiting toxicities reported. Cytokine release syndrome grade 1 was the only serious adverse event related to IMP321 (occurring twice in the same patient in the higher dose group). There were no grade 4 (life-threatening) adverse events related to either IMP321 or paclitaxel. The dose escalation committee confirmed the 30mg dose as the recommended Phase II dose (RP2D) for use in the randomised, placebo-controlled component of the trial.

AIPAC response rate compares favourably to weekly paclitaxel

The pooled preliminary efficacy data from the 15 patients in the safety run-in study are summarised in Exhibit 1. The overall response rate (ORR) was 47% and the disease control rate (DCR, tumour response or stable disease) was 87%. The 47% ORR from the AIPAC safety run-in was consistent with the 50% response rate reported from an earlier Phase I trial,[1] which tested the 6mg dose of IMP321 in combination with weekly paclitaxel in 30 patients.

Exhibit 1: Tumour responses to IMP321/paclitaxel in open-label, run-in phase of AIPAC

Response parameter	%	count
Complete response	0%	(0/15)
Partial response	47%	(7/15)
Stable disease	40%	(6/15)
Progressive disease	13%	(2/15)
Overall response rate	47%	(7/15)
Disease control rate	87%	(13/15)

Source: Prima BioMed poster presentation for Abstract 1062 at ASCO 2017

The company has previously compared the ORR in IMP321/paclitaxel studies to a randomised Phase III study of weekly paclitaxel (days 1, 8 and 15 of a 28-day cycle) as first-line therapy in HER2-negative subjects (Gray[2] et al. 2009), which reported an ORR in patients treated with single-agent paclitaxel of 23%.

We have identified a Phase II study sponsored by Amgen (Martin[3] et al 2011) with a similar design and paclitaxel regimen to the study above. The ORR in HER2-negative patients receiving weekly paclitaxel as first-line chemotherapy treatment for metastatic or locally advanced breast cancer in this study was 41%.

The average of the response rate in the Gray and Martin studies was 32%. While acknowledging the uncertainty inherent in cross-trial comparisons, it is encouraging to see that the response rate to IMP321/paclitaxel combination therapy is higher than the response rate to paclitaxel monotherapy in either of these two trials.

1 Brignone et al. Journal of Translational Medicine 2010, 8:71

2 Gray et al, J ClinOncol. 2009 Oct 20;27(30):4966-72.

3 Martin et al, Lancet Oncol 2011; 12: 369–76

We note that there were minor differences between the Gray and Martin studies and Prima's trials. The published studies used a slightly higher dose of paclitaxel (90mg/m^2 vs 80mg/m^2) and about 30% of subjects in the two published studies cited above were hormone receptor negative whereas these patients are ineligible for enrolment in the AIPAC study. Despite these differences, the two published studies are likely to be a reasonable guide to the response rate that could be anticipated in the control arm of the Phase IIb AIPAC study.

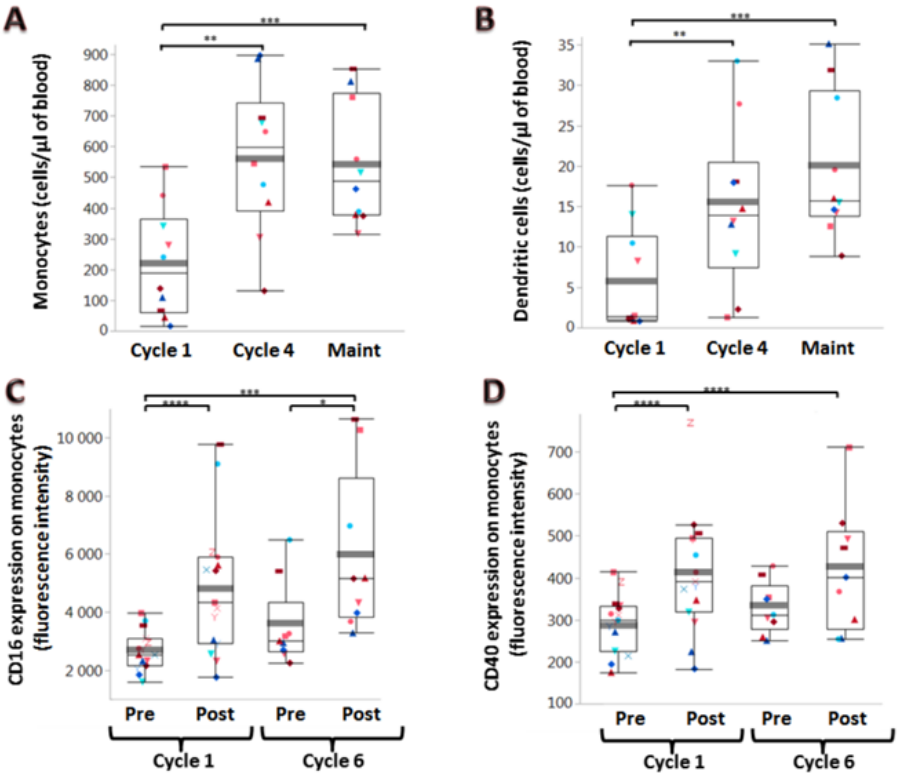
Evidence of sustained immune activation in AIPAC

Prima also presented evidence of sustained proliferation and activation of circulating white blood cells over the course of IMP321/paclitaxel combination therapy. This included sustained increases in circulating antigen-presenting cells (APCs) and subsequent activation of effector cells including CD8 T-cells and natural killer cells.

Exhibit 2 shows that the treatment led to proliferation of APCs, including monocytes and dendritic cells, which was sustained over the 24-week course of treatment (panels A and B). Panels C and D show that injection of IMP321 prompted activation of circulating monocytes from the very first dose, and that monocyte activation was higher at week 22 than at the start of the study.

These data show that IMP321 was effective at activating APCs, in line with its proposed mechanism of action.

Exhibit 2: Sustained increases in number and activation status of circulating APCs



A+B: Samples collected prior to paclitaxel in cycle 1, cycle 4 (i.e. 13 days after 6th IMP321 inj.) and 13 days after the 12th IMP321 inj. (Maint) to monitor the absolute counts of monocytes (CD45$^+$CD14$^+$) and dendritic cells (Lin- HLA-DR$^+$ BDCA-1/-2/3$^+$).

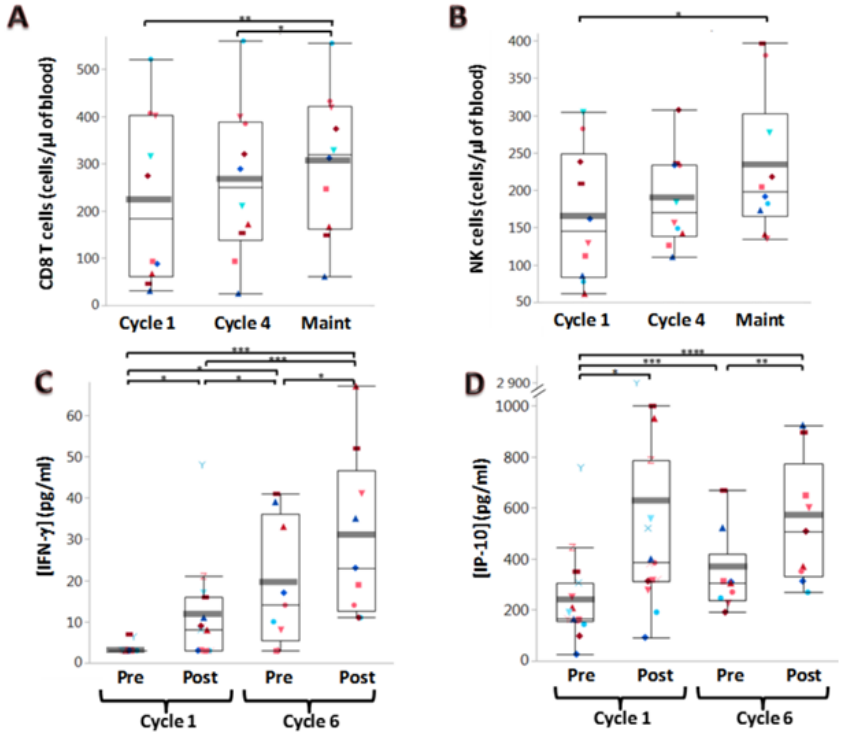
C+D: Samples collected prior to and 2 days-post 1st IMP321 injection (cycle 1) and 12th IMP321 injection (cycle 6). The expression of activation markers, CD16 (C) and CD40 (D), on CD45$^+$CD14$^+$ monocytes was analyzed.

Source: Prima BioMed poster presentation for Abstract 1062 at ASCO 2017

Prima also showed that the activation of the APC network by IMP321 was associated with sustained increases in absolute numbers of effector cells like CD8 T-cells and natural killer cells, as well as sustained increase in Th1 helper T-cell biomarkers like IFN gamma and IP-10.

These changes are suggestive of a stronger cytotoxic cellular response and improved helper T-cell immune status, which are both needed for a potent immune response against the tumour cells.

Exhibit 3: Sustained increases in effector cells and Th1 biomarkers



A+B: Samples collected prior to paclitaxel admin. in cycle 1, cycle 4 (i.e. 13 days after 6th IMP321 inj.) and 13 days after the 12th IMP321 inj. (Maint) to monitor the absolute counts of $CD45^+CD3^+CD8^+CD4^-$ cytotoxic T cells and $CD45^+CD3^-CD16/56^+$ Natural Killer cells.

C+D: Samples collected prior to and from 1 to 48 h after 1st IMP321 injection (cycle 1) and 12th IMP321 injection (at cycle 6)

Source: Prima BioMed poster presentation for Abstract 1062 at ASCO 2017

Prima's chief medical officer Dr Frédéric Triebel pointed out that the increase in APC numbers and their activation has not previously been seen with other immune checkpoint inhibitors. He also viewed the increased numbers of CD8 T-cells and natural killer cells and the effect on Th1 cells to be indicators of potential efficacy of IMP321, as these are known to be related to anti-tumour efficacy in patients.

Recruitment ongoing in randomised component of AIPAC

Prima dosed the first patient in the randomised Phase IIb component of AIPAC in January 2017. The randomised double-blind phase will enrol 226 patients, with half receiving standard paclitaxel chemotherapy on days 1, 8 and 15, plus 30mg of IMP321 on days 2 and 16 of each four-week cycle; the other half will receive paclitaxel plus placebo.

The record of the AIPAC trial on clinicaltrials.gov (NCT02614833) indicates that final data for the progression-free survival (PFS) primary endpoint are expected to be collected in June 2019. Depending on the recruitment rate and PFS observed, we estimate that top-line PFS data could mature sometime between late 2018 and mid-2019.

The European regulator (EMA) has indicated that this trial could be sufficient to support a marketing authorisation if it achieves certain (undisclosed) clinical endpoints.

Keytruda approval validates chemo-immunotherapy approach

In May the US FDA granted accelerated approval for the immune checkpoint inhibitor (ICI) Keytruda (pembrolizumab) in combination with the chemotherapy drugs pemetrexed plus carboplatin as a front-line treatment for non-small cell lung cancer (NSCLC). The Keytruda/chemo combo elicited a 55% ORR vs 29% for the chemo combo alone. Median PFS was 13 months for the Keytruda combo vs 8.9 months for chemo alone.

This is the first approval for chemotherapy plus immunotherapy combination treatment.

Part of the rationale for the chemo-immunotherapy approach is that the cellular debris created when the chemotherapy drug kills cancer cells stimulates an immune response, and that this immune response can be strengthened by including an immunotherapy drug in the treatment regimen. In the case of ICI drugs like Keytruda the immunotherapy strengthens the immune response by taking the brakes off the immune effector cells including cytotoxic T-cells.

Prima is similarly seeking to strengthen the immune response by combining chemotherapy with its IMP321 APC activator. In this case IMP321 acts earlier in the process by up-regulating the extent to which APC cells process the cellular debris and present tumour antigens to T- and B-cells, thereby strengthening the overall immune response.

Exhibit 4: Financial summary

A$'000s	2014	2015	2016	2017e	2018e
Year end 30 June	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	2,020	1,336	1,949	1,253	10,564
R&D expenses	0	(8,952)	(7,060)	(7,271)	(7,489)
SG&A expenses	2,020	(5,723)	(6,983)	(7,122)	(7,336)
EBITDA	(14,003)	(13,345)	(12,093)	(13,141)	(4,262)
Operating Profit (before GW and except.)	(14,395)	(13,671)	(12,275)	(13,144)	(4,269)
Intangible Amortisation	(54)	(1,015)	(1,993)	(1,877)	(1,708)
Exceptionals	0	(18,338)	(47,468)	0	0
Operating Profit	(14,450)	(33,024)	(61,736)	(15,021)	(5,976)
Other	407	538	(1,716)	0	0
Net Interest	713	192	256	418	244
Profit Before Tax (norm)	(13,275)	(12,940)	(13,735)	(12,727)	(4,025)
Profit Before Tax (IFRS)	(13,330)	(32,294)	(63,196)	(14,603)	(5,732)
Tax	(14)	142	1,181	0	0
Profit After Tax (norm)	(13,289)	(12,798)	(12,554)	(12,727)	(4,025)
Profit After Tax (IFRS)	(13,343)	(32,152)	(62,015)	(14,603)	(5,732)
Average Number of Shares Outstanding (m)	1,220.1	1,490.1	2,236.3	2,061.6	2,073.1
EPS - normalised (c)	(1.1)	(0.9)	(0.6)	(0.6)	(0.2)
EPS - IFRS (c)	(1.1)	(2.2)	(2.8)	(0.7)	(0.3)
Dividend per share (c)	0.0	0.0	0.0	0.0	0.0
Gross Margin (%)	N/A	N/A	N/A	N/A	N/A
EBITDA Margin (%)	N/A	N/A	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	N/A	N/A	N/A	N/A	N/A
BALANCE SHEET					
Fixed Assets	694	22,960	20,883	19,031	17,347
Intangible Assets	117	22,662	20,852	18,975	17,267
Tangible Assets	577	298	32	56	79
Other	0	0	0	0	0
Current Assets	24,684	8,023	21,671	8,919	4,871
Stocks	0	0	0	0	0
Debtors	196	315	168	168	168
Cash	23,200	6,760	20,880	8,128	4,080
Other	1,287	948	623	623	623
Current Liabilities	(2,771)	(4,380)	(1,472)	(1,472)	(1,472)
Creditors	(2,669)	(2,791)	(1,444)	(1,444)	(1,444)
Short term borrowings	0	(1,508)	(0)	(0)	(0)
Short term leases	0	0	0	0	0
Other	(102)	(80)	(28)	(28)	(28)
Long Term Liabilities	(15)	(1,914)	(5,765)	(5,765)	(5,765)
Long term borrowings incl. conv. note	0	0	(5,027)	(5,027)	(5,027)
Long term leases	0	0	0	0	0
Other long term liabilities	(15)	(1,914)	(737)	(737)	(737)
Net Assets	22,592	24,690	35,317	20,714	14,981
CASH FLOW					
Operating Cash Flow	(14,908)	(7,785)	(11,594)	(13,141)	(4,262)
Net Interest	705	0	284	418	244
Tax	(24)	(2)	0	0	0
Capex	(104)	(49)	(27)	(28)	(30)
Acquisitions/disposals	0	(20,913)	130	0	0
Financing	6,845	7,745	27,229	0	0
Dividends	0	0	0	0	0
Other	(158)	(164)	0	0	0
Net Cash Flow	(7,643)	(21,168)	16,022	(12,752)	(4,048)
Opening net debt/(cash)	(30,023)	(23,200)	(5,251)	(15,852)	(3,100)
HP finance leases initiated	0	0	0	0	0
Other	820	3,220	(5,421)	0	0
Closing net debt/(cash)	(23,200)	(5,251)	(15,852)	(3,100)	948

Source: Company accounts, Edison Investment Research

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