WILSONS

Equity Research

Date: 18 November 2021

Theme: Company Update

Company

Immutep Limited (IMM)

Efti impresses in HNSCC and aids the young & forgotten in metastatic breast cancer

Recommendation	**OVERWEIGHT**
12-mth target price (AUD)	**$0.91**
Share price @ 17-Nov-21 (AUD)	$0.57
Forecast 12-mth capital return	60.4%
Forecast 12-mth dividend yield	0.0%
12-mth total shareholder return	**60.4%**
Market cap	$482m
Enterprise value	$422m
Shares on issue	854m
Sold short	0.0%
ASX 300 weight	0.0%
Median turnover/day	$1.0m

We maintain our OVERWEIGHT recommendation and a $0.91/sh risked PT on Immutep. The data presented at the Society for Immunotherapy of Cancer (SITC) conference (10-14 Nov) has been the catalyst driving IMM volatility over the past week. Final overall survival (OS) data from the Phase IIb breast cancer program (AIPAC) with Immutep's lead LAG-3 asset, Efti, was incrementally positive compared to the last interim readout (Dec 2020) however the market interpreted top-line data as a miss. What's important to appreciate is that the Phase III program in preparation is focused on key pre-specified subgroups, of which we have seen impressive, and significant, clinical gains with Efti when combined with chemotherapy. Further, we have seen incremental Phase II HNSCC data, highlighting that the addition of Efti to SOC Keytruda has more than doubled the response rates observed in foundational Keytruda studies. The opportunity for Efti to expand the market for this blockbuster, potentially alongside others, presents a valuable option for Immutep, which we assess as likely to attract keen pharma interest, particularly as LAG-3 attention intensifies ahead of LAG-3 target validation in 1Q22 (BMS' relatlimab FDA decision).

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Key points

AIPAC final OS readout supports Phase III. The final OS data from 3 key subgroups showed improvements vs Dec interim readout. Importantly we see a strong case for use in patients <65 years which represent a large addressable cohort with high unmet need.

AIPAC pre-defined subgroups chosen to evaluate factors affecting IO response. Aging, cancer subtype and baseline immune system 'health' are known factors likely to affect response of immune-directed therapies such as Efti, hence why they were pre-specified.

TACTI-002 HNSCC data update impressive. Response rates to an Efti combo continue to be 2-3 times that of Keytruda alone in HNSCC, supporting IMM's new Phase IIb study moving into 1st line therapy. This data displays the prospect for Efti to extend current SOC.

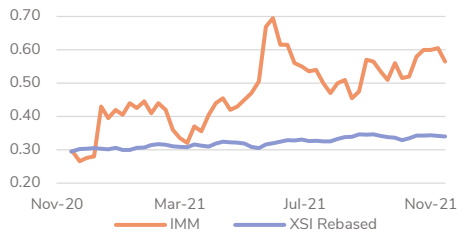
Forecasts. We forecast potential peak revenues of $950M for Efti in mBC, and $720M for Efti in HNSCC; and $350M for Efti in NSCLC (via licensing +$470M milestones).

Valuation. We use a SOTP approach to value IMM based on Efti in core indications (risked PT $0.91/sh) including a) mBC ($0.30), b) HNSCC ($0.09/sh) & c) NSCLC via licensing model ($0.53/sh). Our valuation does not include IMP761 or out-licensed assets. Unrisked PT is $2.33/share.

Risks and catalysts

Risks: a) adverse clinical trial outcomes; b) negative regulator interactions; c) competitive intensity of immuno-oncology field; d) available capital. **Catalysts:** a) achievement of trial endpoints; b) partnership opportunities; c) regulatory approvals; d) corporate activity.

12-mth price performance ($)



	1-mth	6-mth	12-mth
Abs return (%)	4.6	25.6	91.5
Rel return (%)	4.7	16.1	76.4

Earnings forecasts

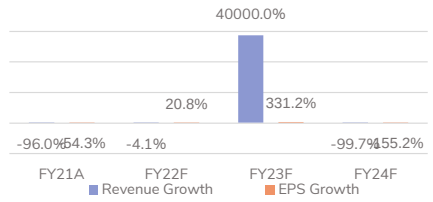
Year-end June (AUD)	FY20A	FY21A	FY22F	FY23F	FY24F
NPAT rep ($m)	-13.4	-30.5	-33.9	78.4	-43.2
NPAT norm ($m)	-13.5	-29.9	-33.9	78.4	-43.2
Consensus NPAT ($m)			-48.2	-6.6	-24.4
EPS norm (cps)	-3.3	-5.0	-4.0	9.2	-5.1
EPS growth (%)	40.5	-54.3	20.8	331.2	-155.2
P/E norm (x)	-17.3	-11.2	-14.2	6.1	-11.1
EV/EBITDA (x)	-36.4	-15.1	-13.1	5.2	-10.2
FCF yield (%)	-2.2	-3.7	-7.2	16.4	-9.1
DPS (cps)	0.0	0.0	0.0	0.0	0.0
Dividend yield (%)	0.0	0.0	0.0	0.0	0.0
Franking (%)	0	0	0	0	0

Source: Company data, Wilsons estimates, Refinitiv

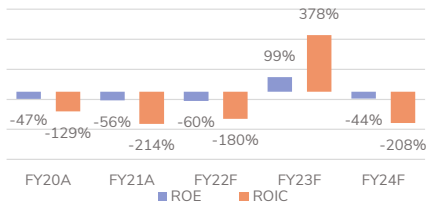
Key changes

		04-Nov	After	Var %
NPAT norm ($m):	FY22F	-33.9	-33.9	0.0%
	FY23F	78.4	78.4	0.0%
	FY24F	-43.2	-43.2	0.0%
EPS: norm (cps)	FY22F	-4.0	-4.0	0.0%
	FY23F	9.2	9.2	0.0%
	FY24F	-5.1	-5.1	0.0%
DPS: (cps)	FY22F	0.0	0.0	0.0%
	FY23F	0.0	0.0	0.0%
	FY24F	0.0	0.0	0.0%
Price target:		0.91	0.91	0.0%
Rating:		O/W	O/W	

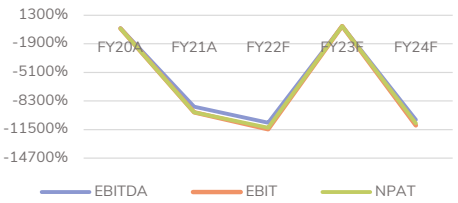
Growth rates



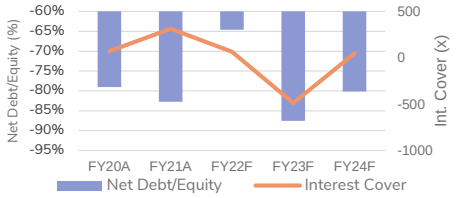
Returns



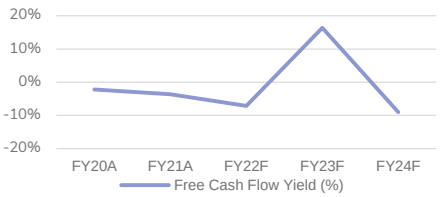
Margin trends



Solvency



Free cash flow yield



Interims ($m)

	1H21A	2H21A	1H22E	2H22E
Sales	0.2	0.1	0.2	0.2
EBITDA	-18.8	-9.1	-15.1	-17.1
EBIT	-19.9	-10.1	-16.2	-18.2
Net profit	**-19.8**	**-10.1**	**-15.9**	**-18.0**
Norm EPS	**-3.8**	**-1.2**	**-1.9**	**-2.1**
EBIT/sales	-	-	-	-
Dividend (c)	0.0	0.0	0.0	0.0
Franking (%)	0.0	0.0	0.0	0.0
Payout ratio	0.0	0.0	0.0	0.0
Adj payout	0.0	0.0	0.0	0.0

Key assumptions

	FY18A	FY19A	FY20A	FY21A	FY22F	FY23F	FY24F
Revenue Growth (%)		-64.4	499.8	-96.0	-4.1	40,000.0	-99.7
EBIT Growth (%)	26.6	45.0	-27.1	119.6	14.7	-327.3	-156.5
NPAT Growth (%)	36.1	43.9	-26.6	122.0	13.3	-331.2	-155.2
EPS Growth (%)			**-40.5**	**54.3**	**-20.8**	**-331.2**	**-155.2**
R&D spend	-10.0	-16.6	-20.4	-17.2	-26.0	-33.0	-35.0
ROA (%)	**-31.1**	**-41.9**	**-30.9**	**-46.5**	**-52.7**	**90.8**	**-41.7**
ROE (%)	**-42.4**	**-63.4**	**-46.7**	**-56.1**	**-60.0**	**98.6**	**-44.4**

Financial ratios

	FY18A	FY19A	FY20A	FY21A	FY22F	FY23F	FY24F
PE (x)	-124.5	-11.1	-18.7	-12.1	-15.3	6.6	-12.0
EV/EBITDA (x)	-41.4	-27.3	-39.8	-16.5	-14.3	5.7	-11.1
Dividend yield (%)	0.0	0.0	0.0	0.0	0.0	0.0	0.0
FCF yield (%)	-1.5	-2.9	-2.1	-3.4	-6.7	15.2	-8.4
Payout ratio (%)	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Adj payout (%)	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Profit and loss ($m)

	FY18A	FY19A	FY20A	FY21A	FY22F	FY23F	FY24F
Sales revenue	3.6	1.3	7.8	0.3	0.3	120.3	0.4
EBITDA	-11.1	-16.9	-11.6	-27.9	-32.2	80.6	-41.6
Depn & amort	1.8	1.9	2.1	2.1	2.2	2.4	2.6
EBIT	**-12.9**	**-18.7**	**-13.7**	**-30.0**	**-34.4**	**78.2**	**-44.2**
Net interest expense	-0.2	-0.4	-0.2	-0.1	-0.5	-0.2	-0.9
Tax	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Minorities/pref divs	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Equity accounted NPAT	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net profit (pre-sig items)	**-12.7**	**-18.3**	**-13.5**	**-29.9**	**-33.9**	**78.4**	**-43.2**
Abns/exts/signif	1.3	0.6	0.1	-0.6	0.0	0.0	0.0
Reported net profit	**-11.4**	**-17.8**	**-13.4**	**-30.5**	**-33.9**	**78.4**	**-43.2**

Cash flow ($m)

	FY18A	FY19A	FY20A	FY21A	FY22F	FY23F	FY24F
EBITDA	-11.1	-16.9	-11.6	-27.9	-32.2	80.6	-41.6
Interest & tax	0.1	0.4	0.2	0.1	0.5	0.2	0.9
Working cap/other	3.2	1.2	0.5	10.2	-2.9	-1.7	-3.1
Operating cash flow	**-7.8**	**-15.3**	**-10.8**	**-17.6**	**-34.6**	**79.0**	**-43.7**
Maintenance capex	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Free cash flow	**-7.8**	**-15.3**	**-10.8**	**-17.6**	**-34.6**	**79.0**	**-43.7**
Dividends paid	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Growth capex	0.0	0.0	0.0	0.0	-0.2	-0.2	-0.2
Invest/disposals	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Oth investing/finance flows	-1.3	-0.8	-1.5	-2.1	0.0	0.0	0.0
Cash flow pre-financing	**-9.1**	**-16.1**	**-12.3**	**-19.8**	**-34.8**	**78.8**	**-43.9**
Funded by equity	19.7	8.8	22.0	55.0	0.0	0.0	0.0
Funded by debt	0.0	0.0	-0.1	-0.2	-0.1	-0.1	-0.1
Funded by cash	-10.6	7.3	-9.6	-35.0	34.9	-78.7	44.0

Balance sheet summary ($m)

	FY18A	FY19A	FY20A	FY21A	FY22F	FY23F	FY24F
Cash	23.5	16.6	26.3	60.6	25.7	104.4	60.4
Current receivables	3.4	5.2	3.3	6.1	5.0	5.0	5.0
Current inventories	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net PPE	0.0	0.1	0.0	0.0	0.2	0.3	0.4
Intangibles/capitalised	18.3	16.9	15.2	12.8	13.1	13.1	13.1
Total assets	**47.0**	**40.5**	**46.6**	**82.0**	**46.6**	**126.0**	**81.6**
Current payables	3.7	5.1	2.9	4.8	2.8	3.5	3.0
Total debt	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total liabilities	**13.5**	**16.2**	**13.3**	**8.8**	**6.8**	**6.8**	**6.3**
Shareholder equity	**33.5**	**24.4**	**33.3**	**73.3**	**39.8**	**119.2**	**75.3**
Total funds employed	**33.5**	**24.4**	**33.3**	**73.3**	**39.8**	**119.2**	**75.3**

AIPAC Phase III well supported for <65y cohort

As noted previously, we see the final Overall Survival (OS) data from the Phase IIb AIPAC study presented at SITC as supportive of Immutep's Phase III registration trial plans in metastatic $HR^+/HER2^-$ breast cancer where they are combining their lead LAG-3 asset, Efti, with chemotherapy (paclitaxel).

At the Society for Immunotherapy of Cancer (SITC) conference, a key IO industry conference, Immutep reported incremental improvements in OS across three key pre-specified patient subgroups. The efficacy of Efti + chemotherapy in these subgroups is critical in that they will inform the Phase III trial design (see **Table 1** below). We keep in mind that OS is the key approvable (FDA, EMA) endpoint for metastatic cancer trials and is the likely primary endpoint for Immutep's upcoming Phase III AIPAC-003 study.

Table 1. Previously reported interim AIPAC OS data vs final OS data from SITC conference

		Median OS benefit of Efti vs placebo		NOTES
	% of AIPAC cohort	Previous data	Updated FINAL data	
Total population	100%	+2.7months HR=0.83 (p=0.140)	+2.9months HR=0.88 (p=0.197)	As expected, non-significant benefit at total group level.
Pre-specified subgroups				
<65 years old	66%	+7.1months HR=0.62 (p=0.012)	**+7.5months HR=0.66 (p=0.017)**	Benefit extended, significance maintained.
Low monocyte (<0.25/nL)	21%	+9.4months HR=0.47 (p=0.02)	**+19.6months HR=0.44 (p=0.008)**	Benefit extended, significance maintained.
Luminal B	49%	+3.8months HR=0.69 (p=0.077)	**+4.2months HR=0.67 (p=0.049)**	Benefit extended, significance gained.

Source: Immutep.

Pre-defined AIPAC subgroups chosen due to known potential differential responses at study outset. We understand that three key patient subgroups (<65 years, low monocyte and Luminal B) among others, were articulated pre-2018, at the time of AIPAC trial design and conception due to their potential likelihood to respond differently to Efti, with influencing factors such as immunosenescence (immune dysfunction occurring with advanced age), more aggressive/proliferative tumour types (i.e. Luminal B), or prior therapy type (i.e. prior taxane exposure) being relevant factors for investigation.

Top-line data miss was expected; impossibility of reaching significance. The AIPAC Phase IIb study was not powered to detect a significant difference in OS. Nor was it powered for any of the three pre-defined subgroups, yet managed to elucidate significant effects. As a reminder, we model the mBC opportunity for Efti as restricted to those under 65 years and those with Luminal B tumours which we estimate to provide an addressable population of ~46,000 in a 2nd or 3rd line metastatic setting (across US and EU markets). Given the overlap commentary that Luminal B patients are often younger, as are those with low monocytes, we are comfortable in focusing on the <65 years cohort as the primary group to progress in AIPAC-003.

Low monocyte data too good to be true? We make this comment not to suggest any data integrity issue, but to comment on just how impressive the gains in OS are with Efti (+19.6 months; p=0.007) with an incremental +10 months added in survival benefit in this subgroup since the December 2020 readout. The mechanism underlying the response in these patients is yet to be clarified at a signalling level. The absence of a ceiling effect in these patients is postulated as potentially contributing to the extreme gains observed with Efti. This is to say, patients with low monocytes are starting off with a weakened immune system ergo they have a greater potential for upside benefit. We note that within the 'low monocyte' subgroup patients with clinical monocytopenia are excluded. There are also questions as to how prior therapy (including taxanes) may be correlated to low baseline monocytes in some patients. We do not yet have clarification regarding the patient overlap between those in both low monocyte and prior taxane therapy subgroups at study outset.

We choose to exclude the low monocyte subgroup from our modelling (~20% AIPAC cohort) given it is unclear how relevant this subgroup is to inform clinical treatment choice. Our understanding is that this is not a commonly defined patient subgroup, nor is it a standard analysis used in treatment decision making, versus say Luminal status. As such we find it hard to see how it would make its way to a label as an approved indication subgroup, notwithstanding the impressive gains. Further understanding of the underlying mechanism in these patients is

bound to inform this view further, and should the same extensive gains be observed in Phase III there could be provision for use in this subgroup with a defined diagnostic companion test, or off-label.

Efti response favours the new SOC: CDK4/6 inhibitors. Exploratory data presented showed that prior CDK4/6 inhibitor therapy is a prognostic factor associated with an increased risk of death in AIPAC cohort patients (+37% risk of death vs those naïve to CDK4/6 inhibitors). The median OS response of these CDK4/6 experienced patients, which accounted for ~44% of the total AIPAC cohort, was reduced overall compared to the median OS response in those without prior CDK4/6 therapy (**Table 4**). This OS reduction was moderated in the Efti treatment arm compared to the placebo arm. Since initiation of the AIPAC trial, the use and popularity of CDK4/6 inhibitors has expanded significantly with CD4/6K inhibitors becoming a 1st line SOC therapy in mBC patients. Efti responding in patients both with and without prior CDK4/6 inhibitor therapy is positive for the future development of Efti in this mBC indication, given the widespread use of this drug class today.

Table 4. Effect of prior CDK4/6 therapy on OS

	Median OS	
	Placebo	Efti
Prior CDK4/6	14.9 months	20.2 months
No prior CDK4/6	20.4 months	21.9 months
Delta	*-5.5 months*	*-1.7months*

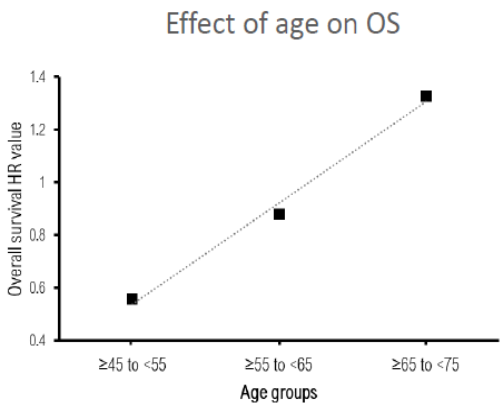
Source: Immutep

Why 65? We note the age subgroup was not correlated to menopausal status of ECOG performance but rather based on immunosenescence and 65 being a standardised age cut off in oncology to define a geriatric patient. In addition, we note the use of ≥65 years as a statistics delineator in major US cancer databases, i.e. SEER. Additionally, this age aligns with US Medicare beneficiary status.

Age correlation to OS HR highlights inconsistent response in older (≥ 65) patients; more data required. A post-hoc analysis of age correlated to OS Hazard Ratio (HR) presented at SITC suggests a detrimental response of Efti versus placebo in the elderly patients (≥65 to <75 years). We note a HR of ~1.3 in elderly (≥65 to <75) versus those in the mid (≥55 to <65; HR ~0.85) and young (≥45 to <55; HR ~0.55) patient age bands (**Figure 1**). This HR suggests older patients may have an increased risk of death due to Efti treatment when compared to placebo.

When looking at the reported OS data we see that this effect (HR >1) could potentially be explained by an aberrant placebo response in the older (≥65) cohort (**Table 5**). This speculation is caveated by the fact we do not have published median OS data for those in the ≥65 cohort (and have relied on a flawed median OS = mean OS equivalency) and that only 27-30 events per group contributed to this age (≥65) bracket.

Figure 1. Age-related correlation between Efti response



Source: Immutep.

Table 5. Placebo group OS in ≥65 years cohort may be aberrantly high?

Median OS						
	Total Population	*(n events)*	< 65 years	*(n events)*	≥ 65 years	*(n events)*
Placebo	17.5 months	83	14.8 months	56	**~23 months ***	27
Efti	20.4 months	81	22.3 months	51	~17.3 months *	30
Impact of Efti	+2.9 months		+7.5 months		~ - 5.7 months *	

*Median OS for ≥ 65 group calculated based on assumption mean OS equivalent to median OS - big caveat to this analysis

Source: Wilsons estimates, Immutep.

Data continues to support Efti MOA. We saw updated correlation data presented at SITC highlighting the positive correlation (R=0.6, p=0.007) between OS and $CD8^+$ T cell counts which supports Efti's intended mechanism of action. This mechanistic data further supports our positive view on Efti in this indication and is often not something that is seen in blinded clinical data sets at this point in development from small biotech players. We appreciate data like this strengthens IMM's appeal to prospective strategic partners.

Current status of Phase III trial plans (AIPAC-003). Our current understanding, as we have written about before, is that the AIPAC-003 trial is likely to focus on patients < 65 years of age and enrol ~460 patients randomised to a 2:1 format (Efti: placebo). Whether Immutep employ a nested approach to capture additional patient subgroups (low monocyte, Luminal B) is yet to be determined. The primary study endpoint is expected to be Overall Survival (OS). As noted by Immutep, changes to paclitaxel backbone therapy is a learning from the AIPAC Phase IIb and we are likely to see paclitaxel use extended beyond a 6-month treatment course (current EU SOC) and be used up until the point of tumour progression (akin to current USA SOC).

Regulators thus far positive. Immutep have received positive scientific feedback on their proposed AIPAC-003 design from the European regulator (EMA) in late October and are in current discussions with the FDA. We expect to hear more about AIPAC-003 finalised trial design in early CY22.

Efti impresses in 2nd line HNSCC

HNSCC 101

HNSCC has high mortality; major unmet dinical need. Head and Neck Squamous Cell Carcinoma (HNSCC) is the sixth most common cancer globally with a high associated mortality rate (66% 5-year survival rate)[1]. HNSCC encompasses a number of cancers including nasopharyngeal, nasal cavity/sinus, oral and oropharyngeal, salivary gland and laryngeal/hypopharyngeal cancer depending on the area of the head/neck in which the tumour/s are located. Squamous cell carcinoma (SCC) describes a cancer of the skin, or epithelium. Approx. 90% of all head and neck cancers are SCCs. If SCC is caught early is relatively curable however once metastasized has a poor prognosis and rapid disease progression.

Keynote-048 trial of pembrolizumab in 1st line mHNSCC supported new SOC. Merck's Keynote-048 Phase III trial of pembrolizumab in 1L metastatic HNSCC supported the 2019 approval of pembrolizumab as a 1L monotherapy (in those with PD-L1 CPS ≥ 1%) and in combination with chemotherapy (for all patients). Anti-PD-1 therapies (including pembrolizumab and nivolumab) had previously only been approved in the 2nd line setting.

We call out Keynote-048 as a key comparator study for Immutep with regards to their TACTI-003 Phase IIb that has just started in 1st line mHNSCC. We compare TACTI-002 data to both Keynote-028 (1L pembrolizumab) and Keynote-040 (2L pembrolizumab) Phase III trials in **Table 1** below to highlight the comparative efficacy of the Efti + pembrolizumab combination vs pembrolizumab alone, noting the caveats of cross-trial comparisons with regards to lack of control group, phase and sample size disparity.

Table 1. Comparison of Efti vs pembrolizumab and SOC in 1st and 2nd line metastatic HNSCC

	Efti + pembrolizumab	Pembrolizumab	Pembrolizumab	Pembro+ chemo	Platinum-based chemo
	IO - IO	IO monotherapy	IO monotherapy	IO - Chemo	Chemo
Study	TACTI-002 Part C	Keynote-040	Keynote-048	Keynote-048	Keynote-040
Phase	II	III	III	III	III
Therapy Line	2nd	2nd	1st	1st	2nd
n	39	247	301	281	248
Demographics (% male)	90%	84%	83%	80%	83%
Median age	62	60	62	61	60
Median PFS	2.1 months	2.1months	2.3 months	4.9 months	2.3 months
HR (for progression)	-	0.96 (p=0.32)	p>0.05	0.84 (p>0.05)	-
PF at 6 months	32%	25%	25%	45%	22%
Median OS	12.6 months	8.4 months	11.6 months	13.0 months	6.9 months
HR (for death)	-	0.80 (p=0.016)	0.83 (p=0.02)	0.77 (p=0.034)	-
Median Duration of response	>9 months	18.4 months	22.6 months	6.7 months	5.0 months
ORR	29.7%	14.6%	16.9%	36.0%	10.1%
Response criteria	iRECIST	RECIST v1.1	RECIST v1.1	RECIST v1.1	RECIST v1.1
Treatment-related Adverse Events (AEs)					
Discontinuation AEs	3%	6%	0%	8%	5%
Grade ≥3 AEs	10%	13%	17%	72%	36%
AEs leading to death	0%	2%	1%	4%	4%

Source: Wilsons, Immutep, Burtness et al (2019), Cohen et al (2018).

We note superior ORR and OS of Efti combo compared to pembrolizumab monotherapy in both 1L and 2L cohorts (30% vs 15-17% and 12.6months vs 8.4-11.6months, respectively). The pembrolizumab + chemotherapy combination has slightly superior efficacy (ORR and OS) to Efti however carries a heavy side effect profile (72% Grade ≥3 AEs vs 10% with Efti) that doesn't outweigh the incremental benefit.

[1] Johnson et al. 2020. Head and neck squamous cell carcinoma. *Nature Reviews Disease Primers*. 6: 92.

TACTI-002 update at SITC highlights high response rate in PD-L1 positive patients with mHNSCC

Updated data released at SITC highlights that the objective response rate (ORR) in PD-L1 positive patients is more than 2x that of pembrolizumab monotherapy when compared across trials (**Table 2**), including across the different PD-L1 expression 'buckets' reported (all-comers, CPS ≥1%, CPS ≥20%).

We had previously noted a 45.8% ORR for those with PD-L1 expression (CPS ≥1%) with Efti. The update at SITC has further split out this response rate into a PD-L1 high (CPS ≥20%) expression group also (**Table 2**). Updated ORR for PD-L1 positive patients (CPS ≥1%) is 40.7% (n=27) with the total (PD-L1 all comers) group importantly maintained at 29.7% ORR.

Table 2. Cross trial efficacy comparison of Efti + pembrolizumab combination in 2L HNSCC versus pembrolizumab (1L, 2L) monotherapy based on PD-L1 expression levels

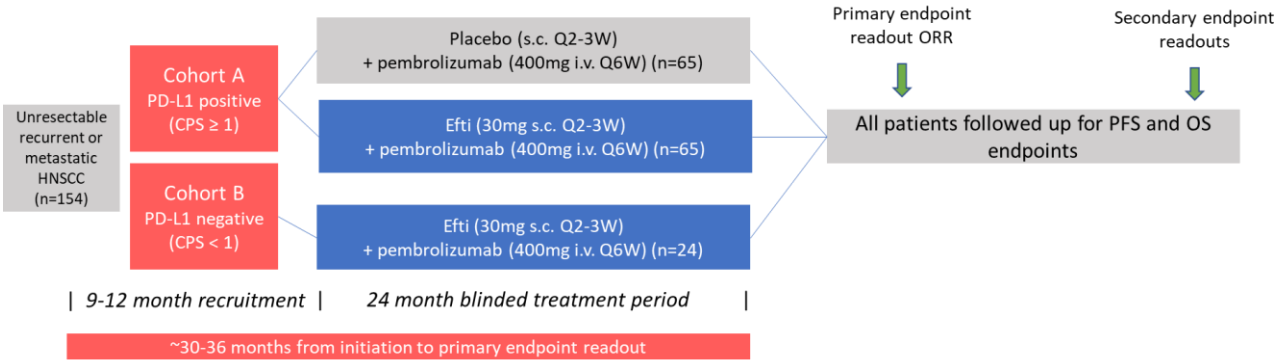
PD-L1 subgroup	Median PFS			ORR			Median OS		
	Efti + pembro (2L)	pembro (2L)	pembro (1L)	Efti + pembro (2L)	pembro (2L)	pembro (1L)	Efti + pembro (2L)	pembro (2L)	pembro (1L)
All (unselected)	2.1months	2.1months	2.3 months	**29.7%**	14.6%	16.9%	**12.6 months**	8.4 months	11.6 months
CPS ≥ 1%	**4.1 months**	-2.1months	3.2 months	**40.7%**	NR	19%	**12.6 months**	8.7 months	12.3 months
CPS ≥ 20%	NR	NR	3.4 months	**64.3%**	NR	23%	NR	NR	14.9 months

NR: Not reported

Note: the green numbers indicate the updated values from SITC. Pembro (2L) data from Keynote-040 trial. Pembro (1L) data from Keynote-048 trial.
Source. Immutep, Cohen et al. (2018)[2], Burtness et al (2019)[3].

SITC data highlights Efti response far exceeds that of pembrolizumab in 1L setting; supports TACTI-003.
We note the comparison between TACTI-002 Part C data and that from Keynote-048 (1L pembrolizumab monotherapy) where we see ORRs in the range of 19-23% for those with PD-L1 positive tumours (CPS ≥1%). Comparatively, the addition of Efti to pembrolizumab has more than doubled this response rate to 41-64% across those with low-high PD-L1 expression overall (**Table 2**). This is a positive readthrough for Immutep heading into the 1st line TACTI-003 Phase IIb trial (NCT04811027) that focuses on those with PD-L1 positive tumours in the randomised cohort (Cohort A; see **Figure 1** for trial design below) with ORR as the primary endpoint.

Figure 1. TACTI-003 trial design summary



Source: Wilsons, Immutep

FDA fast track designation granted for Efti in HNSCC. Immutep received Fast Track Designation (FTD) status for Efti in 1st line HNSCC from the FDA in April of this year based on the TACTI-002 Part C data in HNSCC patients. This provides them with increased access to the FDA in the form of meetings and written communications regarding their trial plans and progress as well as eligibility for Accelerated Approval and/or Priority Review should they meet relevant criteria.

[2] Cohen et al. 2018. Pembrolizumab versus methotrexate, docetaxel or cetuximab for recurrent or metastatic head-and-neck squamous cell carcinoma (KEYNOTE-040): a randomised, open-label, phase 3 study. Lancet. doi.org/10.1016/S0140-6736(18)31999-8
[3] Burtness et al. 2019. Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study. Lancet. doi.org/10.1016/S0140-6736(19)32591-7

Immutep Limited (IMM)

Business description

Immutep (IMM:ASX) (formerly Prima Biomed) is a clinical stage Australian biopharma operating in the immuno-oncology (IO) sector with their portfolio of LAG-3 directed biologics which were first acquired in 2016. Immutep have four assets under development, all with strong IP protection; two of which are out-licensed (LAG525, IMP731) to major development partners (Novartis, GlaxoSmithKline) and have attached milestone and royalty revenue optionality, with the remaining two (IMP321 or 'Efti' and IMP761) being developed in-house for a range of oncology and autoimmune indications. Efti, being Immutep's lead asset in development, is preparing to enter the first registration level Phase III study in metastatic breast cancer advancing its timeline to the clinic. Efti differentiates from other LAG-3 assets in development given its unique mechanism of action. Immutep has strong in-house expertise with their CMO/CSO Dr Frederic Triebel being the one who discovered the LAG-3 checkpoint which is now the basis for a new wave of checkpoint inhibitor development. Immutep has depository listings (ADRs) traded on the NASDAQ (IMMP).

Investment thesis

We maintain our OVERWEIGHT recommendation and a $0.91/sh risked PT on Immutep. The data presented at the Society for Immunotherapy of Cancer (SITC) conference (10-14 Nov) has been the catalyst driving IMM volatility over the past week. Final overall survival (OS) data from the Phase IIb breast cancer program (AIPAC) with Immutep's lead LAG-3 asset, Efti, was incrementally positive compared to the last interim readout (Dec 2020) however the market interpreted top-line data as a miss. What's important to appreciate is that the Phase III program in preparation is focused on key pre-specified subgroups, of which we have seen impressive, and significant, clinical gains with Efti when combined with chemotherapy. Further, we have seen incremental Phase II HNSCC data, highlighting that the addition of Efti to SOC Keytruda has more than doubled the response rates observed in foundational Keytruda studies. The opportunity for Efti to expand the market for this blockbuster, potentially alongside others, presents a valuable option for Immutep, which we assess as likely to attract keen pharma interest, particularly as LAG-3 attention intensifies ahead of LAG-3 target validation in 1Q22 (BMS' relatlimab FDA decision).

Revenue drivers

Market approvals (long term)
Licensing deals (upfront and milestone payments)

Balance sheet

Net cash of ~$106M as of end 1Q FY22.

Margin drivers

Not applicable

Board

Dr Russell Howard – Non-Executive Chairman
Marc Voight – Executive Director
Pete Meyers – Non-Executive Director and Deputy Chairman
Grant Chamberlain - Non-Executive Director

Key issues/catalysts

Clinical trial results
Market approvals
Regulatory interactions with EMA and FDA
Competitor development progress
Indication expansion opportunities
Corporate activity (licensing deals, M&A)

Management

Marc Voight – Chief Executive Officer
Dr Frederic Triebel – Chief Scientific Officer and Chief Medical Officer
Deanne Miller – COO, General Counsel and Company Secretary
Christian Mueller – VP of Strategic Development
Dr Claudia Jacoby – Director of Manufacturing
Dr James Flinn – Director of IP and Innovation
David Fang – Finance Director and Assistant Company Secretary

Risk to view

Unfavourable regulatory reviews
Failure to show adequate clinical efficacy to support approvals
Competition within a busy IO space
Changes in SOC landscape making existing trial programs less relevant (i.e. regarding pembrolizumab, paclitaxel)

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Disclaimers and Disclosures

Recommendation structure and other definitions

Definitions at wilsonsadvisory.com.au/disclosures.

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