WILSONS

Date 27 May 2022

Theme Alert

Sector Healthcare

Company
Immutep Limited (IMM)

Efti continues to win in NSCLC

Recommendation OVERWEIGHT
12-mth target price (AUD) $0.91

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Announcement highlights

Today Immutep have released the abstracts for their 2022 ASCO presentations, including their oral presentation focused on updated interim data from their TACTI-002 Phase II trial in 1st line metastatic non-small cell lung cancer (NSCLC). This new interim data shows that the treatment response achieved with Efti in combination with pembrolizumab (Keytruda®) in the initial n=36 patient data readout (June 2021) was maintained in an expanded cohort of 75 patients (noting that ASCO data presented next week will include further data out to 114 patients).

The Efti + Keytruda combination continues to be superior when compared to Keytruda monotherapy (current standard of care) when looking at overall response rate (ORR) (37.3% vs 27%) (**Table 1**). No detail regarding progression free- or overall survival (PFS or OS) was provided in the abstract today however we anticipate updated interim data (for PFS) to be presented at ASCO next week in Immutep's Oral presentation (3rd June ET).

Key to note, Efti has achieved this superior response in mNSCLC patients in a 1st line setting that is unselected for PD-L1 expression, and are therefore achieving efficacy in an expanded patient population than is currently addressable with standard of care anti-PD-1/L1 monotherapy.

Wilsons' view

Initial analysis

As a reminder, the last interim data readout from this 1st line NSCLC cohort from 36 patients was presented at ASCO 2021. In **Table 1** overleaf we restate this data (far left column) alongside today's updated 75 expanded cohort data (highlighted column), and compare it to existing approved 1st line metastatic NSCLC therapies (right hand side columns).

Efti has achieved response rates equal to Keytruda in PD-L1 negative (TPS <1%) patients. The key takeaway in our view is when comparing the ORR achieved with the Efti combination on a like-for-like basis with Keytruda monotherapy. ORR in a PD-L1 positive (TPS ≥1%) population Efti + Keytruda achieved a 44% response rate which compares on a LFL basis to Keytruda at 27% based on data from their Phase III KEYNOTE-042 trial. **This 17% incremental efficacy uplift is meaningful.** Further, the Efti combination has achieved an ORR of 27.3% in PD-L1 negative patients (TPS <1%) which is on par to that of Keytruda in the positive population – this is an impressive outcome which broadens the applicability of checkpoint inhibitors such as Keytruda beyond only patients with "hot" tumours. We caveat this with the fact we are yet to see PFS and OS data and statistical analysis of these important endpoints (yet to come in time).

All comers approach provides access to entire patient population; a valuable differentiator. Prior approaches with anti-PD-1 therapies (i.e. pembrolizumab and atezolizumab monotherapy) have focused on including only patients with PD-L1 expression, excluding those with nil to very low expression (TPS <1%). As a result, the approved 1st line anti-PD-1 monotherapies are restricted to patients with confirmed PD-L1 positive tumours representing only ~65% of the total metastatic NSCLC population. In the US 65% of these patients are able to be treated with anti-PD-1 monotherapy in a 1st line setting, whilst in Europe only ~30% of patients are eligible based on them requiring a higher PD-L1 expression level (TPS ≥ 50%). There is a clear unmet need for the 35-70% of patients not currently eligible for therapy that may see benefit from an IO approach, prior to moving to chemotherapy which brings with it a toxicity and side effect profile that is far less desirable than immunotherapies. The addition of Efti to pembrolizumab (approved anti-PD-1 monotherapy) highlights there is the ability to broaden the use case for these blockbuster drugs and be able to address 100% of the mNSCLC patient pool. **Table 2** highlights the relative treatment efficacy of the Efti combination across the different PD-L1 cohorts – importantly consistency of effect is maintained.

Table 1. Comparison of Efti vs other checkpoint inhibitors vs SOC in 1st line metastatic NSCLC^

	Efti + pembrolizumab	Efti + pembrolizumab	Pembrolizumab	Atezolizumab	Pembro+ chemo	Nivolumab + ipilimumab	Platinum-based Chemo (SOC)		
Targets	APC activator + Anti-PD-1	APC activator + Anti-PD-1	Anti-PD-1	Anti-PD-L1	Anti-PD-1+ chemo	Anti-PD-1+ Anti-CTLA-4			
FDA approval	-	-	April 2019	May 2020	Oct 2018	May 2020			
Study	TACTI-002 Part A	TACTI-002 Part A extension	Keynote-042	IMpower110	Keynote-407	Checkmate-227	Keynote-042	Keynote-407	IMpower110
Phase	II	II	III	III	III	III	III	III	III
Therapy Line	1st	1st	1st	1st	1st	1st	1st	1st	1st
n	36	**75**	637	277	278	583	637	281	277
Demographics (% male)	69%	NR	71%	71%	79%	67%		84%	70%
Median age	69	NR	63	64	65	64	63	65	65
% current/former smoker	94%	NR	78%	87%	92%	85%	78%	93%	87%
PD-L1 TPS <1%	23%	29%	**nil**	**nil**	34%	32%	**nil**	35%	**nil**
TPS 1-49%	46%	31%	53%	61%	37%	33%	53%	37%	65%
TPS ≥50%	31%	29%	47%	39%	26%	35%	47%	26%	35%
Median PFS	**8.2 m**	**NR**	**5.4 m**	**5.7 m**	**6.4 m**	**7.2 m**	**6.6m**	**4.8 m**	**5.5 m**
HR (for progression)	-	-	1.07, p>0.05	0.77	0.56, p<0.001	0.79	-	-	-
Median OS (months)	**Not yet reached**	**Not yet reached**	**16.7m**	**17.5 m**	**15.9 m**	**17.1 m**	**12.1m**	**11.3 m**	**14.1 m**
HR (for death)	-	-	0.81, p=0.0018	0.83, p>0.05	0.64, p<0.001	0.73	-	-	-
DoR median	>13 m	Not yet reached	20.2 m	not estimatable	7.7 m	19.6 m	8.4m	4.8 m	5.7 m
ORR	**36%**	**37%**	**27%**	**29%**	**58%**	**33%**	**27%**	**38%**	**32%**
Response criteria	iRECIST	iRECIST	RECIST v1.1	RECIST v1.1	RECIST v1.1	RECIST v1.1	RECIST v1.1	RECIST v1.1	RECIST v1.1
Adverse Events (AEs)									
Discontinuation AEs	3.5% #	17%	8%	6%	23%	18%	7%	12%	16%
Grade ≥3 AEs	50% #	NR	18%	34%	70%	33%	41%	68%	57%
Treatment related death	0%	NR	2%	4%	4%	1%	2%	2%	4%

^Note this is not an exhaustive list of all approved IO combinations and drugs ; simply a summary of interesting trial predicates and comparisons.

For trials with PD-L1 subgroups, the most inclusive dataset is shown (i.e. all PD-L1 levels) to make most comparable to TACTI-002 data. i.e. for some IO higher OS data was found in TPS>50% groups etc.

NR = not reported. # total TACTI-002 population (includes HNSCC).

*ORR is shown as the blnded independent central review values, not investigator assessed. * HR when compared to chemotherapy arm.*

Source: Immutep, Wilsons, clinicaltrials.gov, PubMed.

Table 2. Efficacy responses by PD-L1 subgroup

PD-L1 subgroup	Proportion of cohort	ORR	ORR
n		75	36
All (unselected)	100%	37%	36%
<1% TPS	29%	27%	27%
≥1% TPS	67%	44%	44%
<50% TPS	67%	32%	32%
≥50% TPS	29%	55%	54%

Source: Immutep, Wilsons.

Response consistency maintained. The responses across different PD-L1 subgroups with Efti + Keytruda (pembrolizumab) remain consistent when comparing the n=36 patient data (2021 – right hand column) to that reported in today's updated n=75 patient data set. As a reminder, in the PD-L1 negative population (TPS <1%) we saw a 4.1month PFS which is impressive in this cohort with so called "cold" tumours. The ORR data today supports the likely preservation of this PFS response.

Investment case rests on Efti expanding the addressable market for leading IO blockbusters – this data continues to support. The data presented continues to support the thesis that Efti's value lies in its ability to expand the existing addressable market for blockbuster anti-PD-1 therapies such as Keytruda (FY21 US$17B sales) by up to 35%, in the second largest cancer indication globally.

Strengthened fundamentals not reflected in share price. The validation of LAG-3 as a novel immune checkpoint target in March with Bristol Myer's Squibb's relatlimab in March of this year only further validates Immutep's approach to the IO space and de-risks their portfolio. Market conditions have been such that pre-commercial biotech has been hit in sell-offs, with Immutep no exception. On a fundamental basis Immutep are in the strongest position they have ever been with a unique and comprehensive portfolio of assets in development focused on the newest approved immuno-oncology target – LAG-3 – the first new target to be approved since 2016. Also, at a time with other IO target hopefuls, TIGIT, have run aground driving pharma to re-evaluate their pipelines and investments to other targets such as LAG-3. Further to this, Immutep now have strengthened data in their NSCLC program which presents the largest commercial market opportunity for IMM and currently accounts for 58% of our risked valuation.

Earnings implications

None.

Investment view

We maintain our **OVERWEIGHT recommendation on Immutep and $0.91 per share risked price target**, which is comprised of a SOTP focused on their Efti programs in a) metastatic breast cancer $0.30/share, b) HNSCC $0.09/share, and c) NSCLC $0.53/share. Our unrisked PT remains at $2.33 per share.

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