WILSONS ADVISORY

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Theme Alert

Sector Healthcare

Company
Immutep Limited (IMM)

TACTI-003-B | Approvable in HNSCC?

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Investment View

The combination of Efti and KEYTRUDA has achieved impressive efficacy data from Part B of TACTI-003. Results are ahead of the KEYTRUDA/chemotherapy regimens that pass for standard of care in first line HNSCC (for CPS < 1 or 'cold tumour' patients); albeit on a cross-trial comparison basis. Maintain O/W. PT under review, mulling accelerated approval prospects.

Announcement Highlights

Immutep have announced updated data from the TACTI-003-B study in 1L head and neck squamous cell carcinoma (HNSCC). As a reminder, this trial is evaluating Efti, in combination with anti-PD-1 therapy (KEYTRUDA) in PD-L1 non-expressors (CPS < 1). As a reminder, this component of TACTI-003 was uncontrolled. Maturing data from 31 evaluable patients treated with this combo has built upon the strong initial response rates shared earlier this year at ESMO24. At the data cut-off point (31st October), median progression free survival (mPFS) was 5.8 months, (interim) median duration of response was 9.3 months and the proportion of complete responders continued to increase (to 12.9% and 16.1% by RECIST 1.1 and iRECIST, respectively). These results sit well ahead of rival KEYTRUDA with or without chemotherapy. Overall survival has not been reached but with 66% of patients still alive at 12 months, the combo seems well positioned. Our view is that a 2-3 month mOS benefit over the ~11.3 months established in KEYNOTE-048, would be decisive. Whether or not these data are enough to secure accelerated approval is the focus for today's discussions. We estimate US$450M peak sales for Efti in the CPS<1 HNSCC population, should that prove the case (reminding investors that a confirmatory Phase III will be mandated).

Wilsons' View

Initial analysis

Figure 1: TACTI-003-B data to date versus KEYNOTE-048

Comparison of relevant trial programs in 1L mHNSCC

	Efti + pembrolizumab	Pembrolizumab	Pembro+ chemo	Cetuximab + chemo
	IO - IO	IO monotherapy (SOC only in 'hot' tumours)	IO - Chemo (now SOC)	2L SOC or for cold tumour patients
Checkpoint target	PD-1 + LAG-3	PD-1	PD-1	NA
Study	TACTI-003 Part B	Keynote-048	Keynote-048	Keynote-048
Phase	IIb	III	III	III
Therapy Line	1st	1st	1st	1st
n	31	301	281	278
Demographics (% male)	74%	83%	80%	87%
HPV status (% positive)	12.9%^	21%	21%	22%
Current smoker	26%	*	*	*
Median age	64	62	61	61
PD-L1 CPS <1	100%	15%	15%	15%
CPS 1-19	0%	41%	40%	45%
CPS ≥ 20		44%	45%	40%
Median PFS	5.8 months	2.1 months	4.9 months	5.2 months
HR (for progression)	NR	p>0.05	0.84 (p>0.05)	-
PF at 6 months	NR	25%	45%	45%
Median OS	not reached	11.6 months	13.0 months	10.7 months
mOS CPS ≥1	not reached	7.9 months	11.3 months	NR
OS at 12 months	67%	39%	-	-
Median Duration of response	9.3 months	2.6 months	6.7 months	4.3 months
ORR (total)	35.5%	16.9%	36.0%	36.0%
ORR CPS <1	35.5%	5.4%	30.8%	39.5%
ORR CPS ≥1	-	19%	36%	36%
ORR CPS 1-19	-	14.5%	29.3%	33.6%
ORR CPS ≥20	-	23%	38%	43%
DCR (total)	58.1%	44% (32% for CPS<1)	64%	70%

Source: Immutep, Merck, Wilsons Advisory.

KEYNOTE-048 the trial to beat. The current standard of care (SoC) for 1L mHNSCC with PD-L1 negative tumours is a chemotherapy-based regimen, either incorporating a combination with Keytruda (in US) or cetuximab (in EU). In either case, 50% of these patients either refuse or are ineligible for chemotherapy. The metrics to focus on are **ORR** (often supported as a surrogate endpoint for accelerated approval), **OS** (gold standard primary endpoint in oncology) and **DOR** (remembering that **mPFS** is a poor surrogate in this indication). Thus far, the most impressive deltas from SoC are ORR, DOR and the complete response rates (CR: 13%-16%), noting that 0% CPS<1 patients achieved CRs on KEYTRUDA monotherapy (and ~3% with the addition of chemotherapy and/or cetuximab). OS remains the key in positioning the combo for potential accelerated approval. To our minds a 2-3 month benefit over the 10.7-13.0 month range established in KN-048 would be decisive.

Implications of a potential accelerated approval in HNSCC. We've always modelled HNSCC based on waiting for a Phase III pivotal trial and full BLA in 2028. Although on paper, the HNSCC opportunity contributes just 5% to our IMM valuation, the prospect of earlier revenue generation (peak sales estimate of US$450M derived from just 5,000 CPS<1 patients un US/EU5) would lead to a reappraisal of that, clearly. Proximity to revenue could have a profound effect on how IMM stock is perceived and valued in the market.

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