Evaluate Vantage

March 23, 2021

Novartis’s nuclear vision starts to take shape

Amy Brown

A radioligand acquired as part of a $2.1bn deal – and which the sellside believes to be Novartis’s most valuable R&D asset – hits in phase III.

Success in the Vision trial means that Novartis is another step closer to having a second radiopharmaceutical on the market. The win will come as a relief to the company as the stakes were high here, if the numbers associated with the project are anything to go by.

177Lu-PSMA-617 was acquired as part of the $2.1bn Endocyte takeout, a deal remarkable for the fact that the project was apparently worth a fraction of that figure just a year earlier (*From zero to hero, Endocyte completes a remarkable transformation, October 18, 2018*). The sellside considers ‘617 to be Novartis’s most valuable R&D endeavour, with an NPV of $2.8bn, according to *Evaluate Omnium*.

What this says about the health of Novartis’s R&D pipeline is another matter. A look at other assets attracting big numbers reveals something of a mixed bag, and none of them hold substantial near-term hopes.

Phase II data on Novartis’s lead immuno-oncology asset, sabatolimab, should emerge later this year, while asciminib is due to be filed in a heavily pretreated leukaemia population in the coming months. Pivotal data on ligelizumab should start to emerge towards the end of this year and on iptacopan in 2023, but it will be years before the full potential of any of these assets becomes clear.

Novartis's big hopes				
Rank on NPV	**Product**	**Therapy subcategory**	**NPV ($bn)**	**2026e sales ($m)**
On the market….				
1	Cosentyx (marketed)	Anti-IL-17 MAb for psoriasis etc	22.5	6,055
2	Entresto (marketed)	Heart failure	18.3	4,979
3	Leqvio (approved EU, awaiting US decision)	Anti-hyperlipidaemic	10.1	2,017
4	Tafinlar (marketed)	Braf/Mek inhibitor for cancer	9.0	2,135
5	Zolgensma (marketed)	SMA gene therapy	8.6	1,940
Coming next…?				
18	177Lu-PSMA-617 (ph3)	Radioligand for prostate cancer	2.8	553
26	Iptacopan (LNP023, ph3)	Factor B inhibitor for PNH	2.1	398
28	Ligelizumab (ph3)	IgE MAb for chronic urticaria	1.7	532
34	Asciminib (ph3)	Stamp inhibitor for blood cancers	1.4	312
54	Sabatolimab (ph3)	Anti-Tim3 cancer MAb	0.6	109
Source: Evaluate Omnium.				

One caveat to remember here is that big pharma analysts are much less exuberant when it comes to sales forecasts than their small biotech-following colleagues. But this makes it even more surprising that ‘617 is considered Novartis’s biggest R&D hope, on this NPV measure at least.

Radiopharmaceuticals are still considered something of a niche proposition, although the Swiss pharma giant is clearly a believer in the technology’s potential. Hence the Endocyte buyout, and that of Advanced Accelerator Applications, for $3.9bn, in 2017.

That latter move bought Lutathera, which like ‘617 is a lutetium-labelled therapeutic. Lutathera is targeted at neuroendocrine tumours, and carries an NPV of $2.5bn. NETs are a rare type of cancer so Novartis’s hopes for ‘617, in the much larger prostate cancer space, are presumably loftier.

177Lu-PSMA-617's exact potential remains hard to know, however, as today’s news of success in the phase III Vision trial contained no actual data. All Novartis disclosed was that both primary endpoints – overall and radiographic progression-free survival – were met, with no new safety concerns.

The trial enrolled just over 800 patients; the study had been powered to show median OS of 13.7 months and rPFS of six months, with hazard ratios reaching 0.73 and 0.67 respectively. Patients enrolled had relapsed on chemotherapy and an androgen inhibitor, for example Xtandi or Zytiga, and ‘617 was dosed on top of best supportive care, as decided by treating physicians, versus best supportive care.

Development 177Lu-PSMA-617: trial summary		
Trial	**Description**	**Status**
Vision	mCRPC: SOC +/- 177Lu-PSMA-617, post taxane and androgen inhibitor	Top-line positive
PSMAfore	mCRPC chemo-naive: androgen inhibitor or BSC +/- 177Lu-PSMA-617, post alternative androgen inhibitor	About to start
PSMAddition	mHSPC: SOC +/- 177Lu-PSMA-617 (treatment-naive or minimally pretreated)	About to start
Resist-PC	mCRPC: ph2 trial post chemo and androgen inhibitor	Completed ph2
TheraP	mCRPC: 177Lu-PSMA-617 vs chemo; post chemo and androgen inhibitor	Completed ph2
Note: all trials select for PSMA-positive prostate cancer. mCRPC = metastatic castrate-resistant prostate cancer. mHSPC = metastatic hormone-sensitive prostate cancer. Source: clinicaltrials.gov.		

Novartis will likely use data from phase II trials to support US and European filings, which the company plans to submit as soon as possible.

These phase IIs include a relatively large academic-backed trial run in Australia, called TheraP. This pitted ‘617 against chemotherapy in a late-line population, and while it found ‘617 to delay progression and show more activity than Jevtana no benefit on overall survival was seen. The findings of a much smaller Endocyte study were also limited to PSA declines for ‘617.

It sounds as though Novartis has seen much stronger signals in Vision, although the full data are needed to know for sure. It is also notable that in two further phase III trials that the company has planned, ‘617 is also being trialled on top of standard of care, which in the settings being explored is considered to comprise androgen inhibitors.

These new studies would move the radiotherapy into earlier settings, where convincing survival benefits become even more important to show. Should these emerge ‘617 might well warrant the $2.1bn acquisition cost, though the jury will probably remain out for now.