Evaluate Vantage

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Ash 2020 preview – Novartis touts its Tasigna follow-on

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Pivotal data at the upcoming Ash conference make Novartis's asciminib one of the highlights for oncology watchers.

After years in relative obscurity Novartis's BCR-ABL tyrosine kinase inhibitor asciminib could give the Swiss group's chronic myelogenous leukaemia franchise a third pillar, late-breaking pivotal data to be presented at the Ash conference suggest.

The presentation, from the Ascembl study pitting asciminib against Pfizer's Bosulif in third-line or later CML, will be of major interest for investors focusing on blood cancers. Other Ash oncology data include a large array of bispecific antibodies, among which two anti-CD20 assets come from Roche.

For Novartis asciminib is a valuable asset. Its Gleevec blockbuster was the first drug targeting the BCR-ABL oncoprotein to be launched for CML, and it revolutionised treatment of this disease.

Me-too assets followed from Bristol Myers Squibb (Sprycel), Pfizer (Bosulif) and Takeda (Iclusig), and Novartis's own Tasigna is an important first-line drug too. However, Gleevec is now off patent, and Tasigna only has three years' exclusivity left.

Selected BCR-ABL tyrosine kinase inhibitors for CML					
				Sales ($m)	
Drug	**Company**	**Label**	**US patent expiry**	**2019**	**2026e**
Gleevec	Novartis	1st line	2016	1,263	467
Sprycel	Bristol Myers Squibb	1st line	2020	2,110	241
Tasigna	Novartis	1st line	2023	1,880	321
Bosulif	Pfizer	1st line (usually used later)	2024	365	373
Iclusig	Takeda	2nd line	2026	396	584
Asciminib	Novartis	Not approved	Unclear	0	119
Source: EvaluatePharma.					

Now Novartis reckons to have a mechanistic ace up its sleeve. Unlike the approved BCR-ABL assets asciminib specifically hits the oncoprotein's ABL myristoyl pocket, a first-in-class approach that the group claims could combat the build-up of resistance pathways.

The 233-patient Ascembl trial was said in August to have read out positively, and the Ash late-breaker reveals a 24-week molecular response rate, its primary endpoint, of 25.5% for asciminib versus 13.2% for Bosulif, with the difference yielding a p value of 0.029. Severe adverse events occurred less frequently with asciminib than with Bosulif.

As the study enrolled subjects who had failed two or more therapies, data discussion at Ash might focus on baseline imbalances: 52% and 28% of asciminib subjects were third and fourth line respectively, versus 40% and 38% for Bosulif; asciminib's advantage over the Pfizer drug was most pronounced in third-line subjects.

The detail might be important in determining how big a slice of the CML market asciminib might seize. Though Bosulif has a first-line label it is usually used second line or later, and Iclusig, a third-generation drug, is an important second-line (and later) option.

Selected Ash 2020 presentations in oncology (excluding cell therapies)			
Project	**Company**	**Detail**	**Abstract**
Chronic myelogenous leukaemia			
Asciminib (ABL001)	Novartis	Ph3 study, 2L to >6L, major molecular response 25.5% vs 13.2% for Bosulif	LBA-4
Acute myelogenous leukaemia			
GTB-3550	GT Biopharma	Anti-CD16 x CD33 (+ IL-15 linker) trispecific NK cell engager, no responses in 3 pts	65
Sabatolimab (MBG453)	Novartis	Anti-Tim3 MAb, 25 Jun 2020 data cut: 41% ORR in 34 1L pts	657
Lymphoma			
Odronextamab (REGN1979)	Regeneron	Anti-CD20 bispecific, 25 Jun data cut: 53% ORR in 151 pts, incl Car-T refractory	400
Mosunetuzumab	Roche	Anti-CD20 bispecific, 27 May 2020 data cut: 63% ORR (1 relapse) in 19 pts	401
Glofitamab	Roche	Anti-CD20 bispecific, 17 Apr 2020 data cut: 63% ORR in 32 pts	403
Trph-222	BMS/ Triphase Accelerator	Anti-CD22 ADC, lymphoma, 30 Jun 2020 data cut: 23% ORR in 22 pts, incl Car-T refractory	701
MEDI-570	Astrazeneca	Anti-Icos MAb in lymphoma, Jun 2020 data cut: 22% ORR in 18 pts	1151
Multiple myeloma			
MEDI2228	Astrazeneca	Anti-BCMA ADC, 15 May 2020 data cut: 45% ORR in 82 pts	179
REGN5458	Regeneron	Anti-BCMA bispecific, 15 Jun 2020 data cut: 36% ORR in 45 pts	291
TNB-383B	Teneobio/ Abbvie	Anti-BCMA bispecific, 13 Jul 2020 data cut: 37% ORR in 38 pts	293
Talquetamab	J&J	Anti-GPRC5D bispecific, 20 Jul data cut: 78% ORR in 18 pts given IV, 67% ORR in 12 pts given SC dose	290
RG6060	Roche	Anti-FcRH5 bispecific, 13 Apr 2020 data cut: 52% ORR in 29 pts	292

If franchise protection is Novartis's aim with asciminib then similar thinking might lie behind Roche's development of projects that, like the ageing lymphoma/chronic lymphoblastic leukaemia blockbuster Rituxan, target CD20.

To this end the group is presenting mid-stage clinical data on two anti-CD20 bispecifics, mosunetuzumab and glofitamab, which are both now in phase III. A similarly acting asset, Regeneron's odronextamab, is earlier in development, and features in the same Ash session.

The response rates seen so far come from early cuts of the data disclosed in the abstracts, but of more importance will be the updates given at Ash itself, which will presumably comprise results at much later cuts.

Immuno-oncology watchers will note the continued presence of assets targeting once hotly touted antigens like Tim3 and Icos, and there is the usual multitude of BCMA-targeting modalities for multiple myeloma, including for instance Abbvie's TNB-383B.

That last asset might be significant for another reason: Abbvie picked it up from Teneobio last year. With an overall remission rate cited in the abstract of just 52% at the high dose the Ash data could raise further questions about Abbvie's deal-making prowess.

Ash 2020 will take place in virtual format on December 5-8.

Vantage analysis previously summarised upcoming Ash presentations that resulted in early share price moves, and separately those in non-oncology indications.