Evaluate Vantage

July 28, 2021

Amgen doubles down on bispecifics, courtesy of Teneobio

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Curiously, the $900m acquisition will not include many of Teneobio's pipeline projects.

Amgen blazed a trail in bispecific T-cell engagers with the 2014 approval of Blincyto, but it clearly sees the need to shore up its position. A case in point is yesterday's takeover of the private biotech Teneobio, worth $900m in cash up front.

The purchase price is all the more impressive since it does not include many of the bispecifics already in Teneobio's pipeline, as these are to be spun out. As such Amgen's focus is likely on the underlying technology, and perhaps the big pharma partners Teneobio already has on the one hand, and Amgen's recent problems with in-house T-cell engagers on the other, helped focus the mind.

Those problems have included a relatively short half life, which has held back Blincyto, and the toxicity of cytokine release syndrome. Insufficient safety and portfolio overlaps caused Amgen to pause or discontinue several bispecific T-cell engagers (Bites) in its pipeline in February (*Reality Bites for Amgen's bispecifics, February 3, 2021*).

However, the group clearly sees great value in this approach, and will no doubt have been watching Teneobio's progress closely. Since being founded in 2009 the private company has struck deals with Johnson & Johnson, Abbvie, Glaxosmithkline, Gilead, Poseida and others.

The Teneobio approach

One feature of Teneobio's Bites, such as the BCMA-targeting asset TNB-383B, licensed to Abbvie, is their use of a full antibody scaffold with a modified Fc region. This comprises a heavy chain binding CD3 on T cells and a fixed light chain that targets the antigen of choice.

In contrast most of Amgen's Bites are smaller, single-chain molecules lacking an Fc region, while other companies are investigating other bispecific formats, including duobodies, Darpins, fusion proteins and 2+1 constructs.

It is likely that TNB-383B data at Ash last year validated Teneobio's approach. Among 15 multiple myeloma subjects given ≥40mg doses the response rate was 80% and, while cytokine release increased with rising dose, none was reported to be above grade 2.

Still, the Amgen takeover does not include TNB-383B, which Teneobio had put into a subsidiary called Teneoone, which in turn Abbvie opted to buy out last month, no doubt spurred by the Ash data. Similarly, Teneobio's bispecifics against CD19 and HBV, and an anti-CD38 enzyme inhibitor, are to be spun out under their holding subsidiaries to current Teneobio investors before the Amgen deal closes.

Given that antitrust authorities now scrutinise overlaps between even early-stage assets the divestments are no bad thing; Amgen already owns bispecifics against BCMA and CD19, for instance. However, in PSMA targeting Amgen is developing the Bite acapatamab, and will acquire TNB-585 from Teneobio.

How antitrust regulators view the last issue will be a key question as the takeover closes. Since Amgen specifically singles out TNB-585 as a Teneobio project it is acquiring, perhaps it will have no choice but to divest acapatamab.

What Teneobio brings (selected oncology T-cell engagers)…				
Teneobio asset	**Target**	**Status**	**Equivalent Amgen Bite**	**Note**
TNB-383B	BCMA	Abbvie exercised buyout in Jun 2021	Pavrutamab & AMG 420	Pavrutamab ph1 had been paused; AMG 420 no longer in pipeline
TNB-486	CD19	To be spun out under Teneotwo	AMG 562	In ph1, but no longer appears in pipeline list
TNB-585	PSMA	Ph1 in prostate cancer	Acapatamab (AMG 160)	Ph1 in prostate cancer
JNJ-75348780	CD22	Owned by J&J under research collab	None	
Unnamed	FOLR1	Preclinical	None (early work at AACR 2016)	
Unnamed	5T4	Preclinical	None	
…and Amgen's remaining bispecifics				
Project	**Target**	**Status**	**Format**	
AMG 757	DLL3	Ph1 in SCLC & neuroendocrine prostate cancer	Bite	
AMG 330	CD33	Ph1 in myeloid malignancies	Bite	
AMG 673	CD33	Ph1 in AML (had been on hold)	Bite	
AMG 199	Muc17	Ph1 in gastric cancer	Bite	
AMG 427	Flt3	Ph1 in AML	Bite	
AMG 910	CLDN18.2	Ph1 in gastric cancer	Bite	
AMG 509	Steap1	Ph1 in prostate cancer (ex Xencor)	2+1 T-cell engager	
AMG 506	FAP	Ph1 in solid tumours (ex Molecular Partners)	x4-1BB Darpin	
AMG 256	PD-1 x IL21	Ph1 in solid tumours	Fusion protein	
Source: Amgen, Teneobio, Evaluate Pharma & clinicaltrials.gov.				

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