Evaluate Vantage

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Abbvie hopes to turn around the fortunes of Sting

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Continued interest in the Sting pathway might come as a surprise, though secrecy suggests that asset prices are failing.

If Abbvie had revealed how much it paid to acquire Mavupharma yesterday investors would have had a neat way to compare the changing value of assets working on the once highly promising Sting pathway.

As it is they will just have to guess. What cannot be denied, however, is that like many immuno-oncology strategies Sting is not all it was once cracked up to be. That said, Abbvie clearly sees continued promise here, and it must be assumed that it was able to access this at a more realistic price than Bristol-Myers Squibb and Novartis had had to pay a few years ago.

Mavupharma had been launched two years ago with $20m in series A financing from Frazier Healthcare Partners and Alpine Bioventures. Earlier this year it selected the oral project MAVU-104 as its lead Sting pathway enhancer, saying it planned to file an IND for it this year.

Yesterday Abbvie took that decision out of Mavupharma's hands by acquiring it outright without disclosing anything about the deal's terms.

Industry watchers will recall that only a month ago Takeda, which separately has an in-house Sting agonist, TAK-676, licensed Curadev's CRD5500, a small-molecule Sting activator said to be amenable to development as an antibody-drug conjugate. The value of that deal, too, was kept under wraps.

Why the secrecy? After all, just a few years ago Stings were all the rage: in 2015 Novartis paid $225m to get its hands on Aduro's pipeline just before that group went public, and two years later Bristol handed over $300m up front for IFM Therapeutics, which like Mavupharma was privately held and whose most advanced assets were preclinical.

Selected projects activating the Sting pathway			
Project	**Company**	**Status**	**Note**
ADU-S100	Novartis/Aduro	Phase II	2015 deal ($200m cash + $25m equity); disappointed at Asco 2019
MK-1454	Merck & Co	Phase I	Disappointed at Esmo 2018
BMS-986301	Bristol-Myers Squibb (ex IFM)	Phase I	2017 acquisition for $300m; presented at SITC 2018
SB 11285	Spring Bank Pharmaceuticals	Preclinical	IV, intratumoural; separately developing analogues/ADCs
TAK-676	Takeda	Preclinical	
MAVU-104	Abbvie (ex Mavupharma)	Preclinical	2019 acquisition (undisclosed terms); oral ENPP1 inhibitor
exoSTING	Codiak Biosciences	Preclinical	Engineered exosome; early data at SITC 2018
CRD5500	Takeda/Curadev	Preclinical	2019 deal (undisclosed terms); small molecule
VTX-001	Venn Therapeutics	Preclinical	No longer appears in company pipeline
Unnamed	Hitgen	Preclinical	2017 research collaboration with Aduro
TTI-10001	Trillium	Preclinical	Presented at AACR 2019
SYNB1891	Synlogic	Preclinical	
GSK532	Glaxosmithkline	Preclinical	
E7766	Eisai	Preclinical	Presented at SITC 2018
Unnamed	Nimbus Therapeutics	Preclinical	Small molecule
Unnamed	Bicycle Therapeutics	Preclinical	Bicycle conjugate

Perhaps the reason is that in the meantime Sting targeting has underwhelmed. Last October's Esmo conference saw Merck & Co's MK-1454 generate zero remissions in monotherapy, and only a 25% ORR in combination with Keytruda – with none in any PD-(L)1 refractory subjects.

And at this year's Asco meeting Aduro/Novartis's ADU-S100 combined with spartalizumab found responses in just five of 57 evaluable subjects, when some analysts had wanted to see an ORR 20-30% higher than that achieved with anti-PD-(L)1 therapy alone. Aduro is today worth 96% less than when it floated in 2015.

Against this backdrop some might ask why there is perceived value in stimulating Sting, which broadly speaking primes T cells and boosts immune response. But pharma is still desperate to find ways of broadening the anticancer activity of checkpoint blockade, and Abbvie is among the most willing current dealmakers.

It must also be borne in mind that there is more than one way to hit the Sting pathway, and the failure of one mechanism need not necessarily spell the end of all others. Mavupharma's approach has been to inhibit ENPP1, an enzyme that it says negatively regulates Sting.

However much Sting has underwhelmed it cannot be declared dead yet, and Abbvie will be hoping to have got itself a bargain.

This story was updated to add several projects to the competitor table.

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