Evaluate Vantage

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Macrogenics scoops its Asco bounce

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A tiny glimpse at very early data has more than tripled Macrogenics' market cap. The pressure is now on to confirm these signals.

Macrogenics yesterday managed to achieve an early Asco bounce, providing a sneak peek at some data that will be presented at the annual cancer conference – a week before abstracts are due to be released.

Very early data in three pipeline projects piqued interest, sending the stock soaring by a huge a 231% to a two-year high and adding around $750m to the company's market cap. This is quite a rise for updates described as "directionally encouraging" by the typically bullish sellside, and investors who piled in will have to hope that further details support this reaction.

Some extra information should emerge in the Asco abstracts, due to be released on May 13, before full details at the conference that starts at the end of month. But it should be remembered that these impending updates will be very early takes on the efficacy of these projects.

More than margetuximab? The Macrogenics pipeline		
Project	**Mechanism**	**Detail**
Filed		
Margetuximab	Anti-Her2 MAb	H2 2020: final OS from Sophia breast cancer trial and first data from 1L gastric trial, Mahogany
Phase III		
Retifanlimab (MGA012)	Anti-PD-1 MAb	Licensed to Incyte; first data from potentially registrational anal cancer study due H2 2020
Phase I/II		
Flotetuzumab	Anti-CD123 T-cell engaging bispecifc MAb	Some trials halted owing to Covid-19; update on filing plans in AML due Q2 2020; further data at ASH 2020
MGD013	Anti-Lag3 & PD-1 bispecific MAb	Ph1 solid tumour data at Asco; 40% ORR seen in Her2+ tumours
Enoblituzumab	Anti-B7-H3 MAb	Start of H&N phase 2 delayed by Covid-19
MGD019	CTLA 4 & anti-PD-1 bispecific MAb	4 responses in 13 evaluable patients, various tumours, at ≥3mg/kg
MGC018	Anti-B7-H3 ADC	PSA reduction of ≥50% in 5 of 7 mCRPC patients; phase I data at Asco
No update yesterday, and no longer listed in pipeline on website		
MGD007	Anti-gpA33 T-cell engaging bispecific MAb	
MGD009 (orlotamab)	Anti-B7-H3 T-cell engaging bispecific MAb	Was on clinical hold owing to liver tox
MGD014	Anti-HIV bispecific MAb	
Source: EvaluatePharma, company statements.		

One of the main Asco presentations concerns the B7-H3 antibody-drug conjugate MGC018, which is apparently showing promise in prostate cancer. Reductions in PSA of 50% or more were seen in five of seven patients with metastatic castration-resistant disease, Macrogenics disclosed yesterday, and the company plans a dose-expansion cohort in this tumour.

This equates to a 71% response rate on this measure, nearly as good as the impressive results generated by Xtandi in mCRPC: one cut of the Prevail trial found that 80% of patients achieved PSA declines of ≥50%, although of course the subject numbers differ enormously.

B7-H3 is highly expressed on most solid tumours and in particular prostate cancer; the ongoing phase I trial is being conducted in various tumours, and activity has been seen elsewhere, Macrogenics said.

The second Asco presentation of note will involve the Lag3/PD-1 bispecific MGD013. Yesterday, the company teased a 40% ORR seen in “over a dozen” patients with Her2-positive tumours, who were treated with ’013 and margetuximab, Macrogenics’ Her2-targeting antibody. Targeting PD-1 and Her2 has previously only managed to achieve response rates of 0-15%, the company claimed, adding that development of ’013 plus margetuximab would now be prioritised.

MDG013 is in a large phase I solid tumour study, and activity is being seen across several tumour types, including after anti-PD-1 therapy, the company said. Data on this should also be at Asco.

Other shots

Not slated for Asco but also discussed yesterday was MGD019, a bispecific that hits PD-1 and CTLA4 in a large phase I basket study in various advanced solid tumours, where dose escalation has been completed. The company disclosed that of 13 evaluable patients treated at ≥3mg/kg, four responses have been seen, albeit one unconfirmed, in four tumour types.

Macrogenics expect to take forward a much higher dose, which is important because, as Stifel analysts point out, this far exceeds the equivalent doses at which Opdivo and Yervoy are used. According to Macrogenics, dose limiting toxicities were not seen with ‘019, with the project’s safety profile described as “quite favourable”.

Notably, Astrazeneca has put its weight behind a bispecific approach to get the most out of this combination, and further data on ’019, due to emerge later this year, becomes an important event (*Astra turns to bispecifics to solve the treme problem, February 14, 2020*).

Dwindling hopes for the potential of margetuximab, Macrogenics’ most advanced project, have beaten down the company’s stock since over the past 12 months. A final look at overall survival towards the end of the year will determine the project's future, as will the approaching regulatory review of the data.

Data in gastric cancer might salvage the project; objective responses were observed in three of four evaluable patients recruited into the first-line Mahogany trial, the company said yesterday. The plan is to seek accelerated approval on this initial single-arm data, though again these early hints could yet prove misleading.

If yesterday’s presentation was designed to prove that Macrogenics is about more than margetuximab it certainly worked. However, for share price gains to prove durable these hints of clinical activity must also prove robust.