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Triple meeting – low-profile assets boost Merus and Bicycle

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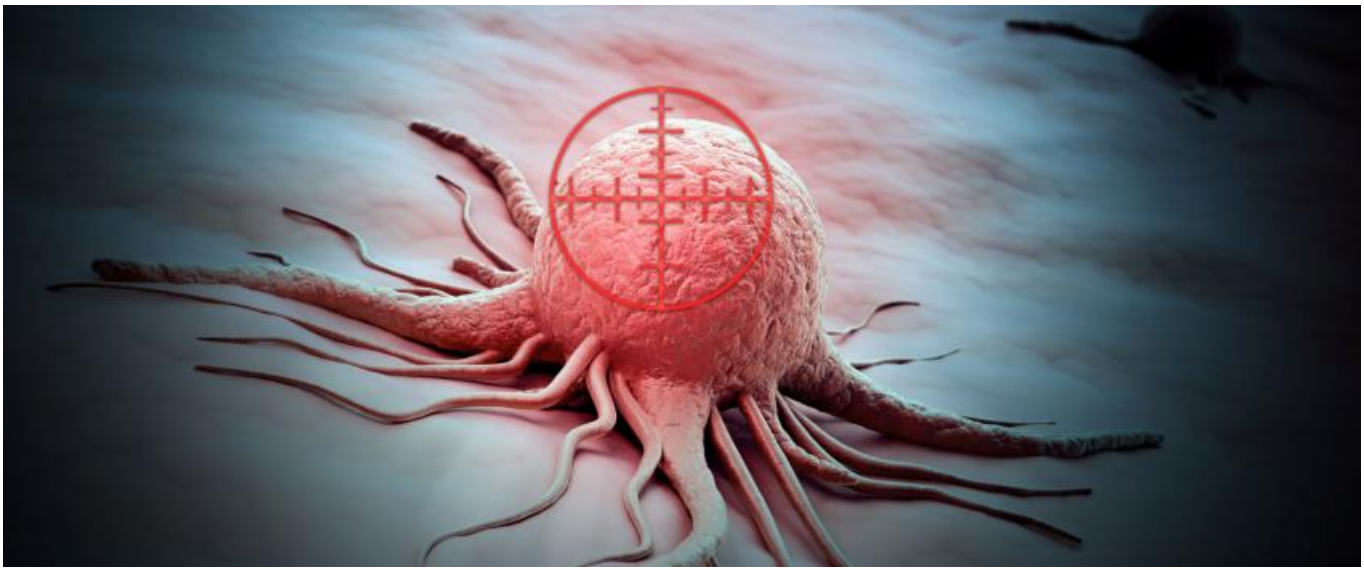

Merus regains some lost pride while Bicycle rides to even greater heights.

Though investors reacted negatively to the early data several biotechs unveiled at the EORTC-NCI-AACR (Triple) symposium that finished yesterday, some presentations did impress.

Perhaps most notable among these were updates from Merus and Bicycle Therapeutics, both concerning somewhat under-the-radar assets that are not these groups' pipeline leads. Bicycle had managed to turn around a post-IPO wobble back in 2019, and the latest data caused it to surge to all-time highs; but Merus has had a tricky 2021, and the Triple meeting presentation allowed it to get over the hump of an Asco disappointment in June.

Merus

The Asco setback concerned Merus's lead targeted therapy, zenocutuzumab, in pancreatic cancer. While the data were positive they ultimately failed to win over investors, who fretted about the practicalities of identifying the patient subgroup in which the therapy might work.

But at the Triple meeting Merus surprised with an encouraging update on a low-profile pipeline project, MCLA-158, a bispecific with a dual mechanism, targeting EGFR and Lgr5.

The company is conducting a phase 1 basket study of MCLA-158 in various solid tumours, and the Triple meeting heard of efficacy data on seven previously treated head and neck cancer patients. Three of these reported partial responses, for a 43% ORR, and the icing on the cake came with the group saying one of these developed into a complete remission after data cut-off.

Leerink analysts pointed out this compared favourably to the 16% ORR that Merck & Co's Keytruda achieved in this setting. The MCLA-158 result is especially encouraging given that a prior readout found no responses in colorectal cancer. Merus was this morning trading 43% above where its stock closed last Wednesday, before the Triple abstract was unveiled.

All eyes now turn to a hotly awaited update on the company's Incyte-partnered PD-L1-targeting bispecific, MCLA-145, due before the year end. A rival bispecific, GEN1046, being developed by Genmab and Biontech, which like MCLA-145 targets PD-L1 and 4-1BB, yielded some intriguing early data last year.

Bicycle

Meanwhile, Bicycle had a Triple meeting presentation on the anti-EphA2 conjugate BT5528, but this only showed a handful of preliminary remissions in phase 1 dose escalation. Rather, it was an update given by the company at the same time on a separate asset, BT8009, which targets nectin-4, that moved its stock.

Notably, neither is the group's most advanced pipeline asset, an honour that belongs to the anti-MMP-14 project BT1718.

The BT8009 data were especially intriguing, as this asset appears to be one of the industry's only nectin-4-targeting agents besides Padcev, Seagen/Astellas's recently launched ADC. Padcev is approved for second/third-line use in urothelial bladder cancer on the strength of two studies, one of which has shown an overall survival benefit versus chemotherapy.

However, the key metric for cross-trial comparisons, which is what investors will now try to do, is ORR, where Padcev has yielded 40-45% at its approved dose. At the Triple meeting Bicycle reported data on third to seventh-line bladder cancer not preselected for nectin-4 expression, and said this yielded one PR in four patients given 2.5mg/m^2 BT8009, and three in seven on 5.0mg/m^2.

On the face of it a 36% ORR looks competitive with Padcev, with the caveat that cross-trial comparisons have serious limitations. More importantly, however, these are relatively low doses; Bicycle's predicted therapeutic range for BT8009 is 7.5mg/m^2 and above, so the data could get considerably better still.

It is clearly too early to tell whether Seagen and Astellas investors should be worried, but those in Bicycle are celebrating: the stock is today worth 29% more than it was last Wednesday, and has now surged 170% year to date.

This story has been corrected to clarify that the BT8009 data were not presented at the Triple meeting.