

A day of soul-searching for CAR-T bulls



Jacob Plieth

Smart investors who had been wondering why, after making a huge splash about CAR-T in 2012, Novartis had grown so reticent about it over the past year or so got their answer today: the Swiss group is disbanding its cell and gene therapy unit.

The company is insisting that this is merely procedural, and that its CAR-T projects will simply be folded into the broad organisation. But the fear is that without a dedicated unit cell therapies will no longer be championed at Novartis, which coupled with yesterday's scathing initiations on Juno and Kite by the bank BTIG should make CAR-T bulls pause for thought.

As it stands of course, timelines for the leading three CAR-T projects remain unchanged, and Novartis's CTL019 is to be filed in the US next year, after Kite's KTE-C19 and before Juno's JCAR015. With the prospect of pivotal data from Kite and Novartis at December's ASH meeting there is still plenty to play for.

But news that Novartis is disbanding the cell therapy unit, [broken today by Endpoints](#), will rock the sector. A Novartis spokesperson confirmed that the 280 of the 400 staff involved would be redeployed, with the remainder likely being let go.

Novartis remains committed to its lead CAR-T programmes, and does not agree that they will now be sidelined, the spokesperson told *EP Vantage*, insisting that the move reflected broader changes at the group. But without its own dedicated business unit CAR-T risks being deprioritised, and follow-on projects could fail to gain traction with R&D heads.

Novartis/Penn CAR-T projects

Project	Target	Indication	Trial ID
CTL019	CD19	Paediatric ALL	NCT02435849
CTL119	CD19	Paediatric ALL	NCT02228096
CART-BCMA	BCMA	Multiple myeloma	NCT02546167
CART22 cells	CD22	ALL	NCT02588456
CART-EGFRvIII	EGFRvIII	Glioblastoma	NCT02209376
CART-meso	Mesothelin	Various	NCT02388828

Certainly this is a big U-turn for the field and for Novartis, which four years ago gave the University of Pennsylvania [cash to build a cell therapy lab in return for rights to CTL019](#), which Penn had until then been struggling to fund, and [declared itself at the forefront of cancer cell therapy](#).

But over the past year Novartis has scarcely made more than a passing mention of CAR-T during quarterly updates. Meanwhile, Juno has struggled with patient death-related CAR-T study halts, while the Penn group has suggested switching away from CTL019 to the humanised CTL119 to overcome the problem of poor persistence ([Therapy focus - How do you solve a problem like CAR-T relapse?, December 22, 2015](#)).

A separate development has been the [recent launch of Penn's own cell therapy spinout, Tmunity Therapeutics](#), by the same team that pioneered CTL019, headed by Dr Carl June. Tmunity is focused on T regulatory cells and engineered T-cell receptors, and there is no suggestion yet of it straying into CAR-T, likely for IP reasons.

But its formation coincides with Novartis's growing reticence on CAR-T, and in the longer term it could be seen as a vehicle that might take back any CAR-T assets that are cut loose by the Swiss group.

Asked about Tmunity the Novartis spokesperson said the group's collaboration was with Penn, and that it

continued to work under its terms to advance CAR-T therapies.

The bear case

Before the Novartis news emerged CAR-T bulls had already had to digest yesterday's initiations by BTIG on Kite with a hold rating, and on Juno with a sell, adding to simmering doubts about Juno's JCAR015 even though its latest safety scare had been resolved quickly.

In a savage analysis of the sector BTIG's Dane Leone said Juno was behind the competition, and Kite, while clearly out in front, had generated limited data. With 2020 sales forecasts of \$738m for KTE-C19 and \$482m for JCAR015/JCAR017 BTIG said it was \$185m and \$217m respectively below Street consensus.

The analysts also said anti-CD19 bispecific antibodies like Blincyto, and Johnson & Johnson/MacroGenics' MGD011, were an underappreciated threat - an argument *EP Vantage* has made separately ([EHA - CAR-T has Blincyto breathing down its neck, June 13, 2016](#)). Juno and Kite opened off 7% and 5% respectively this morning.

MGD011 could soon grow in prominence if data on it are reported at ASH, which could also see Zuma-1 trial results from Kite and pivotal CTL019 data. With ASH still over three months away it is already shaping up to be one of the most important healthcare meetings of 2017.

EP Vantage has published a broad overview of the current opportunities and risks in the CAR-T space. A free copy of the report is [available by download](#).

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