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Novartis Cell Therapy Unit To Close: Implications For CAR-T Could Be Big

by Lucie Ellis-Taitt

Novartis is closing its high-profile cell and gene therapy unit – the one responsible for developing CAR-T therapies. The move suggests Novartis's outlook for the CAR-T field may be changing, though it's not clear why.

Novartis AG's decision to disband its cell and gene therapy unit – the business responsible for developing one of the most advanced CAR-T therapies in the industry – has raised questions about the Swiss pharma's outlook for an area of oncology research that has been thought to be groundbreaking.

It was only four years ago that Novartis in-licensed the CAR-T (chimeric antigen receptor T-cell) technology from the University of Pennsylvania with much fanfare. The high-profile deal was said to involve one of the biggest upfronts ever for an academic collaboration. (Also see "*A New Industry-Academic Model: Novartis And Penn Make A Splash In Cancer Immunotherapy*" - In Vivo, 26 Nov, 2012.) It included CTL019, in a pilot trial in chronic lymphocytic leukemia (CLL) at the time, as well as a commitment from Novartis to invest $20m to pay for a new R&D facility to be called the Center for Advanced Cellular Therapies.

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More recently, Novartis has been downplaying the CAR-T therapy area in presentations to

investors, and the latest news that it will disband the research unit altogether only highlights the uncertainty in the CAR-T field, which holds promise but faces challenges.

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Just 'A Natural Evolution,' Novartis Insists

Despite growing doubts, Novartis insists it remains committed to the CAR-T space and noted it is continuing to advance CTL019 toward regulatory filing at FDA in relapsed/refractory pediatric acute lymphoblastic leukemia (ALL) in early 2017.

"We have made the decision to reintegrate activities conducted by the Cell & Gene Therapies Unit into the larger Novartis organization, as part of a natural evolution of our internal organizational design," Novartis said in a statement. "An isolated unit worked well under our prior pharma division structure, but with a new integrated development model, we can efficiently advance our work on CAR-T as part of our focus in immuno-oncology by reintegrating the functions."

Indeed, Novartis announced in May that it would restructure its oncology business so that it would no longer be under the umbrella of the pharmaceutical division and promoted the head of the oncology division, Bruno Strigini, to CEO of Novartis Oncology reporting directly to CEO Joseph Jimenez. (Also see "*Novartis Rejiggers Pharma To Favor Oncology*" - Scrip, 18 May, 2016.)

The latest action will impact 120 jobs across the cell and gene therapies unit, which currently includes about 400 employees, Novartis said. Some associates previously dedicated to cell and gene therapies will be redeployed to other areas in the immunotherapy space.

The former head of the unit, Oz Azam, will leave the company. Just a few weeks ago he talked enthusiastically about Novartis' future development plans in this area in an interview with *Scrip*.

Azam previously addressed the uncertainties in the field of CAR-T. "We might be treating thousands of patients or tens of thousands of patients. We just don't know yet," Azam said at the time.

Novartis dove quickly and aggressively into CAR-T with its 2012 deal with UPenn, not surprisingly given the company's experience in blood cancer as

Don't Panic! Novartis Is Still Invested In CAR-T Despite 2Q Silence

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Novartis AG's CAR-T cell therapy CTL019, set to be the first in this class to achieve a US FDA

the developer of *Gleevec* (imatinib). But the company missed the other big opportunity building in immuno-oncology at the time – immune checkpoint inhibitors. In what turned out to be a vital misstep, Novartis fell behind immuno-oncology leaders, such as *Bristol-Myers Squibb Co.*, *Roche* and *Merck & Co. Inc.*

filing, might not be an immediate blockbuster owing to its tricky treatment logistics, small initial indication and a lack of physician and patient exposure, but it is still a game changer in immuno-oncology, says Dr. Oz Azam, Novartis's head of cell...

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While companies like Novartis, Juno and Kite focused on CAR-T therapies, Bristol, Merck and Roche all launched the first PD-1/L1 inhibitors for the treatment of solid tumors and others jumped into the field. More recently, data has emerged showing PD-1/L1 inhibitors could be important treatments in blood cancer too – the area targeted initially by CAR-T developers. Bristol's *Opdivo* (nivolumab) was recently approved by FDA for the treatment of Hodgkin's lymphoma, the first checkpoint inhibitor approved for a blood cancer. (Also see "*Bristol's Opdivo Is First Checkpoint Inhibitor Cleared For Blood Cancer*" - Pink Sheet, 17 May, 2016.)

Notably, the leaders in the immune checkpoint space, who are laser-focused on developing combination therapies, haven't shown serious interest in CAR-T.

Whereas immune checkpoint inhibitors are off-the-shelf treatments, CAR-T therapies present specific manufacturing and administration challenges. The first-generation drugs are autologous therapies that involve the extraction of a patient's T-cells from the blood and genetic reprogramming to enable the T-cells to identify particular cancer antigens. The T-cells are then reinfused into the patient, triggering an immune response to fight off cancer.

Promising Efficacy, Troubling CAR-T Side Effects

While some of the early efficacy data has been impressive in cancers expressing CD19, manufacturing and administration present challenges in the commercial market. Meanwhile, the drugs have also shown serious toxicities, which could limit their use in combinations, and it is yet to be seen if they will be applicable to solid tumors.

Most recently, the Phase II ROCKET trial testing Juno's JCAR015 in adults with relapsed/refractory B-cell ALL was put on a clinical hold following three deaths, though the hold was quickly resolved and the trial resumed. (Also see "*Three Deaths In Trial Mean Clinical Hold For Juno's Lead CAR-T Therapy*" - Scrip, 7 Jul, 2016.)

In July, investors started to question Novartis' commitment to CAR-T when the company didn't include CTL019 on a list of 11 potential blockbusters presented during its second quarter

earnings call. (Also see "*Does Novartis Need A Big Immuno-Oncology Deal? Jimenez Says No*" - Scrip, 19 Jul, 2016.)

Datamonitor Healthcare analyst Amanda Micklus told *Scrip* that Novartis' decision to close the cell therapy unit could be a blow to the field.

"The overall reorganization of its cell and gene unit into oncology makes me question how much investment the company will make in the field going forward," Micklus said. "I also wonder if this is going to trigger another mass exodus like we saw several years ago with RNAi."