BIOPHARMADIVE

BRIEF

Bristol Myers finally wins FDA approval for cancer cell therapy

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Published Feb. 5, 2021

Dive Brief:

- The Food and Drug Administration on Friday approved Breyanzi, a cancer cell therapy from Bristol Myers Squibb, for the treatment of late-stage lymphoma.
- Breyanzi, previously called liso-cel, is cleared for use in adults with certain types of large B-cell lymphoma whose cancer has progressed after at least two prior treatments. It's the first cell therapy for Bristol Myers, and the fourth approved in the U.S. for forms of non-Hodgkin lymphoma, joining treatments sold by Novartis and Gilead.
- The approval is a major milestone in a development journey that began with Juno Therapeutics, Breyanzi's original owner. Four years ago, Juno was at the forefront of cancer cell therapy research, and Breyanzi its most advanced treatment. But clinical and regulatory delays held up its progress as acquisitions transferred the program over to Celgene and then Bristol Myers.

Dive Insight:

Breyanzi arrives on the market roughly three years after the U.S. approvals in lymphoma of Yescarta and Kymriah, sold respectively by Gilead and Novartis.

Over that span, physicians have grown more comfortable prescribing the highly complex engineered cell therapies, and both companies have learned hard lessons about the difficulties in producing and delivering them. But neither treatment is a big seller, their use mostly confined to small groups of blood cancer patients who have exhausted other options.

With Breyanzi, Bristol Myers aims to convince doctors its treatment is safer than its competitors, but similarly effective at destroying the malignant B cells that proliferate throughout patients' lymph nodes and bone marrow. But doing so may be a tall order, particularly as the COVID-19 pandemic makes the arduous process of administering treatment in hospitals more difficult.

Bristol Myers expects Breyanzi's side effect profile, which appeared in testing to be less severe than Yescarta and Kymriah, could enable outpatient treatment. Like the other two drugs, however, the FDA approved Breyanzi with a black box warning for the risk of neurotoxicity and a type of immune overreaction known as cytokine release syndrome that's common in patients receiving cell therapy.

The FDA requires patients to be monitored daily — in person or remotely — for the first week after infusion. Patients must remain within proximity to the facility for at least three more weeks thereafter, according to the drug's label. As part of its plan for commercial roll-out of Breyanzi, Bristol Myers will provide wearable monitoring devices that allow patients to track their temperature.

While the side effects to cancer cell therapy are notable, treatment can result in complete remissions that last for many months. About half of the 192 lymphoma patients who received an approved dose of Breyanzi in clinical testing had minimal or no detectable disease after treatment. Another 19% experienced partial responses.

Response rates were similar in the study that led to Yescarta's approval and slightly less in the pivotal trial for Kymriah.

All three treatments are personalized, made up of a patient's own immune cells, which are extracted and shipped to special manufacturing facilities. There, engineers genetically modify the cells to seek out a particular protein that acts as a flag for the cancer. Once keyed to that protein, the souped-up cells are expanded and purified to create a treatment dose that's frozen and shipped back to the patient.

The process is fragile, laborious and, because each dose is specific to each patient, high stakes. Bristol Myers said it can turn around a dose of Breyanzi — from cell extraction to reinfusion — in 24 days, slightly longer than what Gilead and Novartis say they can do with Yescarta and Kymriah.

Bristol Myers will charge $410,300 at list price for Breyanzi, about 10% more than the $373,000 price set by both Gilead and Novartis when they launched their respective treatments. (Kymriah costs $475,000 for use in leukemia, for which it's also approved by the FDA.)

The extremely high prices, drugmakers say, reflect the benefit the treatment delivers as well as the cost of manufacturing and supplying each dose.

Breyanzi is the fourth CAR-T treatment to be cleared by the FDA, along with Yescarta, Kymriah and another therapy Gilead sells as Tecartus for mantle cell lymphoma.

Its approval marks Bristol Myers' entry into the cell therapy space, and the drugmaker hopes to soon follow with an OK for a CAR-T treatment for multiple myeloma, called ide cel. The FDA is due to make a decision by March 27.

But Breyanzi's approval is about five weeks too late for holders of a tradable security known as a contingent value right, or CVR. When acquiring Celgene in 2019, Bristol Myers promised to pay an additional $9 per Celgene share should three of the biotech's experimental drugs win U.S. approval by certain dates.

The first, Zeposia for multiple sclerosis, was cleared on time. But the FDA's review stretched past the Dec. 31, 2020 deadline Bristol Myers had set in the CVR for Breyanzi, terminating the agreement and allowing the pharma to avoid paying CVR holders billions of dollars.

The FDA's review, Bristol Myers said, was drawn out by a required inspection of a third-party manufacturing facility in Texas that makes a component used in Breyanzi's production.

While particularly costly to investors, the latest delay was just one of several that waylaid Breyanzi's development first at Juno and then at Celgene. At one point in 2017, Juno executives had forecast an approval for the drug by 2018, a date that Celgene later pushed back after acquiring the company.

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