2 Beta Thalassemia Drugs Are Fast Approaching the Finish Line

New treatments could be coming from Celgene and bluebird bio that reshape how we treat this life-threatening gene disorder.

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Celgene Corp. (NASDAQ:CELG) and **bluebird bio** (NASDAQ:BLUE) are frenemies. They're working together on a game-changing gene therapy for multiple myeloma, but they're also on a collision course in beta thalassemia, a common genetic disease.

In collaboration with **Acceleron Pharma** (NASDAQ:XLRN), Celgene is developing luspatercept. Meanwhile, bluebird bio's developing LentiGlobin. Pivotal trial results are expected soon for both therapies, and if the data's good, then filings for approval should follow shortly thereafter, making these companies head-to-head competitors in this indication.

IMAGE SOURCE: GETTY IMAGES.

What's beta thalassemia?

There are about 60,000 children born with beta thalassemia every year, including 1,500 per year in the United States. Unfortunately, many of these patients will experience life-threatening organ damage over time because the red blood cell transfusions they require can cause iron overload.

Beta thalassemia is an inherited genetic disorder that prevents patients from adequately producing beta globin, a protein that's necessary for making the oxygen-carrying protein, hemoglobin. Absent adequate hemoglobin, most red blood cells die, so beta thalassemia patients require regular red blood cell transfusions to prevent that from happening.

Unfortunately, those transfusions pose a life-threatening risk to patients because they can result in patients storing more iron in their blood than they can get rid of. Over time, this results in iron building up to levels that can cause irreversible organ damage, such as cirrhosis, diabetes, and heart disease.

Celgene and Acceleron's strategy

Luspatercept is designed to spark production of healthy red blood cells by regulating transforming growth factor beta (TGF-beta) proteins that are involved in late-stage red blood cell differentiation and maturation. By regulating these proteins, Celgene and Acceleron hope to reduce or eliminate the need for frequent blood transfusions.

According to Celgene and Acceleron, luspatercept's late-stage trial met its target enrollment last summer, putting the companies on track to report data from that trial this summer. The primary endpoint of the study is the proportion of patients achieving a 33% or greater lowering of red blood cell transfusion burden from week 13 to week 24 compared to a baseline, which is the 12 weeks prior to receiving luspatercept. A secondary trial endpoint is transfusion burden from week 37 to week 48 versus the baseline period.

It's anyone's guess if luspatercept will clear that primary endpoint hurdle, but in phase 2 studies, the majority of patients achieved a 50% reduction in transfusion burden in any 12-week treatment period when compared to the 12 weeks prior to receiving luspatercept.

If that's any indication (and believe me, it might not be!), then luspatercept could have a decent shot at eclipsing the 33% target in its late-stage study and making its way to the Food and Drug Administration (FDA) later this year.

What bluebird bio's up to

Unlike luspatercept, which is dosed every three weeks, bluebird bio's LentiGlobin is being evaluated as a single-dose therapy. Instead of targeting TGF-beta, LentiGlobin is an ex-vivo approach that inserts a functional human beta-globin gene into a patient's own hematopoietic stem cells. Those re-engineered cells then are infused back into patients in a process called autologous stem cell transplantation.

Recently, bluebird bio reported interim data from two phase 1/2 LentiGlobin trials that's impressive. After one dose of LentiGlobin, 12 of 13 patients who still produced some hemoglobin but were transfusion dependent, didn't require any red blood cell transfusions for a median 27

months. In patients with beta thalassemia major, a severe form of the disorder, transfusions were stopped in three patients, and overall, median transfusion volume fell by 73%.

If the full data set expected later this year confirms these findings, then bluebird bio plans on filing for LentiGlobin's approval in the EU by the end of this year.

Room for two?

The two therapies could face-off against each other someday, but it could be awhile before that happens. Luspatercept's studies are designed to support an FDA approval, but bluebird bio thinks it will need more data before it can secure an approval in the United States.

Unlike in the EU, where regulators have indicated they'll consider data reported later this year, the FDA wants to see results from two additional studies that bluebird bio has underway. One of those trials has an estimated completion date of January 2020, and the other has an estimated completion date of April 2021, according to Clinicaltrials.gov, so it's conceivable that luspatercept won't have to worry about LentiGlobin competing against it in the U.S. for a few years.

Overall, significantly lowering the risk of iron overload in beta thalassemia patients would be a major advancement that could translate into hundreds of millions of dollars in annual sales for these companies. That means approvals could be a big win for patients and investors in Celgene, Acceleron, and bluebird bio.

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Todd Campbell owns shares of Bluebird Bio and Celgene. His clients may have positions in the companies mentioned. The Motley Fool owns shares of and recommends Bluebird Bio and Celgene. The Motley Fool has a disclosure policy.

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