Markets Slaughter Gene Therapy Biotech On Day of FDA Approval? Why—TrialSite Knows

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The U.S. Food and Drug Administration (FDA) approved Casgevy (exagamglogene autotemcel) on December 8, 2023. Casgevy is a gene therapy developed by Vertex Pharmaceuticals and CRISPR Therapeutics. It is the first medicine to be approved in the United States based on the Nobel Prize-winning technology of gene editing. Casgevy is approved to treat sickle cell disease in people aged 12 and older. The goal of the therapy is to help the body produce a fetal form of hemoglobin, which is present at birth. The adult form of hemoglobin is defective in people with sickle cell disease. Also, the FDA approved Lyfgenia is a cell-based gene therapy developed by bluebird bio. Lyfgenia uses a lentiviral vector (gene delivery vehicle) for genetic modification and is approved for the treatment of patients 12 years of age and older with sickle cell disease and a history of vaso-occlusive events.

Casgevy works by disabling a genetic switch that represses the production of fetal hemoglobin after birth. This flips production back on so the body makes red blood cells that don't sickle.

With Lyfgenia, the patient's blood stem cells are genetically modified to produce HbA^{T87Q}, a gene-therapy-derived hemoglobin that functions similarly to hemoglobin A, which is the normal adult hemoglobin produced in persons not affected by sickle cell disease. Red blood cells containing HbA^{T87Q} have a lower risk of sickling and occluding blood flow. These modified stem cells are then delivered to the patient.

Both products are made from the patient's own blood stem cells, which are modified and are given back as a one-time, single-dose infusion as part of a hematopoietic (blood) stem cell transplant. Before treatment, a patient's own stem cells are collected, and then the patient must undergo myeloablative conditioning (high-dose chemotherapy), a process that removes cells from the bone marrow so they can be replaced with the modified cells in Casgevy and Lyfgenia. Patients who received Casgevy or Lyfgenia will be followed in a long-term study to evaluate each product's safety and effectiveness.

Stock Decline?

Why would the stock markets respond with negative movement? Vincent Long, Takeda's Senior Director of External Innovation pointed out on LinkedIn, the professional social network that while approvals typically send shares going up, in the case of these two gene therapies the reverse occurred.

A negative market response met the news, with Vertex initially losing 1% of its value, CRISPR Therapeutics losing 8%, and bluebird bio down 40%!

The Takeda pharmaceutical executive asked, "How can the release of good news result in a loss of ~$250M market cap for bluebird bio in 12 hours?"

Pointing to the "highly unusual" situation involving losses that typically involved a major Phase 3 clinical trial program failure.

Citing *BioSpace* the executive mentioned the steep price points for both cell therapies:

Gene Therapy	Price
Lygenia	$3.1 million
Casegevy	$2.2 million

TrialSite has tracked bluebird and some of its market moves, including legal clashes with San Rocco Therapeutics (San Rocco). In that reporting, *TrialSite* suggests that the latter may actually have licensure rights to the former's intellectual property. Only time and the legal case will tell.

For more on that topic see *TrialSite's* "*Bluebird bio Files IPRS to Invalidate San Rocco Therapeutics Patents—What does this Imply for Investor Risk.*"

Vertex currently trades at $350.15 losing 1.07% on the day the announcement was made. Bluebird bio was massacred, as mentioned, losing 40.54% with the price now at 2.86.

The Takeda executive wonders about the bluebird crash in spite of the good news. A couple of forces are at work. First the FDA as part of the approval issued a black box warning:

"Hematologic malignancy (blood cancer) has occurred in patients treated with Lyfgenia. A black box warning is included in the label for Lyfgenia with information regarding this risk. Patients receiving this product should have lifelong monitoring for these malignancies"

Of course, this will have an impact given that gene therapy is linked to the incidence of leukemia. Secondly is the price point. Already the company has been criticized for high price points for their first gene therapy. In fact, they priced the product out of Germany.

Initially over $2.5 million now bluebird seeks $3.1 million, a sky-high price given the state of the American economy and consumer health, not to mention the black box warning.

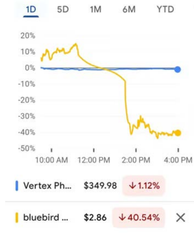
In the meantime, speaking with San Rocco founder and CEO Patick Girondi (See FamilyMan in *TrialSite*) the life science entrepreneur believes their research is making good progress.

San Rocco's vector is derived from the work of Memorial Sloan Kettering renowned scientist, Dr. Michel Sadelain. In 2012, San Rocco safely treated patients in North America in the open clinical trial NCT01639690. To date, San Rocco patients have had no material side effects with significant reductions in blood transfusions. Different than CRISPR and Bluebird Bio, San Rocco's patients were treated with a myelosuppressive chemotherapy regimen and with a vector produced in 2009.

Being safe in patients 7 years longer than CRISPR and 2 years longer than Bluebird, San Rocco scientists claim that their product is a more secure, effective alternative at a fraction of the cost. Girondi informed *TrialSite* that San Rocco will commence a clinical trial in Europe in the third quarter of 2024 and the US shortly after with a tweaked version of the SRT vector produced in 2009.

Back to Vertex and bluebird bio, no gain was seen for the biopharma companies. According to the Takeda executive, the news yesterday "cripples bluebird's market position even further, from $185 per share in 2018, to today's $2.86 per share." https://investor.bluebirdbio.com/news-releases/news-release-details/bluebird-bio-announces-closing-over-allotment-option-public

Takeda's Long asked on LinkedIn "Who will invest in the next gene therapy breakthrough?" Perhaps it will be the next generation of biotech driven by a different value system, focused more on patient care than extraordinary profits.



Call to Action: Change is coming to biotech. *TrialSite* tracks a growing number of life-science-focused equities. If interested, send a request.

References

FDA