5 Cell and Gene Therapy Decisions to Watch in 2024

By Ana Mulero
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In 2023, cell and gene therapy saw an unprecedented surge with seven FDA approvals, and this year, an even greater number of these treatments could reach the market. So far in 2024, the regulator has given the green light to three new CGTs, and at least seven additional cell and gene therapy products are expected to receive approval by year's end, according to a March report from the Alliance for Regenerative Medicine.

"All signs point to 2024 surpassing 2023 as a landmark year for cell and gene therapy," David Barrett, CEO of the American Society of Gene & Cell Therapy (ASGCT), told *BioSpace*.

The first approval this year belonged to Vertex Pharmaceuticals and CRISPR Therapeutics' Casgevy, which won the FDA's nod in January for use in **transfusion-dependent beta thalassemia**. This followed the agency's December 2023 approval of Casgevy as one of the first two cell-based gene therapies to treat patients with **sickle cell disease**. It also represented the first FDA approval of a therapy using CRISPR/Cas9 technology. Then, in February, Iovance Biotherapeutics' **Amtagvi was approved** as the first one-time cell therapy for a solid tumor and the first tumor-infiltrating lymphocytes therapy, for advanced melanoma patients who have worsened after being treated with certain other therapies failed. Finally, last month, the FDA greenlit Orchard Therapeutics' Lenmeldy, which **entered the U.S. market** as the first gene therapy for children with **metachromatic leukodystrophy**, and the world's most expensive drug, with a $4.25 million price tag.

Looking forward, the FDA has upcoming PDUFA dates for several more novel CGTs, including a traditional *in vivo* gene therapy delivered via viral vector, a

couple of gene-corrected cell therapies in which a patient's cells are modified by gene therapy outside of the body and then reinfused, and a new CAR-T.

Two Q1 reports, from **ASGCT** and the **Alliance for Regenerative Medicine**, highlight some of these regulatory actions as potential catalysts for the sector, with approvals poised to propel the CGT space. The ASGCT report includes a list of noteworthy events in Q1 2024, while ARM's report makes the case that 2024 could be a banner year for cell therapy.

Here, *BioSpace* reviews five products under regulatory review that were highlighted by both organizations.

Pfizer's Beqvez

Indication: Hemophilia B
Therapy type: In vivo gene therapy
Action date: April 27

Later this month, the FDA will rule on Pfizer's gene therapy for hemophilia B, **Beqvez**. This engineered version of the factor IX coagulation gene carried by an adeno-associated virus is administered via a single infusion.

Beqvez has been **approved** by Health Canada to treat adults with hemophilia B based on positive data from the Phase III BENEGENE-2 study, which showed a significant reduction in bleeding rate and infusion frequency.

The Big Picture

An FDA approval would put Pfizer in competition with CSL Behring, whose gene therapy Hemgenix, which is also administered via a single intravenous infusion, became the **first FDA-approved gene therapy for hemophilia B** in November 2022. Pricing details for Beqvez are not yet available, but Hemgenix costs $3.5 million per dose. Chris Boshoff, Pfizer's chief oncology officer, told *BioSpace* the company aims to leverage its experience to ensure smooth market entry and efficient delivery to eligible patients.

Abeona Therapeutics' pz-cel

Indication: Recessive dystrophic epidermolysis bullosa
Therapy type: Gene-corrected cell therapy
Action date: May 25

Next up is Abeona Therapeutics' pz-cel, which delivers a functional collagen-producing COL7A1 gene into a patient's own skin cells using a retroviral vector, for the treatment of patients with recessive dystrophic epidermolysis bullosa (RDEB). RDEB, a rare connective tissue disorder, causes severe skin wounds, pain and life-threatening complications stemming from compromised immunity due to a deficiency in the COL7A1 gene, preventing the production of functional type VII collagen.

In November 2023, the FDA **granted priority review** to pz-cel based on clinical data from the Phase III VIITAL study and long-term results from a Phase I/IIa study, which **demonstrated** sustained wound healing and pain reduction.

The Big Picture

Ira Leiderman, managing director of healthcare at Cassel Salpeter, underscored the importance of evaluating therapeutic options against the rarity and impact of the disease. A positive decision on Abeona's pz-cel will help address the high unmet need of RDEB patients and may lead to transformative interventions in this challenging rare genetic disorder, Leiderman told *BioSpace*.

If approved, pz-cel would follow Krystal Biotech's Vyjuvek, the first gene therapy **approved for recessive or dominant DEB** in May 2023. Abeona said in March it is actively preparing for the potential U.S. launch of pz-cel, including discussions with treatment sites and payer engagement.

Rocket Pharmaceuticals' Kresladi

Indication: Leukocyte adhesion deficiency-1
Therapy type: Ex-vivo vector gene therapy
Action date: June 30

While **Rocket Pharmaceuticals** initially anticipated a decision on its gene therapy for leukocyte adhesion deficiency-I (LAD-I) by March, the FDA requested more review time and **extended the deadline** to June 30.

Severe LAD-I, a rare genetic disorder affecting children, is caused by mutations in the ITGB2 gene that lead to life-threatening infections. Without regular bone marrow transplants, survival beyond childhood is rare. Kresladi contains patient-derived hematopoietic stem cells genetically modified with a lentiviral vector to carry functional copies of the ITGB2 gene, crucial for leukocyte adhesion and infection-fighting.

In November 2023, the FDA **accepted** Rocket's BLA for Kresladi with priority review, following positive efficacy and safety data from a global Phase I/II study, in which all nine LAD-I patients were alive 12 to 24 months post-infusion. Significant reductions in infection rates were observed compared to pre-treatment levels, along with the resolution of LAD-I–related skin lesions and restoration of wound healing capabilities.

Kresladi also holds the FDA's Regenerative Medicine Advanced Therapy, Rare Pediatric, Fast Track and Orphan Drug designations.

The Big Picture

This marks Rocket's inaugural product filing and is a notable advancement for patients, offering an alternative to bone marrow transplant, which carries significant risks and may not be readily accessible. Rocket is enhancing its commercial infrastructure in preparation for a potential product launch, including center initiation, channel strategies, education and payer engagement.

Rocket CEO Gaurav Shah told *BioSpace* the FDA is reallocating reviewers to focus on rare diseases and complex biologics, necessitating changes and a transition period. Shah noted that the delayed decision, based on the FDA's

request for clarity on chemistry, manufacturing and controls information submitted by Rocket, is common among CGTs and does not raise significant concerns beyond ensuring the regulator has sufficient resources for the approval process.

Adaptimmune's afami-cel

Indication: Advanced synovial sarcoma
Therapy type: T cell receptor therapy
Action date: August 4

Adaptimmune is gearing up for the potential launch of its inaugural product in the sarcoma franchise, afami-cel, intended for treating advanced synovial sarcoma, with a PDUFA date set for August 4. Afami-cel **received** FDA priority review in January.

Synovial sarcoma, which makes up 5% to 10% of soft tissue sarcomas, typically affects individuals under 30, with a five-year survival rate of 20% for metastatic cases. Recurrence is frequent, necessitating multiple lines of therapy and potential exhaustion of treatment options. Afami-cel is a single-dose engineered T cell receptor therapy targeting MAGE-A4-posititive tumor cells. The therapy's clinical data from the SPEARHEAD-1 trial revealed that about 39% of patients experienced clinical responses, with a median response duration of around 12 months. Median overall survival was about 17 months, contrasting with historical data of less than 12 months for those who received two or more prior lines of therapy. Some 70% of responders to afami-cel were alive two years post-treatment.

The FDA granted afami-cel Orphan Drug Designation for the treatment of soft tissue sarcomas and Regenerative Medicine Advanced Therapy designation.

The Big Picture

If approved, afami-cel would become the first approved engineered T cell therapy for this type of cancer. In November 2023, the Investigational New Drug (IND) for another T cell therapy, lete-cel, was **transferred** from GSK to Adaptimmune for the pivotal IGNYTE-ESO clinical trial, following an interim analysis showing a 40% response rate in synovial sarcoma or myxoid/round cell liposarcoma patients.

Adaptimmune CEO Adrian Rawcliffe said that the clinical results from the pivotal trial position lete-cel as a complement to afami-cel, potentially allowing the company's sarcoma franchise to significantly expand its reach. He noted that leveraging the same commercial infrastructure intended for afami-cel could facilitate the efficient delivery of lete-cel to the market. Afami-cel would become the first engineered T cell therapy for a solid tumor. The franchise, including both afami-cel and lete-cel, "is projected to deliver up to $400 million in U.S. peak year sales," Rawcliffe **said** in March.

Autolus Therapeutics' obe-cel

Indication: B cell acute lymphoblastic leukemia
Therapy type: CAR-T cell therapy
Action date: November 16

In **accepting Autolus Therapeutics**' BLA for its lead next-generation CAR-T therapy obe-cel for relapsed/refractory adult acute lymphoblastic leukemia (ALL) in January, the FDA set a PDUFA target action date of November 16.

Obe-cel, an investigational CD19 CAR-T cell therapy, is designed to enhance clinical activity and safety compared to existing therapies by incorporating a fast target binding off-rate, minimizing T cell activation. In December 2022, Autolus **hailed** the Phase II FELIX trial as a success, as interim analysis showcased an overall remission rate of 70% for obe-cel in leukemia patients. CAR-T cell concentration peaked and persisted at 75% in peripheral blood after a median of 166.5 days post-infusion. The trial also demonstrated positive safety findings.

Obe-cel holds the FDA's Orphan Drug and Regenerative Medicine Advanced Therapy status. Earlier this month, the company;'s obe-cel marketing application was **accepted** by the European Medicines Agency.

The Big Picture

The potential approval of a second cell therapy for solid tumors this year suggests breakthroughs in treating these cancers may be near, Stephen Majors, a spokesperson for the ARM, told *BioSpace*. There is an "increasing

focus on solid tumors," a previously elusive area for cell and gene therapy, he said.

A recent $250 million **deal** granted BioNTech access to obe-cel, with the partner to aid in the launch and development program expansion and receive royalties based on net sales. Autolus expects obe-cel peak sales to exceed $300 million.

Autolus could face competition from Gilead Sciences subsidiary Kite, which in 2021 gained FDA approval for its CAR-T therapy Tecartus, the first such treatment for ALL, achieving a 65% complete remission rate.

*Ana Mulero is a freelance writer based in Puerto Rico. She can be reached at **anacmulero@outlook.com** and @anitamulero on **X**.*