AscellaHealth®

Specialty and Rare Pipeline Digest™

Q3 • 2025

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WELCOME TO ASCELLAHEALTH'S SPECIALTY AND RARE PIPELINE DIGEST™

As the pipeline of new specialty pharmaceuticals continues to evolve, it becomes even more crucial to stay abreast of recent and emerging therapeutic options on the horizon. Our quarterly publication provides all industry stakeholders with important insights into specialty, rare disease and cell and gene therapy pipelines, recent approvals, and upcoming FDA reviews.

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WHO WE ARE

AscellaHealth is a global partner that delivers proven end-to-end solutions to both life sciences and healthcare companies to enhance quality of life for patients with complex, chronic conditions. Every day our team gets critical healthcare products from manufacturers to patients while ensuring an efficient flow of funds between payers and pharma.

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WHAT WE DO

AscellaHealth's global end-to-end solutions for life sciences manufacturers, payers and other stakeholders span the entire product lifecycle and are instrumental in the launch of specialty and rare disease medications, and include:

- Pre-Commercialization & Market Access
- International Specialty Pharmacy Fulfillment
- Exclusive Distribution Partnerships & Supply Chain Logistics
- Patient Support & HUB Services
- Infusion Site of Care & SP Fulfillment Programs
- Medication Access Programs
- Specialty Pharmacy & Medical Benefit Management
- Customized Clinical Programs

Recent Branded Specialty Drug Approvals

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Wegovy (semaglutide)	Novo Nordisk	Subcutaneous	Glucagon-like peptide-1 (GLP-1) agonist	Non-alcoholic steatohepatitis (MASH/NASH)	Approved (08/15/2025)	$17,500	High

On August 15, 2025, the FDA granted accelerated approval to Wegovy 2.4mg injection for the treatment of adults with noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH) with moderate to advanced fibrosis, in combination with a reduced-calorie diet and increased physical activity. The approval does not include patients with cirrhosis.

Non-alcoholic steatohepatitis (NASH), also known as metabolic dysfunction-associated steatohepatitis (MASH), is the most severe form of non-alcoholic fatty liver disease (NAFLD), or metabolic dysfunction-associated fatty liver disease (MAFLD), and is characterized by an accumulation of fat in the liver. MASH affects approximately 5% of U.S. adults. Wegovy is the first glucagon-like peptide-1 receptor agonist (GLP-1 RA) approved for this indication and joins Rezdiffra as the approved therapies for MASH. Wegovy is also approved for chronic weight management in adults and adolescents 12 years of age and older and to reduce the risk of major adverse cardiovascular events (MACE) in adults with cardiovascular disease and either obesity or overweight.

The approval was based on Part 1 of the ongoing two-part trial. At week 72, results showed that 63% of participants treated with Wegovy 2.4mg administered as a subcutaneous injection once weekly in addition to standard of care and lifestyle interventions achieved resolution of steatohepatitis and no worsening of liver fibrosis compared to 34% on placebo. Additionally, 37% of participants on Wegovy demonstrated fibrosis improvement and no worsening of MASH versus 22% in the placebo group. Results from Part 2 of the trial, which will evaluate the effects of semaglutide 2.4 mg on the risk of liver-related clinical events at 240 weeks, are expected in 2029.

Semaglutide will compete with Rezdiffra and the anticipated annual cost of Wegovy therapy for MASH would be significantly less than Rezdiffra, $17,500 vs $50,000, respectively. While no head-to-head studies have been conducted, with the significantly lower cost and comparable efficacy surrogate endpoints, it is anticipated that semaglutide may be in a favorable position to be used prior to Rezdiffra therapy. Since both agents work with different mechanisms of action for MASH, the potential use of both agents concomitantly is unknown and would need additional clinical studies to demonstrate their proper place in therapy.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
INS1007 (brensocatib)	AstraZeneca; Insmed	Oral	Dipeptidyl peptidase-1 (DPP-1) inhibitor	Bronchiectasis	Approved (08/12/2025)	$88,000	Low

On August 12, 2025, the FDA approved Brinsupri (brensocatib) for the treatment of non-cystic fibrosis bronchiectasis (NCFB) in adult and pediatric patients 12 years of age and older. Brinsupri is a dipeptidyl peptidase 1 (DPP1) inhibitor, designed to inhibit the activation of enzymes (neutrophil serine proteases) in neutrophils that are key drivers of chronic airway inflammation in NCFB.

Bronchiectasis is a chronic lung disease characterized by airway inflammation and wall thickening which leads to excessive mucus buildup, frequent infections, cough and shortness of breath. Neutrophils are thought to play a key role in the pathophysiology of bronchiectasis. Brinsupri is the first approved therapy to address the underlying inflammatory process of NCFB.

The approval was supported by a trial which evaluated Brinsupri in patients 12 years of age and older with NCFB. Patients included in the trial were ≥12 years of age, had NCFB confirmed by chest CT scan, and adults were required to have at least two pulmonary exacerbations (defined by the need for antibiotics) in the past 12 months and patients ≥12 years of age were required to have at least one in the past 12 months. Over the 52-week treatment period, patients receiving Brinsupri 10 mg orally once daily had a 21.1% reduction in exacerbations, and those receiving 25 mg once daily had a 19.4% reduction in exacerbations compared to placebo.

There are currently no FDA-approved therapies for bronchiectasis. Brensocatib would likely be added on to background off-label treatments for bronchiectasis such as antibiotics and/or mucolytics.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Alhemo (concizumab)	Novo Nordisk	Subcutaneous	Tissue factor pathway inhibitor (TFPI) antagonist	Hemophilia A or B*	Approved (07/31/2025)	$750,000 (60kg using 0.2mg/kg once daily)	Moderate
Qfitlia (fitusiran sodium)	Sanofi; Genzyme; Alnylam Pharmaceuticals	Injectable	Small interfering RNA (siRNA)	Hemophilia A or B	Approved (03/28/2025)	Annually: $387,360 - 1.937M depending on dose.	Moderate

Hemophilia is an X-linked genetic disease that interferes with the normal coagulation process, which causes bleeding into soft tissues, joints, and internal organs. It can cause severe bleeding and death in traumatic incidents.

On July 31, 2025, the FDA approved Alhemo as a once-daily prophylactic treatment for patients 12 years of age and older with hemophilia A or B (HA/HB) without inhibitors. This expands an earlier approval granted in December 2024 for use in patients with HA/HB with inhibitors.

The expanded approval was based on results from a trial which included patients 12 years of age and older with HA or HB without inhibitors who were given either on-demand factor VIII or IX (without any prophylaxis) or Alhemo prophylaxis. Results showed a statistically significant reduction in annualized bleeding rate (ABR) for Alhemo compared to no prophylaxis: 79% for patients with HB and 86% for those with HA.

Alhemo is the second tissue factor pathway inhibitor (TFPI) antagonist, after Hympavzi, approved for the treatment of hemophilia A and B. It acts to reduce the amount and activity of naturally occurring TFPI, which increases the amount of thrombin that is generated, which is expected to prevent or reduce the frequency of bleeding episodes.

Alhemo will compete directly with Hemlibra, Hympavzi, and Qfitlia in the hemophilia A space and Hympavzi and Qfitlia in the hemophilia B space. All of the agents are given subcutaneously and are self-administered and approved for patients with and without inhibitors, except for Hympavzi, which may potentially receive expanded approval for patients with inhibitors in 2026.

Qfitlia was approved by the FDA on March 28, 2025. Qfitlia is the first antithrombin (AT)-directed small interfering ribonucleic acid (siRNA) approved for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients 12 years of age and older with hemophilia A or B with or without inhibitors. Unlike other hemophilia treatments, Qfitlia can be administered subcutaneously (SC) as infrequently as once every 2 months.

Qfitlia was studied in ATLAS-A/B on males aged 12 years and older with severe hemophilia A or B without inhibitors and were randomly assigned to receive either once-monthly subcutaneous fitusiran prophylaxis or on-demand clotting factor concentrates. The ATLAS-INH trial included male patients with severe hemophilia A or B with inhibitors who were receiving on-demand treatment with bypassing agents (BPA). Study participants were randomly assigned to receive fitusiran monthly prophylaxis or continue with on-demand BPA.

Among participants without inhibitors, fitusiran treatment was associated with a 71% reduction in estimated annualized bleeding rate (ABR) compared with on-demand treatment with clotting factor concentrates. Findings also showed a 73% reduction in estimated ABR in patients with inhibitors who received the antithrombin-based dosing regimen compared with those who received on-demand treatment with BPA.

Qfitlia has the broadest indication (hemophilia A and B with and without inhibitors) and enters a crowded market of SC prophylactic hemophilia therapies. In hemophilia A, it will directly compete with Roche's Hemlibra (emicizumab-kxwh), Pfizer's Hympavzi (marstacimab-hncq), and Novo Nordisk's Alhemo (concizumab-mtci). In hemophilia B, it will directly compete with Hympavzi and Alhemo.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Sephience (sepiapterin)	PTC Therapeutics; Censa Pharmaceuticals	Oral	Phenylalanine hydroxylase activator	Phenylketonuria	Approved (07/28/2025)	$866,000 for an 80kg patient per year	Low

On July 28, 2025, the FDA approved Sephience, a phenylalanine hydroxylase (PAH) activator for the treatment of hyperphenylalaninemia (HPA) in adult and pediatric patients 1 month of age and older with sepiapterin-responsive phenylketonuria (PKU). Sephience is to be used in conjunction with a phenylalanine restricted diet.

Phenylketonuria is a rare condition caused by a defect in the gene that creates an enzyme that can break down Phe, a critical amino acid found in all proteins and many foods. If left poorly managed or untreated, levels of Phe can build up to harmful levels in the body and can cause severe and irreversible disabilities, including permanent intellectual disability, delayed development, memory loss, and seizures, among other brain health complications. It is estimated to affect one in every 13,500 to 19,000 newborns in the US.

Results from the study showed that Sephience provided a 64% greater reduction in blood phenylalanine levels versus placebo, with long-term data demonstrating sustained benefits along with greater dietary freedom. Additionally, 97% of patients participating in the phenylalanine tolerance protocol demonstrated the ability to liberalize their diet while on sepiapterin treatment, with a mean increase in protein intake of 126%.

Sephience will compete directly with BioMarin's Kuvan (sapropterin dihydrochloride), which is a synthetic form of BH4 (an essential enzyme cofactor crucial for the breakdown of the amino acid phenylalanine) and also a PAH activator and is available generically. BioMarin's Palynziq (pegvaliase-pqpz) injection, a Phe-metabolizing enzyme, is approved for patients who are not controlled on existing management and is not appropriate as a first-line therapy. Sephience is also a PAH activator like Kuvan but is a naturally derived form of BH4.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Ekterly (tablet) (sebetralstat)	KalVista Pharmaceuticals	Oral	Plasma kallikrein inhibitor	Hereditary angioedema (Acute treatment)	Approved (07/03/2025)	$16,720 per dose	Moderate
Andembry (garadacimab)	CSL Behring	Subcutaneous	Factor XIIa inhibitor	Hereditary angioedema (Prophylaxis treatment)	Approved (06/16/2025)	$685,200 maintenance treatment per year)	Moderate

On July 7, 2025, the FDA approved Ekterly (sebetralstat), a plasma kallikrein inhibitor, for the treatment of acute attacks of hereditary angioedema (HAE) in adult and pediatric patients 12 years of age and older. Ekterly is the first oral on-demand (OD) treatment option for HAE.

Hereditary angioedema (HAE) is a rare genetic disorder that results in unpredictable, recurrent attacks of localized subcutaneous or mucosal swelling in various parts of the body including the face, hands, feet, airways, and intestinal tract. Attacks can happen at any age after birth. According to the U.S. Hereditary Angioedema Association (HAEA), HAE affects approximately 1 in 10,000 to 1 in 50,000 individuals. Treatment of HAE uses 2 broad strategies for medical management: 1) On-demand therapy to minimize the impact of HAE attacks; and 2) Prophylactic therapy in appropriate patients, to reduce the frequency and severity of attacks.

Approval was based on results from the trial which included patients ≥12 years of age with HAE. Patients received either Ekterly 300mg, 600mg or placebo. Patients in the Ekterly group experienced rapid symptom relief compared to patients who received placebo (1.61 hours with Ekterly 300 mg, 1.79 hours with Ekterly 600 mg, and 6.72 hours with placebo). Although the 300mg dose was studied in the trial, it is not a recommended dose for the treatment of acute HAE attacks. No information in available as to why the manufacturer did not seek the 300mg dose for approval.

Ekterly will compete with intravenously and subcutaneously administered on-demand therapies such as Firazyr (icatibant) and Kalbitor (ecallantide), as well as Berinert (C1 esterase inhibitor [human]), and Ruconest (C1 esterase inhibitor [recombinant]). The costs for the above agents range from 193,000 to 205,000 per year with the exception of Firazyr which is approximately $15,000 per year due to generic availability.

On June 16, 2025 the FDA approved Andembry, as the first monoclonal antibody therapy that specifically targets activated factor XII, thereby reducing the production of bradykinin, a key mediator of inflammation and swelling during HAE attacks. Andembry is a once-monthly subcutaneous treatment indicated for prophylaxis to prevent attacks of hereditary angioedema in adult and pediatric patients 12 years of age and older.

The approval was supported by results from a trial which included a total of 64 patients 12 years of age and older with HAE and at least two confirmed HAE attacks withing a 2-month screening period. Patients received Andembry or placebo. All prophylactic HAE treatments were discontinued; however on-demand rescue medications were permitted during the study.

Results demonstrated that patients treated with Andembry experienced an 89.2% reduction in monthly attack rates compared to placebo. Treatment with Andembry also significantly reduced the need for on-demand treatment and the number of severe attacks.

The efficacy is comparable to the currently available treatments, however the once-monthly dosing interval may provide a dosing frequency advantage over current drugs approved for prophylaxis, such as Cinryze (dosed every 3 to 4 days, IV) and Takhzyro (dosed every 2 or 4 weeks, SC), Haegarda (dosed every 3-4 days, SC), and Orladeyo (dosed once daily, oral).

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Yeztugo (lenacapavir sodium)	Gilead	Subcutaneous	HIV capsid inhibitor	Prophylaxis to reduce risk of sexually acquired HIV-1*	Approved (06/18/2025)	$28,218 per year	Low

On June 18, 2025, the FDA approved Yeztugo for HIV pre-exposure prophylaxis (PrEP) in adults and adolescents weighing at least 35kg who are at risk of HIV acquisition.

The approval was based on results in 2 trials in which Yeztugo was administered twice yearly for PrEP, as a subcutaneous injection. The results of the first study showed the Yeztugo group experienced no infections and superiority compared to Truvada and background HIV (bHIV) incidence in cisgender women. In the second trial, 2 HIV infections occurred in the Yeztugo group, demonstrating a 96% risk reduction in HIV infections and superiority compared to Truvada and bHIV among a diverse range of cisgender men and gender-diverse people.

Lenacapavir was approved as brand name Sunlenca in December 2022 for use in combination with other antiretroviral(s) for the treatment of HIV-1 infection in heavily treatment-experienced (HTE) adults with multidrug-resistant (MDR) HIV-1 infection failing their current antiretroviral regimen due to resistance, intolerance, or safety considerations.

Yeztugo will compete in the PrEP therapy market with other available therapies approved to prevent sexually acquired HIV-infection. They include Truvada (emtricitabine/tenofovir disoproxil fumarate), Descovy (emtricitabine/tenofovir alafenamide) and Apretude (cabotegravir). Truvada and Descovy are administered orally daily, while Apretude is an intramuscular injection administered by a healthcare professional every two months and Yeztugo is a subcutaneous injection administered by a healthcare professional every 6 months after the dose initiation period. Yeztugo is priced slightly higher than the other branded products on an annual basis ($28,200 as compared to Descovy at $26,700 and Apretude at $24,700) and significantly more than the generic Truvada regimen ($215).

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Imaavy (nipocalimab)	Momenta; Johnson & Johnson (Janssen)	Intravenous; Subcutaneous	FcRn antagonist	Myasthenia gravis	Approved (04/29/2025)	$324,000 for an 80kg patient per year	Low

On April 29, 2025, the FDA approved Imaavy, a neonatal Fc receptor (FcRn) blocker indicated for the treatment of generalized myasthenia gravis (gMG) in adult and pediatric patients 12 years of age and older who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive. Patients who are anti-AChR or anti-MuSK antibody positive comprise more than 90% of patients with antibody-positive gMG.

Generalized myasthenia gravis is a chronic, debilitating autoimmune disorder affecting the signals between the nerves and the muscles which causes the muscles to feel weak and easily tired. One of the main symptoms is muscle weakness and tiredness that is worsened by activity and improved by rest. The weakness can affect many areas of the body and about half of those who develop myasthenia gravis experience weakness in the eye muscles first, which can include double vision, blurred vision and drooping eyelids.

Imaavy is administered as an intravenous infusion at an initial dose of 30 mg/kg, followed by maintenance doses of 15 mg/kg every 2 weeks thereafter.

The approval of Imaavy was supported by results from the ongoing Phase 3 Vivacity-MG3 study, which enrolled 199 adults with gMG, 153 of whom were antibody positive. The efficacy of Imaavy was measured using the Myasthenia Gravis-Activities of Daily Living (MG-ADL) scale. Patients who received Imaavy plus standard-of-care (SOC) therapy demonstrated a statistically significant improvement in MG-ADL scores versus patients who received SOC plus placebo at 24 weeks. Patients who received Imaavy also experienced a reduction in autoantibody levels of up to 75% from the first dose through 24 weeks. In the ongoing study, which includes patients 12–17 years of age with gMG who are anti-AChR or anti-MuSK antibody positive, Imaavy plus SOC has demonstrated a 69% reduction in total serum immunoglobulin G (IgG) over 24 weeks.

Imaavy is the first FcRn blocker approved for anti-AChR and anti-MuSK antibody-positive adult and pediatric patients with gMG aged 12 and older. It will compete directly with several FcRn blockers approved to treat gMG in adults: Vyvgart (efgartigimod alfa-fcab) and Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc), and Rystiggo (rozanolixizumab-noli). In pediatric patients 12 years of age and older, there are no direct competitors that are FcRn blockers; however, Imaavy may compete with other available complement inhibitors (e.g., Soliris, Ultomiris) in pediatric patients who are anti-AChR antibody positive. For an 80-kg patient, the annual WAC for maintenance dosing is $324,480.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Livmarli (tablet) (maralixibat Chloride)	Mirum Pharmaceuticals	Oral	Ileal bile acid transporter (IBAT) inhibitor	Pruritus in progressive familial intrahepatic cholestasis (PFIC)*; Alagille syndrome*	Approved (04/10/2025)	$454,000 (ALGS) $1.3 million (PFIC)	Low

Livmarli was approved in September 2021 as the first and only medication to treat cholestatic pruritus in ALGS patients aged 1 year and older. In March 2024, the FDA then granted approval for Livmarli use in patients aged 5 years and older with progressive familial intrahepatic cholestasis (PFIC), and most recently in April 2025, the FDA approved Livmarli tablets for patients with Alagille syndrome (ALGS) and (PFIC).

ALGS is a rare genetic disorder that results in abnormally narrow, malformed bile ducts, which are also reduced in number, leading to bile accumulation in the liver. This leads, ultimately, to progressive liver disease. ALGS incidence is estimated to be present in 1 in every 30,000 people.

Progressive familial intrahepatic cholestasis is a group of ultra-rare genetic disorders that disrupt bile formation. PFIC usually develops in infancy, although it can develop into young adulthood, and is characterized by cholestasis, jaundice, and intense pruritus. Patients typically develop fibrosis and end-stage liver disease before adulthood, which can be fatal if untreated. PFIC affects approximately 600 children in the United States and 15,000 individuals worldwide.

Livmarli will continue to compete directly with Bylvay (odevixibat), another IBAT inhibitor. Bylvay is approved for the treatment of cholestatic pruritus in patients with PFIC 3 months of age and older and in patients with ALGS 12 months of age and older.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Vanrafia (atrasentan hydrochloride)	Novartis; Chinook Therapeutics	Oral	Endothelin receptor antagonist (ERA)	IgA nephropathy	Approved (04/02/2025)	$162,500 per year	Low

On April 2, 2025, the FDA granted accelerated approval to Novartis' Vanrafia (atrasentan), a selective endothelin type A receptor (ETAR) antagonist, to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression.

IgA nephropathy is an autoimmune disease that occurs when antibodies accumulate and are deposited in your kidneys, causing inflammation and kidney damage. Immunoglobulin A (IgA) and other antibodies damage the glomeruli, tiny blood vessels in your kidneys that filter blood, causing your kidneys to leak blood and protein into your urine. The damage may also lead to the scarring of the nephrons, the filtering units where the glomeruli are located. Currently, there is no cure for IgAN, but there are recently approved therapies that have been shown to slow progression of the disease. The treatment of IgAN is still largely centered around renin-angiotensin system (RAS) inhibition via angiotensin-converting enzyme (ACE) inhibitors (e.g., Vasotec, Zestril, Accupril, Lotensin) and angiotensin receptor blockers (ARBs) (e.g., Micardis, Cozaar, Benicar, Avapro), with or without sodium-glucose contransporter-2 (SGLT2) inhibitors (e.g., Invokana, Farxiga, Jardiance, etc.) as the standard of care (SOC). Approximately 30% to 40% of patients with IgAN have disease that is not well controlled on SOC therapies and are likely to require the use of more recently approved, novel approved therapies.

The approval was granted based on the Phase 3 study, which demonstrated that Vanrafia reduced proteinuria by 36.1% compared to placebo. Among the 29 patients taking SGLT2 inhibitors (Invokana, Faxiga, Jardiance), Vanrafia demonstrated a 37.4% reduction in proteinuria compared with placebo. It has not yet been established whether Vanrafia slows kidney function decline in patients with IgAN. The study is also evaluating the effect of Vanrafia on disease progression as measured by decline in estimated glomerular filtration rate at week 136.

Vanrafia will directly compete with Filspari (sparsentan), also an oral, once-daily treatment. Filspari contains an inherent angiotensin receptor blocker (ARB) component, whereas Vanrafia will need to be combined with a RASi (i.e. ACE inhibitor or ARBs). The annual cost of Varafia is approximately $162,000 which is slightly higher than Filspari, which is priced at approximately $150,000 per year.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Submission Type
PTC743 (vatiquinone)	Dainippon Pharmaceutical; Edison Pharma; PTC Therapeutics	Oral	Tocotrienol; Lipoxygenase inhibitor	Friedreich's ataxia	Pending (08/19/2025)	NDA

Vatiquinone (PTC-743) is a small molecule designed to block the activity of 15-lipoxygenase, an enzyme that regulates neuroinflammation processes involved in Friedreich's ataxia (FA) in children and adults.

Friedreich ataxia (FA) is a rare, inherited disorder that causes progressive damage to the nervous system. This can cause movement and sensory symptoms and trouble with walking and gait. In FA, nerve fibers in the spinal cord and peripheral nerves break down, becoming thinner. The cerebellum, part of the brain that coordinates balance and movement, is most affected. Symptoms typically begin between the ages of five and 15, although they sometimes appear after age 25.

The trial evaluating the efficacy of vatiquinone enrolled 146 adults and children 7 years and older who were able to walk at least 10 feet in one minute, with or without assistance. Participants received either vatiquinone three times daily, at a dose based on weight, or a placebo for about 1.5 years. The trial's main goal was vatiquinone's impact on the modified Friedreich Ataxia Rating Scale (mFARS) scores, a disease progression measure focusing on swallowing and speech, upper and lower limb coordination, and upright stability. A key secondary measure was a change in activities of daily living as assessed by the FARS Activities of daily living (FARS-ADL) score.

Although 72 weeks of vatiquinone improved the mean mFARS scores by 1.6 points compared with the placebo, the difference was not statistically significant. However, vatiquinone did significantly outperform the placebo at slowing decline in the upright stability subscale of the mFARS. The subscale assesses a person's ability to balance upright.

Current treatments for Friedreich's ataxia focus on alleviating specific symptoms rather than addressing the root cause. These symptom-targeted therapies remain the cornerstone of Friedreich's ataxia care. Vatiquinone will compete with the only other medication approved for the treatment of FA, Skyclarys, which was approved in 2023 for adults and adolescents aged 16 years and older.

The estimated cost is projected to be approximately $375,000 per year.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Submission Type
IONIS-PKK-LRx (donidalorsen sodium)	Ionis Pharmaceuticals	Subcutaneous	Antisense oligonucleotide	Hereditary angioedema (prophylaxis)	Pending (08/21/2025)	NDA

Donidalorsen is an antisense oligonucleotide designed to target and block the production of prekallikrein (PKK), a precursor of plasma kallikrein. It is intended to lower levels of plasma kallikrein and subsequently lower the risk of swelling attacks in adult and pediatric patients 12 years of age and older. Donidalorsen is under development as a once monthly/every 2 month subcutaneous (SC) injection for the prevention of HAE attacks.

HAE is a genetic disorder wherein swelling attacks are driven by the overproduction of the signaling molecule bradykinin. Treatment of HAE includes on-demand treatments to control swelling attacks and long-term prophylactic therapies taken regularly to reduce the risk of attacks.

The new drug application was based on results from the phase 3 OASIS-HAE and OASISplus studies and the ongoing phase 2 open-label extension (OLE) study. In the ongoing phase 2 OLE and phase 3 studies, donidalorsen was found to reduce HAE attacks with an overall sustained mean reduction rate of 96% from baseline. This result was maintained for up to 3 years.

If approved, donidalorsen would be the first once monthly/every 2 months SC prekallikrein antisense oligonucleotide for the prevention of HAE attacks. It would compete with the following prophylactic products:

- CSL's Haegarda administered SC twice weekly (every 3 or 4 days).
- Takeda's Takhzyro, which is dosed SC every 2 weeks. Takhzyro's dosing interval can be extended to every 4 weeks in patients that are well controlled for 6 months.
- BioCryst's Orladeyo administered orally once daily. In May 2025, BioCryst announced real-world evidence on the use of Orladeyo in adolescents and people with severe HAE showing a significant and sustained reduction in HAE attacks through 18 months of follow-up after beginning treatment.
- Takeda's Cinryze administered intravenously twice a week (every 3 or 4 days).

Donidalorsen's comparable efficacy and once monthly/every 2-month dosing interval may provide an administration frequency advantage over other plasma kallikrein inhibitors (e.g. Takhzyro and Orladeyo).

The estimated annual cost is between $500,000 and $750,000.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Submission Type
SAR442168 (Tolebrutinib)	Sanofi; Principia Biopharma	Oral	Bruton's tyrosine kinase inhibitor	Secondary progressive multiple sclerosis	Pending (09/28/2025)	NDA

SAR442168 is an investigational, oral, brain-penetrant, selective small-molecule inhibitor of Bruton's tyrosine kinase (BTK) being investigated for the treatment of multiple sclerosis. BTK is a protein important for the proliferation of immune cells, particularly B-cells. By blocking BTK, it is expected that SAR442168 can reduce inflammation that damages the nervous system in MS.

Multiple sclerosis (MS) is a chronic, inflammatory, immune-mediated disease of the central nervous system (CNS) that disrupts communications within the brain and between the brain and body. MS is among the most common causes of neurological disability in young adults, with first symptoms often appearing between the ages of 20 and 40 years, and it occurs 2–3 times more frequently in women than in men.

MS is characterized as relapsing-remitting or progressive. Relapsing-remitting MS (RRMS) is the initial presentation in 85% to 90% of MS patients. Progressive MS consists of both primary progressive MS (PPMS) and secondary progressive MS (SPMS). The clinical course in PPMS and SPMS differs from RRMS by increasing neurologic disability that occurs independent of, or in the absence of, relapses.

The study was designed to assess the dose-response relationship after 12 weeks of treatment with SAR442168, by measuring the number of new brain lesions on MRI. The study had a cross-over design. Participants were divided into two groups of 60. One group received one of four doses of SAR442168 for the first 12 weeks of the trial, then crossed over to receive a placebo for an additional four weeks. The other group received the same treatment, but in the opposite order.

Results showed that treatment with SAR442168 at its highest daily dose (60mg daily) resulted in an 85% relative reduction in new T1 lesions, and an 89% relative reduction in T2 lesions. T1 lesions are areas of active, ongoing inflammation. T2 lesions are areas where inflammation has caused damage, regardless of whether there is ongoing inflammation at the time of the scan.

If approved, it will be the first BTKi for MS and the first therapy specifically approved for non-relapsing secondary progressive multiple sclerosis.

The potential yearly cost is estimated to be $110,000-$120,000.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Submission Type
Winrevair (sotatercept)	Bristol-Myers Squibb; Merck & Co (MSD); Celgene; Acceleron	Subcutaneous	TGF-beta inhibitor	Pulmonary arterial hypertension*	Pending (10/25/2025)	sBLA

On July 2, 2025, the FDA granted priority review to a supplemental Biologics License Application aiming to update the US product label for sotatercept-csrk that would expand the indication to reduce the risk of a composite of all-cause death, lung transplantation, and related hospitalization > 24 hours compared to placebo in pulmonary arterial hypertension (PAH). Pulmonary arterial hypertension is a rare, incurable, progressive form of pulmonary hypertension (PH) that is estimated to make up about 3% of all cases of PH. PAH is associated with significant morbidity and mortality, with patients with the most severe disease requiring lung transplant. The estimated average 5-year mortality rate is about 35%–40% but can vary greatly depending on the underlying cause of PAH. The prognosis is worse if left untreated.

Winrevair was originally approved on March 26, 2024, for the treatment of adults with pulmonary arterial hypertension (PAH) to increase exercise capacity, improve World Health Organization (WHO) functional class, and reduce the risk of clinical worsening events. Winrevair is the first activin signaling inhibitor to be approved and is the first treatment for PAH that has the potential to be disease-modifying, although additional evidence is needed to establish this. All other approved therapies for PAH work by promoting vasodilation.

The projected yearly cost for patients weighing 89 kg or less is $238,000 and for patients weighing more than 89kg, the annual cost is $476,000.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Submission Type
Wegovy (semaglutide)	Novo Nordisk	Subcutaneous	Glucagon-like peptide-1 (GLP-1) agonist	Heart failure in patients with obesity*	Pending (2H 2025)	sNDA
Ozempic (semaglutide)	Novo Nordisk	Subcutaneous	Glucagon-like peptide-1 (GLP-1) agonist	Peripheral arterial disease (PAD)*	Pending (10/2025)	sNDA
Rybelsus (semaglutide)	Novo Nordisk	Oral	Glucagon-like peptide-1 (GLP-1) agonist	Reduce cardiovascular mortality in patients with type 2 diabetes*	Pending (10/2025)	sNDA
NN9932 (semaglutide)	Novo Nordisk	Oral	Glucagon-like peptide-1 (GLP-1) agonist	Obesity*; Reduce cardiovascular mortality in patients with obesity*	Pending (4Q 2025)	sNDA

Wegovy is a GLP-1 receptor antagonist (RA) that was initially approved in June 2021 for chronic weight management in adults with obesity or overweight with at least one weight-related comorbid condition. Since then, Wegovy has received three additional indications:

- December 2022: Approved in pediatric patients 12 years of age and older with obesity.
- March 2024: Approved to reduce the risk of major adverse cardiovascular events (MACEs), including CV death, nonfatal MI, and nonfatal stroke, in adults with established CVD and either obesity or overweight.
- August 2025: Approved for the treatment of adults with noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH) with moderate to advanced fibrosis, in combination with a reduced-calorie diet and increased physical activity.

Wegovy was evaluated in 529 patients who had heart failure with preserved ejection fraction and a body mass index of 30 or higher to receive once weekly semaglutide (2.4mg) or placebo for 52 weeks. Results of the study found a mean change from baseline in the Kansas City Cardiomyopathy Questionnaire Clinical Summary Score (KCCQ-CSS) of 16.6 points in patients treated with Wegovy compared to 8.7 points with placebo. The mean change from baseline in the 6-minute walk distance was 21.5 meters with semaglutide versus 1.2 meters with placebo. The mean percentage change in bodyweight was -13.3% with semaglutide and -2.6% with placebo.

The annual cost is estimated to be around $17,500, similar to the cost for other indications.

Ozempic is a GLP-1 RA that was initially approved for the treatment of type 2 diabetes in 2017. The label then expanded in 2020 for the treatment of cardiovascular risk reduction in adults with type 2 diabetes and known heart disease, and in January 2025, it received approval to reduce the risk of worsening kidney disease and cardiovascular death in adults with type 2 diabetes and chronic kidney disease.

Currently, it is being investigated as a treatment option for adult patients with type 2 diabetes and symptomatic peripheral arterial disease (PAD). It is estimated that 20% of symptomatic patients with peripheral artery disease have diabetes.

PAD is a slow and progressive disorder of blood vessels. Narrowing, blockage or spasms in a blood vessel can cause PAD. It may affect any blood vessel outside of the heart. This includes the arteries, veins, or lymphatic vessels. Organs supplied by these vessels, such as the brain or legs, may not get enough blood flow for health function. The legs and feet are most often affected. The most common cause of PAD is atherosclerosis, which is the buildup of plaque inside the artery wall. The plaque reduces the amount of blood flow to the limbs, which decreases the oxygen and nutrients sent to the tissue.

In the trial, Ozempic significantly improved walking distance, symptoms such as pain, and quality of life in patients with symptomatic PAD and type 2 diabetes, compared with placebo. It also was associated with reductions in disease progression and use of rescue therapy and improvement in ankle-brachial index. The ankle-brachial index is a comparison of the blood pressure in the ankle with the blood pressure in the arm. There was also a clinically meaningful median treatment difference of 26.4 meters (approximately 87 feet, or about a third the length of an American football field) on a 12% incline, compared to placebo at 52 weeks.

The cost is projected to be between $10,000 and $20,000 annually.

Rybelsus is also being investigated to reduce the risk of major adverse cardiovascular events (MACE) in adults with type 2 diabetes. Rybelsus, the oral form of semaglutide, was first approved by the FDA for the treatment of type 2 diabetes in September 2019. In January 2023, it was updated to allow for its use as a first-line therapy for type 2 diabetes.

The study evaluating its safety and efficacy for MACE enlisted almost 10,000 adults over the age of 50 with type 2 diabetes and atherosclerotic cardiovascular disease and/or chronic kidney disease. Investigators wanted to assess Rybelsus 14mg compared with placebo on cardiovascular outcomes. The results showed that Rybelsus 14mg demonstrated a 14% reduction in the risk of major adverse cardiovascular event, including cardiovascular death, nonfatal myocardial infarction or nonfatal stroke.

Trulicity, Ozempic, and Rybelsus are additional treatment options for MACE risk reduction in people with T2D and established CVD and/or CKD.

The projected annual cost is approximately $12,000.

NN9932, an oral semaglutide, is being investigated for chronic weight management and obesity. The trial, which was 64-weeks long, evaluated once-daily oral semaglutide 25 mg vs placebo in 307 adults with obesity or overweight with one or more comorbidities. The mean baseline body weight was 105.9 kg, and patients treated with oral semaglutide experienced a 13.6% weight loss compared to a 2.2% reduction with placebo in an intent to treat (ITT) population. These results are not as significant as the weight loss seen with other agents such as Zepbound. In a study evaluating the safety and efficacy of Zepbound (tirzepatide) compared with Wegovy (semaglutide) in adults with obesity or overweight and at least one weight-related comorbidity without diabetes showed that patients in the Zepbound group achieved a weight reduction of 20.2% compared to 13.7% in the Wegovy group at week 72. The Zepbound group also lost an average of 50.3 lb., while those on Wegovy lost 33.1 lb.

Although head-to-head trials are ongoing, Zepbound appears to offer the most weight reduction as compared to both injectable and oral competitors. Despite the weight loss, there are still patients who are not willing to self-inject. Of the approved oral therapies, Qsymia offers high value; however, its use is limited by various safety concerns, including a Risk Evaluation and Mitigation Strategy (REMS) program due to the risk of birth defects.

If approved, oral semaglutide would become the first oral formulation of a GLP-1 indicated for chronic weight management and will compete with all approved chronic weight management agents, including other oral non-GLP-1 RA therapies such as Xenical, Contrave, and Qsymia, as well as injectable GLP-1 RZ agents such as Saxenda, Wegovy, and Zepbound. The projected cost is estimated to be $18,000 per year.

GLP-1 label expansion is expected and other potential future uses and may include pending positive clinical trial results:

Drug	Indication if Approved
Rybelsus	Alzheimer's Disease (Phase III)
Ozempic	Alzheimer's Disease (Phase III)
Zepbound	Non-alcoholic steatohepatitis (NASH) (Phase II) Chronic Kidney Disease (Phase II)

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Submission Type
VIS649 (sibeprenlimab)	Otsuka; Visterra	Intravenous; Subcutaneous	Anti-a proliferation-inducing ligand (APRIL) antibody	IgA nephropathy	Pending (11/28/2025)	BLA
Atacicept (atacicept)	EMD Serono (Merck KGaA) Vera Therapeutics	Subcutaneous	Anti-B-cell activation factor BAFF) antibody	IgA nephropathy	Q1 2026	BLA

VIS649 (sibeprenlimab) is currently being investigated to treat patients with immunoglobulin A nephropathy (IgAN), a chronic kidney disease. It is a monoclonal antibody that inhibits the activity of APRIL, a cytokine in the tumor necrosis factor family. By binding and inhibiting APRIL, sibeprenlimab may help reduce the amount of immunoglobulin A (IgA) and galactose-deficient IgA1 (Gd-IgA1) levels, which helps to decrease immune complex creation.

Immunoglobulin A nephropathy (IgAN) is an autoimmune kidney disease in which immunoglobulin A (IgA) accumulates and attacks the glomeruli. This impairs the kidney's ability to filter, causing blood and protein to leak into the urine. The exact cause of IgAN is unknown, but essentially, the body creates abnormal IgA proteins, which it then recognizes as foreign substances. When the body attacks these proteins, they form clusters, which are eventually deposited in the kidneys, causing inflammation and damage. When patients have an active infection, most commonly a respiratory infection, these IgA protein clusters circulate more and are deposited in the kidneys.

The trial evaluated the efficacy and safety of sibeprenlimab 400mg administered subcutaneously every four weeks, compared to placebo. The trial included 510 adult patients with IgAN who were receiving standard-of-care therapy (defined as maximally tolerated ACE inhibitor [e.g., lisinopril, enalapril] or ARB [e.g., losartan, valsartan] +/- SGLT-2 inhibitor [e.g., Invokana, Farxiga]). Patients treated with sibeprenlimab achieved a 51.2% reduction in proteinuria at nine months of treatment compared to placebo.

If approved, it will be the first APRIL antibody for IgAN. The projected annual cost is between $200,000 and $300,000.

Atacicept is an investigational recombinant fusion protein for the treatment of IgAN. It targets a pair of cytokines called BAFF and APRIL that stimulate production of the autoantibodies that mistakenly target the body's own tissue.

The trial to evaluate safety and efficacy included 431 adults with IgA nephropathy. Patients were given either atacicept 150mg, self-administered at home via once weekly subcutaneous injection, or placebo. At week 36, patients treated with atacicept achieved a 46% reduction from baseline in proteinuria as measured by 24-hour urine protein-to-creatinine ratio (UPCR), with a significant and clinically meaningful 42% reduction in UPCR compared to placebo. This trial is ongoing and expected to be completed in 2027.

The projected annual cost is between $200,000 and $300,000.

GENE THERAPY

Gene therapies work by replacing or modifying the disease-causing gene to treat or cure a disease. While only a small number of diseases are currently treatable with gene therapies, there are more than 500 gene therapies undergoing research to make sure they are safe and effective.

Recent FDA Approvals

Papzimeos™ (zopapogene imadenovec-drba) / Precigen

Route	Mechanism of Action	Proposed Indication	Approval (PDUFA) Date	Projected Estimated Cost
Subcutaneous	Gene Therapy	Recurrent Respiratory Papillomatosis	8/15/2025	$300,000–$500,000 per treatment course

Zopapogene imadenovec is a non-replicating adenoviral vector-based immunotherapy approved for adults with recurrent respiratory papillomatosis (RRP). RRP is a chronic disease caused by infection with human papillomavirus (HPV) types 6 and 11, leading to the growth of benign papillomas in the larynx, trachea, or lungs. These papillomas can cause hoarseness, airway obstruction, and require repeated surgical removal. Standard care has relied on recurrent surgical debulking. Zopapogene imadenovec induces an immune response against HPV 6 and HPV 11 proteins. Treatment works by stimulating the immune system to recognize and eliminate papilloma tissue driven by HPV infection, aiming to reduce the need for repeated surgeries.

On August 15, 2025, the FDA approved Papzimeos for the treatment of adult patients with RRP, marking it as the first therapy targeting the root viral cause of the disease. The approval was based on results from the open-label, single-arm, phase I/II study, which evaluated zopapogene imadenovec in 38 adults with RRP who had undergone at least three prior debulking procedures in the year before study entry.

Results showed that 51% (18/35) of patients who received the recommended dose achieved a complete response at 12 months, defined as no need for surgical intervention. Among these responders, 43% (15/35) maintained a complete response throughout 24 months.

The recommended therapeutic dosing of Papzimeos is 5×10^{11} PU per injection, administered subcutaneously four times over a 12 week interval. Participants treated with the lower investigational dose of 1×10^{11} PU per injection did not achieve complete responses, indicating the higher dose is required for clinical efficacy.

The most common adverse reactions reported with zopapogene imadenovec included injection site reactions, fatigue, chills, fever, myalgia, and nausea. Like other adenoviral vector-based therapies, there is also a risk of thrombotic events due to potential development of prothrombotic antibodies.

Papzimeos is anticipated to be available through identified specialty centers in late 2025.

Gene Pipeline

The following gene therapies could be approved within the next 12 months.

Clemidsogene lanparvovec (RGX-121) / Regenxbio

Route	Mechanism of Action	Proposed Indication	Approval (PDUFA) Date	Projected Estimated Cost
Intracisternal / Intrathecal	Gene Therapy	Hunter syndrome	February 8, 2026	$2M–$3M (One time)

Hunter syndrome (MPS II) is a rare, X-linked lysosomal storage disorder caused by a deficiency of the enzyme iduronate-2-sulfatase (IDS). Without IDS, glycosaminoglycans (GAGs) accumulate throughout the body and brain, leading to multi-organ disease, neurocognitive decline, airway obstruction, cardiac disease, and premature death. Current enzyme replacement therapies (ERTs) improve somatic symptoms but do not cross the blood–brain barrier, leaving neurological manifestations untreated. Clemidsogene lanparvovec (RGX-121) is a one-time gene therapy that addresses both somatic and neurological disease. Using an AAV9 vector, RGX-121 delivers a functional copy of the IDS gene to cells in the central nervous system and periphery, enabling production of IDS enzyme. This approach reduces GAG accumulation.

Interim data from Phase I/II/III trials have shown reductions in CSF and plasma GAGs, sustained enzyme activity, and trends toward stabilization of neurocognitive function compared with the natural history of the disease. Patients also demonstrated improved biomarker profiles consistent with therapeutic effect. Safety to date has been favorable, with no unexpected serious adverse events reported.

The FDA accepted the BLA under priority review with an original PDUFA date of November 9, 2025, but later extended to February 8, 2026 to allow review of additional long-term data. If approved, RGX-121 would be the first approved gene therapy for Hunter syndrome and could offer a one-time treatment option that addresses both systemic and neurological disease manifestations.

UX111 (ABO-102) / Ultragenyx

Route	Mechanism of Action	Proposed Indication	Approval (PDUFA) Date	Projected Estimated Cost
Intravenous	Gene Therapy	Sanfilippo Syndrome Type A	TBD	$2M–$3M (One time)

Sanfilippo syndrome type A (MPS IIIA) is a rare, fatal lysosomal storage disorder characterized by rapid neurodegeneration with onset in early childhood. Caused by pathogenic variants in the SGSH gene, the disease leads to deficiency of the sulfamidase enzyme, resulting in abnormal accumulation of heparan sulfate and progressive cell damage. Children present with developmental delays followed by cognitive, language, and motor decline, behavioral abnormalities, and early death, with a median life expectancy of about 15 years. The condition affects an estimated 3,000–5,000 patients worldwide. There are currently no approved therapies.

UX111 is a one-time intravenous gene therapy that addresses the underlying SGSH enzyme deficiency. Using an AAV9 vector, the therapy delivers a functional copy of the SGSH gene to patient cells. Transduced cells produce and secrete sulfamidase, which can be taken up by other cells to restore enzyme activity and reduce heparan sulfate accumulation. UX111 has received Fast Track, Rare Pediatric Disease, and Orphan Drug designations.

Data from the Transpher A trial and long-term follow-up studies, demonstrated that UX111 reduced heparan sulfate levels in cerebrospinal fluid (CSF) regardless of patient age or disease stage at treatment. Additionally, patients showed statistically significant improvements in Bayley-III cognitive, receptive communication, and expressive communication scores compared to natural history controls. The clinical endpoints correlated with biochemical reductions in CSF heparan sulfate. The most common treatment-related adverse events were transient elevations in liver enzymes, which were mild to moderate in severity and resolved.

The FDA accepted the Biologics License Application (BLA) for UX111 under Priority Review, with an original PDUFA date of August 18, 2025. However, in July 2025, the FDA issued a Complete Response Letter (CRL) for deficiencies in Chemistry, Manufacturing, and Controls (CMC). Ultragenyx is addressing these issues and plans to resubmit the BLA with a new PDUFA date of February 8, 2026.

If approved, UX111 would be the first approved therapy for Sanfilippo syndrome type A.

RP-L102 (mozafancogene autotemcel)/Rocket

Route	Mechanism of Action	Proposed Indication	Approval (PDUFA) Date	Projected Estimated Cost
Intravenous	Gene Therapy	Fanconi Anemia	TBD	$2M - $3M

Fanconi anemia (FA) is a rare and serious inherited blood disorder that leads to bone marrow failure. It prevents bone marrow from making enough new blood cells for the body to work properly or can also cause bone marrow to make faulty blood cells. This can lead to serious health problems such as leukemia. In the United States, about 31 babies are born with the disease each year, with about one in every 181 people in the United States is a carrier of Fanconi anemia.

Mozafancogene is an investigational gene therapy product that contains patient derived stem cells that have been genetically modified and infused back into the patient with the goal of preventing bone marrow failure. The current standard of care treatment for FA is stem cell transplantation, which is associated with significant toxicities and complications. About 80% of patients with FA will require a transplant within the first decade of their life. Results from a global clinical trial demonstrated that mozafancogene conferred sustained genetic correction in 8 of 12 evaluable patients with more than 12 months of follow up. The safety profile remains favorable with no known significant preliminary safety signals.

Rocket initiated a rolling Biologics License Application (BLA) for RP-L102 in November 2024; however, on August 7, 2025, the company announced it was pausing additional investments in the FA program, delaying FDA approval at least beyond 2026 or potentially not pursuing a BLA approval.

Kresladi (marnetegragene autotemcel)/Rocket

Route	Mechanism of Action	Proposed Indication	Approval (PDUFA) Date	Projected Estimated Cost
Intravenous	Gene Therapy	Primary immunodeficiency; severe leukocyte adhesion deficiency	TBD	$3M - $3.5M

Severe Leukocyte Adhesion Deficiency-I (LAD-I) is a rare pediatric disease caused by mutations in the ITGB2 gene. This gene is responsible for producing a component of CD18, a key protein that facilitates the immune response against infections. As a result, white blood cells, or leukocytes, do not function normally. Children with this disease experience life-threatening bacterial and fungal infections that respond poorly to antibiotics and antifungal medications. Children who survive infancy experience recurrent severe infections including pneumonia, mouth ulcers, necrotic skin ulcers, and blood infections. LAD-I is estimated to impact between 800 to 1,000 children in the United States and Europe. Currently the only potential curative treatment is a stem cell transplant and itself is associated with substantial morbidity and mortality. However, without a successful bone marrow transplant, survival beyond childhood is rare.

Marnetegragene is an investigational one-time gene therapy that contains patient-derived stem cells that have been genetically modified to deliver a functional copy of the ITGB2 gene. Positive data from a global Phase I/II study of marnetegragene demonstrated 100% overall survival at 12 months post-infusion and for the entire 12-to-24-month duration of follow-up for all nine LAD-I patients. Data also showed large decreases compared with pre-treatment history in the incidences of significant infections, combined with evidence of resolution of LAD-I-related skin lesions and restoration of wound repair capabilities. It was well tolerated in all patients with no serious treatment related adverse events.

The PDUFA date for Kresladi was originally set for March 31, 2024, but the FDA extended the review period by three months to June 30, 2024, to allow additional time to review clarifying Chemistry, Manufacturing, and Controls (CMC) information submitted by Rocket in response to FDA information requests. However, in July 2025, Rocket announced a reorganization that shifted prioritization toward other programs. As a result, regulatory progress for Kresladi has been delayed, and no new PDUFA date has been set.

CELL THERAPY

Cell therapy works to treat diseases by restoring or altering certain sets of cells or by using cells to carry a therapy through the body. With cell therapy, cells are cultivated or modified outside the body before being injected into the patient. The cells may originate from the patient or a donor.

Cell Pipeline

The following gene therapies could be approved within the next 12 months.

Deramiocel (CAP-1002) / Capricor Therapeutics

Route	Mechanism of Action	Proposed Indication	Approval (PDUFA) Date	Estimated Cost
Intravenous	Cell Therapy	Duchenne muscular dystrophy cardiomyopathy	8/31/2025	$750,000 annually

Deramiocel (CAP-1002) is an investigational allogeneic cell therapy indicated for Duchenne muscular dystrophy (DMD). DMD is a progressive X-linked neuromuscular disorder caused by mutations in the DMD gene, which encodes dystrophin, a protein essential for muscle stability. As the disease advances, cardiac muscle is progressively affected, leading to DMD-associated cardiomyopathy.

Current treatment of DMD cardiomyopathy includes corticosteroids and cardioprotective medications, which may slow progression but do not directly target the underlying cardiac pathology. Deramiocel is composed of cardiosphere-derived cells (CDCs), a type of stromal cell harvested from donor heart tissue. These exert therapeutic effects via paracrine signaling, including the release of extracellular vesicles that promote anti-inflammatory and anti-fibrotic effects in damaged myocardium.

In March 2025, Capricor Therapeutics announced that the FDA had accepted its Biologics License Application (BLA) for deramiocel for the treatment of DMD-associated cardiomyopathy. The application was granted Priority Review, with a PDUFA target action date of August 31, 2025.

The BLA is supported by data from the Phase 2 HOPE-2 study, which evaluated the safety and efficacy of deramiocel in DMD patients. In the HOPE-2 trial, a total of 8 patients were randomly assigned to deramiocel and 12 patients to placebo. The mean 12-month change from baseline in mid-level elbow favored deramiocel over placebo (percentile difference, 36.2%; 95% CI, 12.7-59.7; difference, 2.6 points; P = .014). Individuals who received deramiocel had an improvement in left ventricular ejection fraction (LVEF), with an average increase of 1.2% across the overall cohort and a more pronounced 3.0% increase among patients who had a baseline LVEF of 45% or higher. Additionally, reductions were observed in both left ventricular end systolic volume (LVESV) and end diastolic volume (LVEDV), indicating favorable changes in cardiac chamber size and function.

Following the completion of the HOPE-2 study, eligible participants who wished to remain on treatment entered the open label extension (OLE) study where they received deramiocel every 3 months. Over a three-year period, patients receiving the therapy experienced a significant improvement in skeletal muscle function, evidenced by a 3.7-point gain on the Performance of Upper Limb (PUL) scale compared to an external control group, indicating a slowing of disease progression.

In July 2025, the FDA issued a Complete Response Letter (CRL), stating that the application did not demonstrate enough evidence of effectiveness and that certain Chemistry, Manufacturing, and Controls (CMC) issues remained unresolved. In August 2025, Capricor announced it had held a meeting with the FDA to discuss the CRL and reported that all FDA inspection findings had been resolved. Capricor plans to resubmit the BLA with additional data from the ongoing Phase 3 HOPE-3 trial, with results expected in late 2025.

If approved, deramiocel would become the first cell therapy approved specifically for DMD-cardiomyopathy and could be administered as a lifelong, quarterly treatment.

Tabelecleucel (Ebvallo)/Atara Biotherapeutics, Inc.

Route	Mechanism of Action	Proposed Indication	Approval (PDUFA) Date	Estimated Cost
Intravenous	Cell Therapy	Relapsed/refractory Epstein-Barr Virus-Positive Posttransplant Lymphoproliferative Disease	1/10/2026	$1.5 million - $2.5 million annually

Epstein-Barr Virus (EBV) positive post-transplant lymphoproliferative disease (EBV+ PTLD) is a complication that can occur following solid organ transplantation, resulting from the reactivation of EBV in immunosuppressed patients. EBV is a common virus that typically remains dormant in the body after an initial infection, but in transplant recipients, the immunosuppressive medications used to prevent organ rejection can impair the body's ability to control the virus. This leads to abnormal proliferation of B lymphocytes, which may progress to lymphoma or other forms of cancer. The condition most commonly affects individuals who are EBV seronegative prior to transplantation and receive an EBV-positive organ, increasing their susceptibility to the disease.

Management involves reducing the levels of immunosuppressive therapy to allow for immune recovery. Additional treatments may include antiviral therapies and targeted immunotherapies, such as rituximab.

Tabelecleucel (Ebvallo) is an allogeneic EBV-specific T-cell immunotherapy aimed at treating relapsed/refractory EBV+ PTLD by utilizing donor-derived T-cells that are specifically engineered to target and attack cells infected with EBV.

In May 2024, Atara Biotherapeutics submitted a BLA to the FDA for tabelecleucel. In December 2024, updated results from the phase III ALLELE clinical trial were presented at the 66th American Society of Hematology Annual Meeting. The study included 75 patients with the primary endpoint being the overall response rate (ORR), along with secondary endpoints of duration of response (DOR), overall survival (OS), and time to response (TTR). The study found that tabelecleucel achieved a 51% ORR and a 28% complete response rate with a median DOR of 23 months and median OS of 18.4 months. Safety results were consistent with prior studies, with no reports of cytokine release syndrome, tumor flare reactions, or graft vs. host disease.

However, on January 16, 2025, the FDA issued a complete response letter (CRL) regarding the BLA. The CRL was related to observations as part of a standard pre-license inspection of a third-party manufacturing facility for Ebvallo. As a result, the FDA has halted trials of Ebvallo due to the compliance issues found at the third-party manufacturing facility.

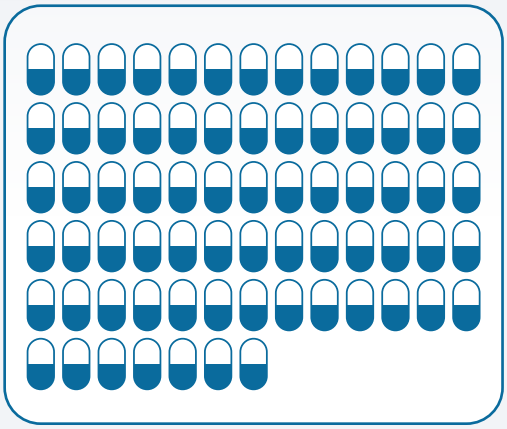
In May 2025, the FDA lifted the clinical hold on the Phase III ALLELE trial, allowing development to resume. Atara resubmitted the BLA in July 2025 and the FDA accepted it under Priority Review. A new PDUFA date has been set for January 10, 2026.

The Institute for Clinical and Economic Review (ICER) evaluated tabelecleucel and concluded that current evidence indicates tabelecleucel has a net health benefit compared to standard of care, extending survival in patients with relapsed or refractory EBV+ PTLD. The therapy was deemed cost-effective if priced between $143,900 and $273,700 per treatment cycle, however pricing has not yet been disclosed.

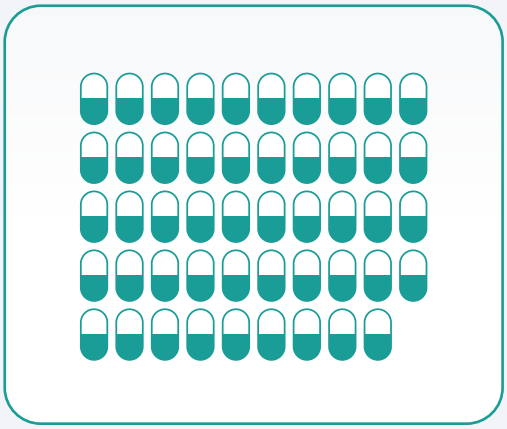
Ebvallo has already been approved in Europe in December 2022 for treating relapsed/refractory EBV+ PTLD in patients aged 2 years and older.

Biosimilars Pipeline

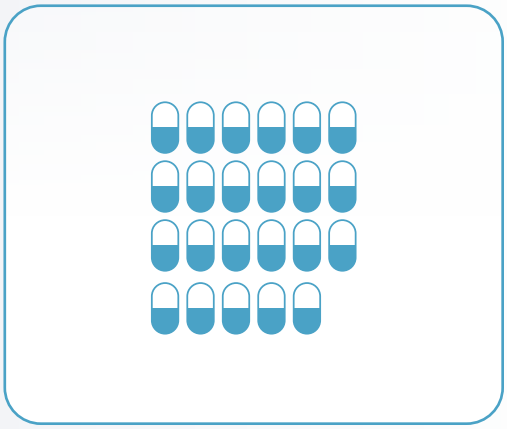
QUICK FACTS



72 FDA Approved Biosimilars to Date



49 Launched Biosimilars



23 Approved Interchangeable Biosimilars

The U.S. Food and Drug Administration has proposed that biosimilar drugs seeking agency's interchangeable designation will no longer need studies showing the impact of switching between them and the branded drug. There have been no changes or updates to this proposal and the draft guidance remains the current status quo while awaiting finalization.

Recent FDA Approvals

FDA Approves First Interchangeable Insulin Aspart Biosimilar, Kirsty® (insulin aspart-xjhz)

On July 15, 2025, the FDA approved Kirsty® (insulin aspart-xjhz), the first interchangeable biosimilar to reference Novolog® (insulin aspart). Kirsty is a rapid-acting insulin indicated to improve glycemic control in adults and pediatric patients with diabetes. It can be administered subcutaneously and may also be used via continuous subcutaneous infusion or intravenous administration. Kirsty is the second insulin aspart biosimilar approved by the FDA, following Merilog® (insulin aspart-szjj), which was approved in February 2025 as the first biosimilar referencing Novolog®.

Kirsty was also approved as an interchangeable biosimilar. As an interchangeable biosimilar, Kirsty can be substituted for Novolog at the pharmacy, as state laws allow, without consulting the prescriber, much like the process for dispensing generic medications.

Approval was based on data demonstrating bioequivalence between Kirsty and Novolog, with no clinically meaningful differences in efficacy, safety, pharmacokinetics, or immunogenicity. Adverse effects associated with Kirsty include risks of hypoglycemia, severe allergic reactions, and hypokalemia. Common adverse effects include injection site reactions, rash, lipodystrophy, weight gain, and peripheral edema.

Kirsty will be available as a 3-mL single-patient-use prefilled pen and a 10-mL multiple-dose vial. No official launch date has been announced yet.

FDA Expands Approval for Actemra Biosimilar, Avtozma®

On August 6, 2025, the FDA approved an expanded indication for Avtozma® (tocilizumab-anoh), a biosimilar to Actemra®, to include the treatment of cytokine release syndrome (CRS) in adults and pediatric patients aged 2 years and older.

CRS is a systemic inflammatory response caused by rapid cytokine release, with symptoms ranging from mild flu-like illness to severe complications such as hypotension, respiratory distress, and multi-organ failure. Tocilizumab is a humanized monoclonal antibody that acts as an interleukin-6 (IL-6) receptor antagonist, blocking IL-6 signaling to reduce the inflammatory cascade that drives CRS, a life-threatening complication often associated with Chimeric Antigen Receptor (CAR) T-cell therapy.

The expanded approval was supported by a comprehensive data package that demonstrated biosimilarity to Actemra. A global phase 3 study in patients with moderate to severe rheumatoid arthritis assessed efficacy, pharmacokinetics, safety, and immunogenicity, showing no clinically meaningful differences compared to the reference product. The FDA did not require new CRS-specific clinical trials; instead, approval was extrapolated from rheumatoid arthritis data and analytical evidence to cover all Actemra's approved indications, including CRS.

Avtozma IV is expected to become available in the U.S. in September 2025.

Upcoming Biosimilars

Lucamzi™- Biosimilar to Lucentis®

In May 2024, Xbrane Biopharma and STADA Arzneimittel announced a partnership with Valorum Biologics to commercialize Lucamzi (ranibizumab), a biosimilar to Lucentis. Ranibizumab is an anti-VEGF (vascular endothelial growth factor) monoclonal antibody fragment used in the treatment of serious retinal disorders, including neovascular (wet) age-related macular degeneration (nAMD), diabetic macular edema (DME), and retinal vein occlusion (RVO).

The Biologics License Application (BLA) for Lucamzi is based on data from a randomized, double-blind, multicenter phase III study comparing Lucamzi to reference ranibizumab in patients with nAMD. The study's primary endpoint was the mean change in best-corrected visual acuity (BCVA) from baseline to week 8. Results demonstrated therapeutic equivalence between Lucamzi and Lucentis with no clinically meaningful differences observed in efficacy, safety, or immunogenicity through the study duration, however, Lucamzi is not designated as interchangeable with Lucentis.

Additionally, data supporting Lucamzi included a pharmacokinetic study conducted in healthy volunteers, which showed that Lucamzi had comparable pharmacokinetic properties, safety, and tolerability to Lucentis.

The FDA has set an action date of October 21, 2025, for Lucamzi's BLA resubmission. If approved, Lucamzi is expected to launch in 2026.

BAT2506™ – Biosimilar to Simponi®

In July 2025, Bio-Thera Solutions and Accord BioPharma announced that the FDA had accepted Biologics License Application (BLA) for BAT2506, a proposed biosimilar to Simponi (golimumab). Golimumab is a tumor necrosis factor (TNF) inhibitor used for the treatment of rheumatoid arthritis, psoriatic arthritis, ulcerative colitis, and ankylosing spondylitis.

The BLA for BAT2506 is supported by a comprehensive data package, including analytical, pharmacokinetic, safety, and efficacy results comparing BAT2506 with the reference product. Data from a global phase III clinical trial in patients with rheumatoid arthritis demonstrated therapeutic equivalence, with no clinically meaningful differences observed in efficacy, safety, or immunogenicity.

This is the second FDA submission for a Simponi biosimilar, following Alvotech and Teva's filing in January 2025. An FDA decision on BAT2506 is expected in Q2 2026.

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AscellaHealth partners with life sciences manufacturers around the world, enabling them to successfully commercialize therapies for complex, chronic conditions. Our comprehensive suite of services guides clients through every stage of the process, from clinical trials through approval, pre-commercialization support and ultimately transitioning patients on to therapy.

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