AscellaHealth®

Specialty and Rare Pipeline Digest™

Q4 • 2025

AscellaHealth 1055 Westlakes Dr. Suite 200 Berwyn, PA 19312 | info@ascellahealth.com

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.

TABLE OF CONTENTS

About AscellaHealth

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.

Visit **ascellahealth.com**.

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

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Orladeyo granules (berotralstat hydrochloride)	BioCryst	Oral	Plasma kallikrein inhibitor	Prophylaxis against angioedema attacks in hereditary angioedema	Approved (12/12/2025)	$580,000 per year	Moderate

On December 12, 2025, the FDA approved the use of an oral pellet formulation of once-daily Orladeyo for prophylactic therapy in pediatric patients with hereditary angioedema (HAE) aged 2 to < 12 years of age. Orladeyo was originally approved as a capsule formulation, to prevent attacks of HAE in people 12 years of age and older.

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. It affects approximately 1 in 10,000 to 1 in 50,000 individuals in the United States. Treatment includes both on-demand therapy and prophylactic therapy. On-demand therapy is given to minimize the impact of an HAE attack and prophylactic therapy is given to certain patients to reduce the frequency and severity of attacks. Products for on-demand include Firazyr, icatibant, Berinert, Kalbitor and Ruconest. Cinryze, Haegarda, Takhzyro Orladeyo, Andembry and Dawnzera are approved for prophylaxis.

The trial evaluated prophylactic therapy for HAE in patients aged 2 to 11 years. The results showed berotralstat provided early and sustained reductions in monthly attack rates. Orladeyo demonstrated early and sustained attack rate reduction, with 65.5% of patients attack-free at 1 month and 70.4% of patients attack free at month 12. Orladeyo was also safe and well tolerated with the most commonly reported treatment adverse events being nasopharyngitis.

It is the first oral prophylaxis treatment for HAE in patients 2 to 11 years and will compete with Takhzyro® (lanadelumab), which is administered subcutaneously.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Uplizna (inebilizumab)	AstraZeneca; Amgen; MedImmune; Horizon Therapeutics; Viela Bio	Intravenous	Anti-CD19 antibody	Myasthenia gravis	Approved (12/11/2025)	$200,000-$300,000 per year	Low

On December 11, 2025, the FDA approved Uplizna, a CD19+ B cell-directed monoclonal antibody, for the treatment of generalized myasthenia gravis (gMG) in adults who are anti-acetylcholine receptor (AChR) and anti-muscle specific tyrosine kinase (MuSK) antibody positive. This is the first and only CD19-Targeted B-Cell therapy approved for gMG. Uplizna was originally approved for neuromyelitis optica spectrum disorder and IgG4-related disease-two immune-mediated disorder in which B cell depletion has shown meaningful clinical benefit.

Myasthenia gravis (MG) is an autoimmune neuromuscular disorder characterized by muscle weakness that worsens throughout the day and with activity. The disease usually targets muscles in the eyes, face, neck, arms, and legs. The disease can strike anyone at any age but is more frequently seen in young women (age 20 and 30) and men aged 50 and older. A myasthenia crisis can involve difficulty in swallowing or breathing. The cause is unknown and there is no cure, but early detection and medical management can help people live longer and more functional lives.

The approval was supported by data from one of the largest studies to include both anti-AChR and anti-MuSK Ab+ patients and the first to successfully incorporate a steroid taper into its protocol. The primary endpoint was change from baseline in Myasthenia Gravis Activities of Daily Living scale (MG-ADL) score at week 26. Results showed that participants in the Uplizna group experienced a higher decrease in MG-ADL score compared with placebo at week 26.

Uplizna is the first treatment for gMG that can be administered every 6 months and will compete with Imaavy® (nipocalimab) and Rystiggo® (rozanolixizumab) in patients who are anti–MuSK Ab+ and all other approved treatment options for patients who are anti–AChR Ab+ (e.g., Vyvgart® (efgartigimod), Soliris® (eculizumab), Zilbrysq® (zilucoplan), Ultomiris® (ravulizumab).

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Voyxact (sibeprenlimab-szsi)	Otsuka; Visterra	Intravenous; Subcutaneous	Anti-a proliferation-inducing ligand (APRIL) antibody	IgA nephropathy	Approved (11/25/2025)	≈$200,000-300,000 per year	Moderate

On November 25, 2025, the FDA approved Voyxact to reduce proteinuria (protein in the urine) in adults with primary immunoglobulin A nephropathy (IgAN) at risk for disease progression.

IgA nephropathy (IgAN) is an autoimmune condition in which IgA proteins build up in the kidneys and damage the glomeruli, the structures responsible for filtering the blood. As a result, the kidneys become less effective at filtering waste, leading to blood and protein leaking into the urine. Patients often experience reddish or tea-colored urine, flank discomfort, ankle swelling, and elevated blood pressure. Over time, IgAN can lead to serious kidney impairment. After 10 or more years of living with the disease, up to 40% of patients may progress to end-stage renal disease (ESRD), requiring dialysis or a kidney transplant. Treatment therefore focuses on slowing or preventing progression to ESRD.

Voyxact binds and blocks the actions of anti-a proliferation-inducing ligand antibody (APRIL), a cytokine that stimulates the production of abnormal IgA. Approval was based on a trial which included adults with biopsy-confirmed IgAN. Patients were given either Voyxact or placebo. Results showed that after 9 months of therapy, Voyxact cut levels of protein in the urine by 51.2% compared to a 2% increase in the placebo group.

Voyxact will compete with several approved therapies that target different drivers of the disease. Key competitors include Filspari® (sparsentan) and Varafia® (atrasentan), both oral endothelin-receptor antagonists. Tarpeyo® (targeted-release budesonide), which regulates the immune system in reducing the production of IgA that builds up in the kidneys and Fabhalta® (iptacopan) which inhibits the complement pathway and serves patients whose disease is complement driven. Voyxact is a self-administered, subcutaneous injection given every four weeks. Otsuka has not yet disclosed pricing or product availability.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Redemplo (plozasiran)	Arrowhead	Subcutaneous	Small interfering RNA (siRNA)	Familial chylomicronemia syndrome (FCS)	Approved (11/18/2025)	$60,000 per year	Low

On November 18, 2025, the FDA approved Redemplo (plozasiran) as an adjunct to diet to reduce triglycerides in adult patients with familial chylomicronemia syndrome (FCS). It reduces the production of apolipoprotein C-III (APOC3), a key regulator of triglyceride metabolism. Familial chylomicronemia syndrome (FCS) is a rare genetic disorder estimated to affect 1-2 individuals per million. It is characterized by very high levels of a type of fat known as triglycerides. These triglycerides are carried in the blood by large structures called chylomicrons. Chylomicrons help move triglycerides to different parts of the body where they are needed for energy and fat storage. The hallmark of FCS is persistent and severe hypertriglyceridemia, which can exceed 1,000mg/dL. This increases the risk of acute pancreatitis, a potentially life-threatening condition where the pancreas becomes inflamed, and its function disrupted. Additionally, other symptoms

include severe frequent stomach and back pain, enlarged liver or spleen, fatty deposits in the retina of the eye, yellowish, waxy-like deposits of fatty material in the skin, known as xanthomas, bloating and indigestion, depression, anxiety, fatigue, memory loss or brain fog.

The primary treatment for FCS is a highly restrictive low-fat diet to minimize triglyceride intake and reduce chylomicron production.

The study evaluating the safety and efficacy of plozasiran included 75 adults with genetically or clinically diagnosed FCS. The patients received either plozasiran (25mg or 50mg) or a placebo, administered subcutaneously every 3 months for 1 year. Results after 10 months showed triglyceride levels reduced by 80% with the 25mg dose and 78% with the 50mg dose, but only 17% with the placebo. Plozasiran also met all key secondary endpoints and demonstrated statistical significance versus placebo, including a decrease in the incidence of acute pancreatitis events with 8% in the plozasiran group and 20% in the placebo group.

Redemplo will compete with Tryngolza® (olezarsen), an apo-C-III-directed antisense oligonucleotide, approved in December 2024 as the first treatment for FCS. Tryngolza is also self-administered subcutaneously but dosed once monthly and is more costly at around $595,000 per year.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Lynkuet (elinzanetant)	Bayer	Oral	Neurokinin-1 (NK1) receptor antagonist; Neurokinin-3 (NK3) receptor antagonist	Vasomotor symptoms due to menopause (hot flashes)	Approved (10/24/2025)	$7,600 per year	Moderate

On October 24, 2025, The FDA approved Lynkuet (elinzanetant), an NK1 and NK3 receptor antagonist, for the treatment of moderate to severe hot flashes due to menopause. These symptoms affect more than 80% of women during menopause and can last for several years, significantly impacting sleep, comfort, and overall quality of life.

Lynkuet works differently compared to traditional hormone replacement therapies in that it targets the neurochemical pathways in the brain that trigger hot flashes rather than replacing estrogen or progesterone levels. It works by blocking specific brain receptors that become overactive when estrogen levels drop, helping to reduce heat surges and sweating and helping to regulate body temperature. A similar nonhormonal drug, Veozah®, approved in 2023, blocks only the NK3 receptor. Targeting the additional receptor potentially may help improve sleep.

The approval was based on data from two trials which included 796 menopausal women who had at least 50 moderate to severe hot flashes, including nighttime hot flashes, per week. Participants received either elinzanetant 120mg or placebo, once daily at bedtime for 12 weeks. Findings showed that elinzanetant significantly reduced the frequency and severity of moderate-to-severe vasomotor symptoms (VMS). Additionally, they found a significant reduction in frequency of VMS at week 1, improvement in sleep disturbances and menopause-related quality of life. Results from the long-term extension trial showed safety of elinzanetant over 52 weeks was consistent with finding from the two trials.

Hormone therapy (HT) has been the most common treatment for menopausal symptoms. However, it is not suitable for women with a history of breast cancer, heart disease or blood clots. The risks of HT differ depending on type, dose, duration of use, route of administration, timing of initiation, and whether a progestogen is used. On November 10, 2025, the U.S. Department of Health and Human Services (HHS) announced that the FDA will begin removing Boxed Warnings from menopausal hormone replacement therapies (HRTs). Removal of the Boxed Warning from HRT products follows a comprehensive review of the current literature and recommendations from a July 17, 2025 FDA advisory panel meeting. Evidence indicates that women who initiate HRT within 10 years of the onset of menopause (generally before 60 years of age) have a reduction in all-cause mortality and fractures. Women may also reduce their risk of cardiovascular disease (CVD) by as much as 50%, Alzheimer's disease by 35%, and bone fractures by 50%–60%. The FDA's recommended labeling changes also include to start systemic HRT within 10 years of menopause onset, or before 60 years of age. Lynkuet will compete with hormone therapy such as estrogen and estrogen-progesterone combination products as well as with Veozah, however it does not carry a boxed warning for hepatotoxicity as seen with Veozah.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Winrevair (sotatercept)	Bristol-Myers Squibb; Merck & Co (MSD); Celgene; Acceleron	Subcutaneous	TGF-beta inhibitor	Pulmonary arterial hypertension*	Approved (10/24/2025)	$252,500 per year	Moderate

On October 24, the FDA approved an expanded indication for Winrevair for the treatment of Pulmonary Arterial Hypertension (PAH) to include clinical components of hospitalization, lung transplantation and death. Winrevair was initially approved in 2024 for the treatment of adults with PAH to increase exercise capacity, improve WHO Functional Class (FC), and reduce the risk of clinical worsening events.

Pulmonary arterial hypertension is a progressive disorder characterized by abnormally high blood pressure in the pulmonary artery. It occurs when most of the very small arteries throughout the lungs narrow in diameter, which increases the resistance to blood flow through the lungs. To overcome the increased resistance, blood pressure increases in the pulmonary artery and in the right ventricle of the heart, which can damage the right ventricle.

The expanded label is based on a trial that showed that adding Winrevair to background therapy demonstrated a statistically significant and clinically meaningful 76% reduction in the risk of major morbidity and mortality outcomes in adults with PAH WHO functional class III or IV compared to placebo. Based on the efficacy findings, the trial ended early with patients given the opportunity to receive Winrevair as part of the open-label long-term follow-up study.

Winrevair is primarily used as an add-on therapy in adults receiving dual treatment with an endothelin receptor antagonist (e.g., Letairis, Tracleer) and phosphodiesterase type 5 inhibitor (e.g., Adcirca, Revatio), or triple therapy including a prostacyclin pathway agent (e.g., Tyvaso, Orenitram). Winrevair is the first treatment for PAH that works through a mechanism of action that does not involve vasodilation and is the first treatment that has the potential to be disease-modifying, although long-term evidence is needed to establish this.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Rybelsus (3, 7, 14 mg; 1.5, 4, 9 mg) (semaglutide)	Novo Nordisk	Oral	Glucagon-like peptide-1 (GLP-1) agonist	Reduce cardiovascular mortality in patients with type 2 diabetes*	Approved (10/17/2025)	$12,137 per year	Moderate

Rybelsus was first approved in 2019 as an add-on to diet and exercise to help improve glycemic control in adults with type 2 diabetes (T2D). On October 17, 2025, its indication was expanded to include reducing the risk of major adverse cardiovascular events (MACE)—cardiovascular death, nonfatal myocardial infarction (MI), or nonfatal stroke—in adults with T2D who are at high risk. This makes Rybelsus the first and only oral GLP-1 receptor agonist to carry this designation.

Approval was based on results from the SOUL trial which enrolled 9,650 patients with T2D and established cardiovascular disease (coronary artery disease, cerebrovascular disease, symptomatic peripheral artery disease) and/or chronic kidney disease). The primary objective was to evaluate Rybelsus 14mg, in addition to standard of care, on reducing the risk of MACE. The results showed that MACE occurred in 12.0% of patients in the semaglutide group and 13.8% in the placebo group. Furthermore, semaglutide 14mg reduced the risk of MACE by 14% at 4 years compared to placebo, in addition to standard therapies.

Rybelsus joins Novo Nordisk's Ozempic (semaglutide) and Victoza (liraglutide), as well as Eli Lilly's Trulicity (dulaglutide), all of which already include MACE risk-reduction indications. Notably, Lilly intends to submit cardiovascular outcomes trial (CVOT) data for Mounjaro (tirzepatide) to the FDA by the end of 2025, with a label expansion for this indication expected in 2026.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Jascayd (nerandomilast)	Boehringer Ingelheim	Oral	Phosphodiesterase-4 (PDE4) Inhibitor	Idiopathic pulmonary fibrosis	Approved (10/07/2025)	$197,000 per year	Low

On October 7, 2025, the FDA approved Jascayd (nerandomilast), an oral preferential inhibitor of phosphodietsterase-4B (PDE4B), for the treatment of idiopathic pulmonary fibrosis (IPF) in adult patients. It may be used as monotherapy or in combination with Esbriet® (pirfenidone) or Ofev® (nintedanib).

Jascayd works by blocking PDE4, which plays a crucial role in inflammation and tissue damage. This helps slow progression of lung scarring and reduce inflammation.

Idiopathic pulmonary fibrosis is a chronic, progressive form of interstitial pneumonia. Although considered rare, it is the most frequently encountered type of interstitial lung disease. IPF is characterized by ongoing fibrotic changes that gradually destroy lung tissue. Its clinical course is highly variable and unpredictable—some patients deteriorate rapidly and die within months, while others may remain relatively stable for years. The underlying cause remains unknown, giving rise to the term "idiopathic." Symptoms typically develop gradually, with most patients experiencing progressive shortness of breath and a persistent, dry cough. Additional features may include reduced appetite and weight loss. Overall, IPF carries a poor prognosis and is often fatal.

The approval is supported by data from two trials, which both included adults 40 years of age and older with IPF with or without background antifibrotic therapy (i.e., Ofev or Esbriet). Patients were also required to have a Forced Vital Capacity (FVC) greater than or equal to 45% of predicted normal. FVC is the maximum amount of air a person can forcefully exhale from the lungs after taking a deep breath. In IPF, scarring and fibrosis reduce lung elasticity, meaning FVC tends to decline over time.

Findings from one study showed that nerandomilast led to a slower decline in absolute change from baseline in FVC compared with placebo over 52 weeks of treatment. Jascayd performed significantly better than the placebo at slowing FVC decline after a year of treatment. Additionally, the study showed that it may reduce the risk of death for people with IPF. The second trial results showed that patients taking Jascayd, with or without background antifibrotic treatments, had a reduction in FVC at Week 12 of 91mL, which indicated a slower decline in FVC compared to placebo. In both trials, Jascayd demonstrated similar efficacy in patients with or without concomitant IPF treatments. However, in the FIBRONEER-IPF study, the data showed that participants taking pirfenidone did not experience a benefit from the 9-mg dose.

Jascayd may face competition from Tyvaso (treprostinil) as early as mid-2027, pending FDA approval. Jascayd is also currently under FDA review for another lung condition called progressive pulmonary fibrosis (PPF), with a decision expected late in 4Q 2025.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Rhapsido (remibrutinib)	Novartis	Oral	Bruton's tyrosine kinase inhibitor	Chronic idiopathic urticaria (CIU)*	Approved (09/30/2025)	$55,000 per year	Low

On September 30, 2025, the FDA approved Rhapsido, the first oral Bruton's tyrosine kinase (BTK) inhibitor for adults with chronic spontaneous urticaria (CSU) who continue to experience symptoms despite treatment with H1 antihistamines. This marks the first approved targeted oral therapy for CSU. CSU is a condition characterized by the development of recurrent wheals (hives), angioedema, or both for a period of six weeks or longer and the cause is unknown.

The approval was supported by two identical, 52-week trials, which enrolled patients with persistent CSU symptoms after standard or higher-dose second-generation H1 antihistamines. The primary endpoint—change from baseline to Week 12 in the 7-day urticaria activity score (UAS7), ranging from 0 to 42—was met in both studies. Both trials also showed that Rhapsido outperformed placebo on standard measures of itch, hive counts and overall disease activity at 12 weeks, with significantly more patients reporting control of symptoms after 2 weeks of treatment. Approximately one-third were free of itch and hives by week 12.

Beyond CSU, remibrutinib is being evaluated for several other immune-mediated conditions, including chronic inducible urticaria, food allergies, hidradenitis suppurativa, myasthenia gravis, and multiple sclerosis.

The 2022 treatment guidelines recommend Xolair® after inadequate response to standard-dose second-generation H1 antihistamines and after dose escalation up to four times the approved amount. Rhapsido and Dupixent® are expected to be incorporated in similar positions once guidelines are updated.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Keytruda Qlex (Berahyaluronidase Alfa; Pembrolizumab)	Merck & Co (MSD); Alteogen	Subcutaneous	Programmed cell death 1 (PD-1) inhibitor; Endoglycosidase	Kidney cancer; Bladder cancer; Melanoma; Biliary tract cancer; Cutaneous squamous cell carcinoma (CSCC); Non-small cell lung cancer (NSCLC); Colorectal cancer; Solid tumors*; Mesothelioma; Gastric cancer; Merkel cell carcinoma; Gastroesophageal junction cancer; Cervical cancer; Esophageal cancer; Liver cancer; Endometrial cancer; Squamous cell carcinoma; Urothelial cancer; Breast cancer	Approved (09/19/2025)	$204,500	Moderate

On September 19, 2025, the FDA approved Keytruda® Qlex, a subcutaneous formulation of pembrolizumab, in adult and pediatric patients 12 years and older with solid tumor indications approved for the IV formulation of pembrolizumab. Pembrolizumab is an anti-programmed cell death protein 1 (PD-1) treatment that increases the ability of the body's immune system to help detect and fight tumor cells. Currently Keytruda, as monotherapy or in combination with other agents, has over 40 indications approved across 18 types of cancer.

The approval was based on results from a trial which was conducted to evaluate the subcutaneous formulation versus the IV formulation in treatment-naïve, non-squamous NSCLC. The results demonstrated that subcutaneous pembrolizumab and berahyaluronidase alfa led to similar concentrations of the drug in the blood. Additionally, there were no significant differences in progression free survival, overall survival, overall response rate or pharmacokinetics.

Keytruda Qlex is the third FDA-approved SC checkpoint inhibitor, following Tecentriq® Hybreza and Opdivo® Qvantig.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Vonvendi (vonicog Alfa)	Shire; Takeda; Baxalta	Intravenous	Von Willebrand factor	Von Willebrand disease; Von Willebrand disease*	Approved (09/05/2025)	$28,500	Low

The FDA approved expanded use of Vonvendi for routine preventative use in adults 18 years and older for all types of von Willebrand disease (VWD), along with treatment of bleeding episodes and perioperative use in children with VWD. Previously, Vonvendi was approved only for on-demand treatment of bleeding episodes and perioperative use in adults and preventative use only in adults with Type 3 VWD, the most serious type. Von Willebrand disease is a bleeding disorder in which the blood does not clot properly due to a deficiency or defect in von Willebrand factor (VWF) protein.

Approval was based on several trials which demonstrated successful treatment control of bleeding episodes and the use of perioperative management in patients with VWD of all ages, along with success for prevention of bleeding episodes in adults with VWD.

Vonvendi is the only recombinant (non-plasma derived) VWF product approved for VWD, and this is the first recombinant VWF product approved for pediatric patients. Prior to this approval, only plasma derived VWF products were available to the pediatric population.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Wayrilz (rilzabrutinib)	Sanofi; Principia Biopharma	Oral	Bruton's tyrosine kinase inhibitor	Immune thrombocytopenia	Approved (08/29/2025)	$17,500 per month	Low

On August 29, 2025, the FDA approved Wayrilz for the treatment of adult patients with persistent or chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment. Wayrliz is the first Bruton's tyrosine kinase inhibitor approved for ITP and it is taken orally twice daily.

Chronic immune thrombocytopenia is an acquired autoimmune disorder characterized by a low platelet count due to the immune system attacking and destroying platelets, which are essential for blood clotting. Symptoms include bleeding, ranging from mild bruising to severe and potentially life-threatening bleeding in the GI tract, brain or urinary tract.

The approval was based on a trial in which patients initially received 12 weeks of treatment and patients who achieved platelet count response were eligible to continue treatment for the full 24 weeks. At the end of the 24 weeks, an open-label period followed. Patients received either rilzabrutinib or placebo twice daily. Concomitant ITP medications were allowed at stable doses. Following 24 weeks of therapy, 23% of participants in the BTK inhibitor arm met the criteria for a durable platelet response—platelet levels ≥50,000/μL at over eight of the final 12 measurement visits—while no patients in the placebo arm achieved this endpoint. In addition, patients who received Wayrilz experienced a faster time to first platelet response and longer duration of platelet response than those who received placebo. Rescue medication was required by 33% and 58% of patients receiving Wayrilz and placebo, respectively. Wayrilz recipients additionally showed a mean 10.6-point improvement across nine health-related quality-of-life metrics on the ITP questionnaire, compared with a 2.3-point improvement observed with placebo.

Wayrilz will likely be used after more established second-line products such as Nplate® (romiplostim), Doptelet® (avatrombopag maleate), Alvaiz® (eltrombopag choline), Tavalisse® (fostamatinib disodium), and Promacta® (eltrombopag olamine), which recently had generics introduced.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Dawnzera (donidalorsen Sodium)	Ionis Pharmaceuticals	Injectable; Subcutaneous	Antisense oligonucleotide	Hereditary angioedema	Approved (08/21/2025)	$747,000 for every 4 week regimen	Moderate

On August 21, 2025, the FDA approved Dawnzera for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients 12 years of age and older. Dawnzera is the first RNA-targeted therapy approved for HAE that reduces plasma prekallikrein (PKK) production by selectively targeting PKK messenger RNA (mRNA). By lowering PKK levels, donidalorsen prevents excessive bradykinin generation therapy reducing the frequency and severity of attacks.

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. It affects approximately 1 in 10,000 to 1 in 50,000 individuals in the United States. Treatment includes both on-demand therapy and prophylactic therapy. On-demand therapy is given to minimize the impact of an HAE attack and prophylactic therapy is given to certain patients to reduce the frequency and severity of attacks. Products for on-demand include Firazyr®, icatibant, Berinert®, Ekterly®, Kalbitor® and Ruconest®. Cinryze®, Haegarda®, Takhzyro®, Orladeyo, and Andembry are approved for prophylaxis.

The approval was supported by data from the OASIS-HAE trial, a 24-week trial that included 90 patients 12 years and older with HAE who had at least 2 confirmed attacks during the 8-week run-in period. Participants received either donidalorsen 80mg once every 4 weeks, donidalorsen 80mg every 8 weeks or placebo. Results showed an 81% reduction in HAE attack rate with donidalorsen every 4 weeks and a 55% reduction in every 8-week dosing, compared to placebo. When measured from the second dose of Dawnzera, the Q4W dosing reduced mean HAE attacks by 87% and moderate to severe attacks by approximately 90% versus placebo at Week 24.

Dawnzera is the third HAE treatment to enter the market this year, after Ekterly (sebetralstat, oral, on-demand) and Andembry (garadacimab, once-monthly subcutaneous injection for prophylaxis).

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Submission Type
LIB003 (lerodalcibep)	LIB Therapeutics	Subcutaneous	PCSK9 inhibitor	Atherosclerotic vascular disease risk due to hypercholesterolemia; Homozygous familial hypercholesterolemia (HoFH); Heterozygous familial hypercholesterolemia (HeFH)	Pending (12/12/2025)	BLA
MK-0616 (enlicitide decanoate)	Merck & Co (MSD) UCB	Oral	PCSK9 inhibitor	Hypercholesterolemia Heterozygous familial hypercholesterolemia (HeFH)	Phase III	NDA

Lerodalcibep is an investigational treatment aimed at lowering low-density lipoprotein cholesterol (LDL-C) in patients with atherosclerotic cardiovascular disease (ASCVD), or those at very high or high risk of ASCVD. The BLA also includes patients with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), and patients aged 10 years or older with homozygous familial hypercholesterolemia. Lerodalcibep is a novel, small protein-binding third-generation PCSK9 inhibitor, and has been developed as a more convenient, once-monthly, single small-volume, subcutaneous injection that will not require refrigeration at home or in travel.

The BLA was supported by data from multiple studies that evaluated the efficacy and safety of lerodalcibep. It encompasses 2,900 patients-including 2,300 patients that were on maximally tolerated statin and other oral agents that required further LDL-C reductions. In these trials lerodalcibep was dosed once monthly for up to 52 weeks, with over 2,400 patients having continued treatment in the 72-week extension study. The results showed that lerodalcibep demonstrated sustained LDL-C reductions of > 60% in patients with, or at very-high or high risk of, cardiovascular disease (CVD) and >50% in those with heterozygous familial hypercholesterolemia (FH) who have more severe LDL-C elevations.

Lerodalcibep will be used as an add on therapy to oral lipid lowering therapy and will compete most directly with the approved PCSK9 inhibitors, which include Repatha, Praluent, and Leqvio. The estimated cost is between $10,000 - $20,000 per year.

Enlicitide is an oral investigational PCSK9 inhibitor designed to block the PCSK9 protein's interaction with LDL receptors. This results in greater numbers of receptors available on the cell surface to remove LDL cholesterol from the blood. This is the same mechanism of action as current PSCK9 inhibitors, but in a daily pill form.

The Phase III study enrolled 2,912 adults. Patients either had a prior heart attack or stroke or were at intermediate to high risk for a first cardiovascular event. Almost all participants had a history of statin therapy, and all of them had LDL-C levels above recommended thresholds despite at least moderate- or high-intensity statin therapy; 26% were also taking ezetimibe. Participants received either enlicitide 20mg once daily or placebo for 52 weeks.

Results after 24 weeks showed that patients receiving enlicitide experienced a 55.8% greater reduction in LDL-C compared with placebo. Additionally, enlicitide also significantly reduced other atherogenic lipids including non-high-density lipoprotein cholesterol reduced by 53%; this is a combination of all types of cholesterol except for HDL (good cholesterol). A 50% reduction in apolipoprotein B, a protein that helps carry fat and various "bad" types of cholesterol throughout the body; a 28% reduction in lipoprotein a, a type of lipoprotein that is structurally similar to LDL, determined by genetics and a risk factor for heart disease.

Serious side effects were similar between enlicitide and placebo, 10% vs. 12%, respectively and a small proportion of participants.

Enlicitide may be the first oral PCSK9 inhibitor and will compete with other currently available injectable PCSK9 inhibitors, including the monoclonal antibodies (Praluent and Repatha) and RNA inhibitors (Leqvio). The estimated annual cost is expected to be approximately $15,000.

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 (12/28/2025)	NDA

Tolebrutinib is a brain-penetrant Bruton's tyrosine kinase (BTK) inhibitor under development for non-relapsing secondary progressive multiple sclerosis (nr SPMS) that aims to slow disability accumulation independent of relapse activity in adults. Multiple sclerosis is a chronic, inflammatory, immune-mediated disease of the central nervous system that disrupts the communication between the brain and body. Symptoms include vision problems, numbness, tingling fatigue, muscle weakness and balance and coordination issues. Non-relapsing secondary progressive MS is a type of MS in which symptoms slowly get worse with fewer or no relapses. This is typically diagnosed after the relapsing remitting phase, which has periods of aggressive flare ups, followed by periods of remission.

Tolebrutinib, an oral therapy, was given breakthrough therapy designation by the FDA based on positive data from the HERCULES trial. Results from the HERCULES trial showed that the risk of disability progression was 31% lower with tolebrutinib compared to placebo. Additionally, it increased the odds of six-month confirmed disability improvement by 88% and reduced the rate of new or enlarging lesions on MRI scans by 38%.

If approved, tolebrutinib would be the first BTKi for MS and the first therapy specifically approved for non-relapsing SPMS. The estimated annual cost is between $100,000-$200,000.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Submission Type
CORT125134 (relacorilant)	Corcept Therapeutics	Oral	Glucocorticoid antagonist	Cushing's syndrome	Pending (12/30/2025)	NDA

Relacorilant is a selective glucocorticoid receptor modulator in development for the treatment of Cushing's syndrome. It acts as a selective cortisol modulator, by binding to the glucocorticoid receptor but not to other hormone receptors in the body.

Cushing's syndrome refers to a constellation of symptoms that occur from chronic exposure to excess amounts of cortisol and can be caused by an abnormality in the adrenal or pituitary glands or by long term corticosteroid use or tumors in the body. The primary symptoms include weight gain, muscle weakness, acne, hypertension, hyperglycemia, fatigue, hyperhidrosis, fatty deposits, especially in the midsection, the face and between the shoulders and the upper back. It is more prevalent in females than in males.

Results from the GRACE study showed that treatment with relacorilant led to clinically meaningful improvements in hypertension, hyperglycemia, and other symptoms of Cushing syndrome such as body weight, waist circumference, and cognition. These results were supported by data from the confirmatory phase 3 GRADIENT trial, which also demonstrated improvements in a broad range of hypercortisolism signs and symptoms.

Its mechanism of action is unique compared to Korlym, another glucocorticoid antagonist, in that it has no affinity for the progesterone receptor; therefore, it does not cause antiprogesterone side effects including endometrial hypertrophy, irregular vaginal bleeding, and risk of pregnancy termination.

The estimated cost is approximately $650,000 - $750,000 per year.

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
NN9932 (semaglutide)	Novo Nordisk	Oral	Glucagon-like peptide-1 (GLP-1) agonist	Obesity*; Reduce cardiovascular mortality in patients with obesity*	Pending (4Q 2025)	NDA
LY3502970 (orforglipron)	Chugai Eli Lilly	Oral	GLP-1 agonist	Improve glycemic control in type 2 diabetes Obesity Sleep apnea Hypertension in obesity	Phase III	NDA

Wegovy is a GLP-1 receptor agonist (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.

NN9932, an oral version of 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 injectable GLP-1 agents such as Wegovy and Zepbound. In a study evaluating the safety and efficacy of Zepbound (tirzepatide) compared with Wegovy (injectable 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.

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 RA agents such as Saxenda, Wegovy, and Zepbound. Rybelsus, another oral GLP-1 receptor agonist approved in 2019 for managing blood sugar levels in Type 2 diabetes also contains semaglutide and while not FDA-approved for weight loss, clinical trials have shown it can lead to weight reduction.

The FDA also approved a label expansion for Rybelsus to reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes who are at high risk for these events. This makes Rybelsus the first and only oral glucagon-like peptide-1 receptor agonist with the MACE risk reduction.

On November 24, 2025, Novo Nordisk announced the top-line results from the trials investigating semaglutide in symptomatic Alzheimer's disease. They concluded that treatment with semaglutide resulted in improvement of Alzheimer's disease-related biomarkers in both trials, this did not translate into a delay of disease progression. The study was discontinued based on the efficacy results observed.

Orforglipron is an oral non-peptidic GLP-1 RA that is under investigation for both T2D and obesity. The trial compared orforglipron to oral semaglutide, assessing glycemic control and weight loss. Participants were randomly assigned in a 1:1:1:1 ration to receive either 12 mg or 36 mg of orforglipron or 7 mg or 14 mg of oral semaglutide.

Orforglipron lowered A1C by an average of 1.9% (12 mg) and 2.2% (36 mg) compared to 1.1% (7 mg) and 1.4% (14 mg) with oral semaglutide at 52 weeks. A secondary endpoint saw participants on the highest orforglipron dose achieve an A1C <5.7% compared to 12.5% taking the highest dose of oral semaglutide. Orforglipron was also superior to oral semaglutide for weight loss, as participants taking orforglipron lost an average of 14.6 lbs (6.7%; 12 mg) and 19.7 lbs (9.2%; 36 mg) compared to 7.9 lbs (3.7%; 7 mg) and 11 lbs (5.3%; 14 mg) with oral semaglutide. This represents a 73.6% greater relative weight loss at the highest dose comparison. It is also being studied for cardiovascular outcomes and obstructive sleep apnea indications.

Orforglipron is also being evaluated in patients with obesity or overweight with weight-related comorbidities without type 2 diabetes as well as patients with obesity or overweight with type 2 diabetes. Additionally, it is being investigated in the treatment of Obstructive Sleep Apneas in people with obesity or overweight and hypertension in people with obesity or overweight.

If oral semaglutide and orforglipron are approved for weight loss, they will be the only oral GLP-1 RAs available. In addition to the weight loss and A1C differences seen, oral semaglutide has strict mealtime requirements while orforglipron can be taken any time of day. The estimated cost of these agents is expected to be between $10,000 - $20,000 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	Type 2 Diabetes-Higher Doses (Phase III)
Ozempic	Alzheimer's Disease (Phase III) Peripheral Arterial Disease (Pending)
Zepbound	Non-alcoholic steatohepatitis (NASH) (Phase II) Chronic Kidney Disease (Phase II)

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Submission Type
Sogroya (somapacitan)	Novo Nordisk	Subcutaneous	Growth hormone	Small for gestational age (SGA); Short stature associated with Noonan syndrome; Idiopathic short stature	Pending (1Q 2026)	sBLA

Somapacitan is a human growth hormone analog first approved by the FDA in August 2020 for use in adults with growth hormone deficiency. It was then approved in April 2023 for the treatment of children aged 2.5 years and older who have growth failure due to inadequate secretion of endogenous growth hormone. It is now being investigated in the treatment of children 2 to 10 years of age with either Noonan syndrome (NS), Turner Syndrome (TS), idiopathic short stature (ISS) and born small for gestational age (SGA).

The study investigated treatment with once weekly Sogroya compared to once daily Norditropin, another growth hormone currently available. Results showed that in children born with SGA, Sogroya demonstrated superior annual heigh velocity (HV) compared to a lower dose of Norditropin (11 vs 9.4 cm/year) and was non-inferior to a higher dose (11 vs 11.1 cm/year). Sogroya was also found to be superior in children with NS (10.4 vs 9.2 cm/year). In children with ISS, Sogroya achieved non-inferior growth results, with both groups demonstrating 10.5 cm/year. Results for patients with TS are expected later this year. The safety profile of Sogroya was found to be similar to that of once-daily Norditropin.

Sogroya offers the convenience of once weekly administration and if approved, it would be the first once-weekly growth hormone product indicated for the treatment of short stature associated with conditions beyond GH deficiency.

The estimated annual cost is between $50,000 - $100,000.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Submission Type
Awiqli (insulin icodec)	Novo Nordisk	Subcutaneous	Insulin/insulin analog	Improve glycemic control in type 2 diabetes	Pending (03/2026)	BLA

Awiqli is being investigated as a once-weekly subcutaneous basal insulin analog for the treatment of adults with Type 2 diabetes. Novo Nordisk submitted the application for Awiqli in April 2023 for use in patients with either Type 1 or Type 2 diabetes.

In May 24, 2024, the FDA's Endocrinologic and Metabolic Drugs Advisory Committee (EMDAC) voted 7 to 4 that the benefits of Awiqli did not outweigh its risks for improving glycemic control in adult patients with T1D. The FDA cited concerns regarding the rate of hypoglycemia observed for the product in the ONWARDS 6 trial. In the trial, insulin icodec was associated with 50% to 80% more clinically significant or severe hypoglycemia compared to insulin degludec at Week 52.

The company decided to prioritize the resubmission in adults with Type 2 diabetes and a new trial for patients with Type 1 diabetes is planned. The ONWARDS clinical development program for once-weekly insulin icodec currently comprises of five phase 3a global clinical trials, involving more than 4,000 adults with type 2 diabetes.

The different trials showed that once-weekly insulin icodec had higher hemoglobin A1c reduction, with no significant difference in fasting plasma glucose compared with other insulin analogues. The percentage of time spent in the target glycemic range was comparatively similar between insulin icodec and the comparators. The subgroup analysis of once-weekly insulin icodec with individual insulin analogues (glargine U100 and degludec) showed that insulin icodec had similar efficacy with insulin glargine U100 but superior efficacy with higher HbA1c reduction with insulin icodec compared with insulin degludec.

The safety profile was comparable between insulin icodec and glargine U100, whereas insulin icodec reported higher incidence of hypoglycemia events and any adverse events when compared with degludec. Any adverse events and adverse events related to basal insulin were comparably similar in insulin icodec and comparators. The estimated cost, assuming 40 units per day is less than $5,000 per year.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Submission Type
RMC-6236 (daraxonrasib)	Revolution Medicines	Oral	Rat sarcoma (RAS) (ON) inhibitor	Pancreatic Cancer	Phase III	NDA

RMC-6236 is a potent, direct, multiselective RAS (ON) inhibitor designed to target oncogenic RAS mutations in pancreatic ductal adenocarcinoma. RAS drive mutations are present in nearly all pancreatic cancer cases. Daraxonrasib suppresses RAS signaling by blocking the interaction of RAS(ON) with its downstream effectors. It does so by targeting oncogenic RAS mutations that are common drivers of major cancers, including pancreatic ductal adenocarcinoma (PDAC), non-small cell lung cancer (NSCLC) and colorectal cancer (CRC).

PDAC is a type of pancreatic cancer and is the most common form of the disease. PDAC represents approximately 92% of all pancreatic cancer cases. Approximately 80% of PDAC cases are diagnosed at an advanced or metastatic stage due to lack of symptoms. Metastatic PDAC continues to be a leading cause of cancer-related deaths in the U.S., with a five-year survival rate of approximately 3%.

The trial is evaluating daraxonrasib with a G12X mutant PDAC, they are also evaluating the treatment in other cohorts with different mutations. They will be analyzing the progression-free survival and overall survival.

The Phase 1 results demonstrated a median PFS of 8.8 months in RAS G12X mutant PDAC and 8.5 months in broader RAS-mutant cohorts. The estimated primary completion date of the Phase III trial is June 2026. Based on these trial results, the company received one of the first FDA non-transferable vouchers under the new Commissioner's National Priority Voucher pilot program which began accepting applications in July. This program has the goal of accelerating the development and review of certain drugs and biological products, which typically can take between 10 to 12 months. Approval for daraxonrasib may occur less than 1 month after submission.

The cost of other RAS inhibitors, such as Krazati, is approximately $270,000 per year; however, the cost of daraxonrasib may be at a premium due to the preliminary clinical trial results, novel mechanism of targeting the RAS proteins, broader mutation coverage and the FDA priority voucher.

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

Itvisma® (Onasemnogene abeparvovec-brve) / Novartis

Route	Mechanism of Action	Proposed Indication	Approval (PDUFA) Date	Projected Estimated Cost
Intrathecal	Gene Therapy	Spinal Muscular Atrophy	11/24/2025	Estimated $2.5M per one-time treatment

On November 24, 2025, the FDA approved onasemnogene abeparvovec-brve, Itvisma, for patients aged 2 years through adulthood. Itvisma is the first gene-replacement therapy available for a broad SMA population beyond infancy and is approved for adolescents, teens, and adults living with spinal muscular atrophy (SMA) who have a confirmed mutation in the survival motor neuron 1 (SMN1) gene. SMA is a progressive neuromuscular disorder characterized by degeneration of motor neurons in the spinal cord, leading to muscle weakness, impaired mobility, respiratory complications, and loss of functional independence. Prior to this approval, gene-replacement therapy options were limited to infants and very young children, leaving a significant gap in treatment for older patients. Itvisma delivers a functional copy of the SMN1 gene using an adeno-associated viral (AAV9) vector. The therapy is designed to restore continuous SMN protein expression in motor neurons. By targeting the underlying genetic defect, Itvisma aims to stabilize and improve motor function as well as reduce disease progression.

Approval was supported by results from the Phase III STEER trial and the Phase IIIb STRENGTH study, which evaluated efficacy and safety across treatment-naïve patients and those transitioning from previous SMA therapies. In STEER, treatment-naïve patients with SMA Type 2 demonstrated significant gains in motor function. At 52 weeks, Itvisma improved Hammersmith Functional Motor Scale Expanded (HFMSE) scores by a mean of +2.39 points compared with +0.51 points in the sham group. Safety was comparable to controls. The most common side effects included were pneumonia and vomiting.

The STRENGTH trial evaluated individuals previously treated with risdiplam (Evrysdi®) or nusinersen (Spinraza®) for several years prior to switching to Itvisma. Across this population, Itvisma stabilized motor function, demonstrating a +1.05 point mean change in HFMSE through Week 52. Safety findings were consistent with STEER, with common side effects including common cold, pyrexia, and vomiting.

Itvisma is delivered via intrathecal injection as a single-dose and is expected to be available through neuromuscular centers and designated gene-therapy sites of care 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	2/8/2026	$2M–$3M (One time)

Hunter syndrome (MPS II) is a rare, X-linked lysosomal storage disorder caused by a deficiency of 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 AAV9 gene therapy designed to address both somatic and neurological disease by delivering a functional copy of the IDS gene to cells in the central nervous system and periphery, enabling endogenous IDS enzyme production and reducing GAG accumulation.

Interim data from Phase I/II/III trials have shown reductions in CSF and plasma GAGs, sustained IDS enzyme activity, and trends toward stabilization of neurocognitive function compared with natural history. Patients demonstrated improved biomarker profiles consistent with therapeutic effect. Safety to date has been favorable, with no unexpected serious adverse events reported. Additionally, new 12-month pivotal data released in September 2025 showed greater than 80% reductions in CSF heparan sulfate disaccharide D2S6 (HS-D2S6), continued IDS enzyme activity, and sustained neurodevelopmental stability. No new safety issues emerged during the 12-month follow-up.

In August 2025, the FDA completed pre-license and bioresearch monitoring inspections for the RGX-121 program with no observations, and no new safety concerns have been raised during the ongoing review. The FDA accepted the BLA under Priority Review with an original PDUFA date of November 9, 2025, later extended to February 8, 2026 to allow review of additional long-term data.

If approved, RGX-121 would be the first gene therapy for Hunter syndrome, offering a single-dose treatment that addresses both systemic and neurological disease manifestations.

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	3/28/2026	$3M - $3.5M

Severe Leukocyte Adhesion Deficiency-I (LAD-I) is a rare pediatric disease caused by mutations in the ITGB2 gene, which encodes the CD18 protein essential for normal leukocyte adhesion and immune response. Children with LAD-I experience severe, recurrent bacterial and fungal infections that respond poorly to antibiotics and antifungal therapies. Those who survive infancy often develop pneumonia, mouth ulcers, necrotic skin lesions, and bloodstream infections. LAD-I affects an estimated 800–1,000 children across the United States and Europe. The only potentially curative treatment is allogeneic stem cell transplantation, which carries substantial morbidity and mortality; without a successful transplant, survival beyond childhood is rare.

Marnetegragene is an investigational one-time autologous gene therapy that uses patient-derived stem cells genetically modified to deliver a functional copy of the ITGB2 gene. In a global Phase I/II study, marnetegragene demonstrated 100% overall survival at 12 months and throughout the 12–24 months of follow-up in all nine treated patients. Large reductions in clinically significant infections were observed compared with pretreatment history, along with resolution of LAD-I–related skin lesions and restoration of wound repair capability. The therapy was well tolerated, with no serious treatment-related adverse events reported.

The FDA first accepted the BLA for Kresladi with Priority Review in October 2023. In June 2024, the FDA issued a Complete Response Letter (CRL) requesting additional Chemistry, Manufacturing, and Controls (CMC) information. The company resubmitted the BLA in October 2025, and the FDA has assigned a new PDUFA action date of March 28, 2026, marking the second full review cycle for Kresladi.

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.

Recent FDA Approvals

Route	Mechanism of Action	Proposed Indication	Approval (PDUFA) Date	Projected Estimated Cost
Intravenous	Cell Therapy	Relapsed or refractory marginal zone lymphoma after two or more lines of systemic therapy	12/4/25	$450,000

FDA Expands Indication for Breyanzi for Relapsed/Refractory Marginal Zone Lymphoma

Breyanzi is a type of chimeric antigen receptor (CAR) T-cell therapy that uses the patient's own T-cells to promote T-cell activation, proliferation, and secretion of inflammatory cytokines, leading to targeted destruction of CD19-expressing cancer cells. Breyanzi was first approved in 2021 as a third-line or later treatment for large B-cell lymphoma, and in 2022 its indication was extended to include second-line therapy for certain B-cell malignancies.

On December 4, 2025, the FDA approved Breyanzi as the first CAR-T cell therapy for the treatment of adult patients with relapsed or refractory marginal zone lymphoma (MZL) who have received two or more prior lines of systemic therapy.

Breyanzi is administered as a one-time infusion following lymphodepleting chemotherapy. The approval was based on the results of the marginal zone lymphoma cohort within the TRANSCEND FL clinical trial. The primary outcome measure was overall response rate, with secondary endpoints including complete response rate, duration of response, progression-free survival, and safety. The trial demonstrated an overall response rate of 95.5%, while the complete response rate was 62.1%, with durable responses observed at a median follow-up of approximately 21.6 months. The most common adverse reactions included cytokine release syndrome (CRS), neurologic toxicities, cytopenias, fatigue, musculoskeletal pain, constipation, and infections.

Breyanzi is only available through a Risk Evaluation and Mitigation Strategy (REMS) program due to risks of fatal or life-threatening CRS and neurologic events.

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	TBD	$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 increasingly 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 myocardial pathology. Deramiocel is composed of cardiosphere-derived cells (CDCs), a type of stromal cell harvested from donor heart tissue. These cells 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 and granted it Priority Review. In July 2025, the FDA issued a Complete Response Letter (CRL), stating that the application did not demonstrate sufficient evidence of effectiveness and that certain Chemistry, Manufacturing, and Controls (CMC) issues remained unresolved. In August 2025, Capricor reported that inspection findings had been resolved. However, no new PDUFA date has been assigned. The company intends to resubmit the BLA after incorporating additional data from the ongoing Phase 3 HOPE-3 trial, with updated results expected in late 2025 or early 2026.

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 HOPE-2, 8 patients were assigned to deramiocel and 12 to placebo. The mean 12-month change from baseline in mid-level elbow function favored deramiocel (percentile difference 36.2%; 95% CI 12.7–59.7; difference 2.6 points; P = .014). Individuals who received deramiocel had an average 1.2% improvement in left ventricular ejection fraction (LVEF), with a more pronounced 3.0% increase among patients with baseline LVEF ≥45%. Reductions in left ventricular end-systolic volume (LVESV) and end-diastolic volume (LVEDV) indicated favorable cardiac remodeling.

Following HOPE-2, eligible participants who wished to continue treatment entered the open-label extension (OLE) study, receiving deramiocel every 3 months. Over three years, treated patients demonstrated a 3.7-point gain on the Performance of Upper Limb (PUL) scale versus external controls, indicating a slowing of skeletal muscle decline.

If approved, deramiocel would become the first cell therapy specifically indicated for DMD-associated cardiomyopathy and would be administered quarterly as a long-term 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.

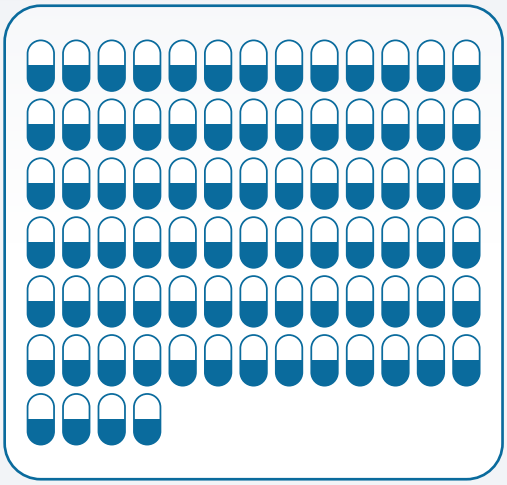
In May 2025, the FDA lifted the clinical hold on the Phase III ALLELE trial, allowing development to resume. Atara resubmitted the BLA in July 2025 and the FDA accepted it under Priority Review. A new PDUFA date has been set for January 10, 2026.

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.

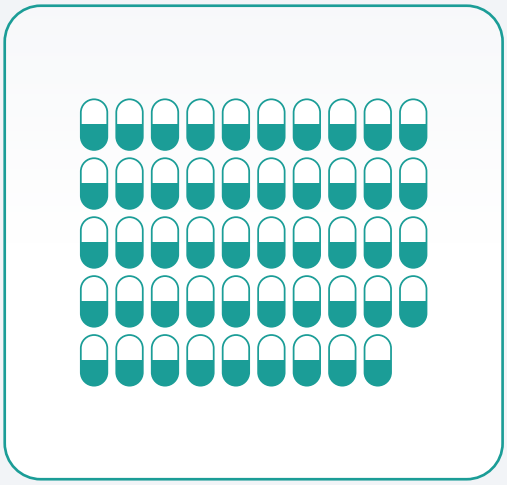
Ebvallo has already been approved in Europe in December 2022 for treating relapsed/refractory EBV+ PTLD in patients aged 2 years and older.

Biosimilars Pipeline

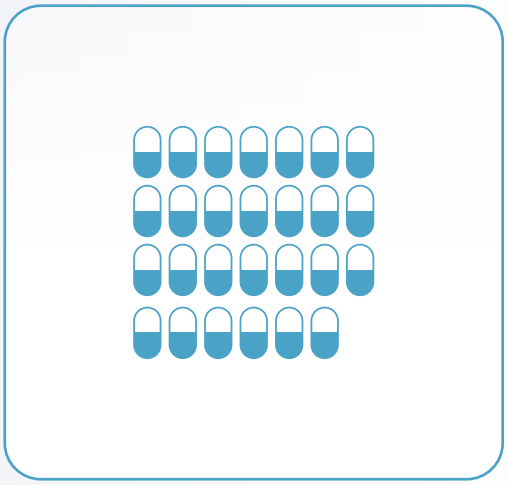
QUICK FACTS



82 FDA Approved Biosimilars to Date



49 Launched Biosimilars



27 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. This continues having biosimilars being able to gain an interchangeable designation while others are not seeking this labeling.

Recent FDA Approvals

FDA Approves Multiple Denosumab Biosimilars and New Interchangeable Products for Prolia® and Xgeva®

Throughout 2025, the FDA approved several additional denosumab biosimilars referencing Prolia® and Xgeva®, bringing the total number of approved denosumab biosimilars to 15.

Denosumab is a human monoclonal antibody that binds to RANKL, preventing activation of the RANK receptor on osteoclasts and inhibiting bone resorption. The following table summarizes the current FDA-approved denosumab biosimilars, including their reference products, approval dates, interchangeability status and pricing comparison:

Biosimilar	Reference Product	Approval Date	Interchangeable Designation	Discount to Reference Product
Ospomyv	Prolia	February 13, 2025	No	48%
Stoboclo	Prolia	March 4, 2025	Yes	5%
Conexxence	Prolia	March 25, 2025	Yes	3%
Bildyos	Prolia	August 29, 2025	No	55%
Bosaya	Prolia	September 16, 2025	No (Provisional interchangeability)	Not available
Enoby	Prolia	September 26, 2025	No	Not available
Osvyrti	Prolia	November 20, 2025	No	Not available
Wyost	Prolia / Xgeva	March 5, 2024	Yes	7%
Jubbonti	Prolia / Xgeva	March 5, 2024	Yes	14.5%
Xbryk	Xgeva	February 13, 2025	No	48%
Osenvelt	Xgeva	March 4, 2025	Yes	5%
Bomyntra	Xgeva	March 25, 2025	Yes	3%
Bilprevda	Xgeva	August 29, 2025	No	51%
Aukelso	Xgeva	September 16, 2025	No (Provisional interchangeability)	Not available
Xtrenbo	Xgeva	September 26, 2025	No	Not available
Jubereq	Xgeva	November 20, 2025	No	Not available

The denosumab products Prolia and Xgeva serve as the reference biologics for these biosimilars and are distinguished by their specific indications, dosing schedules, and formulations. Prolia is primarily used in the treatment of osteoporosis and other conditions involving bone loss. It is approved for use in postmenopausal women and men at high risk for fracture, as well as individuals receiving hormonal therapy for breast or prostate cancer that causes bone loss. Prolia is administered as a 60mg subcutaneous injection once every six months and is available in a prefilled syringe containing 60mg/mL.

Xgeva, on the other hand, is used in oncologic settings. It is indicated for the prevention of skeletal-related events in patients with bone metastases from solid tumors, multiple myeloma involving bone, giant cell tumor of bone (GCTB) in adults and skeletally mature adolescents, and for hypercalcemia of malignancy refractory to bisphosphonates. Xgeva is administered at a higher dose and more frequently at 120mg subcutaneously every 4 weeks and is available as a single-use vial containing 120mg/1.7mL (70 mg/mL).

Previous biosimilars approved include Wyost® and Jubbonti® were the first to receive interchangeability, followed by Stobocclo® and Osenvelt®. Conexxence® and Bomyntra® subsequently obtained full interchangeability designations as well. In addition to these six interchangeable products, Bosaya® and Aukelso® were granted provisional

interchangeability status. Together, these designations expand substitution options across both indications and facilitating potential cost saving opportunities.

These designations were supported by analytical and comparative clinical data, including pharmacokinetic, safety, and immunogenicity results from studies in postmenopausal women with osteoporosis demonstrating no clinically meaningful differences from the reference biologics.

No launch dates or pricing have been set for recently approved biosimilars.

FDA Approves Sixth Eylea® Biosimilar, Eydenzelt® (aflibercept-boav)

On October 13, 2025, the FDA approved Eydenzelt® (aflibercept-boav), an aflibercept biosimilar referencing Eylea® (aflibercept) for the treatment of neovascular (wet) age-related macular degeneration, macular edema following retinal vein occlusion, diabetic macular edema, and diabetic retinopathy. Eydenzelt is an anti–vascular endothelial growth factor (VEGF) inhibitor designed to block the growth and leakage of abnormal blood vessels in the retina, helping preserve vision in patients with retinal diseases.

Its approval was based on analytical, nonclinical, and clinical data demonstrating no clinically meaningful differences from Eylea in terms of pharmacokinetics, safety, efficacy, and immunogenicity. In a randomized, double-masked, multicenter phase 3 study in patients with diabetic macular edema, Eydenzelt met predefined equivalence criteria for the primary endpoint, change in best corrected visual acuity from baseline to week 8, and showed consistent trends across secondary endpoints.

Eydenzelt is the sixth aflibercept biosimilar, following Pavblu® (aflibercept-ayyh), Enzeevu® (aflibercept-abzv), Ahzantive® (aflibercept-mrbb), Yesafili® (aflibercept-jbvf), and Opuviz® (aflibercept-yszy). Like other aflibercept products, Eydenzelt is administered intravitreally as a 2 mg (0.05 mL of 40 mg/mL) injectable solution in a physician's office. The launch date and pricing for Eydenzelt has not yet been announced.

FDA Approves First Perjeta® Biosimilar, Poherdy® (pertuzumab-dpzb)

On November 18, 2025, the FDA approved Poherdy® (pertuzumab-dpzb), the first biosimilar to reference Perjeta® (pertuzumab). Poherdy is a HER2/neu receptor antagonist indicated for the treatment of HER2-positive breast cancer in adult patients. Specific indications include the following:

- HER2-positive metastatic breast cancer
- Used with trastuzumab and docetaxel
- For adults who have not previously received anti-HER2 therapy or chemotherapy for metastatic disease
- Neoadjuvant treatment of HER2-positive breast cancer
- For locally advanced, inflammatory, or early-stage HER2-positive disease
- Used with trastuzumab and chemotherapy
- Adjuvant treatment of HER2-positive early breast cancer
- For patients at high risk of recurrence
- Used with trastuzumab and chemotherapy

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

Approval of Poherdy was based on comprehensive analytical, structural, and functional comparisons demonstrating high similarity to Perjeta, with no clinically meaningful differences in safety, efficacy, pharmacokinetics, or immunogenicity. Clinical data included human pharmacokinetic similarity studies and comparative assessments in patients with early HER2-positive, hormone receptor–negative breast cancer in the neoadjuvant setting.

Adverse effects associated with Poherdy include risks of infusion-related reactions, cardiotoxicity, fetal harm, and hypersensitivity reactions. Other common adverse effects may include diarrhea, alopecia, neutropenia, nausea, fatigue, and rash.

No official launch date or pricing for Poherdy has been announced.

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).

Clinical data supporting Lucamzi demonstrated no clinically meaningful differences in efficacy, safety, immunogenicity, or pharmacokinetic profile compared with the reference product ranibizumab. Although therapeutic equivalence to Lucentis was confirmed across phase III and pharmacokinetic studies, Lucamzi does not carry an FDA interchangeability designation.

The FDA initially set an action date of October 21, 2025, for Lucamzi's BLA resubmission; however, they issued a Complete Response Letter (CRL) on October 19, 2025, citing unresolved manufacturing-site observations identified during re-inspection of a contract manufacturing facility. No issues were raised regarding the clinical or analytical components of the BLA.

Xbrane has since announced that it will re-submit the BLA in March 2026 following completion of corrective actions, with an anticipated six-month review timeline. As a result, the projected approval date is now expected in September 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. The application for BAT2506 also includes a request for the product to be designated as an interchangeable biosimilar. The estimated approval date is May 16, 2026.

GP40141 – Biosimilar to Nplate®

On August 25, 2025, new clinical data published in EJHaem showed that the romiplostim biosimilar candidate GP40141 demonstrated therapeutic equivalence to reference romiplostim (Nplate®) for the treatment of immune thrombocytopenia (ITP). Romiplostim, a thrombopoietin receptor agonist (TPO-RA), is widely used to stimulate platelet production in patients with persistent or chronic ITP.

The multicenter, single-blind, randomized controlled phase 3 trial evaluated GP40141 in 136 adults with persistent or chronic ITP. Patients were randomized 1:1 to receive either GP40141 or reference romiplostim for 26 weeks. The primary end point was the proportion of patients achieving a platelet response (≥50 × 10^9/L) at week 11. GP40141 met the predefined equivalence criteria: 78% of patients in the GP40141 group achieved a platelet response compared with 85% in the reference group. Durable platelet response rates, bleeding events, and overall safety outcomes were also comparable.

Adverse events occurred in 22 patients receiving GP40141 and 18 patients receiving the reference product, with no significant difference in the frequency or severity of AEs. The most common adverse event was petechiae, followed by mucosal bleeding.

If approved, GP40141 would become the first biosimilar to romiplostim. No FDA submission or anticipated approval date has been announced yet.

AscellaHealth®

ABOUT ASCELLAHEALTH

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.

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.

Our global expertise in specialty fulfillment, data analytics and patient support/HUB services allows us to streamline product launch, provide an ecosystem of financial support to our partners and ensure patients have access to therapies they need for better outcomes.

Visit **www.AscellaHealth.com**

1055 Westlakes Dr., Suite 200
Berwyn, PA 19312
877.389.9040
info@ascellahealth.com

AscellaHealth's Specialty Pharmacy is located in St. Louis, MO. AscellaHealth Europe is comprised of locations in Dublin, Ireland and Manchester, England.