AscellaHealth®

Specialty Drug Management:

Strategies to Effectively Control Costs Amid Escalating Prices

June 2025

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INTRODUCTION

The rising cost of specialty pharmaceuticals presents a growing concern for payers across the healthcare ecosystem. As more innovative and complex therapies enter the market, particularly in the areas of rare diseases—including autoimmune disorders, chronic conditions, and oncology and hematology-related conditions—the economic burden continues to expand. **Specialty drugs now account for over 50% of total prescription drug spending** despite serving a comparatively small percentage of the patient population. Without a strategic approach to cost containment, payers face increasing difficulty balancing access, affordability, and budget sustainability.

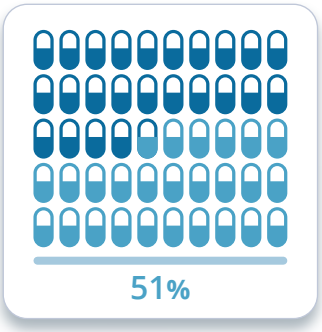
From optimizing site-of-care decisions to leveraging advanced analytics and implementing value-based contracts, this white paper will examine a range of challenges and actionable strategies for payers to manage specialty drug costs more effectively—with a core focus on integrating effective cost-control methods to improve clinical outcomes and increase member satisfaction.

OVERVIEW OF THE CURRENT SPECIALTY PHARMACEUTICAL LANDSCAPE

The specialty pharmaceutical market is experiencing remarkable growth, attributed to an increasing demand for targeted therapies that harness cutting-edge advancements in commercial life sciences. This surge is fueled by a combination of factors, including significant breakthroughs in drug development and supportive regulatory frameworks that facilitate expedited approvals for these types of treatments.

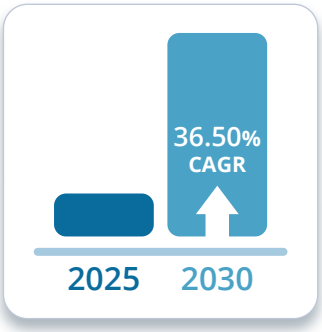
Key Trends and Statistics:

Specialty drugs now represent **51%** of healthcare costs, underscoring their dominant share in pharmaceutical expenditures (*IQVIA Institute, 2023*).



The cell and gene therapy (CGT) market, valued at **$3.22 billion in 2022**, is projected to reach **$25.58 billion by 2028**, with a compound annual growth rate (CAGR) of 41.25% (*Market Research Future, 2023*).

The broader specialty pharmaceutical market is anticipated to grow from **$16.03 billion in 2025** to **$75.94 billion by 2030**, representing a CAGR of 36.50% (*Grand View Research, 2023*).



As the specialty pharmaceutical market continues to evolve, it is crucial to comprehend the complex dynamics surrounding the introduction of new therapies. Specialty pharmaceuticals often entail intricate manufacturing processes that differ substantially from traditional medications. They may also require cutting-edge technologies, rigorous quality control measures, and robust supply chain management to ensure their effectiveness and safety.

Moreover, unique storage and handling requirements present additional challenges in the specialty pharmaceutical sector. Many therapies are sensitive to environmental factors such as temperature and light, necessitating precise conditions for transportation and storage to preserve their potency. These factors add layers of complexity that stakeholders must learn how to navigate, from manufacturers to patients and providers.

Personalized administration protocols are also an aspect to consider, as many specialty drugs are tailored to specific patient populations or individual genetic profiles. This personalized approach not only enhances treatment efficacy but also imposes specific logistical and healthcare delivery considerations, requiring ongoing collaboration among providers, pharmacists, and patients.

Specialty pharmaceuticals exist within a dynamic and multifaceted environment where technological innovation, regulatory direction, and patient-centric approaches represent the future of therapeutic development and delivery. Its steady market growth reflects an expanding pipeline of specialty treatments, particularly in gene therapies, immunotherapies, and biosimilars. However, it also introduces volatility in forecasting and payer planning, increasing the need for more refined and strategic cost management strategies.

DIFFICULTIES PAYERS FACE IN MANAGING SPECIALTY DRUG COSTS

The financial implications of the upward trajectory of specialty pharmaceuticals extend well beyond drug acquisition costs. Payers encounter a host of operational, clinical, and economic challenges as they navigate the evolving landscape, including:

Escalating Financial Burden: The rising cost of specialty drugs places direct pressure on payer budgets, with some therapies priced in the range of hundreds of thousands or even millions of dollars. This steep increase in costs makes affordability a major concern for payers looking to offer their members a fair balance of access and coverage.

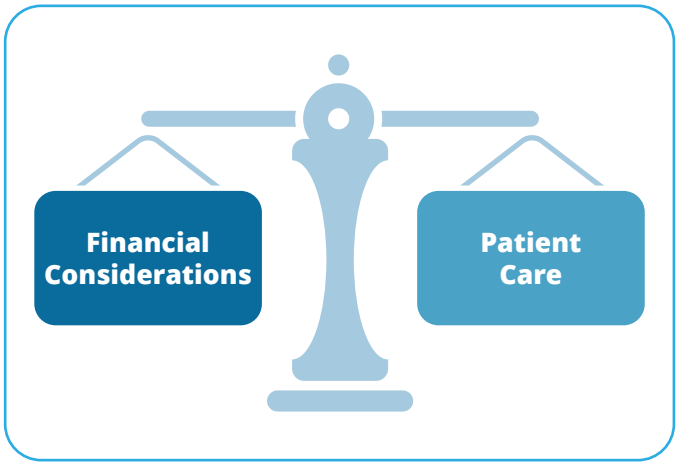
Increased Patient Demand: As awareness of new treatments grows, so does patient and provider demand—often before comprehensive coverage policies or reimbursement mechanisms are entirely in place. This surge of activity can overwhelm resources, especially when compounded with the administration of patient assistance programs.

Complexity of Therapy Management: Many specialty therapies require customized care coordination, prior authorization, specialized testing, or post-treatment monitoring. Managing these additional factors increases the administrative burden and raises the risk of delays, denials, and suboptimal therapeutic performance.

Market Access and Reimbursement Gaps: Novel therapies often launch before long-term clinical results are well-established. Without sufficient evidence of cost-effectiveness, payers may hesitate to offer broad-based coverage, resulting in limited access and potential disparities in care.

STRATEGIES TO HELP PAYERS CONTROL COSTS AND IMPROVE OUTCOMES

To effectively address the complex challenges associated with specialty drug management, payers must implement a comprehensive and integrated strategy that prioritizes stakeholder collaboration, operational efficiency, and data utilization. This multifaceted approach should be designed to not only control costs but also improve treatment outcomes. By applying best practices and adopting innovative solutions, payers can build a framework that balances financial considerations with a commitment to patient-centered care.



The following strategies outline a clear pathway for effectively managing costs while helping enhance the patient experience in the rapidly evolving specialty pharmaceuticals landscape.

Enhanced Operational Workflows

Streamlining operational processes can yield significant cost savings. By expediting claims processing, proactively managing prior authorizations, and centralizing case management, payers can significantly reduce delays, cut administrative waste, and improve the member experience. Efficient workflows enable payers to respond more effectively to the dynamic specialty pharmaceutical market.

Site of Care Optimization

Not all treatment sites carry the same cost or clinical suitability. By partnering with a progressive service provider like AscellaHealth, payers can utilize member-level data—including diagnosis, comorbidities, and geographic proximity—to direct care to the most cost-effective and clinically appropriate setting. For example, **shifting eligible infusions from hospital outpatient departments to ambulatory infusion centers or in-home care** can yield substantial savings without compromising standards of care or target health goals while at the same time improving patient satisfaction.

Patient-Centric Care Coordination

Comprehensive patient care coordination is vital in delivering effective specialty therapy management. Payers can streamline the patient journey by managing critical details such as referral logistics, appointment scheduling, and provider communication. This improved support leads to better treatment adherence, reduces the likelihood of missed appointments, and helps prevent inefficiencies and unnecessary visits to emergency care.

Collaborative Care Models

Integrating care delivery across stakeholders—payers, providers, specialty pharmacies, and patients—reduces friction points and fosters shared accountability. These collaborative models align therapy goals, reduce duplicative services and simplify communication. Cross-functional care teams are tasked with proactively managing side effects, monitoring adherence, and identifying cases where early intervention may be necessary. This improved approach to care delivery reduces waste and increases cost efficiency across the healthcare system.

Comprehensive Specialty Network

Establishing a broad specialty drug network ensures payers have access to new and breakthrough therapies, including limited distribution drugs. Centralizing procurement through a comprehensive specialty network provider like AscellaHealth—which provides 100% access to all specialty medications on the market—enables better pricing transparency, supports budgeting accuracy, and reduces delays in therapy initiation. This streamlined approach supports both clinical effectiveness and operational efficiency.

Value-Based Contracts (VBCs)

Value-based contracts (VBCs) effectively align financial incentives with the real-world success of therapeutic interventions. These agreements can include outcome guarantees, indication-based pricing, or bundled payment structures—prioritizing value over volume. By tying reimbursement to therapeutic effectiveness, VBCs enable payers to control healthcare costs while facilitating the adoption of therapies that demonstrate actual performance rather than the promise of performance. This shift fosters a more accountable healthcare environment and pharmaceutical marketplace and ensures patients receive the most effective treatments for their specific health conditions.

Leveraging Data and Advanced Analytics

Data-driven insights enable payers to make informed decisions regarding therapy selection, formulary placement, and member engagement. Real-world evidence (RWE) plays a crucial role in identifying cost-effective alternatives within therapeutic classes, supporting value-based decision-making. Additionally, predictive analytics and AI tools are becoming increasingly effective at recognizing patients at risk of non-adherence, enabling timely and targeted interventions.

PREPARING FOR THE FUTURE

As specialty drug innovation accelerates, it is crucial for payers to not only keep pace but also evolve their strategies to remain agile, efficient, and focused on patient needs. The future of specialty drug management will depend on the development of adaptive infrastructures and embracing predictive, proactive solutions that enhance decision-making and improve the overall quality and coordination of patient care.

To achieve this, organizations should look to partner with an experienced specialty pharmacy and healthcare solutions provider like AscellaHealth to help them transform their approach to specialty drug management across several key areas:

- **Advanced Utilization Management:** Modernizing utilization management protocols—through streamlined prior authorization, dynamic formulary design, and evidence-based therapy pathways—can reduce administrative burden while maintaining clinical efficiency. These enhancements help ensure the right patients receive the right therapies at the right time.
- **Investment in Patient Support Infrastructure:** Expanding services such as financial assistance, dedicated care coordination, medication counseling, and extended support can reduce non-adherence and improve overall patient success. In addition, leveraging proactive engagement tools (e.g., mobile apps or SMS reminders) can further reinforce long-term therapy adherence.
- **Monitoring Regulatory and Market Trends:** Staying ahead of new drug launches, biosimilar competition, and pricing legislation will be critical. Payers must strengthen internal capacity to quickly assess and respond to emerging therapies, particularly those with accelerated approval pathways. This flexibility will be essential to control costs and maintain clinical relevance in a rapidly evolving environment.

CONCLUSION

As the specialty drug market evolves, payers face a pivotal opportunity to redefine their approach to cost management. Rather than relying on traditional containment strategies, forward-leaning organizations must embrace integrated, data-informed, and patient-centered solutions. By enhancing operational workflows, optimizing care settings, building comprehensive networks, and investing in collaborative, value-based care models, payers can successfully manage costs while simultaneously improving clinical outcomes.

If your organization is struggling with rising drug costs amid an increasing demand for specialty treatments—look no further than AscellaHealth. As a trusted partner in Specialty Pharmacy Management, AscellaHealth provides flexible and scalable specialty pharmacy management solutions to optimize cost savings, streamline operations, and improve access to breakthrough treatments for your members.

- **Reduce Costs by Up to 50% with Site of Care Optimization*** – Transition patients from high-cost hospitals to ambulatory infusion centers (AICs) or home-based settings.
- **Ensure 100% Access to Specialty Therapies** – Gain full access to all Limited Distribution Drugs (LDDs) and Exclusive Distribution Drugs (EDDs).
- **Unlock Sustained Drug Savings with GPO Discount Management** – Including direct access to 60+ medical and pharmacy specialty drugs with no bundling requirements.
- **Gain Real-Time Financial Control with Integrated Claims Management** – Achieve full financial visibility and accurate claims processing powered by real-time data insights.
- **Deliver Seamless Patient Support with White-Glove Care Coordination** – Go beyond access with hands-on care coordination that guides patients from first call to final dose.

**Results will differ per client and per patient depending on the drug regimen and site of care utilized for infusion.*

Visit AscellaHealth.com or email us at businessdevelopment@ascellahealth.com to learn how our proven suite of solutions optimizes specialty drug management, reduces unnecessary costs, and supports enhanced patient experiences for your members.

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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.

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

AscellaHealth®

Specialty and Rare Pipeline Digest™

Q2 • 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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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

Recent Branded Specialty Drug Approvals

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Nucala (mepolizumab)	GSK	Subcutaneous	Interleukin 5 (IL-5) antagonist	COPD with eosinophilic bronchitis	Approved (05/22/2025)	$50,000	Moderate

On May 22, 2025, GSK announced the FDA approval of Nucala for an additional indication as add-on maintenance treatment for adults with inadequately controlled Chronic Obstructive Pulmonary Disease (COPD) and an eosinophilic phenotype.

COPD is a progressive inflammatory lung disease that includes chronic bronchitis and/or emphysema. A subset of patients with COPD also have an increase in blood eosinophils, a type of white blood cell that is a biomarker for inflammation.

Nucala is a subcutaneous IL-5 inhibitor that works by tamping down the inflammatory cascade, which in many diseases, such as COPD, is hyper-activated. Nucala is also approved for severe asthma, chronic rhinosinusitis with nasal polyps, eosinophilic granulomatosis with polyangiitis and hypereosinophilic syndrome.

Nucala's approval was based on data from the two trials in which Nucala showed a statistically significant reduction in the annualized rate of moderate/severe exacerbations vs. placebo in COPD patients with an eosinophilic phenotype when added to triple inhaled therapy. Triple therapy consists of an inhaled corticosteroid, a long-acting bronchodilator and a long-acting muscarinic antagonist. Some available triple therapy combination products include Trelegy Ellipta and Breztri Aerosphere.

Nucala is the only approved biologic evaluated in patients with an eosinophilic phenotype characterized by a blood eosinophil count (BEC) threshold as low as ≥150 cells/μL. Dupixent was the first biologic approved for COPD in patients with an eosinophilic phenotype with blood eosinophils ≥300 cells/μL. Approximately 70% of COPD patients in the US who are inadequately controlled on inhaled triple therapy and continue to exacerbate have a BEC starting at 150 cells/μL and above, representing over a million people at risk of exacerbations. Nucala will compete with Dupixent and Fasenra, which is currently in Phase 3 studies for eosinophilic COPD.

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
Vyvgart Hytrulo PFS	Argenx	Subcutaneous	FcRn antagonist	Myasthenia gravis; Chronic inflammatory demyelinating polyneuropathy (CIDP)	Approved (04/10/2025)	$330,000 for gMG and $870,000 for CIDP 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.

gMG 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 Phase 2/3 Vibrance-MG 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: argenx's Vyvgart (efgartigimod alfa-fcab) and Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase-qvfc), and UCB's 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.

On April 10, 2025, Vyvgart Hytrulo PFS received FDA approval for generalized myasthenia gravis (gMG). The Vyvgart Hytrulo PFS for self-injection is approved as a 20-to-30-second subcutaneous injection administered by a patient, caregiver, or healthcare professional. Patients are able to self-inject after proper instruction in subcutaneous injection technique.

gMG 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.

The approval of Vyvgart Hytrulo PFS for self-injection is supported by data from studies evaluating its bioequivalence to Vyvgart Hytrulo in a vial. This approval represented the first FcRn antagonist for gMG treatment option that may be self-administered. Additionally, Vyvgart Hytrulo was approved for the treatment of adult patients with chronic inflammatory demyelinating polyneuropathy.

Chronic inflammatory demyelinating polyneuropathy (CIDP) is a rare neurological disorder in which there is inflammation of nerve roots and peripheral nerves and destruction of the fatty protective covering (myelin sheath) of the nerve fibers. Myelin allows nerve fibers to transmit signals very rapidly (40-60 meters/second). Loss or damage to myelin can cause slowing or blockage of the nerve signals and can lead to loss of nerve fibers. This causes weakness, paralysis and/or impairment in motor function, especially of the arms and legs.

Vyvgart Hytrulo was initially approved on June 20, 2023, for the treatment of adult patients with gMG who are anti-acetylcholine receptor antibody positive. It is the first neonatal Fc receptor blocker approved for the treatment of CIDP. Approval for the CIDP indication was based on the Phase 3 ADHERE trial. Vyvgart Hytrulo-treated patients maintained a clinical response to treatment longer than those on placebo as evidenced by a statistically significant and clinically relevant reduction (61%) in risk of relapse.

Vyvgart PFS provides added flexibility in treatment and represents the first self-administered FcRn antagonist treatment option for gMG and CIDP.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Rinvoq (tablet) (upadacitinib)	AbbVie	Oral	Janus kinase (JAK) inhibitor	Giant cell arteritis (Temporal arteritis)	Approved (04/28/2025)	$82,000 per year	Low

The FDA approved Rinvoq tablet in April 2025 for an additional indication for the treatment of giant cel arteritis in adult patients. This is the 9th approved indication for Rinvoq. Other indications include atopic dermatitis, ulcerative colitis, Crohn's disease, ankylosing spondylitis, non-radiographic axial spondyloarthritis, polyarticular juvenile idiopathic arthritis, rheumatoid arthritis and psoriatic arthritis. Giant cell arteritis (GCA), also known as temporal arteritis, is an autoimmune disease that causes inflammation of the temporal and other cranial arteries, the aorta, and other large and medium arteries. If left untreated, the disease can lead to blindness, aortic aneurysm, or stroke.

Inflammation causes a narrowing or blockage of blood vessels, which interrupts blood flow. The symptoms of GCA can vary. Many people have severe headaches and scalp tenderness, particularly around the temples. GCA can affect eyesight, causing sudden vision loss or double vision. Blindness caused by GCA generally happens first in one eye but can also happen in the other eye if the condition is not treated.

The approval was supported by results from the Phase 3 trial which showed that 46% of patients taking Rinvoq 15mg once daily in combination with a 26-week steroid taper regimen achieved sustained remission from week 12 through week 52 compared to 29% of patients in the placebo group.

Systemic corticosteroids are the cornerstone treatment for GCA. The only other approved treatment is Actemra (tocilizumab), an interleukin-6 receptor antagonist. Novartis is evaluating Cosentyx to treat GCA and Tremfya failed a Phase 3 trial in June 2024 that was evaluating it to treat GCA. Rinvoq is the first JAK inhibitor approved to treat GCA.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Dupixent (dupilumab)	Sanofi; Genzyme; Regeneron	Subcutaneous	Interleukin 4 receptor (IL-4R) antagonist	Chronic idiopathic urticaria (CIU)*	Approved (04/18/2025)	$51,000 per year	Low

On April 18, 2025, the FDA approved Dupixent for the treatment of adults and pediatric patients >12 years of age with chronic idiopathic urticaria (CIU) who remain symptomatic despite antihistamine treatment. Dupixent is also approved for the following indications: atopic dermatitis, asthma, chronic rhinosinusitis with nasal polyps, eosinophilic esophagitis, prurigo nodularis and chronic obstructive pulmonary disease.

CIU is defined by the presence of hives daily or almost daily for at least six weeks. Patients typically present with recurrent, pruritic, wheal-and-flare lesions that fade within 24 hours without scarring. It has a peak incidence between the ages of 20 and 40 years, lasting one to five years in most patients, but longer in severe cases.

Approval is based on data from two phase 3 clinical studies which included biologic-naïve patients aged 12 years and older who were symptomatic despite the use of antihistamines and assessed Dupixent as an add-on therapy to standard-of-care antihistamines, compared to antihistamines alone. Patients demonstrated reductions in itch severity and urticaria activity compared to placebo at 24 weeks.

Dupixent competes with Xolair (the only other biologic currently approved for CIU), which is also indicated to treat patients > 12 years of age with CIU who are refractory to antihistamines. The cost of Dupixent is approximately $51,000 compared to Xolair at $73,000 per year.

Second generation antihistamines , such as Zyrtec, Claritin and Xyzal are the cornerstone treatment for CIU, however less than 50% of patients gain control with monotherapy. Additionally, leukotriene receptor antagonists, such as Singulair, Accolate, are also used as well as short term courses of corticosteroids.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
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

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.

Hemophilia is an X-linked genetic disease that interferes with the normal coagulation process, which causes bleeding into soft tissue, joints, and internal organs. There are several types of hemophilia, including hemophilia A and hemophilia B, with or without inhibitors; and the disease may be severe, moderate or mild based on the amount of clotting factors in the blood. Typically, treatment consists of administering intravenous clotting factors several times per week, to replace the missing clotting factors in the blood.

In ATLAS-A/B, males aged 12 years and older with severe hemophilia A or B without inhibitors 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.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Tremfya (guselkumab)	Johnson & Johnson (Janssen); MorphoSys	Intravenous; Subcutaneous	Interleukin 23 (IL-23) antagonist	Crohn's disease	Approved (03/20/2025)	$95,000 per year	Low

On March 20, 2025, Johnson & Johnson's Tremfya (guselkumab) received FDA approval for a label expansion for the treatment of adults with moderately to severely active Crohn's disease (CD). Tremfya is the first interleukin (IL)-23 inhibitor to offer both a subcutaneous (SC) and an intravenous (IV) induction option for this indication.

Crohn's disease is an inflammatory bowel disease that affects the lining of the digestive tract. It can cause abdominal pain, diarrhea, weight loss, anemia, and fatigue.

In the GALAXI 2 and GALAXI 3 studies, patients who received 200 mg of Tremfya IV at Weeks 0, 4, and 8 showed statistically significantly higher rates of clinical remission and endoscopic response at Week 12 than patients who received placebo. Additionally, Tremfya demonstrated superiority to Stelara (ustekinumab) across all pooled secondary endoscopic endpoints. Of the randomized patients, 52% had previously failed at least one biologic therapy. In the GRAVITI study, Tremfya 400 mcg SC at Weeks 0, 4, and 8 met the co-primary endpoints of clinical remission and endoscopic response at Week 12 versus placebo.

Tremfya was first approved in July 2017 for the treatment of moderate to severe plaque psoriasis. Since then, Tremfya has also received label expansions for the treatment of active psoriatic arthritis and moderately to severely active ulcerative colitis.

Other interleukin inhibitors that are currently available for the treatment of CD include Stelara, which now has several low cost biosimilars available, as well as Skyrizi and Omvoh.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Amvuttra (vutrisiran sodium)	Alnylam Pharmaceuticals	Subcutaneous	Small interfering RNA (siRNA)	Transthyretin amyloid cardiomyopathy (ATTR-CM)	Approved (03/20/2025)	$477,000 per year	Low

On March 20, 2025, Amvuttra was approved for the treatment of transthyretin amyloid cardiomyopathy (ATTR-CM), a rapidly progressive and fatal form of CM cardiomyopathy. Amvuttra is a TTR silencer, representing a novel mechanism of action to the category. It works by reducing the amount of a protein called transthyretin (TTR) in the body, which is misfolded and can lead to amyloid deposits in tissues, including nerves and the heart. The buildup of abnormal proteins is called amyloid deposits.

The expanded approval of Amvuttra was supported by results of the Phase 3 trial, in which Amvuttra reduced the risk of all-cause mortality and recurrent cardiovascular events by 28% versus placebo through the 36-month study period. Approximately 40% of patients were also receiving tafamidis at baseline, and benefit was shown in the Amvuttra arm for both the overall population (including those also on tafamidis) and for patients receiving only Amvuttra.

Amvuttra was first approved in June 2022 to treat adults with polyneuropathy of hereditary transthyretin-mediated amyloidosis (hATTR-PN). Amvuttra is the first drug approved to treat both hATTR-PN and ATTR-CM, and it is administered subcutaneously once every 3 months by a healthcare professional. Amvuttra joins Pfizer's Vyndaqel/Vyndamax and BridgeBio's Attruby, which are TTR stabilizers. Amvuttra is priced almost double of the currently available TTR stabilizer therapies.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Cost	Impact
Fabhalta (iptacopan)	Novartis	Oral	Complement inhibitors	C3 glomerulopathy	Approved (03/20/2025)	$566,000	Low

On March 20, 2025, the FDA granted a label expansion for Novartis' Fabhalta (iptacopan), an oral complement factor B inhibitor, for the treatment of adults with complement 3 glomerulopathy (C3G), to reduce proteinuria. Fabhalta is the first FDA-approved treatment for C3G, an ultra-rare, progressive kidney disease.

C3G is a rare disease that causes inflammation and damage to the kidney glomeruli, which are responsible for filtering blood and producing urine. In C3G, the complement system (proteins in the blood that play a critical role in the immune system) becomes abnormally activated. Complement products can become lodged in the glomeruli causing them to become leaky and harming their ability to filter blood. Waste products and toxins then build up in the blood, which decreases the kidneys' ability to balance salts and minerals, decreases urine production, and causes continued kidney damage.

Common symptoms of C3G include blood in the urine, protein in the urine (proteinuria), low levels of protein in the blood, high blood pressure, fatigue, swelling, and decreased kidney function. Approximately half the people affected with C3G develop kidney failure within 10 years of diagnosis.

The approval of Fabhalta for C3G was based on efficacy and safety data from the Phase 3 APPEAR-C3G study. The study included 74 adults with biopsy-confirmed native kidney C3G. The study was comprised of a 6-month randomized, double-blind period during which patients received Fabhalta 200 mg or placebo orally twice daily, followed by a 6-month period during which all patients received Fabhalta. The results showed that Fabhalta was superior to placebo in reducing proteinuria after 6 months of treatment.

This is the third approved indication for Fabhalta, which received initial FDA approval on March 26, 2024, for the treatment of adults with paroxysmal nocturnal hemoglobinuria (PNH). The dose of Fabhalta is the same (200 mg twice daily) in all three indications - PNH, IgA Nephropathy, and C3G.

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 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 ALIGN 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 Travere Therapeutics' 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
Ekterly (tablet) (sebetralstat)	KalVista Pharmaceuticals	Oral	Plasma kallikrein inhibitor	Hereditary angioedema (on demand)	Pending (06/17/2025)	NDA
IONIS-PKK-LRx (donidalorsen sodium)	Ionis Pharmaceuticals	Subcutaneous	Antisense oligonucleotide	Hereditary angioedema (prophylaxis)	Pending (08/21/2025)	NDA

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.

Sebetralstat is an investigational oral plasma kallikrein inhibitor under investigation for on-demand treatment of Hereditary Angioedema (HAE) attacks in adults and in patients aged 12 years and older. Sebetralstat is designed to reduce the molecule's levels by blocking the activity of kallikrein, the enzyme that produces bradykinin.

For sebetralstat, finding from the trial showed that patients experienced significantly faster symptom relief from HAE attacks as compared with placebo. The median time to beginning of symptom relief was reported to be 1.61 hours with sebetralstat 300mg, 1.79 hours with sebetralstat 600mg, and 6.72 hours with placebo. Additionally, participants receiving sebetralstat achieved a significantly faster time to reduction in attack severity and faster time to complete attack resolution compared to placebo.

Sebetralstat would be a more convenient oral option compared to current intravenous therapies, Ruconest and Berinert, and subcutaneous Firazyr or Kalbitor. The estimated yearly cost is $240,000.

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 months subcutaneous (SC) injection for the prevention of HAE 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
GS-6207 (twice-yearly) (lenacapavir)	Gilead	Oral; subcutaneous	HIV capsid inhibitor	Prophylaxis to reduce risk of sexually acquired HIV-1	Pending (06/19/2025)	NDA

Lenacapavir, a first-in-class inhibitor of HIV-1 capsid function, is being investigated as a twice-yearly injection for the prevention of HIV as pre-exposure prophylaxis (PrEP). It was previously approved in 2022 for multi-drug-resistant HIV treatment.

Lenacapavir is being evaluated in two separate trials with one trial analyzing lenacapavir in women and adolescent girls aged 16 to 25 years of age. They were assigned to receive twice-yearly lenacapavir, once daily oral Descovy (emtricitabine 200mg/tenofovir alafenamide 25mg), or once daily oral Truvada (emtricitabine 200mg/tenofovir disoproxil fumarate 300mg). Results showed zero infection was seen in the lenacapavir group, while 1.5% and 1.8% of patients in the Truvada and Descovy group contracted HIV, respectively. However, there were several patients in both the Truvada and Descovy group that were non-compliant with the medication, which could have contributed to the higher rates of infection.

The second study enrolled cisgender men, transgender women, transgender men, and gender nonbinary people aged 16 years and older who have sex with male partners and are at risk for HIV infection. Study participants were randomly assigned to receive lenacapavir or Truvada. Findings showed there were 2 HIV infections in the lenacapavir group, corresponding to 99.9% effectiveness. There were 9 incident cases in the Truvada group. Twice-yearly lenacapavir was found to be 89% more effective than once daily Truvada at preventing HIV infections.

The original approval of Descovy for PreP was based on a study which compared the efficacy and safety of Descovy to reduce the risk of acquiring HIV-1 infection in HIV-seronegative men or transgender women, comparing once daily Descovy to Truvada. Results showed that the rate of infection for the Descovy groups was 0.26% compared to a rate of 0.56% in the Truvada group. Additionally, the original approval of Truvada for PreP was based on a study which included HIV-seronegative men or transgender women. This study evaluated the safety and efficacy of Truvada compared to placebo. Of the 2,499 enrolled subjects, 1,251 received TRUVADA and 1,248 received placebo. The results showed that 3.8% of patients in the Truvada group became HIV-positive, compared to 6.7% in the placebo group. In addition to Truvada and Descovy, lenacapavir will also compete with injectable Apretude in this indication. Apretude is administered every other month; lenacapavir may be administered twice yearly for PrEP.

The yearly cost is projected to be between $20,000 -$50,000.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Submission Type
NP001 (sodium chlorite)	Neuvivo; Neuraltus Pharmaceuticals	Intravenous	Neuroprotective agent	Lou Gehrig's disease (amyotrophic lateral sclerosis (ALS))	Pending (2Q 2025)	NDA

ALS [also known as Lou Gehrig's disease] is a fatal, progressive, neurodegenerative disorder that affects upper and lower motor neurons. A loss of motor neurons in the brain and spinal cord initially leads to focal weakness, with muscle weakness spreading over time. Most patients will die of respiratory failure within 2-5 years of onset. The average survival rate for amyotrophic lateral sclerosis (ALS) from the time of diagnosis is 3-5 years, with an incidence in the United States of 2 newly diagnosed cases within a population of 100,000 people.

NP001 is an immunotherapy designed to restore balance within a dysfunctional innate immune system where pro- and anti-inflammatory processes are no longer in equilibrium. By regaining balance, NP001 may help slow the progression of ALS and preserve skeletal muscle function, including the diaphragm.

Only 3 therapies have been approved for ALS; riluzole, Radicava (IV and oral suspension), and Qalsody. None of the current therapies stop the progression of ALS, and they only modestly slow the progression of disease. Qalsody is approved for a rare genetic form of ALS, SOD1 ALS. Riluzole has shown to slightly increase overall survival (2-3 months) although it has not been shown to have an effect on physical functioning.

Radicava has not been shown to have an effect on overall survival at this time; however, it has been shown to have an effect on physical functioning. Although the FDA approved Radicava with a broad label for ALS, the early-onset ALS patients (those patients newly diagnosed with definite or probable ALS) had a greater magnitude of effect.

Three studies were completed to evaluate the safety and efficacy of NP001. The first study evaluated multiple doses of NP001 and the possible efficacy in patients with ALS. Results demonstrated that no significant benefit was seen with NP001 in ALS progression over a 6-month period. There was a slow Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R) scores decline in the NP001 treatment groups in patients with high systemic inflammation at baseline. In this subset of patients, there was a 41% reduction in progression with high-dose (2mg/kg) NP001 vs placebo, compared with 13% decrease for the group as a whole. In a subset of patients, symptom progression halted in a dose-dependent fashion: 25% vs 19% vs 11% in the 2 mg/kg, 1 mg/kg, and placebo groups, respectively.

In another trial, NP001 failed to meet the primary endpoint, showing no significant differences between placebo and active treatment with respect to change in ALSFRS-R scores or vital capacity (secondary endpoint). An analysis of participants with systemic inflammation who participated in the trials above also demonstrated that NP001-treated participants had a 36% slower decline in their ALSFRS-R scores over the six-month period compared with the placebo group.

NP001 did not show a significant benefit in ALS progression over a 6-month treatment period, however it did help to preserve lung function in the treatment group. If approved, NP001 would be the first disease-modifying treatment with a novel mechanism of action for patients with ALS having uncontrolled inflammation. The estimated annual cost is $100,000 - $200,000 per year.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Submission Type
Alhemo (concizumab)	Novo Nordisk; Dicerna Pharmaceuticals	Subcutaneous	Tissue factor pathway inhibitor (TFPI) antagonist	Hemophilia A or B*	Pending (07/2025)	BLA

On December 20, 2024, the FDA approved Novo Nordisk's Alhemo (concizumab-mtci), a tissue factor pathway inhibitor (TFPI) antagonist, to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients ≥12 years of age with hemophilia A (congenital factor VIII [FVIII] deficiency) with FVIII inhibitors or hemophilia B (congenital factor IX [FIX] deficiency) with FIX inhibitors.

It is now being investigated to expand its current indication to include the prevention or reduction of the frequency of bleeding episodes in adult and pediatric patients ≥12 years of age with hemophilia A (congenital factor VIII [FVIII] deficiency) without FVIII inhibitors or hemophilia B (congenital factor IX [FIX] deficiency) without FIX inhibitors in addition to those with inhibitors for hemophilia A and B.

Alhemo is the second TFPI antagonist approved for the treatment of hemophilia A and B. Unlike traditional hemophilia treatments that replace clotting factors, Alhemo reduces the amount, and therefore, the activity of, naturally occurring TFPI. This increases the amount of thrombin that is generated, which is expected to prevent or reduce the frequency of bleeding episodes.

The study evaluating the safety and efficacy of Alhemo in patients with hemophilia A and B without inhibitors included male patients 12 years of age or older who had severe hemophilia A, moderate or severe hemophilia B and did not have inhibitors. Additionally, these participants were on replacement treatment within 24 weeks before screening. After a pause due to non-fatal blood clots that arose in three patients, the study resumed. Patients were treated with either concizumab or on-demand clotting factor. The primary endpoint was the number of treated spontaneous and traumatic bleeding episodes for patient with hemophilia A and hemophilia B separately. Patients treated with concizumab, administered subcutaneously daily for at least 32 weeks using an injector pen reduced mean annualized bleeding rates by 86% in patients with hemophilia A and by 79% in patients with hemophilia B, compared with no prophylaxis.

The cost for a 70kg patient is approximately between $960,000 to 1.1 million annually.

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
SRK-015 (apitegromab)	Scholar Rock	Intravenous	Myostatin inhibitor	Spinal muscular atrophy	Pending (09/22/2025)	BLA

Apitegromab is an investigational muscle-targeted add-on treatment being developed to provide improvement in motor function for people living with spinal muscular atrophy (SMA) who are receiving an SMN-targeted treatment such as Evrysdi and Spinraza. It is the first add-on treatment designed to boost patients' muscle strength by targeting the muscle protein myostatin.

SMA is a genetic disorder that causes progressive muscle weakness and wasting due to the loss of motor neurons in the spinal cord. It is caused by a mutation in a gene which leads to insufficient levels of the SMN protein, which is essential for motor neuron survival. Myostatin is primarily present in skeletal muscles to inhibit muscle growth, helping to maintain a balanced and healthy muscle mass under typical conditions. Apitegromab works by selectively binding to the precursor of myostatin, preventing its conversion into its active form. By reducing levels of mature myostatin, apitegromab should increase muscle mass and improve motor function in people with SMA.

The efficacy and safety of apitegromab was based on a trial of 188 people with SMA who were on stable treatment with Spinraza or Evrysdi, were unable to walk, but could sit independently. A total of 156 patients ages 2 to 12 were assigned to apitegromab at 10mg/kg or 20mg/kg or a placebo intravenously every 4 weeks for 12 months. The remining 32 patients, ages 13 to 21, were assigned to apitegromab at 20mg/kg or placebo intravenously every 12 months. Results showed that patients treated with either dose of apitegromab demonstrated a statistically significant and clinically meaning improvement in motor function compared to placebo, and treatment was well tolerated.

Apitegromab will be used as additive therapy to patients who are currently on either Evrysdi or Spinraza treatments. There is not current information available on the use in patients who have received the gene therapy SMA treatment, Zolgensma. The estimated annual cost is between $250,000-$500,000. This therapy cost would be additional to the current annual cost of Evrysdi or Spinraza therapy (i.e., $427,000-$475,000).

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Submission Type
Kerendia (finerenone)	Bayer	Oral	Mineralocorticoid receptor antagonist	Heart failure*	Pending (3Q 2025)	sNDA

Finerenone is a non-steroidal, selective mineralocorticoid receptor antagonist that has been shown to block the harmful effects of the overactivated mineralocorticoid receptor (MR) system. MR overactivation is a major driver of heart and kidney damage. In 2021, Kerendia was approved to reduce risk of kidney function decline, kidney failure, cardiovascular death, non-fatal heart attacks, and hospitalization for heart failure in adults with Chronic Kidney Disease associated with Type 2 diabetes.

Kerendia is now being investigated in the treatment of patients with heart failure with a left ventricular ejection fraction (LVEF) of ≥40%. Ejection fraction is a condition in which the left side of the heart stiffens and cannot pump blood properly. Nearly 7 million people in the United States are affected by heart failure.

The trial evaluating the safety and efficacy of finerenone included over 6,000 patients aged 40 and over with symptomatic mildly reduced (HFmrEF) or preserved ejection fraction (HFpEF) heart failure with LVEF ≥40%. Patients were randomized to receive either finerenone at a maximum dose once daily or placebo, in addition to existing background therapy. Results showed that Kerendia significantly reduced the risk of cardiovascular death and total heart failure events, which are defined as hospitalizations or urgent visits, by 16% over a median duration of 32 months compared with placebo. Kerendia also significantly reduced total heart failure events and improved patient-reported outcomes.

If approved, finerenone would be the first non-steroidal, selective mineralocorticoid receptor (MR) antagonist for the treatment of HF. Currently, generic MR antagonists, spironolactone and eplerenone, are guideline-recommended treatments for HfrEF and HFpEF. The annual cost is estimated to be around $10,000.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Submission Type
Tremfya (guselkumab)	Johnson & Johnson (Janssen); MorphoSys	Intravenous; Subcutaneous	Interleukin 23 (IL-23) antagonist	Ulcerative Colitis	Pending (09/2025)	sBLA

Tremfya is a monoclonal antibody that targets IL-23 and is being investigated for the induction treatment of ulcerative colitis in adults. Tremfya is currently approved for plaque psoriasis, psoriatic arthritis, moderate to severely active Crohn's disease and moderate to severe ulcerative colitis.

Ulcerative colitis (UC) is a chronic disease of the large intestine, in which the lining of the colon becomes inflamed and develops tiny open sores, or ulcers. This condition is the result of your immune system's overactive response. It is a form of inflammatory bowel disease (IBD).

In the study evaluating subcutaneous induction therapy in adults with moderately to severely active UC, investigators found that patients treated with guselkumab 400 mg subcutaneous induction followed by 100 mg every 8 weeks or 200 mg every 4 weeks as maintenance therapy demonstrated clinical remission at 35.3% and 36.4%, respectively, compared with the placebo at 9.4%. Clinical response was seen at 63.3% and 61.4%, respectively, compared with 30.9% for the placebo. Further, symptomatic remission was 54.7% and 50%, respectively, and endoscopic improvement was 40.3% and 45%, respectively, compared with the placebo at 25.2% and 12.2%, respectively.

In the long-term extension study, investigators found that 72% of patients were in clinical remission, with 99% of patients remaining corticosteroid-free for 8 or more weeks, and 43% were in endoscopic remission at 92 weeks.

Stelara, an IL-12 &-23 antagonist, also developed by J&J, now has several significantly less expensive biosimilars market available. Tremfya will be entering a very crowded market in the UC space. If approved, Tremfya will be the only IL-23 inhibitor with a fully SC induction and maintenance regimen. The cost is projected to be approximately $100,000 annually.

Brand (Generic)	Manufacturer	Route	Mechanism of Action	Indication	Stage	Submission Type
Zepbound (tirzepatide)	Eli Lilly	Subcutaneous	Glucagon-like peptide-1 (GLP-1) agonist; Glucose-dependent insulinotropic polypeptide (GIP) receptor agonist	Heart failure in patients with obesity*	Withdrawn	sNDA
Wegovy (semaglutide)	Novo Nordisk	Subcutaneous	Glucagon-like peptide-1 (GLP-1) agonist	Heart failure in patients with obesity* Non-alcoholic steatohepatitis (NASH)	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

Tirzepatide is a long-acting agonist of glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptors, approved by the U.S. Food and Drug Administration for treatment of Type 2 diabetes for weight management in people with overweight or obesity. On December 20, 2024, the FDA approved tirzepatide under the brand name Zepbound for moderate to severe obstructive sleep apnea and obesity, and on November 8, 2023 for the treatment of adults with obesity or those who are overweight who also have a weigh-related comorbid condition. On May 13, 2022, the FDA approved tirzepatide under the brand name Mounjaro to improve blood sugar control in adults with type 2 diabetes (T2D), as an addition to diet and exercise. On May 1, 2025, Eli Lilly announced that it withdrew its FDA application for tirzepatide for the treatment of heart failure with preserved ejection fraction in patients with obesity. The withdrawal followed discussions with the FDA indicating it would require an additional confirmatory clinical trial to support the application.

Wegovy is a GLP-1 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 two 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.

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.

Wegovy is also currently being investigated for the treatment of heart failure in patients with obesity and it is also being investigated as monotherapy in non-alcoholic steatohepatitis (MASH/NASH). Part 1 of the study, which included 800 adults with MASH with stage 2 or 3 fibrosis, were randomized to receive either placebo or semaglutide 2.4mg SC once weekly in addition to standard of care. The trial showed that 37.0% of patients in the semaglutide arm versus 22.5% of those in the placebo arm achieved improvement in liver fibrosis with no worsening of steatohepatitis, and 62.9% of patients in the semaglutide arm versus 34.1% of those in the placebo arm achieved resolution of steatohepatitis with no worsening of liver fibrosis. The trial is ongoing and will evaluate semaglutide 2.4 mg in a total of 1,200 adults for 240 weeks. 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.

Novo announced that 32.8% of patients receiving semaglutide 2.4 mg achieved both resolution of MASH and improvement in fibrosis. Additionally, they noted that 88% of semaglutide patients had stayed on the drug at week 72 and that 75% of those patients were on the 2.4 mg dose. Approval is expected by the 3Q 2025.

Given its favorable glycemic and weight loss profile, semaglutide will likely be an attractive treatment option if approved and would compete with Rezdiffra. If approved, the anticipated annual cost of Wegovy therapy for MASH would be significantly less than Rezdiffra, $17,500 vs $50,000, respectively.

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 as the only GLP-1 RA 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 fee 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 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. Rybelsus would be an additional oral GLP-1 RA treatment option for MACE risk reduction in people with T2D and established CVD and/or CKD. The projected annual cost is approximately $12,000.

GLP-1 label expansion is expected and other potential future uses potentially 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) Heart failure in patients with obesity (Phase III) Chronic Kidney Disease (Phase II)

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; Heterozygous familial hypercholesterolemia (HeFH)*; Homozygous familial hypercholesterolemia (HoFH)	Pending (12/12/2025)	BLA

Lerodalcibep is a novel small protein with a high affinity for PCSK9, a protein in the liver that helps regulate LDL cholesterol levels. By blocking the PCSK9, it allows the body to more effectively clear LDL cholesterol from the bloodstream.

The trial enrolled 922 patients and just over half had not yet had a heart attack or stroke but were at high or very high risk for one. Patients were randomly assigned to one of two groups: two-thirds received monthly treatment with 300mg (1.2ml) of lerodalcibep and one-third a monthly dose of a matching placebo. Both groups continued their diet and existing cholesterol-lowering medications. At one year, 824 patients (89%) had completed the study, with a similar dropout rate in both the lerodalcibep and placebo groups. Patients assigned to lerodalcibep achieved an average placebo-adjusted percentage reduction in LDL cholesterol between 56% (at week 52) and 63% (the average of weeks 50 and 52). More than 90% of patients in the lerodalcibep group achieved a reduction of 50% or more in their LDL cholesterol levels and attained the target LDL cholesterol level for their risk group during the 52-week study. In the placebo group, 16% of patients achieved both goals.

Among patients treated with lerodalcibep, levels of apolipoprotein B—a protein that transports LDL cholesterol through the bloodstream—fell by an average of 43% and levels of lipoprotein (a), another "bad" cholesterol variant that contributes to cardiovascular risk, fell by 33%.

Lerodalcibep will be used as an add on therapy to oral lipid lowering therapy and will compete with the other approved PCSK9 inhibitors, Repatha, Praluent and Leqvio.

The LIBerate-003 (LIBerate-HoFH) study evaluated lerodalcibep vs Repatha (evolocumab) in 65 patients with HoFH. Findings showed mean reduction in LDL-C was -9.6% with lerodalcibep and -11.7% with evolocumab. LDL-C responses were reported to be highly variable but similar with both treatments in individual participants.

Additionally, on May 29, 2024, the LIBerate-VI study comparing lerodalcibep vs Leqvio (inclisiran) showed that the LDL decreased from baseline with lerodalcibep by 53% compared to 45.3% with inclisiran. More patients achieved the EAS/ESC targets with lerodalcibep than with inclisiran of >50% reduction in LDL-C from baseline (62% vs 50%) and LDL-C target of <55 mg/dL (67% vs 50%).

Praluent and Repatha are monoclonal antibodies that are administered via subcutaneous injection every two to four weeks. Leqvio, on the other hand, employs a small-interfering RNA technology to decrease PCSK9 production in the liver. The estimated cost is projected to be $10,000-$20,000 per year.

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 antagonist, meaning it blocks the activity of cortisol without affecting other hormone receptors. It is being investigated as a treatment for Cushing's syndrome, a condition caused by prolonged exposure to high levels of cortisol.

Cushing's syndrome is a hormonal disorder caused by prolonged exposure to high levels of the hormone cortisol. The syndrome can cause a wide variety of symptoms, which include fatty hump between the shoulders, a rounded face and pink or purple stretch marks on the skin. It can also lead to high blood pressure, bone loss, and in some cases type 2 diabetes.

The trial was a 2-part clinical trial, with the first part being an open-label phase where 152 patients with Cushing's syndrome and either hypertension, hyperglycemia, or both received relacorilant for 22 weeks. In the first portion of the trial, 63% of patients with hypertension met the study's response criteria, with use associated with rapid and sustained improvements for both systolic and diastolic blood pressure at 22 weeks. Among those with hyperglycemia, all patients achieved clinically meaningful and statistically significant improvements in glucose metabolism, with 50% meeting the study's response criteria.

The second part of the trial consisted as a double-blind, randomized, withdrawal period, with the maintenance of blood pressure control serving as the primary outcome of interest. In this portion of the trial, patients who met response criteria in the first part of the trial were randomized 1:1 to continue relacorilant or switch to placebo therapy for 12 weeks.

Results indicated loss of blood pressure control was 83% less likely to occur among patients relieving relacorilant compared to placebo. Investigators pointed out similar blood pressure trends to part 1 of the trial, with results favoring use of relacorilant over placebo therapy for 24-hour systolic and diastolic blood pressure, daytime systolic and diastolic blood pressure, and nighttime systolic and diastolic blood pressure.

If approved, relacorilant will be an alternative therapy for Korlym since it does not bind to the progesterone receptor and may minimize progesterone related adverse effects such as vaginal bleeding, uterine thickening and pregnancy complications . The estimated annual price is between $400,000-500,000.

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

Fitusiran (Qfitlia)/Sanofi Pharmaceuticals

Route	Mechanism of Action	Proposed Indication	Approval (PDUFA) Date	Projected Estimated Cost
Subcutaneous	Gene Therapy	Hemophilia A and B	3/28/2025	$750,000 - $1M Annually

Hemophilia is an X-linked recessive genetic disorder that primarily affects males, although in rare cases, females can have the disorder. It is caused by mutations in the genes that encode coagulation factors. This causes bleeding into soft tissue, joints, and internal organs. There are two types of hemophilia: hemophilia A is caused by a deficiency in coagulation factor VIII (FVIII), and hemophilia B is caused by a deficiency in coagulation factor IX (FIX).

Depending on severity and bleed frequency, patients with hemophilia A may receive prophylaxis with IV infused FVIII products or Hemlibra, a subcutaneous administered bispecific antibody designed to mimic the function of FVIII. About 30% of patients with severe hemophilia A and 3%–13% of patients with mild or moderate hemophilia A develop antibodies to FVIII, known as inhibitors. Patients with inhibitors are treated with Hemlibra or with high-dose FVIII in combination with blood products that bypass the inhibited clotting factors. Hemophilia treatment options include factor replacement therapies and extended life factor replacement therapies (e.g., Altuviiio), Hemlibra and the recently approved tissue factor pathway inhibitors (i.e., Alhemo, Hympavzi) or gene therapies (i.e., Roctavian, Hemgenix) that address the underlying genetic cause.

Fitusiran is a gene therapy that contains small interference RNA (siRNA) therapy, as a treatment option for hemophilia A and B patients, regardless of their inhibitor status. Positive results from the ATLAS clinical development program were published in April 2023. The ATLAS-INH study is a randomized, open-label Phase III study designed to evaluate the safety and efficacy of fitusiran in males ≥12 years with severe hemophilia A or B with inhibitors to factor VIII or IX. Patients receiving on-demand treatment with bypassing agents (BPA) were randomized to receive fitusiran prophylaxis or continue with on-demand BPA. The primary endpoint was annualized bleeding rate. Results have shown that 66% of fitusiran-treated patients experienced zero monthly bleeding episodes, compared to 5% of control patients who were treated with an on-demand bypassing agent.

ATLAS-A/B is a Phase III randomized, open-label study investigating the efficacy and safety of fitusiran in males ≥12 years with severe hemophilia A or B without inhibitors who had previously been treated with on-demand clotting factor concentrates. Patients were randomized to receive fitusiran or on-demand clotting factor concentrates. The primary endpoint was annualized bleeding rate. Fifty-one percent of those receiving fitusiran showed zero monthly bleeding episodes, compared to 5% of those treated with on-demand clotting factors.

Fitusiran carries a boxed warning for potentially serious adverse reactions, including thrombotic events, acute and recurrent gallbladder disease, and hepatotoxicity. An additional warning noted liver toxicity and the need to monitor liver blood tests. The most commonly reported side effects occurring in more than 10% of patients were viral infections, nasopharyngitis, and bacterial infections.

Fitusiran is likely to compete with other hemophilia agents. Fitusiran differs from other gene therapies, as it is administered monthly via a SC injection, while many gene therapies such as Roctavian offer one-time infusions for long-term clotting factor production. Compared to non-gene therapy options, many of these agents require frequent infusions often on multiple doses per week, weekly or biweekly basis. Fitusiran's monthly dosing could provide a less frequent dosing option for patients. Fitusiran provides another long-acting prophylactic therapy treatment option for individuals with hemophilia A or B.

Gene Pipeline

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

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.

Mozafancogene has fast track, rare pediatric, and orphan drug designations. Rocket has initiated a rolling Biologics License Application (BLA) for RP-L102.

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. Rocket has already met with FDA leaders from the Center for Biologics Evaluation and Research (CBER) to resolve and provide additional CMC information needed to support the drug's approval. It is unclear when the new anticipated approval date will be.

If approved, Kresladi would be the first therapy available for patients with severe LAD-I without the need for a matched donor, as well as the first FDA-approved therapy for this indication.

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

Prademagene zamikeracel (Zevaskyn)/ Abeona Therapeutics

Route	Mechanism of Action	Proposed Indication	Approval (PDUFA) Date	Estimated Cost
Intravenous	Cell Therapy	Recessive dystrophic epidermolysis bullosa	4/29/2025	$1M - $2M Annually

Prademagene zamikeracel is an investigational autologous epidermal cell sheet therapy for patients 6 years of age and older with recessive dystrophic epidermolysis bullosa (RDEB). Dystrophic epidermolysis bullosa is a genetic disorder caused by mutations in the COL7A1 gene, leading to fragile skin that blisters and scars easily, with severe forms also affecting internal linings like the esophagus.

The condition can be inherited dominantly or recessively, with RDEB being more severe and associated with complications like chronic wounds, scarring, and a heightened risk of aggressive skin cancer. Current management of DEB consists of wound care, pain management, and infection prevention. Available pharmacologic agents include Vyjuvek™ and Filsuvez™.

Prademagene zamikeracel is manufactured for each patient from autologously derived keratinocytes that are corrected with functional COL7A1 genes using an AAV vector. The corrected cells are grown as cultures, then surgically transplanted once as cell "sheets" onto the patient's wounds to enable normal Type VII expression and skin function.

On April 22, 2024, Abeona announced that it received a complete response letter (CRL) from the FDA regarding the BLA for prademagene zamikeracel for the treatment of RDEB. The FDA requested additional information regarding certain manufacturing testing methods to satisfy Chemistry Manufacturing and Controls (CMC) requirements before the BLA can be approved. On August 8, 2024, Abeona shared data and reports addressing almost all deficiencies noted in the CRL. In October 2024, Abeona resubmitted its BLA to the FDA, addressing the CMC requirements outlined in the FDA's complete response letter. This BLA was accepted by the FDA in November 2024 and prademagene zamikeracel was approved in April 2025.

The approval of prademagene zamikeracel is based on the pivotal phase 3 VIITAL study, which met its coprimary efficacy endpoints, demonstrating statistically significant healing of 50% or more from baseline in large chronic RDEB wounds and pain reduction from baseline evaluated 6 months after treatment. In 43 large and chronic wounds treated with a single application of prademagene zamikeracel, 81% showed 50% or more healing when evaluated at 6 months, compared with 16% in 43 matched control wounds treated with standard of care ($P < 0.001$).

Results from a phase I/II trial has alluded to longer-term improvement at treated sites with prademagene zamikeracel. This trial was a single-center, open-label study investigating 38 chronic wounds across 7 patients. These findings demonstrated that a single surgical application of prademagene zamikeracel was associated with long-term improvement at the treated sites over a median follow-up of approximately 6.9 years.

Prademagene zamikeracel will likely compete with Vyjuvek and Filsuvez. The estimated annual cost for Filsuvez is approximately $585,000, while Vyjuvek is approximately $630,000. These competing agents may provide a lower cost option for patients with DEB when compared to prademagene zamikeracel. However, cost will vary significantly among patients based on the frequency of wound dressing changes, the total body surface area of open wounds, and disease severity. Prademagene zamikeracel is expected to be available in the third quarter of 2025.

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.

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

Zevorcabtagene autoleucel (zevor-cel)/CARsgen Therapeutics

Route	Mechanism of Action	Proposed Indication	Approval (PDUFA) Date	Estimated Cost
Intravenous	Cell Therapy	Relapsed/Refractory Multiple Myeloma	TBD	$250,000-$500,000

Zevorcabtagene autoleucel is a fully human, autologous BCMA (B-cell maturation antigen) CAR T-cell product for the treatment of adult patients with relapsed/refractory multiple myeloma. Multiple myeloma is a type of cancer that begins in plasma cells, a type of white blood cell found in the bone marrow. These abnormal plasma cells grow uncontrollably and produce abnormal proteins, which can cause damage to the bones, kidneys, and other organs. Symptoms include bone pain, fatigue, frequent infections, and high calcium levels. Treatment options include chemotherapy, immunotherapy, stem cell transplants, and targeted therapies, aiming to manage the disease and improve the patient's quality of life. Multiple myeloma accounts for approximately 10% of all hematological cancers.

The drug was approved in China in February 2024 and has been granted breakthrough therapy designation by the FDA and is currently under investigation in phase II studies.

A Phase Ib/II LUMMICAR study evaluated the safety and efficacy of zevorcabtagene autoleucel in relapsed/refractory multiple myeloma. In December 2023, the FDA put a clinical hold on this study due to chemistry, manufacturing, and control issues. However, in November 2024, the FDA lifted these holds, but no additional clinical information has been made available.

Most recent findings for zevor-cel looked at 102 patients with relapsed/refractory multiple myeloma who had received at least 3 prior lines of therapy including an immunomodulatory drug and a proteasome inhibitor. The objective response rate (ORR) was 92.2%, the stringent complete response (sCR) or complete response (CR) was 71.6%. With a median follow-up of 20.3 (range: 0.4 to 27) months, the median duration of response (DOR), progression-free survival (PFS), and overall survival (OS) data were not mature and therefore, 18-month (18m) and estimated 30-month (30m) event free rates were used as efficacy outcomes for subgroup analyses. The DOR, PFS and OS were not impacted by age or ISS. These subgroup analyses indicate that baseline characteristics have minimal impact on the clinical efficacy of zevorcabtagene autoleucel, demonstrating that even relapsed/ refractory multiple myeloma patients with poor prognostic factors may potentially benefit from zevorcabtagene autoleucel.

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	TBD	$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.

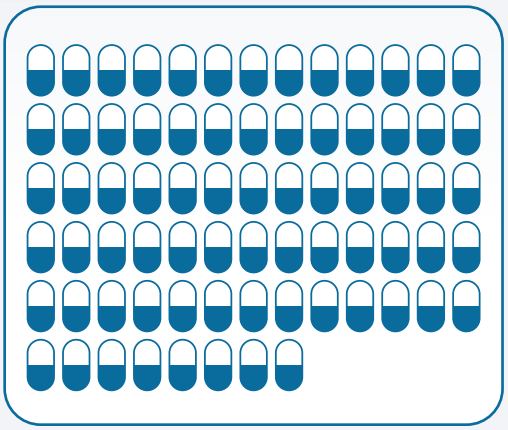
However, on January 16, 2025, the FDA issued a complete response letter (CRL) regarding the BLA. The CRL was related to observations as part of a standard pre-license inspection of a third-party manufacturing facility for Ebvallo. As a result, the FDA has halted trials of Ebvallo due to the compliance issues found at the third-party manufacturing facility. No update has been given on lifting the FDA hold.

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.

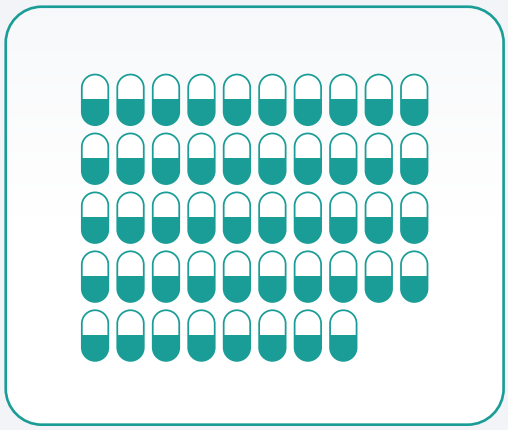
Ebvallo has already been approved in Europe in December 2022 for treating relapsed/refractory EBV+ PTLD in patients aged 2 years and older.

Biosimilars Pipeline

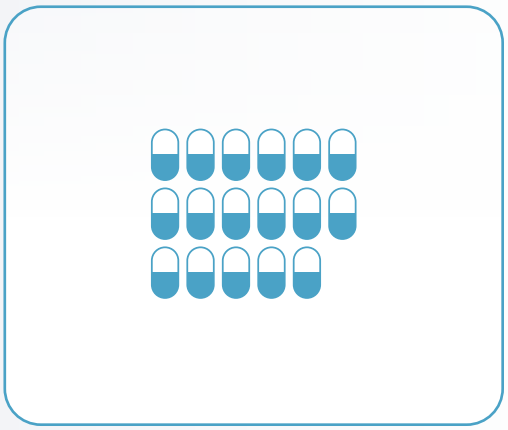
QUICK FACTS



73 FDA Approved Biosimilars to Date



48 Launched Biosimilars



17 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 Eighth Biosimilar, Starjemza®, to Stelara® (ustekinumab)

On May 15, 2025, the FDA approved Starjemza® (ustekinumab-hmny), the eighth biosimilar to Stelara® (ustekinumab). Starjemza is developed under a license agreement between Hikma Pharmaceuticals and Bio-Thera Solutions. Starjemza is a monoclonal antibody targeting interleukins IL-12 and IL-23, used to treat moderate to severe plaque psoriasis, psoriatic arthritis, Crohn's disease, and ulcerative colitis.

The approval of Starjemza was based on two clinical studies. A phase I, randomized, double-blind, single-dose, 3-arm study assessed the pharmacokinetics, safety, and immunogenicity of Starjemza compared to Stelara in healthy volunteers. Results showed that Starjemza was similar to Stelara with no clinically meaningful differences in efficacy, safety, or immunogenicity.

Additionally, a phase III, multicenter, randomized, double-blind study compared the efficacy, safety, and immunogenicity of Starjemza to Stelara in patients with moderate to severe plaque psoriasis. Among 278 participants, the average difference in the percent change from baseline in Psoriasis Area and Severity Index (PASI) scores at weeks 8 and 12 were 0.964 and 1.774, respectively. Both treatment groups showed similar outcomes across key secondary endpoints.

Other approved biosimilars to Stelara include Wezlana® (ustekinumab-auub), Selarsdi® (ustekinumab-aekn), Pyzchiva® (ustekinumab-ttwe), Otulfi® (ustekinumab-aauz), Yesintek® (ustekinumab-kfce), and Steqeyma® (ustekinumab-stba), and Imuldosa® (ustekinumab-srlf).

With the availability of multiple biosimilars for Stelara, current available biosimilar pricing is in the range of 80-90% discounts as compared to the reference product. Stelara is also one of the initial products selected for the Maximum Fair Price (MFP) program, as determined by the Centers for Medicare & Medicaid Services (CMS). The initial discount for the Medicare Part D program is a 66% discount from its 2023 list price.

FDA Approves Sixth Avastin Biosimilar, Jobevne® (bevacizumab-nwgd)

On April 9, 2025, the FDA approved Biocon Biologics' Jobevne® (bevacizumab-nwgd), the sixth biosimilar to reference Avastin® (bevacizumab). Jobevne is a recombinant humanized monoclonal antibody that inhibits angiogenesis by blocking the action of vascular endothelial growth factor A (VEGF-A). Jobevne slows the growth of new blood vessels in tumors and is used to treat various cancers including colorectal cancer, non–small cell lung cancer, glioblastoma, renal cell carcinoma, cervical cancer, ovarian cancer, fallopian tube cancer, and primary peritoneal cancer.

The approval for Jobevne (bevacizumab-nwgd) was based on a comprehensive package of comparative pharmacokinetic, safety, efficacy, nonclinical, structural, analytical and functional data, which showed that Jobevne was similar to Avastin (bevacizumab). The data demonstrated that there were no clinically meaningful differences between Jobevne and Avastin in terms of pharmacokinetics, safety, efficacy, and immunogenicity.

Other approved biosimilars to Avastin include Vegzelma® (bevacizumab-adcd), Mvasi® (bevacizumab-awwb), Zirabev® (bevacizumab-bvzr), Alymsys® (bevacizumab-maly), and Avzivi® (bevacizumab-tnjn).

FDA Approves Additional Denosumab Biosimilars, Conexxence and Bomyntra

On March 25, 2025, the FDA approved Conexxence® and Bomyntra® (denosumab-bnht), biosimilars referencing Prolia® and Xgeva®, respectively, for the treatment of multiple bone-related conditions. Conexxence is indicated for patients at high risk for fracture, including those with postmenopausal osteoporosis, glucocorticoid-induced osteoporosis, or bone loss due to certain cancer therapies. Bomyntra is indicated for the prevention of skeletal-related events in patients with multiple myeloma and bone metastases from solid tumors, and for the treatment of hypercalcemia of malignancy, and giant cell tumor of bone.

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 60 mg subcutaneous injection once every six months and is available in a prefilled syringe containing 60 mg/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 120 mg subcutaneously every 4 weeks and is available as a single-use vial containing 120 mg/1.7 mL (70 mg/mL).

Approval of denosumab-bnht was based on data from two comparative clinical studies. One study evaluated pharmacokinetics, pharmacodynamics, and immunogenicity in healthy volunteers, while the second was a randomized study in women with postmenopausal osteoporosis that assessed efficacy, pharmacodynamics, safety, and immunogenicity. The results demonstrated no clinically meaningful differences between denosumab-bnht and its reference products across all endpoints.

Adverse events associated with denosumab-bnht include back pain, arthralgia, headache, hypercholesterolemia, and musculoskeletal pain in patients with osteoporosis.

Conexxence® is available as a 60 mg/mL solution in a single-dose prefilled syringe for subcutaneous use. Bomyntra® is available as a 120 mg/1.7 mL solution in either a single-dose vial or prefilled syringe. Denosumab products, including Conexxence and Bomyntra, are administered by healthcare professionals to ensure proper injection technique, accurate dosing, monitoring for serious side effects, and compliance with regulatory safety standards. Conexxence® and Bomyntra® are expected to launch mid-2025.

FDA Approves Omlyclo®, the first biosimilar to Xolair®

On May 28, 2025, the FDA approved Celltrion's Omlyclo® (omalizumab-igec), the first biosimilar to reference Xolair® (omalizumab), for the treatment of multiple allergic and inflammatory conditions. Omlyclo is indicated for the treatment of moderate to severe persistent asthma, chronic rhinosinusitis with nasal polyps, IgE-mediated food allergy, and chronic spontaneous urticaria. Omlyclo is indicated for the treatment of moderate to severe persistent asthma, chronic rhinosinusitis with nasal polyps, IgE-mediated food allergy, and chronic spontaneous urticaria.

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

Approval was based on data from a double-blind, randomized, active-controlled, parallel-group phase III study involving 619 patients with chronic spontaneous urticaria (CSU) up to week 40. Patients were randomized to receive 300 mg or 150 mg of Omlyclo or reference product every 4 weeks. From Week 12, patients who received Omlyclo were continued on Omlyclo, and patients who received 300mg of the reference product were re-randomized in a 1:1 ratio to switch to Omlyclo or to continue reference product. From Week 24, patients were followed up until Week 40 without dosing. The trial demonstrated bioequivalence between Omlyclo and Xolair in terms of efficacy, safety, pharmacokinetics, and immunogenicity.

Adverse events associated with Omlyclo® include injection site reactions, fever, headache, dizziness, and arthralgia. Similar to Xolair®, Omlyclo® also has a boxed warning for anaphylaxis.

Omlyclo is available in two subcutaneous single-dose prefilled syringe formulations: 75 mg/0.5 mL and 150 mg/mL, matching the respective Xolair doses.

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 Lucamz and Lucentis® with no clinically meaningful differences observed in efficacy, safety, or immunogenicity through the study duration.

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®.

Lucamzi's FDA review and approval are anticipated in late 2025.

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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.

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