carelon Rx

Drug and biologic pipeline update Q3 2025

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CarelonRx's quarterly Drug and biologic pipeline update

Our Q3 2025 update features three agents with anticipated approvals in 2025: brensocatib for bronchiectasis, apitegromab for spinal muscular atrophy (SMA), and clemidsogene lanparvovec for mucopolysaccharidosis II (MPS II). Other select drugs and biologics in the pipeline, including gene therapies and biosimilars, are also highlighted. An overview of the use of artificial intelligence to support regulatory decision making for drug and biologic products is also provided. Other topics this quarter include an update on potential future Keytruda® indications, as well as a subcutaneous formulation, and an overview of recent Kidney Disease: Improving Global Outcomes (KDIGO) guidelines.

CarelonRx continues to closely monitor the drug and biologic pipeline and to provide this free publication as part of our mission to improve health, reduce waste, lower total cost of care for pharmacy and medical services, and estimate future cost impact.

Top emerging new therapies

Brensocatib

Condition:
Bronchiectasis is a chronic lung condition in which the bronchial airways become permanently dilated with thickened walls and weakened cilia due to a cycle of infection, inflammation, and lung tissue damage. This may lead to the pooling of mucus and airway obstruction. Potential symptoms include chronic cough, excessive sputum production, shortness of breath, and recurrent infections. Acute exacerbations may lead to progressive lung damage. An estimated 500,000 individuals have been diagnosed with bronchiectasis in the US.

Role in treatment:
The primary treatment for bronchiectasis not caused by an underlying disease like cystic fibrosis is the management of symptoms and prevention of complications. Brensocatib would be the first Food and Drug Administration (FDA)-approved treatment for this condition. It works by inhibiting an enzyme responsible for activating neutrophils, a type of white blood cell, which can accumulate in airways and cause inflammation and damage to the lungs.

Efficacy:
The New Drug Application submitted to the FDA was supported by data from the randomized, double-blind, placebo-controlled, 52-week ASPEN trial. The primary endpoint was met, demonstrating statistically significant reductions in the annualized rate of pulmonary exacerbations (PEs) versus placebo.

Safety:
Brensocatib was well tolerated in the ASPEN trial. Treatment-emergent adverse events occurring in at least 5% of trial subjects included Coronavirus disease 2019 (COVID-19) infection, nasopharyngitis, cough, and headache.

Financial impact:
If approved, brensocatib will be the first treatment option for non-cystic fibrosis-related bronchiectasis. The cost is unknown at this time. Expected peak sales are estimated to be greater than $5 billion[1].

CarelonRx view:
Treatment options for non-cystic fibrosis related bronchiectasis are currently limited to symptom management and prevention of complications. Brensocatib may provide the first FDA-approved treatment for reducing pulmonary exacerbations in this disease. Brensocatib is also in development for hidradenitis suppurativa and chronic rhinosinusitis without nasal polyps.

Product:
Brensocatib

Indication:
Non-cystic fibrosis related bronchiectasis

Estimated FDA approval:
August 2025

Therapeutic class:
Dipeptidyl peptidase 1 (DPP1) inhibitor

Route of administration:
Oral

FDA designations:
Breakthrough; Priority

Manufacturer:
Insmed

Apitegromab

Condition:
Spinal muscular atrophy (SMA) is an autosomal recessive neurodegenerative disease, occurring in 5 to 13 per 100,000 live births. It is the leading genetic cause of death in infants. Most typically, SMA results from a deletion or mutation in the *SMN1* gene, which leads to a decreased expression of the SMN protein and degeneration of motor neurons in the spinal cord and brainstem. Individuals experience progressive muscle weakness and, in severe cases, death. The *SMN2* gene also encodes the SMN protein, but 90 to 95% of translated protein is nonfunctional; individuals with a higher copy number of *SMN2* generally manifest with a milder disease.

Role in treatment:
Prior to the approval of disease-modifying treatments, SMA care was mainly supportive. The focus was on nutrition and respiratory assistance as well as treatment or prevention of complications of weakness.

Three disease-modifying treatments have been approved to preserve motor neurons, improve muscle function, and extend lives in the past decade. None are definitive cures. Intrathecal Spinraza™ and oral Evrysdi® are SMN2-splicing modifiers that enhance the effectiveness of SMN2 genes and are approved for use in both pediatrics and adults. Intravenous Zolgensma® was approved as a gene therapy for individuals with SMA who are less than 2 years old. SMA agents have demonstrated greater efficacy when administered earlier in treatment prior to the onset of extensive nerve damage. Evidence to support the efficacy of concurrent or sequential use of agents for SMA is limited.

Apitegromab is an intravenously administered myostatin inhibitor for add-on treatment of SMA. It would be the first muscle-targeted therapy for disease management and aims to improve motor function.

Efficacy:
The New Drug Application submitted to the FDA for apitegromab is supported by data from the TOPAZ phase 2 and SAPPHIRE phase 3 clinical trials. Non-ambulatory individuals with SMA receiving background Spinraza or Evrysdi achieved significant and clinically meaningful improvements in motor function compared to placebo at 12 months. The benefit was noted across all pre-specified subgroups (type of SMN-targeted therapy, age at SMN-targeted therapy initiation, and geographic region).

Safety:
In clinical trials, apitegromab was well tolerated, with an overall safety profile similar to that of the placebo group.

Financial impact:
The price of apitegromab is unknown. Used as add-on therapy, apitegromab would add cost to currently available disease-modifying therapies.

CarelonRx view:
If approved, apitegromab would offer an additional therapeutic option for non-ambulant individuals with SMA. A unique mechanism of action for the improvement of motor function in individuals with SMA would likely be well-received. It is expected to be used in individuals who are non-ambulant and receiving background Spinraza or Evrysdi. Adding apitegromab to the treatment regimen for these SMA individuals will increase costs. Apitegromab is not currently being studied for use in individuals who previously received Zolgensma.

Of note, apitegromab is also being studied in overweight and obese adults receiving glucagon-like peptide-1 (GLP-1) therapy with the goal of lean muscle preservation during and after treatment.

Product:
Apitegromab

Indication:
Spinal muscular atrophy (SMA)

Estimated FDA approval:
September 2025

Therapeutic class:
Myostatin inhibitor

Route of administration:
Intravenous

FDA designations:
Fast track; Orphan drug; Rare pediatric disease

Manufacturer:
Scholar Rock, Inc.

Clemidsogene lanparvovec

Condition:
Mucopolysaccharidosis type II (MPS II), also known as Hunter syndrome, is a genetic disorder caused by a deficiency in the enzyme needed to break down complex sugar molecules. Affecting mostly boys, MPS II symptoms typically begin around 1 to 3 years of age. In its severe form, MPS II can cause cognitive and physical developmental delays, which result in early death, or it can present in a milder form with fewer symptoms, allowing people to live into their 60s and 70s. It is estimated that MPS II occurs in approximately 1 in 135,000 births.

Role in treatment:
The current standard of care for treating severe forms of MPS II involves a weekly intravenous infusion of the enzyme replacement therapy Elaprase® (idursulfase). Elaprase has been shown to improve some symptoms associated with MPS II, such as walking distance in people treated; however, it cannot cross the blood-brain barrier. Clemidsogene, administered directly into the central nervous system (CNS), uses a viral vector to penetrate cells and deliver functional copies of the *iduronate-2-sulfatase (IDS)* gene. The delivery of the *IDS* gene aims to provide a permanent source of the deficient enzyme in people with MPS II with the hope of addressing a broader range of manifestations, including neurocognitive symptoms.

Efficacy:
The pivotal CAMPSITE trial is evaluating males who are at least 4 months old and up to 5 years of age with severe MPS II either taking Elaprase or who are Elaprase naïve. Clemidsogene is administered as a one-time treatment. The company is using a surrogate biomarker endpoint to seek accelerated approval; confirmatory data will be required after approval to confirm clinical benefit. People given the pivotal dose met the primary endpoint with statistical significance, showing a reduction in cerebrospinal fluid (CSF) levels of heparan sulfate 16 weeks after treatment, a proposed biomarker of brain activity in MPS II.

Safety:
One serious adverse event occurred with clemidsogene, elevation in liver enzymes, and resolved with treatment.

Financial impact:
The price of clemidsogene is unknown. However, it could be priced similarly to other gene therapies for rare diseases at $3M or more per one-time treatment.

CarelonRx view:
Preliminary data show that a handful of boys treated with clemidsogene were able to stop Elaprase treatment or remain Elaprase-naïve. However, in clinical practice, it remains unclear whether people will require Elaprase treatment after receiving clemidsogene. While the primary biomarker surrogate efficacy endpoint was met with statistical significance, important questions remain, such as evaluating changes in clinical efficacy outcomes, like acquisition of developmental skills, and determining the potential durability with clemidsogene.

Product:
Clemidsogene lanparvovec

Indication:
Mucopolysaccharidosis type II (MPS II)

Estimated FDA approval:
November 2025

Therapeutic class:
Gene therapy

Route of administration:
Image guided intracisternal injection

FDA designations:
Fast track; Orphan; Priority review; Rare pediatric disease; Regenerative medicine advanced therapy (RMAT)

Manufacturer:
RegenxBio

Other significant product approvals

Other product approvals expected to reach the market in the next 12 months*

Drug or biologic manufacturer	Indication/route	Place in therapy	Estimated approval date	Impact on overall drug or medical spend
Delgocitinib Leo Pharma	Atopic dermatitis/topical	**Addition to class:** specifically for atopic dermatitis of the hand	Second half of 2025	
Translarna (ataluren) PTC Therapeutics	Duchenne muscular dystrophy/oral	**First in class:** for treatment of nonsense mutation disease	Third quarter 2025	
Zongertinib Boehringer Ingelheim	Non-small cell lung cancer (NSCLC), second-line treatment/oral	**First in class:** for Individuals with NSCLC whose tumors have human epidermal growth factor receptor-2 (HER2) mutations; first oral targeted therapy for this population	Third quarter 2025	
Elinzanetant Bayer	Menopause, vasomotor symptoms/oral	**Addition to class:** non-hormonal therapy; would compete with Veozah®	08/01/2025	
LNZ-100 (aceclidine) Lenz Therapeutics	Presbyopia/ophthalmic	**Addition to class:** would compete with Vuity® and Qlosi™	08/08/2025	
Brensocatib Insmed	Bronchiectasis/oral	**First in class:** would be first FDA-approved agent for this indication	08/12/2025	
Rebisufligene etisparvovec (UX111) Ultragenyx Pharmaceutical	Mucopolysaccharidosis IIIA/IV	**First in class:** gene therapy; would be first FDA-approved agent for this indication	08/18/2025	
ONC201 (dordaviprone) Chimerix	Brain cancer/oral	**First in class:** would be first FDA-approved agent for recurrent H3 K27M-mutant gliomas	08/18/2025	

*As of May 22, 2025.

In addition to treatments listed previously, these important drugs and biologics are scheduled to receive Food and Drug Administration (FDA) approval within the next 12 months.*

Orphan drug/rare disease; expected to be high cost, but with minimal impact to overall drug/medical spend due to low utilization

Potential to significantly increase overall drug/ medical spend

New entrant into current or future high-spend/ trending category

No significant impact to incremental spend due to replacement of existing competitors based on initial analysis

Other product approvals expected to reach the market in the next 12 months* (continued)

Drug or biologic manufacturer	Indication/route	Place in therapy	Estimated approval date	Impact on overall drug or medical spend
Vatiquinone PTC Therapeutics	Friedreich's ataxia, in adults and children/oral	**First in class:** would be first FDA-approved agent for children with this disease	08/19/2025	
Donidalorsen Ionis	Hereditary angioedema /subcutaneous injection (SC)	**Addition to class:** prophylaxis to prevent attacks	08/21/2025	
SL-1009 (sodium dichloroacetate) Saol Therapeutics	Pyruvate dehydrogenase complex deficiency/oral	**First in class:** would be first FDA-approved agent for this indication	08/27/2025	
Zopapogene imadenovec (PRGN-2012) Precigen	Recurrent respiratory papillomatosis/ SC	**First in class:** would be first FDA-approved gene-based therapeutic vaccine for this indication	08/27/2025	
Rilzabrutinib Principia BioPharma	Immune thrombocytopenic purpura (ITP)/oral	**Addition to class:** first Bruton's tyrosine kinase (BTK) for this indication	08/29/2025	
Narsoplimab Omeros Corporation	Transplant-associated thrombotic microangiopathy/IV	**First in class:** would be first FDA-approved treatment for this indication	September 2025	
N115 (sodium pyruvate) EmphyCorp	Idiopathic pulmonary fibrosis (IPF)/intranasal	**Addition to class:** for coughing associated with IPF	09/12/2025	
Apitegromab Scholar Rock	Spinal muscular atrophy (SMA)/IV	**First in class:** muscle-targeted therapy to improve motor function for people living with SMA who are receiving survival motor neuron (SMN)-targeted treatment	09/22/2025	

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Other product approvals expected to reach the market in the next 12 months* (continued)

Drug or biologic manufacturer	Indication/route	Place in therapy	Estimated approval date	Impact on overall drug or medical spend
Paltusotine Crinetics Pharmaceuticals	Acromegaly/oral	**Addition to class:** for individuals who are treatment naïve or those switching from other therapies	09/25/2025	
Tolebrutinib Sanofi	Multiple sclerosis, secondary progressive/ oral	**Addition to class:** would be first Bruton's tyrosine kinase (BTK) inhibitor approved for multiple sclerosis	09/28/2025	
Troriluzole Biohaven	Spinocerebellar ataxia/ oral	**First in class:** would be first FDA-approved agent for this indication	Fourth quarter 2025	
Tradipitant Vanda Pharmaceuticals	Motion sickness/oral	**Addition to class:** will compete with over the counter (OTC) options for motion sickness	Between 10/01/25 and 12/31/25	
NP-001 (sodium chlorite) Neuvivo	Amyotrophic lateral sclerosis/IV	**First in class:** potential disease-modifying therapy	10/07/2025	
Doxecitine/ doxribtimine UCB	Thymidine kinase 2 deficiency/oral	**Addition to class:** would be first FDA-approved agent for this indication	10/27/2025	
Clemidsogene lanparvovec Regenxbio	Mucopolysaccharidosis II/IV	**First in class:** would be first gene therapy for this indication	11/09/2025	
Plozasiran Arrowhead Pharmaceuticals	Familial chylomicronemia syndrome/SC	**Addition to class:** potential advantage of quarterly dosing	11/18/2025	

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Other product approvals expected to reach the market in the next 12 months* (continued)

Drug or biologic manufacturer	Indication/route	Place in therapy	Estimated approval date	Impact on overall drug or medical spend
Sibeprenlimab Otsuka Holdings	Immunoglobulin A nephropathy (IgAN)/SC	**First in class:** would be the first injectable product approved for IgAN	11/28/2025	
TransCon CNP (navepegritide) Ascendis	Achondroplasia/SC	**Addition to class:** potential advantage of weekly dosing	11/30/2025	
Lerodalcibep LIB Therapeutics	Dyslipidemia; Hypercholesterolemia/SC	**Addition to class:** third generation proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor	12/12/2025	
Depemokimab GlaxoSmithKline	Asthma; Rhinosinusitis with nasal polyps/SC	**Addition to class:** potential advantage of every 6 month dosing	12/16/2025	
Aficamten Cytokinetics	Symptomatic obstructive hypertrophic cardiomyopathy (HCM)/ oral	**Addition to class:** would compete with Camzyos®; quicker onset; potential for improved safety	12/16/2025	
Relacorilant Corcept	Cushing's syndrome/oral	**Addition to class:** next-generation competitive antagonist of the glucocorticoid II (GR-II) receptor	12/30/2025	
Etuvetidigene autotemcel Fondazione Telethon	Wiskott-Aldrich Syndrome (WAS)/IV	**First in class:** would be first FDA-approved treatment for this indication	03/11/2026	
Bysanti (milsaperidone) Vanda Pharmaceuticals	Schizophrenia; Bipolar disorder/oral	**Addition to class:** active metabolite of iloperidone	03/31/2026	

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*As of May 22, 2025.

The Food and Drug Administration (FDA) requires all approved biologic products, including reference, biosimilar, and interchangeable products, be evaluated for safety and efficacy to determine whether the benefits outweigh any known potential risks.

Reference biologics undergo several phases of clinical studies to establish safety and effectiveness before they are FDA-approved. Clinical trials begin with early, small-scale, Phase 1 studies and move toward late-stage, large scale, Phase 3 studies. After the biologic has entered the market, post-marketing monitoring continues to assess the safety, efficacy, and clinical benefit in a larger population.

Biosimilar products are highly similar to their reference product in terms of structure and function and lack clinically meaningful differences in terms of safety and efficacy. Biosimilar products may be approved for all or some of the reference product indications due to patent exclusivity.

Prescriptions for biosimilar products need to be written for the biosimilar by name. Biosimilar products that are granted interchangeability are allowed to be substituted for their reference biologic without the intervention of the prescriber. This is similar to how generic drugs may be substituted for brand name drugs. Unlike reference biologics, biosimilar products are not required to submit evidence to establish safety and efficacy. However, a biosimilar manufacturer must submit clinical trial data that establishes biosimilarity with the reference product

Biosimilar pipeline update

Currently seventy-one biosimilar products are FDA approved in the United States which represent eighteen unique reference biologic products. Recent approvals include Omlyclo® (omalizumab-igec) and Bomyntra® and Conexxence® (denosumab-bnht) in March 2025; Jobevne® (bevacizumab-nwgd) in April 2025; and Starjemza™ (ustekinumab-hmny) in May 2025. Fifty-three of the approved products have been launched.

Biosimilar products awaiting launch and/or approval*

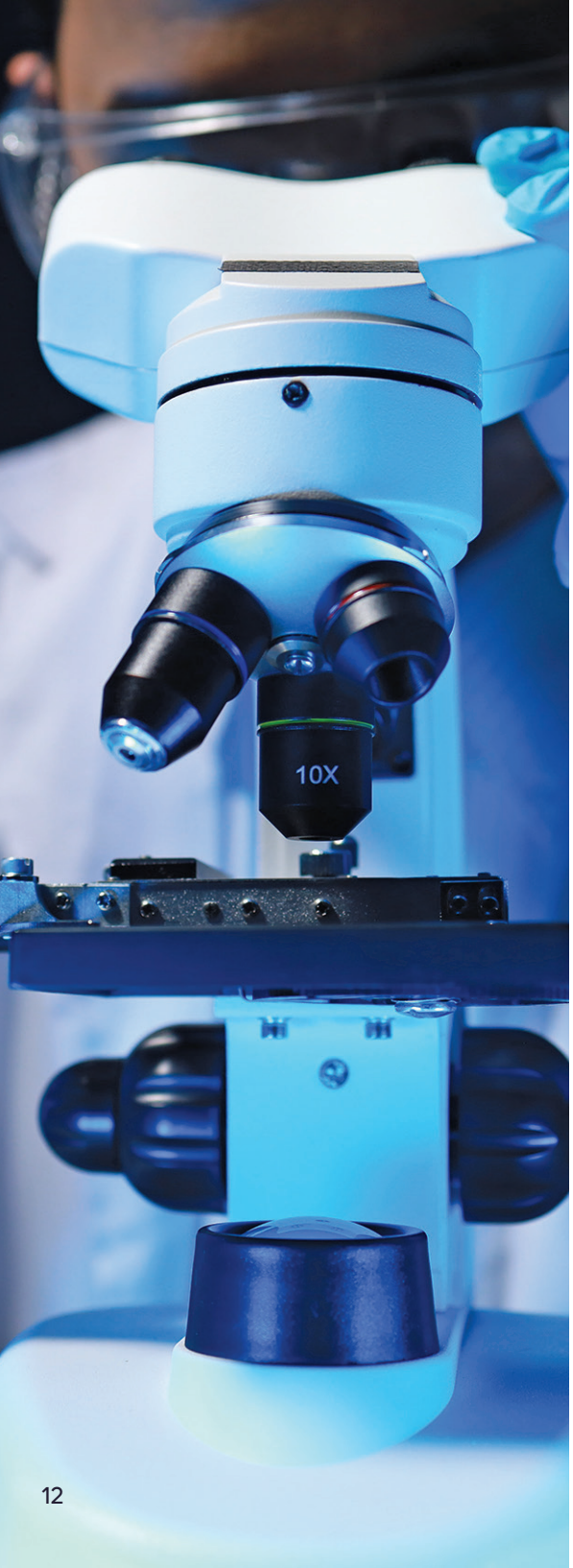
Brand name	Brand manufacturer	Biosimilar name	Biosimilar manufacturer	FDA approval*
Actemra®	Roche; Chugai; Genentech	Avtozma®	Celltrion	1/24/2025
		Tocilizumab Celltrion		
Avastin®	Genentech; Roche	Avzivi®	Bio-Thera Solutions; Sandoz	12/6/2023
		Jobevne	Biocon; Mylan; Viatris	4/9/2025
		FKB238	Centus Biotherapeutics; AstraZeneca; Fujifilm Kyowa Kirin	Pending
Enbrel®	Amgen; Immunex	Erelzi™	Sandoz	8/30/2016
		Eticovo™	Samsung Bioepis	4/25/2019
Eylea®	Regeneron	Ahzantive®	Formycon; Santo Holding; Bioeq; Klinge Pharma	6/28/2024
		Enzeevu™	Sandoz; Hexal	8/9/2024
		Opuviz™	Samsung Bioepis; Biogen	5/20/2024
		Yesafili™	Momenta; Mylan; Johnson & Johnson; Biocon; Viatris	5/20/2024
		AVT06	Alvotech; Teva; Alvogen	Pending
		CT-P42	Celltrion	Pending
Humalog®	Eli Lilly	GL-LIS	Gan & Lee; Sandoz	Pending
Humalog Pen				Pending
Humalog U-100 KwikPen				Pending

*As of June 6, 2025. Excludes biosimilars that are FDA approved and have launched.

Biosimilar products awaiting launch and/or approval* (continued)

Brand name	Brand manufacturer	Biosimilar name	Biosimilar manufacturer	FDA approval*
Humira® (100 mg/mL)	AbbVie	Adalimumab AbbVie	AbbVie	11/3/2023
Lantus Solostar®	Sanofi	GL-GLA	Gan & Lee; Sandoz	Pending
Lucentis®	Roche; Genentech	Lucamzi	Xbrane; Valorum Biologics; Stada	Pending
Neulasta®	Amgen	Lapelga	Apotex; Accord; Intas	Pending
Neupogen®	Amgen	Grastofil	Apotex; Accord; Intas	Pending
Novolog® (10 mL vial)	Novo Nordisk	Merilog™	Sanofi	2/14/2025
Novolog FlexPen				
Novolog FlexTouch				
Novolog PenFill				
Novolog® (10 mL vial)	Novo Nordisk	AMP-004	Amphastar	Pending
Novolog FlexPen				
Novolog FlexTouch				
Novolog PenFill				
Novolog (10 mL vial)	Novo Nordisk	GL-ASP	Gan & Lee; Sandoz	Pending
Novolog FlexPen				
Novolog FlexTouch				
Novolog PenFill				
Perjeta®	Genentech; Roche	HLX11	Henlius; Organon	Pending

*As of June 6, 2025. Excludes biosimilars that are FDA approved and have launched.



Biosimilar products awaiting launch and/or approval* (continued)

Brand name	Brand manufacturer	Biosimilar name	Biosimilar manufacturer	FDA approval*
Prolia®/Xgeva®	Amgen	Bomyntra/Conexxence	Fresenius Kabi	3/25/2025
		Denosumab Fresenius	Fresenius Kabi	3/25/2025
		Denosumab Samsung Bioepis	Samsung Bioepis; Samsung Biologics	2/13/2025
		Jubbonti®/Wyost®	Sandoz	3/5/2024
		Ospomyv™/Xbryk™	Samsung Bioepis; Samsung Biologics	2/13/2025
		Stoboclo®/Osenvelt®	Celltrion	2/28/2025
		AVT03	Alvotech; Dr. Reddy's; Alvogen	Pending
		Bmab 1000	Biocon	Pending
		HLX14	Henlius; Organon	Pending
		INTP23	Intas; Accord	Pending
		MB09	mAbxience; Insud Pharma; Fresenius Kabi; Amneal	Pending
		RGB-14	Gedeon Richter; Hikma	Pending
		TVB-009P	Teva	Pending
Simponi®/Simponi Aria	Johnson & Johnson	AVT05	Alvotech; Teva; Alvogen	Pending
Stelara®	Johnson & Johnson	Imuldosa™	Amgen	5/28/2024
		Starjemza	Samsung Bioepis	7/19/2024
		Ustekinumab Alvotech	Alvotech; Teva	10/18/2024
Tysabri® IV	Biogen; Royalty Pharma	Imuldosa™	Polpharma; Sandoz	8/24/2023
Xolair®	Roche; Genentech; Novartis	Omalizumab Celltrion	Celltrion	3/7/2025
		Omlyclo	Celltrion	3/7/2025

*As of June 6, 2025. Excludes biosimilars that are FDA approved and have launched

Gene therapies in the pipeline

Gene therapy is a novel approach to treatment that introduces genetic material into an individual's body to help fight various diseases. To differentiate gene therapy products, we break them into two broad categories: gene therapy and gene-based therapeutics. The main difference is that gene therapies are usually single treatments that aim to treat or cure a genetic disease, while gene-based therapeutics require multiple treatments.

The following gene therapies and gene-based therapeutics are scheduled to receive an FDA decision in the next 12 months, or we expect they could file a biologics license application (BLA) with the FDA in 2025/2026. The price of gene therapies has traditionally been announced after FDA-approval, making prediction of pipeline therapy pricing a particular challenge. We anticipate the majority of future gene therapy approvals will fall within the range of costs associated with the current FDA approved gene therapies, between $2 to $4 million.

Gene and gene-based therapies with submitted applications for potential FDA-approval in 2025/2026*

Gene therapy/ gene-based therapy	Indication/route and frequency	Place in therapy	Estimated approval date
Vusolimogene oderparepvec Replimune	Advanced melanoma/multiple injections directly into the tumor	Addition to class; gene-based oncolytic immunotherapy; used in combination with Opdivo® Uses viral vector (herpes simplex virus).	07/22/2025 (filed)
Rebisufligene etisparvovec Abeona	Mucopolysaccharidosis IIIA (Sanfilippo Type A)/single intravenous (IV) infusion	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	08/18/2025 (filed)
Zopapogene imadenovec Precigen	Recurrent respiratory papillomatosis (RRP)/multiple subcutaneous (SC) doses	First gene-based therapeutic multidose vaccine; will compete with surgery. Uses viral vector (Precigen's AdenoVerse®; gorilla adenovectors).	08/27/2025 (filed)
Clemidsogene lanparvovec Regenxbio	Mucopolysaccharidosis II (MPS II; Hunter syndrome)/single intracisternal or intracerebroventricular injection	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	11/09/2025 (filed)
Mozafancogene autotemcel Rocket	Fanconi anemia (FA)/single IV infusion	First gene therapy for this indication. Uses viral vector (lentivirus).	2H25 (initiated rolling BLA)
Marnetegragene autotemcel Rocket	Leukocyte adhesion deficiency-I/ single IV infusion	First gene therapy for this indication. Uses viral vector (lentivirus).	2025 (FDA-denied; plans to refile)
Etuvetidigene autotemcel Fondazione	Wiskott-Aldrich Syndrome/single IV infusion	First gene therapy for this indication. Uses viral vector (lentivirus).	03/11/2026 (filed)

*As of May 22, 2025

Gene and gene-based therapies of significant interest with potential FDA-submissions in 2025/2026*

Gene therapy/ gene-based therapy	Indication/route	Place in therapy	Estimated approval date
Botaretigene sparoparvovec Johnson & Johnson	X-linked retinitis pigmentosa (XLRP)/single subretinal injection	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2025
Cretostimogene grenadenorepvec Novartis	Bacillus Calmette-Guérin (BCG) unresponsive, non-muscle invasive bladder cancer (NMIBC)/multiple intravesical doses	Second gene-based therapeutic; would compete with Adstiladrin®. Uses viral vector (adeno-associated virus).	2025
Pariglasgene brecaparvovec Ultragenyx	Glycogen storage disease type Ia/single IV infusion	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2025
Sonpiretigene isteparvovec Nanoscope	Retinitis Pigmentosa (RP)/single intravitreal injection	First mutation-agnostic gene therapy for RP. Uses viral vector (adeno-associated virus).	2025
Giroctocogene fitelparvovec Sangamo	Hemophilia A/single IV infusion	Second gene therapy for hemophilia A; will compete with FVIII products, Hemlibra, and Roctavian. Uses viral vector (adeno-associated virus).	2025-2026
Rivunatpagene miziparvovec Ultragenyx	Wilson disease/single IV infusion	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2025-2026
RP-A501 Rocket	Danon disease/single IV infusion	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2025-2026
Zolgensma® (onasemnogene abeparvovec) Novartis	Spinal muscular atrophy (SMA) Type 2/single intrathecal infusion	Potential expanded indication for Zolgensma to include children 2 to < 18 years of age with SMA Type 2; will compete with Spinraza® and Evrysdi®. Uses viral vector (adeno-associated virus).	2025-2026
AAV-AQP1 MeiraGTx Holdings	Radiation-Induced Xerostomia/ single intraparotid injection	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2026
Bidridistrogene xeboparvovec Sarepta	Limb-girdle muscular dystrophy (LGMD) Subtype 2E/R4/single IV infusion	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2026
Dabocemagene autoficel Castle Creek Biosciences	Dystrophic epidermolysis bullosa (DEB)/multiple intradermal injections	Third localized gene-based wound therapeutic for this indication; will compete with Vyjuvek and Zevaskyn™. Uses viral vector (lentivirus)..	2026
Elevidys (delandistrogene moxeparvovec-rokl) Sarepta	Duchenne muscular dystrophy (DMD)/single IV infusion	Potential to expand approval to include individuals 4 years of age and younger with DMD. Uses viral vector (adeno-associated virus).	2026

*As of May 22, 2025

Gene therapy/ gene-based therapy	Indication/route	Place in therapy	Estimated approval date
Isaralgagene civaparvovec Sangamo	Fabry disease/single IV infusion	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2026
Surabgene lomparvovec Regenxbio	Neovascular age-related macular degeneration (wet AMD)/single subretinal and/or suprachoroidal injection	First gene therapy for this indication; will compete with treatments requiring multiple intravitreal injections such as Eylea® and Vabysmo®. Uses viral vector (adeno-associated virus).	2026
Vyjuvek (beremagene geperpavec-svdt) Krystal Biotech	Dystrophic epidermolysis bullosa (DEB)/multiple ophthalmic doses	Potential to expand approval to include an ophthalmic formulation of Vyjuvek to treat ocular complications secondary to DEB. Uses viral vector (herpes simplex virus).	2026
AMT-130 uniQure	Huntington's disease/stereotaxic surgery with single infusion into the brain	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2026-2027
Avalotcagene ontaparvovec Ultragenyx	Ornithine transcarbamylase (OTC) deficiency/single IV infusion	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2026-2027
BBP-812 Aspa	Canavan disease/single IV infusion	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2026-2027
Engensis; donaperminogene seltoplasmid Helixmith	Wilson disease/single IV infusion	First gene-based therapeutic for these indications. Uses non-viral vector (plasmid deoxyribonucleic acid (DNA)).	2026-2027
Generx® (alferminogene tadenovec) Gene Biotherapeutics	Angina/single intracoronary infusion	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2026-2027
NTLA-2002 Intellia	Hereditary angioedema (HAE)/ single IV infusion	First gene therapy for this indication. Uses gene editing, delivered by lipid nanoparticles.	2026-2027
OCU400 Ocugen	Retinitis pigmentosa (RP)/single subretinal injection	Potential to be first gene therapy for RP associated with *RHO* mutations; may also get approval for people with any other RP associated mutation with a clinical phenotype of RP. Uses viral vector (adeno-associated virus).	2026-2027
OTL-203 Orchard	Mucopolysaccharidosis I (MPS I; Hurler Syndrome)/single IV infusion	First gene therapy for this indication. Uses viral vector (lentivirus).	2026-2027
RGX-202 Regenxbio	Duchenne muscular dystrophy (DMD)/single IV infusion	Second gene therapy for DMD; will compete with Elevidys. Uses viral vector (adeno-associated virus).	2026-2027

*As of May 22, 2025

Gene therapy/ gene-based therapy	Indication/route	Place in therapy	Estimated approval date
RP-L301 Rocket	Pyruvate Kinase Deficiency (PKD)/single IV infusion	First gene therapy for this indication. Uses viral vector (lentivirus).	2026-2027
Tavokinogene telseplasmid (TAVO) OncoSec Medical	Metastatic melanoma/multiple intratumoral injections	Addition to class; gene-based oncolytic immunotherapy; used in combination with Keytruda®; uses non-viral vector (plasmid DNA).	2026-2027
TG-C Kolon TissueGene	Osteoarthritis of the knee/ multiple intraarticular injections	First gene-based therapeutic for this indication; potential to compete with intraarticular steroid injections and knee replacement surgery. Uses viral vector (retrovirus).	2026-2027
Aglatimagene besadenovec Candel	Intermediate-to-high-risk localized prostate cancer/ multiple intratumoral injections	First localized gene-based viral immunotherapy for this indication; used in combination with an oral anti-herpes drug, such as valacyclovir, to destroy cancer cells. Uses viral vector (adeno-associated virus).	2027
Detalimogene voraplasmid enGene	BCG unresponsive, NMIBC/ multiple intravesical instillations	Third gene-based therapeutic for NMIBC; will compete with Adstiladrin and cretostimogene grenadenorepvec, if approved. Uses viral vector (adeno-associated virus).	2027
LX2006 Lexeo	Friedreich's Ataxia Cardiomyopathy/single IV infusion	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2027
Laruparetigene zovaparvovec Beacon	X-linked retinitis pigmentosa (XLRP)/single subretinal injection	Second gene therapy for this indication; potential to compete with botaretigene sparoparvovec, if its approved. Uses non-viral vector (Dually Derivatized Oligochitosan® (DDX) platform).	2027
Lenadogene nolparvovec (Lumevoq®) GenSight	Leber Hereditary Optic Neuropathy (LHON)/single intravitreal injection	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2027

*As of May 22, 2025

FDA draft guidance: considerations for the use of artificial intelligence to support regulatory decision-making for drug and biological products

The Food and Drug Administration (FDA) recently released draft guidance for industry and other interested parties on the use of artificial intelligence (AI) to produce information or data intended to support regulatory decision-making regarding safety, effectiveness, or quality for drugs . This guidance provides a risk-based credibility assessment framework that may be used for establishing and evaluating the credibility of an AI model tailored to a specific context of use through a 7-step process. The process begins with defining the question of interest that will be addressed by the AI model, defining the context of use, and assessing the model risk to develop a plan for establishing AI credibility. After executing the plan, the final steps include documenting results addressing any deviations from the plan and determining the adequacy of the AI model for its specific context of use.

Many concerns about the use of AI models in the drug product life cycle are addressed by the risk-based credibility assessment plan, including issues regarding the quality of data used to develop the AI models, transparency in model development, determining the accuracy of the model, and model performance over time. The credibility assessment plan guides sponsors and interested parties to provide complete documentation at every step of AI model development. The guidance emphasizes early and continuous engagement with the FDA throughout the development of this plan to set expectations and identify potential challenges. This is crucial, as AI models are meant to assist but not completely replace a clinician's judgement regarding safety or efficacy during a trial.

Designing quality clinical trials at any stage of drug development requires careful planning before trial initiation to determine a protocol that drives decisions, such as who qualifies for the trial, what assessments will be conducted, when assessments will be conducted, and what data will be collected. It ensures that all safety events are captured during the trial and people are treated equally. The protocol ensures consistency and should remain unchanged over time, producing data that ultimately support the final FDA-approved labeling.

One hypothetical example provided in the draft guidance involves the use of AI to determine which individuals were at high versus low risk of having a life-threatening drug-related adverse reaction, criteria that are normally defined in the trial protocol. Using AI alone to determine which people are at high risk and should receive additional 24-hour inpatient monitoring may introduce an unintended variable into the trial that could impact data consistency and does not help guide how a drug should be used and monitored post-approval. With the growing use of AI in healthcare, it is important to emphasize the use of AI models as a tool to *support* a clinician's decision-making, especially in clinical trials used to support the efficacy and safety of new drugs.

Market trends

Keytruda treatment landscape and pipeline

Keytruda ® is a widely used antineoplastic agent with dozens of approved indications, and this number is growing. It is a programmed death receptor-1 (PD-1) blocking antibody approved by the Food and Drug Administration (FDA) for approximately 42 different indications, covering more than 20 types of cancer. This immunotherapy, known as an immune checkpoint inhibitor, is typically administered every three weeks as an intravenous (IV) infusion over 30 minutes, or the dose may be doubled and given every 6 weeks. It may be used as first-line therapy, subsequent therapy, for advanced or metastatic disease, prior to surgical resection to reduce tumor size, or after surgery to ensure the elimination of all cancer cells.

While Keytruda holds many FDA-approved indications as well as strong recommendations from the National Comprehensive Cancer Network (NCCN), the manufacturer continues to study the efficacy and safety of Keytruda in additional cancer types, in combination with other agents, and as a new dosage form.

Phase 3 studies are underway to expand the use of Keytruda to those with prostate, ovarian, or small cell lung cancer; hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2-) breast cancer; and as adjuvant therapy in hepatocellular carcinoma. In addition, there are numerous phase 1 and 2 studies evaluating Keytruda use in other cancers and lines of therapy that may become approved indications if the data are favorable.

The manufacturer has submitted an application to the FDA for the combination of pembrolizumab and berahyaluronidase, an enzyme similar to hyaluronidase that breaks down hyaluronic acid within the tissue and increases the absorption of drugs into that tissue, for all previously approved solid tumor indications for Keytruda. Subcutaneous administration has the advantage of reduced preparation and administration time compared to IV administration. If approved, this would be the third subcutaneous checkpoint inhibitor following Opdivo Qvantig™ and Tecentriq Hybreza™, which target PD-1 and programmed death-ligand 1 (PD-L1), respectively. A decision from the FDA is expected to come in September 2025.

With the patent for Keytruda anticipated to expire in the next few years, a number of applications are expected for biosimilar products. A biosimilar is a biologic product that is highly similar to, and has no clinically meaningful differences from, an existing FDA-approved biologic. Biosimilars are made with the same types of living sources as the reference product, are administered the same way, and have the same strength, dosage, potential treatment benefits, and potential side effects. The FDA approves biosimilars through an abbreviated pathway that does not require a clinical study for all approved indications of the reference product. There are currently seven biosimilars to Keytruda in phase 3 trials that could provide potential for cost savings if approved.

Recent KDIGO guideline updates

Kidney Disease: Improving Global Outcomes (KDIGO) is a global organization that develops and implements evidence-based clinical practice guidelines for the evaluation, management, and treatment of various kidney diseases. New guidelines are published and older guidelines are updated based on the availability of new evidence that may alter recommendations.

Current knowledge and practice in measuring kidney function and predicting the risk of disease progression have evolved as individuals with kidney diseases are increasingly included in clinical trials. Many drugs for kidney diseases and related complications are in the pipeline, and new therapies have positively influenced prognosis. Since last year, KDIGO has published one new guideline and four guideline updates. Two updates are also currently under review and are expected to be published later this year. Topics include chronic kidney disease (CKD), anemia in CKD, autosomal dominant polycystic kidney disease (ADPKD), and glomerular diseases. Glomerular diseases directly affect the kidneys' ability to filter blood and can progress to CKD if untreated. Lupus nephritis, nephrotic syndrome, antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, immunoglobulin A (IgA) nephropathy (IgAN) and IgA vasculitis (IgAV) are glomerular diseases included in recent KDIGO guideline updates.

Treatment for kidney diseases mainly focuses on preventing disease progression, achieved through lifestyle modification and management of risk factors such as high blood pressure and diabetes. Glomerular diseases caused by the immune system are also managed with glucocorticoids and other immunosuppressive medications. Many key guideline updates relate to the availability of new drugs for the treatment of these diseases, as shown in the table below.

Guideline topic[2]	Brief disease background	Key medication therapy updates
CKD, 2024 Last updated: 2012	• Abnormality of kidney structure or function that affects the ability to filter blood • Can lead to high blood pressure, heart disease, stroke, early death	*Note: These recommendations are updates to the CKD guideline, but are not new recommendations; they refer to the KDIGO 2022 Diabetes in CKD guideline* • Strong recommendation for sodium-glucose co-transporter 2 inhibitors (SGLT2i) in individuals with CKD and type 2 diabetes (T2D) to decrease risk of disease progression and reduce cardiovascular (CV) risk o Farxiga® (dapagliflozin) o nvokana® (canagliflozin) o Jardiance® (empagliflozin) • Strong recommendation for glucagon-like-peptide 1 (GLP-1) receptor agonists with documented CV benefits in adults with T2D and CKD who have not achieved glycemic targets o Ozempic® (semaglutide) o Victoza® (liraglutide) o Trulicity® (dulaglutide) • Suggest nonsteroidal mineralocorticoid receptor antagonist with proven kidney or CV benefit for certain adults with T2D and CKD o Kerendia® (finerenone)
ANCA-associated vasculitis, 2024 Last updated: 2021	• Antibodies in the blood and inflammation of small blood vessels that can affect kidneys and other organs • Causes protein and blood in urine	• Recommendations to decrease glucocorticoid use to achieve disease remission • New practice point: Tavneos® (avacopan) for add-on therapy to achieve disease remission as an alternative to glucocorticoids
Lupus nephritis, 2024 Last updated: 2021	• Inflammation of the glomeruli in individuals with systemic lupus erythematosus	• New options to add onto glucocorticoids and other immunosuppressant drugs for initial treatment o Benlysta® (belimumab) o Lupkynis® (voclosporin)
Nephrotic syndrome in children, 2025 Last updated: 2021	• Damage to glomeruli causes too much protein in the urine, leading to fluid buildup in the body	• New treatment algorithm on which immunosuppressive therapy to use in children responsive to glucocorticoids who later relapse or become steroid-dependent

ADPKD, 2025 New guideline	• Genetic condition that causes kidney cysts • Can lead to high blood pressure, kidney stones, blood in urine, kidney pain and infections	• Delay disease progression with tolvaptan
IgAN and IgAV Last updated: 2021	• Buildup of IgA in kidneys causes inflammation and damage to glomeruli, leading to protein in the urine	*Guideline currently under review; potential updates:* • Tarpeyo® (budesonide) and Filspari® (sparsentan) to slow kidney function decline • Fabhalta® (iptacopan) and Vanrafia® (atrasentan) to decrease protein in the urine
Anemia in CKD Last updated: 2012	• Damage to kidneys leads to decreased red blood cell production	*Guideline currently under review; potential updates:* • Vafseo® (vadadustat) to treat anemia in individuals receiving dialysis

References

1. Investing.com: *Earnings call: Insmed reports strong Q3 growth, eyes brensocatib launch* (May 2025): **investing.com**.
2. KDGIO.org: *Kidney Disease: Improving Global Outcomes (KDIGO) Guidelines.* (June 4, 2025): **https://kdigo.org/guidelines/**

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