carelon Rx

Drug and biologic pipeline update Q2 2025

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CarelonRx's quarterly Drug and biologic pipeline update

Our Q2 2025 update spotlights three agents of interest with anticipated approvals in 2025 or 2026: vusolimogene oderparepvec for melanoma, sodium dichloroacetate for pyruvate dehydrogenase complex deficiency, and sonpiretigene isteparvovec for retinitis pigmentosa. Other select drugs and biologics in the pipeline, including gene therapies and biosimilars, are also highlighted. A review of Food and Drug Administration (FDA) approvals from 2024 is provided. Other topics this quarter include overviews of treatment landscapes and pipelines for hemophilia and myasthenia gravis.

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

Top emerging new therapies

Sonpiretigene isteparvovec

Condition:
Retinitis pigmentosa (RP) is a broad term that encompasses a complex group of inherited retinal dystrophies caused by mutations in over 200 different genes. Individuals with RP experience progressive degeneration and loss of retinal cells over time leading to differing levels of vision loss, with a few mutations resulting in complete blindness. RP is estimated to affect 1 in 3,700 individuals in the U.S. and Europe. Nanoscope estimates approximately 100,000 individuals in the U.S. have RP.

Role in treatment:
Sonpiretigene isteparvovec is seeking to become the second FDA-approved gene therapy for RP. Using a viral vector to penetrate retinal cells, sonpiretigene isteparvovec delivers a *multi-characteristic opsin* (MCO) gene expression cassette that helps retinal cells detect light. Unlike Luxturna® (voretigene neparvovec-rzyl), the first gene therapy ever FDA-approved in 2017, which is specifically for the treatment of individuals with confirmed biallelic *RPE65* mutations, sonpiretigene isteparvovec can be given to any individual diagnosed with RP who has severe vision loss, regardless of their underlying mutation.

Efficacy:
The pivotal phase 2b RESTORE trial evaluated 28 legally blind individuals with severe and permanent vision loss associated with advanced RP. The primary endpoint was met with statistical significance with the sonpiretigene isteparvovec treatment group demonstrating a greater improvement in visual acuity from baseline to one year after treatment compared to the control group. In addition, 52- and 76-weeks after being treated with sonpiretigene isteparvovec 39% and 56%, respectively, of individuals gained 3-lines or more of vision, using a standardized vision chart to assess visual acuity.

Safety:
Sonpiretigene isteparvovec delivery resulted in no serious adverse events. The most common adverse events were related to anterior chamber cell inflammation and ocular hypertension, both managed by topical ophthalmic medications.

Financial impact:
The price of sonpiretigene isteparvovec is unknown. However, it could be priced similarly to other gene therapies for rare diseases at $3M or more per one-time treatment. Depending on visual acuity, one or both eyes in an individual with RP could be eligible for treatment.

CarelonRx view:
While RP is one of the most prevalent inherited retinal disorders, sonpiretigene isteparvovec is seeking approval for the group of individuals with permanent and severe vision loss caused by advanced RP. If approved, sonpiretigene isteparvovec may become the first mutation-agnostic gene therapy option for legally blind individuals with advanced RP. It remains unknown how long the visual acuity gains seen in select individuals treated with sonpiretigene isteparvovec in trials will last.

Product:
Sonpiretigene isteparvovec

Indication:
Retinitis pigmentosa

Estimated FDA approval:
2025

Therapeutic class:
Gene therapy

Route of administration:
Intravitreal injection

FDA designations:
Fast Track; Orphan

Manufacturer:
Nanoscope Therapeutics

Vusolimogene oderparepvec

Condition:
Melanoma, the fifth most common cancer, is the most advanced type of skin cancer. Of the different skin cancers, melanoma causes the most deaths because it is more likely to spread to other parts of the body. In 2024, there were approximately 100,000 newly diagnosed cases and melanoma was estimated to have caused 8,000 deaths in the US.

Vusolimogene oderparepvec (RP1) is an injection administered directly into an individual's tumor with the goal of maximizing an immune response to treatment. RP1 is an oncolytic immunotherapy that uses a genetically modified strain of the herpes simplex virus (HSV) to deliver two immune activating proteins.

Role in treatment:
RP1 has submitted for approval in combination with Opdivo® (nivolumab injection) for the treatment of advanced melanoma. Opdivo is a programmed death receptor-1 (PD-1) blocking antibody carrying an indication for the treatment of unresectable or metastatic melanoma for individuals as monotherapy or in combination with Yervoy® (ipilimumab injection), human cytotoxic T-lymphocyte antigen 4 (CTLA-4)-blocking antibody. RP1 submitted for anti-PD1 failed melanoma.

RP1, an off-the shelf immunotherapy, will compete indirectly with Amtagvi® (lifileucel injection), a personalized tumor-derived immunotherapy, for people with unresectable or metastatic melanoma. Amtagvi is given as a single-dose infusion but its use is limited to people with acceptable health status as it also requires the use of highly toxic chemotherapy.

Efficacy:
RP1 filed for accelerated approval based on initial data from the IGNYTE, early phase clinical trial. IGNYTE evaluated individuals given RP1 injections in combination with Opdivo which resulted in a 34% overall response rate, demonstrating clinical activity in individuals who had previously failed treatment with an anti-PD1. The confirmatory Phase 3 trial, IGNYTE-3, has begun. It is evaluating RP1 in combination with Opdivo in individuals whose advanced melanoma has progressed on anti-PD1 and anti-CTLA-4 treatments compared to treatment of physician's choice. The dosing regimen for RP1 in the IGNYTE-3 trial is unclear; however, RP1 was given every 2 weeks for a total of 8 cycles in the IGNYTE trial, with an option to reinitiate RP1 beyond 8 cycles if prespecified criteria were met.

Safety:
Overall, 89% of side effects were rated as grade 1 and 2, or mild to moderate severity, in the IGNYTE trial. Of the grade 3 events, none occurred in more than 5% of individuals. There were five grade 4 events and no grade 5 events.

Financial impact:
The price of RP1 is unknown. However, RP1 treatment will be used in combination with Opdivo which carries an annual wholesale acquisition cost of approximately $202,000 for melanoma. Amtagvi carries a one-time wholesale acquisition cost of $515,000.

Product:
Vusolimogene oderparepvec (RP1)

Indication:
Advanced melanoma

Estimated FDA approval:
July 2025

Therapeutic class:
Oncolytic immunotherapy

Route of administration:
Intratumoral injections

FDA designations:
Breakthrough; Priority

Manufacturer:
Replimune

CarelonRx view:
The company anticipates approximately 10,500 individuals may be eligible for RP1 in the US based on estimates of how many people progress while on anti-PD1 therapy and how many would potentially have lesions addressable with RP1 (i.e., superficial lesions or deeper lesions that require image guided injection). There are many remaining questions with RP1, including its price and if it will compete with Amtagvi. The confirmatory IGNYTE-3 trial will determine if initial results from early phase trials will translate to an overall improvement in survival when RP1 is added to Opdivo for individuals with advanced melanoma.

SL-1009 (sodium dichloroacetate)

Condition:
Pyruvate dehydrogenase complex deficiency (PDCD) is a rare metabolic disorder that affects carbohydrate metabolism and the breakdown of nutrients for energy. It is caused by mutations leading to an enzyme deficiency. It primarily affects the nervous system and skeletal muscle. Symptoms may begin shortly after birth or appear later in childhood and include extreme tiredness, poor feeding, rapid breathing, developmental delay, uncontrolled movements, low muscle tone, abnormal eye movements, and seizures. It is estimated that 300-500 people are currently being treated in the US with an overall prevalence of as high as 2,000.

Role in treatment:
Sodium dichloroacetate would be the first Food and Drug Administration (FDA)-approved treatment for PDCD. It works by inhibiting enzymes that may be overexpressed in PDCD. This leads to increased energy production. Dosing will be individualized based on a genetic test that determines whether a person is a fast or slow metabolizer.

Efficacy:
The New Drug Application submitted to the FDA was supported by positive data from a phase 3 study and a survival analysis. The phase 3 study evaluated daily Observer Reported Outcomes to measure changes in motor domains and safety compared with placebo. The survival analysis compared outcomes in the phase 3 data with an external, untreated natural history cohort.

Safety:
In the phase 3 study, individuals treated with sodium dichloroacetate were dose-stratified after randomization using a proprietary test to identify genotypes and provide individualized dosing. The goal was to reduce adverse events such as peripheral neuropathy.

Financial impact:
If approved, sodium dichloroacetate will be the first treatment option for PDCD. The cost is unknown at this time but it will likely be high, similar to what is seen for other FDA-approved treatments in orphan diseases.

CarelonRx view:
Treatment options for PDCD are limited to symptom management and a ketogenic diet. Sodium dichloroacetate may provide the first FDA-approved treatment for this rare metabolic disease. If approved, individualized genetically driven dosing will also be available.

Product:
SL-1009 (sodium dichloroacetate)

Indication:
Pyruvate dehydrogenase complex deficiency (PDCD)

Estimated FDA approval:
May 2025

Therapeutic class:
Pyruvate dehydrogenase kinase (PDK) inhibitor

Route of administration:
Oral

FDA designations:
Fast track; Orphan drug; Priority

Manufacturer:
Saol Therapeutics

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
Atrasentan AbbVie	Immunoglobulin A (IgA) nephropathy/oral	**Addition to class:** would compete with Filspari® and Fabhalta®	Between May and June 2025	⊗
SL-1009 (sodium dichloroacetate) Saol Therapeutics	Pyruvate dehydrogenase complex deficiency/oral	**First in class:** would be first FDA-approved agent for this indication	05/27/2025	🔬
AR-15512 Aerie Pharmaceuticals	Dry eye disease/ ophthalmic	**First in class:** novel mechanism of action in dry eye; rapid onset of action	05/30/2025	⊗
Delgocitinib Leo Pharma	Atopic dermatitis/topical	**Addition to class:** specifically for atopic dermatitis of the hand	Second half of 2025	⊗
Clesrovimab Merck	Respiratory syncytial virus (RSV)/intramuscular (IM)	**Addition to class:** prophylactic monoclonal antibody; would compete with Beyfortus	06/10/2025	⊗
VesiGel® (mitomycin) UroGen	Bladder cancer/ intravesical	**Addition to class:** for low-grade intermediate-risk non-muscle invasive bladder cancer (LG-IR-NMIBC)	06/13/2025	⊗

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

*As of February 25, 2025.

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
Sebetralstat KalVista Pharmaceuticals	Hereditary angioedema, on-demand treatment/ oral	**Addition to class:** would be the first oral option for on-demand treatment	06/17/2025	
Zycubo™ (copper histidine) Cyprium Therapeutics	Menkes kinky hair syndrome/subcutaneous (SC)	**Addition to class:** would be first FDA-approved agent for this indication	06/30/2025	
Avutometinib Verastem	Ovarian cancer, low-grade serous ovarian cancer (LGSOC)/oral	**Addition to class:** in combination with defactinib for recurrent KRAS mutant disease	06/30/2025	
Defactinib Verastem	Ovarian cancer, low-grade serous ovarian cancer (LGSOC)/oral	**Addition to class:** in combination with avutometinib for recurrent KRAS mutant disease	06/30/2025	
Troriluzole Biohaven	Spinocerebellar ataxia/oral	**First in class:** would be first FDA-approved agent for this indication	Third quarter 2025	
Translarna (ataluren) PTC Therapeutics	Duchenne muscular dystrophy/oral	**First in class:** for treatment of nonsense mutation disease	Third quarter 2025	
Pegzilarginase Aeglea BioTherapeutics	Arginase 1 deficiency (ARG1-D)/intravenous (IV)	**First in class:** would be first FDA-approved agent for this indication	07/05/2025	
Vusolimogene oderparepvec Replimune	Advanced melanoma/ intratumoral	**Addition to class:** oncolytic immunotherapy; used in combination with Opdivo®	07/22/2025	

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Drug or biologic manufacturer	Indication/route	Place in therapy	Estimated approval date	Impact on overall drug or medical spend
Sepiapterin PTC Therapeutics	Phenylketonuria/oral	**Addition to class:** would compete with Kuvan® and its generics	07/30/2025	
Elinzanetant Bayer	Menopause, vasomotor symptoms/oral	**Addition to class:** non-hormonal therapy; would compete with Veozah®	08/01/2025	
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	
Donidalorsen Ionis	Hereditary angioedema/SC	**Addition to class:** prophylaxis to prevent attacks	08/21/2025	
Zopapogene imadenovec (PRGN-2012) Precigen	Recurrent respiratory papillomatosis/SC	**First in class:** would be first FDA-approved gene-based therapeutic 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	
Aficamten Cytokinetics	Symptomatic obstructive hypertrophic cardiomyopathy (HCM)/oral	**Addition to class:** would compete with Camzyos®; quicker onset; potential for improved safety	09/26/2025	

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*As of February 25, 2025.

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
LNZ-100 (aceclidine) Lenz Therapeutics	Presbyopia/ophthalmic	**Addition to class:** would compete with Vuity® and Qlosi™	08/08/2025	⊗
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	🔬
Paltusotine Crinetics Pharmaceuticals	Acromegaly/oral	**Addition to class:** for individuals who are treatment naïve or those switching from other therapies	09/25/2025	⊗
Telisotuzumab vedotin AbbVie	Non-small cell lung cancer (NSCLC)/IV	**First in class:** for c-Met–overexpressing disease	09/27/2025	⊗
NP-001 (sodium chlorite) Neuvivo	Amyotrophic lateral sclerosis/IV	**First in class:** potential disease-modifying therapy	10/07/2025	⊗
Plozasiran Arrowhead Pharmaceuticals	Familial chylomicronemia syndrome/SC	**Addition to class:** potential advantage of quarterly dosing	11/18/2025	🔬
Lerodalcibep LIB Therapeutics	Dyslipidemia/ Hypercholesterolemia/SC	**Addition to class:** third generation proprotein convertase subtilisin/ kexin type 9 (PCSK9) inhibitor	12/12/2025	⊗

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*As of February 25, 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 sixty-seven biosimilar products are FDA approved in the United States. Recent approvals include Steqeyma® (ustekinumab-stba) in December 2024; Avtozma® (tocilizumab-anoh) in January 2025; and Ospomyv™ and Xbryk™ (denosumab-dssb), Merilog™ (insulin aspart-szjj), and Stoboclo® and Osenvelt® (denoxumab-bmwo) in February 2025.

Biologic products with biosimilars in Phase 3 clinical trials*

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
		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 March 6, 2025. Excludes biosimilars that are FDA approved and have launched.

Biologic products with biosimilars in Phase 3 clinical trials* (continued)

Brand name	Brand manufacturer	Biosimilar name	Biosimilar manufacturer	FDA approval*
Humira® (100 mg/mL)	AbbVie	Adalimumab AbbVie	AbbVie	11/3/2023
		Hadlima HC	Samsung Bioepis; Organon	Pending
		Yuflyma	Celltrion	Pending
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 March 6, 2025. Excludes biosimilars that are FDA approved and have launched.

Biologic products with biosimilars in Phase 3 clinical trials* (continued)

Brand name	Brand manufacturer	Biosimilar name	Biosimilar manufacturer	FDA approval*
Prolia®/Xgeva®	Amgen	Denosumab Samsung Bioepis	Samsung Bioepis; Samsung Biologics	2/13/2025
		Ospomyv/Xbryk	Samsung Bioepis; Samsung Biologics	2/13/2025
		Stoboclo/Osenvelt	Celltrion	2/28/2025
		Jubbonti®/Wyost®	Sandoz	3/5/2024
		AVT03	Alvotech; Dr. Reddy's; Alvogen	Pending
		Bmab 1000	Biocon	Pending
		FKS518	Fresenius Kabi	Pending
		HLX14	Henlius; Organon	Pending
		INTP23	Intas; Accord	Pending
		RGB-14-P	Gedeon Richter; Hikma	Pending
		TVB-009P	Teva	Pending
Simponi®/Simponi Aria	Johnson & Johnson	AVT05	Alvotech; Teva; Alvogen	Pending
Soliris®	Alexion; AstraZeneca	Bkemv™	Amgen	5/28/2024
		Epysqli™	Samsung Bioepis	7/19/2024
Stelara®	Johnson & Johnson	Imuldosa™	Dong-A Pharmaceutical; Intas; Meiji Seika; Accord	10/10/2024
		Ustekinumab Alvotech	Alvotech; Teva	10/18/2024
		BAT2206	Bio-Thera Solutions; Hikma	Pending
Tysabri® IV	Biogen; Royalty Pharma	Tyruko®	Polpharma; Sandoz	8/24/2023
Xolair®	Roche; Genentech; Novartis	CT-P39	Celltrion	Pending

*As of March 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
Prademagene zamikeracel (Pz-cel; EB-101) Abeona	Dystrophic epidermolysis bullosa (DEB)/multiple surgically placed skin-graft	Competing to be the second localized gene-based wound therapeutic for people 6 and older with DEB; will compete with Vyjuvek™. Uses viral vector (adeno-associated virus).	04/29/2025
Vusolimogene oderparepvec (RP-1) Replimune	Advanced melanoma/multiple injections directly into the tumor	First localized gene-based therapeutic for this indication; used in combination with Opdivo® for adults with advanced melanoma who have previously received an anti-PD1 containing regimen. Uses viral vector (herpes simplex virus).	07/22/2025 (filed)
Rebisufligene etisparvovec (UX111) Ultragenyx Pharmaceutical	Mucopolysaccharidosis IIIA (Sanfilippo Type A)/single intravenous (IV) infusion	Competing with OTL-201 to be first gene therapy for this indication. Uses viral vector (adeno-associated virus).	08/18/2025 (filed)
Zopapogene imadenovec (PRGN-2012) 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).	Mid-2025 (filed)

*As of February 24, 2025

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
RGX-121 Regenxbio	Mucopolysaccharidosis II (MPS II; Hunter syndrome)/ single intracisternal or intracerebroventricular injection	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2H25 (initiated rolling BLA)
RP-L102 Rocket	Fanconi anemia (FA)/single IV infusion	First gene therapy for this indication. Uses viral vector (lentivirus).	2H25 (initiated rolling BLA)
Marnetegragene autotemcel (RP-L201) Rocket	Leukocyte adhesion deficiency-I/single IV infusion	First gene therapy for this indication. Uses viral vector (lentivirus).	2025 (FDA-denied; plans to refile)

*As of February 24, 2025

Gene and gene-based therapies of significant interest with potential FDA-submissions in 2025-2027*

Gene therapy/ gene-based therapy	Indication/route	Place in therapy	Estimated approval date
Cretostimogene grenadenorepvec (CG0070) Novartis	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 (DTX401) Ultragenyx	Glycogen storage disease type Ia/single IV infusion	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2025
Sonpiretigene isteparvovec (MCO-010) Nanoscope	Retinitis Pigmentosa (RP)/single IV infusion	First mutation-agnostic gene therapy for RP. Uses viral vector (adeno-associated virus).	2025
Generx® (alferminogene tadenovec) Gene Biotherapeutics	Angina/single intracoronary infusion	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2025-2026
Giroctocogene fitelparvovec (PF-07055480; SB-525) Pfizer and Sangamo	Hemophilia A/single IV infusion	Competing with SPK-8011 to be second gene therapy for hemophilia A; will compete with FVIII products, Hemlibra, and Roctavian. 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
TAVO (tavokinogene telseplasmid) OncoSec Medical	Metastatic melanoma/multiple intratumoral injections	First gene therapy for this indication. Uses non-viral vector (plasmid DNA).	2025-2026
UX701 Ultragenyx	Wilson 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

*As of February 24, 2025

Gene and gene-based therapies of significant interest with potential FDA-submissions in 2025-2027*

Gene therapy/ gene-based therapy	Indication/route	Place in therapy	Estimated approval date
ABBV-RGX-314 Regenxbio	Neovascular age-related macular degeneration (wet AMD) and diabetic retinopathy/ 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
Bidridistrogene xeboparvovec (SRP-9003) 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 (D-Fi; FCX-007) Castle Creek Biosciences	Dystrophic epidermolysis bullosa (DEB)/multiple intradermal injections	Competing to be the second localized gene-based wound therapeutic for people 2 and older with DEB; will compete with Vyjuvek. 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
Engensis; donaperminogene seltoplasmid Helixmith	Diabetic peripheral neuropathy and Diabetic foot and other ulcers/multiple intramuscular injections	First gene-based therapy for these indications. Uses non-viral vector (plasmid deoxyribonucleic acid (DNA)).	2026
Isaralgagene civaparvovec (ST-920) Sangamo	Fabry disease/single IV infusion	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2026
LX2006 Lexeo	Friedreich's Ataxia Cardiomyopathy/single IV infusion	First gene therapy for this indication. 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

*As of February 24, 2025

Gene and gene-based therapies of significant interest with potential FDA-submissions in 2025-2027*

Gene therapy/ gene-based therapy	Indication/route	Place in therapy	Estimated approval date
BBP-812 Aspa	Canavan disease/ single IV infusion	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2026-2027
Avalotcagene ontaparvovec (DTX301) Ultragenyx	Ornithine transcarbamylase (OTC) deficiency/ single IV 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. Uses gene editing.	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
RP-L301 Rocket	Pyruvate Kinase Deficiency (PKD)/single IV infusion	First gene therapy for this indication. Uses viral vector (lentivirus).	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 (CAN-2409) Candel	Intermediate-to-high-risk localized prostate cancer/ multiple intratumoral injections	First localized gene-based therapeutic for this indication; designed as a viral immunotherapy; used in combination with an oral anti-herpes drug, such as valacyclovir, to destroy cancer cells. Uses viral vector (adeno-associated virus).	2027

*As of February 24, 2025

Gene and gene-based therapies of significant interest with potential FDA-submissions in 2025-2027*

Gene therapy/ gene-based therapy	Indication/route	Place in therapy	Estimated approval date
Detalimogene voraplasmid enGene	Non-muscle invasive bladder cancer (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
Laruparetigene zovaparvovec (laru-zova; AGTC-501) 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 viral vector (adeno-associated virus).	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 February 24, 2025

Analysis: 2024 year in review for novel drug approvals

The Food and Drug Administration (FDA) Center for Drug Evaluation and Research (CDER) releases an annual report entitled *Advancing Health Through Innovation: New Drug Therapy Approvals*. The report summarizes notable approvals for the prior year.

Below are approval highlights from the 2024 report (2023 numbers in parentheses):

- 50 (55) therapies approved in total
- 24 (20) first in class therapies (unique mechanisms of action)
- 26 (28) therapies approved for orphan diseases (affect < 200,000 people in US)
- 22 (25) therapies approved with Fast Track status
- 18 (9) therapies approved as Breakthrough Therapies
- 28 (31) therapies approved with Priority Review status (6-month review versus 10-month for standard review)
- 7 (9) therapies approved under Accelerated Approval (confirmatory trials must be conducted)
- 33 (36) of the 50 (55) approvals used one or more expedited programs (Fast Track Designation, Breakthrough Therapy Designation, Priority Review, and/or Accelerated Approval)
- 47 (49) of the 50 (55) approvals came on or before the Prescription Drug User Fee Act (PDUFA) goal date

Market trends

Hemophilia treatment landscape and pipeline

While the mainstay of treatment for hemophilia, a life-threatening disorder in which the blood does not clot properly, is to restore the body's deficient levels of clotting factors using plasma-derived or recombinant clotting factor VIII or IX for hemophilia A or B, respectively, a number of novel therapeutics have been approved in recent years with many more in the pipeline.

The use of clotting factor concentrates (CFC) as either prophylactic or acute treatment is limited by the lengthy, costly and frequent number of infusions as well as the risk of developing inhibitors, which prevent the treatment from working and make a bleed difficult to stop. The Food and Drug Administration (FDA) has approved agents that either bypass the factors in the clotting cascade that are blocked by the inhibitor (FEIBA®, NovoSeven®, or SevenFact®), mimic the factor without being affected by the inhibitor (Hemlibra®), or target other anti-clotting factors such as Alhemo®. MIM8 and fitusiran are in development to mimic clotting factor VIIIa and reduce antithrombin, respectively.

Another approach to the treatment of hemophilia is to fix the cells in the liver that make the clotting factor using a modified virus to carry a gene for that clotting factor to the liver cell. This is known as gene therapy and the FDA has approved three products (Beqvez®, Hemgenix®, Roctavian®); however, the manufacturer of Beqvez has recently indicated that Beqvez will no longer be available due to low demand.[1] Giroctocogene fitelparvovec is in late stage development with positive data from a Phase 3 study recently released. While gene therapy has the potential to eliminate the need for prophylactic factor replacement, the duration of effect remains a question as declining factor levels have been observed over several years of data. Also, longer term studies are needed to ensure there are no additional complications.

Even with a variety of factor products and other prophylactic treatments, managing hemophilia effectively remains challenging due to the associated costs and burdens. Some gene therapies have gained approval, and others are in development, along with alternative strategies aimed at enhancing factor activity or decreasing natural anticoagulants.

Agents recently approved by the FDA

Agent manufacturer	Class	Indication	Route, frequency	Approval date
Hemlibra Genentech	Bispecific factor IXa- and factor X-directed antibody	Prophylaxis in adults and pediatrics newborn and older with hemophilia A, with or without inhibitors	Subcutaneous (SC); once weekly, once every 2 weeks or once every 4 weeks	11/16/2017
Hympavzi™ Pfizer	Tissue factor pathway inhibitor (TPFI) antagonist	Prophylaxis in adults and pediatrics 12 years and older with hemophilia A or B, without inhibitors	SC; once weekly	10/11/2024
Alhemo Novo Nordisk	TPFI antagonist	Prophylaxis in adults and pediatrics 12 years and older with hemophilia A or B, with inhibitors	SC; once daily	12/20/2024
Gene therapies				
Hemgenix CSL Behring	Adeno-associated virus (AAV) vector-based gene therapy	Treatment of adults with hemophilia B who are on factor IX prophylaxis, have life-threatening bleeding, or repeated serious spontaneous bleeds	Intravenous (IV); single dose	11/22/2022
Roctavian BioMarin	AAV vector-based gene therapy	Treatment of adults with severe hemophilia A without pre-existing antibodies to AAV serotype 5	IV; single dose	07/30/2023

Pipeline agents for hemophilia*

Agent manufacturer	Class	Indication studied	Route, frequency	FDA target action date
Giroctocogene fitelparvovec (SB-525) Sangamo	AAV vector-based gene therapy	Treatment of adults with moderately severe to severe hemophilia A	IV; single dose	Phase 3 study data released; potential to file in 2025
Fitusiran Alnylam	Small interfering RNA	Treatment of hemophilia A or B, with or without inhibitors	SC; once monthly or every other month	03/28/2025
MIM8 Novo Nordisk	FVIIIa mimetic bispecific antibody	Prophylaxis for hemophilia A, with or without inhibitors	SC; once weekly, once every 2 weeks or once monthly prophylaxis	Submission expected in 2025

*As of March 12, 2025

Myasthenia gravis: treatment landscape and pipeline

Generalized myasthenia gravis (gMG) is a rare autoimmune disorder that causes weakness in voluntary muscles. These muscles are involved in moving the limbs, eyes, and face, chewing, swallowing, speaking, and breathing. Younger women (below age 40) and older men (above age 60) are more likely to have gMG, although it can occur at any age.

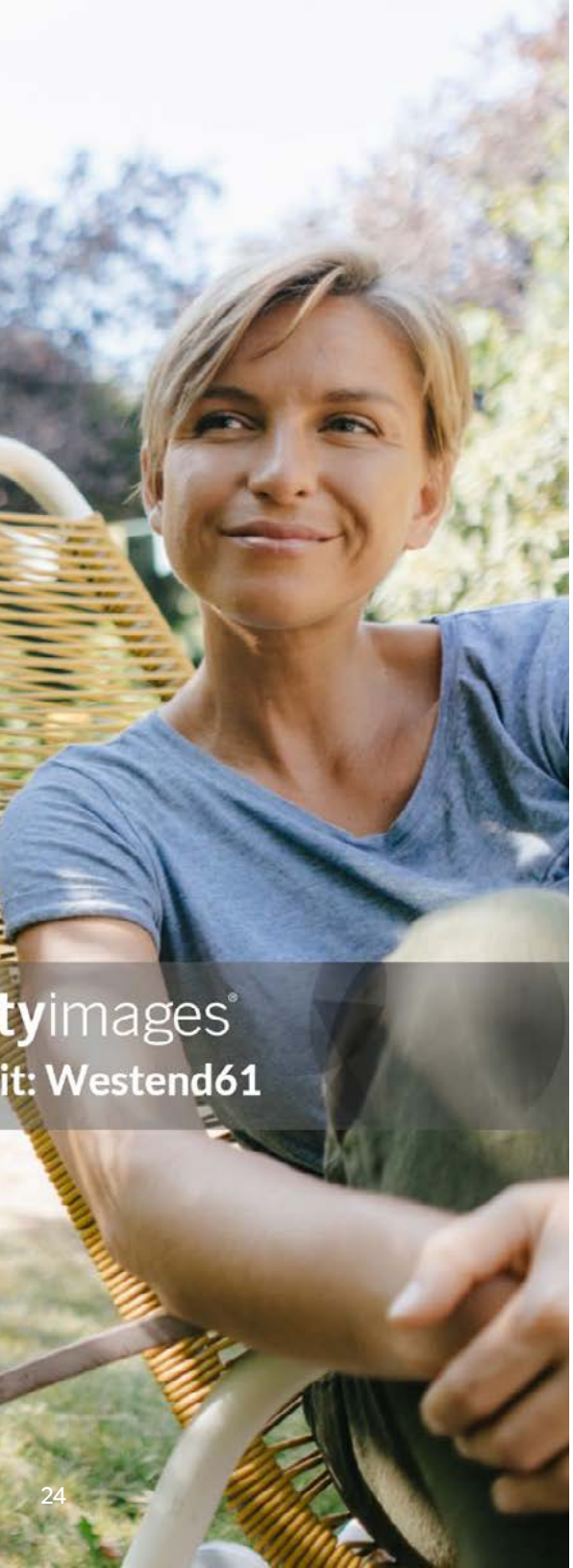
In gMG, antibodies produced by one's own immune system block acetylcholine at nerve-muscle junctions, resulting in impaired muscle contraction. Symptoms often worsen after physical activity and may include weakness in the limbs and eyes, changes in vision or facial expressions, difficulty swallowing or speaking, and shortness of breath.

gMG is classified by antibody status and the most common type is anti-acetylcholine receptor antibody positive. Knowing the antibody status can help guide selection of therapy.

Seropositive or Seronegative	Antibodies	% of individuals with gMG
+	Acetylcholine receptor (AChR)	85%
	Muscle-specific tyrosine kinase (MuSK)	8%
	Low-density lipoprotein receptor-related protein 4 (LRP4)	1%
-	No antibodies for AChR, MuSK, or LRP4	6-10%

While there is no cure, treatments are available which can improve symptoms of gMG. Treatment for most individuals begins with an acetylcholinesterase inhibitor, like pyridostigmine. Corticosteroids or other immunosuppressives may be used in those not meeting treatment goals after a trial of pyridostigmine.

Several injectable therapies have been Food and Drug Administration (FDA)-approved in recent years for gMG including three complement inhibitors (Soliris®, Ultomiris®, and Zilbrysq®) and three neonatal Fc receptor blockers (Rystiggo®, Vyvgart®, and Vyvgart Hytrulo®). All are indicated for AChR+ gMG in adults. Soliris carries an additional indication for pediatrics 6 years and older with AChR+ gMG. Rystiggo carries an additional indication for adults with MuSK+ gMG. Each of these treatments, except for Zilbrysq which may be self-injected subcutaneously (SC) at home once daily, require healthcare provider administration and are given by SC or intravenous (IV) infusions. Rystiggo, Vyvgart, and Vyvgart Hytrulo are administered weekly during treatment cycles lasting 4 to 6 weeks. Soliris and Ultomiris maintenance doses are administered every 2 to 3 and 8 weeks, respectively. These treatments are currently considered after conventional therapies for severe, refractory gMG. Other alternatives for refractory disease include chronic plasma exchange and IV immunoglobulin.



The landscape of treatments for gMG continues to evolve, with many agents in the pipeline. CarelonRx is closely following medications in late-stage development (table below). Nipocalimab is the next agent anticipated for FDA-approval in April 2025. Like Vyvgart, nipocalimab is an IV neonatal Fc receptor blocker. If approved, it would be the first agent available for LRP4+ individuals representing about 1% of the gMG population. Multiple mechanisms of action and routes of administration are in development for gMG, including two oral agents Fabhalta® and Mavenclad® which are currently approved for other indications.

Agents for gMG in late-stage development*

Agent	Manufacturer	Route **	Mechanism	Antibodies studied	Development status
ALXN1720 (gefurulimab)	AstraZeneca	SC	Complement inhibitor	AChR+	Phase 3
Batoclimab	Immunovant	SC	Neonatal Fc receptor blocker	AChR+	Phase 3
Descartes-08	Cartesian Therapeutics	IV	Autologous mRNA chimeric antigen receptor T-cell cell therapy	AChR+	Phase 3
Fabhalta (iptacopan)	Novartis	Oral	Complement inhibitor	AChR+	Phase 3
Telitacicept	RongChange Biopharmaceuticals	SC	Recombinant fusion protein	AChR+ & MuSK+	Phase 3
Uplizna® (inebilizumab)	Viela Bio	IV	CD19-directed cytolytic antibody	AChR+ & MuSK+	Phase 3
Cemdisiran (+/- Pozelimab)	Alnylam Pharmaceuticals	SC	RNA interference; Complement inhibitor	AChR+ & LRP4+	Phase 3
Nipocalimab	J&J	IV	Neonatal Fc receptor blocker	AChR+, MuSK+, & LRP4+	Pending approval (April 2025)
Mavenclad (cladribine)	Merck	Oral	Purine nucleoside analogue	AChR+, MuSK+, LRP4+, & seronegative	Phase 3

*As of March 12, 2025

**Key: IV = intravenous; SC = subcutaneous

References

1. BioPharmaDive: *Pfizer stops selling hemophilia gene therapy, citing weak demand* (accessed March 2025): **biopharmadive.com**

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