carelon Rx

Drug and biologic pipeline update Q1 2025

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CarelonRx's quarterly Drug and biologic pipeline update

Our Q1 2025 update features summaries of three agents of interest with anticipated approvals in 2025 or 2026: sebetralstat for hereditary angioedema, elinzanetant for vasomotor symptoms, and DTX401 for glycogen storage disease. Other select drugs and biologics in the pipeline, including gene therapies and biosimilars, are also highlighted. A summary of epinephrine products for anaphylaxis is provided. Other topics this quarter include overviews of treatment landscapes and pipelines for immunoglobulin A (IgA) nephropathy, hypertrophic cardiomyopathy, and amyloidosis.

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

Sebetralstat

Condition:

Hereditary angioedema (HAE) is a rare genetic condition that affects an estimated 1 in 50,000 individuals. There are three distinct types of HAE; types I (deficiency of C1 esterase inhibitor (C1-INH)) and II (dysfunction of C1-INH) are the most prevalent. C1-INH helps regulate the plasma bradykinin-forming cascade and the kallikrein-kinin pathway. HAE attacks result from the excessive production of bradykinin that causes edema, affecting the skin, gastrointestinal system, or upper respiratory tract. Individuals may experience swelling and pain that can significantly impact their daily activity, lead to physical changes, and, in serious cases (e.g., involving swelling of the throat), can be fatal.

Role in treatment:

There is no cure for HAE. Management focuses on trigger avoidance, treatment of acute attacks, and prevention of further attacks. Common triggers include dental and medical procedures, stress, menstruation, pregnancy, and infection.

The United States Hereditary Angioedema Association emphasizes that individuals with HAE should have immediate access to on-demand medications that can be administered at the onset of an attack. Guidelines advocate for the use of self-administered treatments whenever possible and stress the importance of treating all attacks promptly, regardless of location or severity.

First-line therapy options for acute attacks include C1-INH concentrates Berinert® and Ruconest®, a bradykinin antagonist icatibant, and a kallikrein inhibitor Kalbitor®. Berinert and Ruconest are administered by short intravenous infusion while generic icatibant and Kalbitor are administered by subcutaneous injection. Kalbitor is considered clinically unfavorable because it has a higher risk of serious anaphylactic reactions than Berinert and Ruconest; for this reason, Kalbitor must be administered by a healthcare professional. Generic icatibant (Firazyr®) is not associated with anaphylaxis.

Sebetralstat is an orally administered plasma kallikrein inhibitor for on-demand treatment of acute attacks in adults and adolescents with HAE.

Individuals who experience frequent or severe HAE attacks may be considered for long-term prophylaxis.

Options include C1-INH concentrates (intravenous Cinryze® and subcutaneous Haegarda®) and kallikrein inhibitors (subcutaneous Takhzyro® and oral Orladeyo®).

Efficacy:

The New Drug Application submitted to the Food and Drug Administration (FDA) for sebetralstat is supported by data from the KONFIDENT phase 3 clinical trial. Individuals receiving sebetralstat experienced shorter times to the beginning of symptom relief, reduction in attack severity, and shorter times to complete attack resolution compared with individuals receiving placebo.

Safety:

In the KONFIDENT trial, sebetralstat was well-tolerated, with an overall safety profile similar to that of the placebo group.

Financial impact:

If approved, sebetralstat would offer a more convenient oral option for the on-demand treatment of acute HAE attacks. Sebetralstat may be priced at a premium to existing agents due to its potential oral dosing advantage. Sebetralstat is also being studied as an oral disintegrating tablet formulation and for use in a pediatric population (ages 2 to 11 years).

CarelonRx view:

The prospect of an oral agent for treating acute HAE attacks may generate interest. While clinical data is limited, indirect comparisons suggest similar safety and efficacy to existing first-line agents. Sebetralstat may provide an advantage over parenteral products, potentially allowing for easier and earlier administration, which could lead to better clinical outcomes.

Product:
Sebetralstat

Indication:
Hereditary angioedema (HAE) on-demand treatment

Estimated FDA approval:
June 2025

Therapeutic class:
Plasma kallikrein inhibitor

Route of administration:
Oral

FDA designations:
Fast track; Orphan drug

Manufacturer:
KalVista Pharmaceuticals

Elinzanetant

Condition:
Menopause occurs when a woman stops having periods, on average at age 50. For many, changes in hormone levels associated with menopause cause bothersome VMS (i.e. hot flashes) and/or genitourinary syndrome of menopause (GSM), a term collectively involving vaginal atrophy, dryness and painful intercourse. Symptoms can start years before menopause and fluctuate over time, with up to 80% of women experiencing VMS.

Role in treatment:
Not all women require treatment for their symptoms. If approved, elinzanetant would join Veozah® (fezolinetant) as the second, once daily, oral, FDA-approved neurokinin (NK) receptor antagonist for the treatment of VMS due to menopause. Elinzanetant is a dual NK-1 and NK-3 receptor antagonist, whereas Veozah is a NK-3 receptor antagonist.

These NK receptor antagonists compete with another oral nonhormonal therapy, generically available low dose paroxetine, as well as several hormone replacement therapies (e.g. estrogen) FDA-approved for VMS. Paroxetine and the hormonal therapies carry black box warnings, which the FDA uses to warn of potential harms with their use. Elinzanetant has the potential to join Veozah and provide another nonhormonal option for women who cannot use existing therapies due to their side effects or associated risks.

Efficacy:
The OASIS 1 and 2 trials, evaluating women with VMS associated with menopause, specifically hot flashes, showed elinzanetant treatment significantly decreased the frequency and severity of VMS after 12 weeks compared to placebo.

Safety:
The most common side effects with elinzanetant were headache and fatigue. No liver-toxicity was observed in trials. Taking Veozah can result in elevations in liver enzymes, warranting monitoring and sometimes treatment discontinuation per FDA labeling. It remains unclear if elinzanetant data, with its similar mechanism of action, will support a similar FDA label.

Financial impact:
The price of elinzanetant is unknown. However, it will likely be priced similarly to Veozah to compete in the market. Veozah carries a wholesale acquisition cost of $550 per month.

CarelonRx view:
While hormone therapy works to reduce VMS, its use should be limited to the shortest amount of time needed due to an increased risk of blood clots, strokes, and some cancers. If approved, elinzanetant would be an additional alternative to using hormone replacement therapies to manage VMS.

Product:
Elinzanetant

Indication:
Treatment of moderate to severe vasomotor symptoms (VMS) associated with menopause

Estimated FDA approval:
August 2025

Therapeutic class:
Dual neurokinin-1 and 3 (NK-1 and 3) receptor antagonist

Route of administration:
Oral

FDA designations:
None

Manufacturer:
Bayer

DTX401

Condition:

Glycogen storage disease type Ia (GSDIa) is a rare autosomal-recessive disorder that results in a deficiency of the glucose-6-phosphate (G6P) hydrolase enzyme. G6P is an essential component in glycogen metabolism, a process that helps to maintain steady blood glucose levels. Diagnosis is confirmed with genetic testing usually before a person turns one year of age after presenting with symptoms such as severe low blood glucose levels, lactic acidosis, seizures, enlarged liver, and an overall failure to thrive. GSDIa accounts for approximately 80% of the overall GSD1 (a and b) population with an incidence of 1 in 100,000 live births. Ultragenyx estimates a prevalence of 6,000 people worldwide with GSDIa.

Role in treatment:

If approved, DTX401 would be the first treatment and the first gene therapy FDA-approved for GSDIa. Currently, people with GSDIa rely on using oral glucose replacement therapy (e.g., uncooked cornstarch), administered up to eight times a day at regular intervals including overnight, to prevent low blood glucose levels between meals and related complications. The only potential cure for GSD1a is a liver transplant.

DTX401 is a one-time infusion that uses an adeno-associated viral (AAV) vector to deliver a transgene with the goal to produce normally functioning G6P.

Efficacy:

The pivotal phase 3, randomized, placebo controlled, cross-over, GlucoGene trial evaluated 44 people aged eight years and older with GSD1a who were receiving cornstarch treatment. The primary endpoint measured the change from baseline to week 48 in their daily cornstarch intake. The trial found people given DTX401 had a statistically greater mean reduction (41%) in their daily cornstarch intake compared to placebo (10%) while also maintaining blood glucose control. In addition, DTX401 treatment resulted in an average reduction of approximately 1 fewer cornstarch dose per day compared to the placebo group.

Safety:

AAV-induced hepatic effects with administration of DTX401 were all considered non-serious and managed with steroids. Liver enzyme elevations occurred in 76% of people given DTX401 compared to 12% with placebo. Four infusion related reactions (IRR) occurred, 2 in each treatment arm. After implementing a protocol change which included slowing the treatment infusion, no additional IRR occurred.

Financial impact:

The price of DTX401 is unknown. However, it will likely be priced similarly to other gene therapies for rare diseases at $3M or more per one-time treatment.

CarelonRx view:

DTX401 would be the first gene therapy approved for GSDIa introducing the possibility for people to achieve a reduction in their daily cornstarch consumption, both a reduction in dosage quantity and dosing frequency. While emerging data supports this disease-modifying agent based on its reduction of cornstarch dosing quantity and frequency, it is unclear how long these effects will last.

Product:
DTX401

Indication:
Treatment of glycogen storage disease type Ia (GSDIa)

Estimated FDA approval:
2025

Therapeutic class:
Gene therapy

Route of administration:
Intravenous

FDA designations:
Fast Track; Orphan; Regenerative Medicine Advanced Therapy (RMAT)

Manufacturer:
Ultragenyx

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
Camrelizumab Elevar Therapeutics	Liver cancer, first- line/ intravenous (IV)	**Addition to class:** programmed cell death protein 1 (PD-1) inhibitor for use in combination with rivoceranib, also under FDA review	03/20/2025	
Rivoceranib Elevar Therapeutics	Liver cancer, first-line/IV	**Addition to class:** tyrosine kinase inhibitor for use in combination with camrelizumab, also under FDA review	03/20/2025	
Etripamil Milestone Pharmaceuticals	Supraventricular tachycardia/intranasal	**Addition to class:** rapid-response therapy that is self- administered	03/28/2025	
Fitusiran Alnylam	Hemophilia A or B/ subcutaneous (SC)	**Addition to class:**for individuals with or without inhibitors	03/28/2025	
Reproxalap Aldeyra Therapeutics	Dry eyes/ophthalmic	**First in class:** new mechanism of action for dry eye	04/02/2025	
Prademagene zamikeracel (Pz-cel; EB-101) Abeona Therapeutics	Dystrophic epidermolysis bullosa (DEB)/surgically placed skin-graft	**Addition to class:** would be second localized gene-based wound therapeutic for this indication; will compete with Vyjuvek; uses viral vector (adeno-associated virus)	04/29/2025	
Atrasentan AbbVie	Immunoglobulin A (IgA) nephropathy/oral	**Addition to class:** would compete with Filspari® and Fabhalta®	Between May and June 2025	

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 December 19, 2024

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
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	⊗
Concizumab Novo Nordisk	Hemophilia A or B/SC	**Addition to class:** for adults and adolescents with inhibitors	05/31/2025	⊗
Avutometinib Verastem	Ovarian cancer, low-grade serous ovarian cancer (LGSOC)/oral	**Addition to class:** in combination with defactinib for recurrent KRAS mutant disease	Mid-2025	⊗
Defactinib Verastem	Ovarian cancer, low-grade serous ovarian cancer (LGSOC)/oral	**Addition to class:** in combination with avutometinib for recurrent KRAS mutant disease	Mid-2025	⊗
Delgocitinib Leo Pharma	Atopic dermatitis/ topical	**Addition to class:** specifically for atopic dermatitis of the hand	Second half of 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	⊗
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	⊗
Pegzilarginase Aeglea BioTherapeutics	Arginase 1 deficiency (ARG1-D)/IV	**First in class:** would be first FDA- approved agent for this indication	07/05/2025	⊗

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*As of December 19, 2024

Other products 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
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	⊗
Aficamten Cytokinetics	Symptomatic obstructive hypertrophic cardiomyopathy (HCM)/oral	**Addition to class:** would compete with Camzyos®; quicker onset; potential for improved safety	08/08/2025	⊗
LNZ-100 (aceclidine) Lenz Therapeutics	Presbyopia/ophthalmic	**Addition to class:** would compete with Vuity® and Qlosi™	08/08/2025	⊗
Nipocalimab Momenta	Myasthenia gravis/IV	**Addition to class:** same class as Vyvgart®, Vyvgart® Hytrulo, and Rystiggo®	08/29/2025	⊗
Paltusotine Crinetics Pharmaceuticals	Acromegaly/oral	**Addition to class:** for individuals who are treatment naïve or those switching from other therapies	09/26/2025	⊗
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	⊗

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*As of December 19, 2024

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-three biosimilar products are FDA-approved in the United States, including six approved in the second half of 2024: Enzeevu™ (aflibercept-abzv), Epysqli® (eculizumab-aagh), Imuldosa® (ustekinumab-srlf), Otulfi™ (ustekinumab-aauz), Pavblu™ (aflibercept-ayyh), Yesintek™ (ustekinumab), and Steqeyma® (ustekinumab-stba).

Biosimilar products awaiting launch and/or approval*

Brand name	Brand manufactuer	Biosimilar name	Biosimilar anufacturer	FDA approval*
Actemra® IV/SC	Roche; Chugai; Genentech	CT-P47	Celltrion	Pending
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
		CT-P42	Celltrion	Pending
Herceptin®	Roche; Genentech	Hercessi™	Henlius; Accord; Intas	4/25/2024
		TX05	Tanvex	Pending

*As of December 19, 2024. Excludes biosimilars that are FDA approved and have launched.

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

Brand name	Brand manufactuer	Biosimilar name	Biosimilar anufacturer	FDA approval*
Humalog® Humalog Pen Humalog U-100 KwikPen	Eli Lilly	GL-LIS	Gan & Lee; Sandoz	Pending
Humira® (100 mg/mL)	AbbVie	Adalimumab AbbVie	AbbVie	11/3/2023
Lantus Solostar®	Sanofi	GL-GLA	Gan & Lee; Sandoz	Pending
Neulasta®	Amgen	Lapelga	Apotex; Accord; Intas	Pending
Neupogen®	Amgen	Nypozi®	Tanvex	6/28/2024
		Grastofil	Apotex; Accord; Intas	Pending
Novolog® (10 mL vial) Novolog FlexPen Novolog FlexTouch Novolog PenFill	Novo Nordisk	AMP-004	Amphastar	Pending
Novolog (10 mL vial) Novolog FlexPen Novolog FlexTouch Novolog PenFill	Novo Nordisk	GL-ASP	Gan & Lee; Sandoz	Pending

*As of December 19, 2024. Excludes biosimilars that are FDA approved and have launched.

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

Brand name	Brand manufactuer	Biosimilar name	Biosimilar anufacturer	FDA approval*
Prolia®	Amgen	Jubbonti®	Sandoz	3/5/2024
		CT-P41-P	Celltrion	Pending
		FKS518	Fresenius Kabi	Between March and April 2025
		HLX14	Henlius; Organon	Pending
		INTP23	Intas; Accord	Pending
		SB16-P	Samsung Bioepis	Pending
		TVB-009P	Teva	Pending
Soliris®	Alexion; AstraZeneca	Bkemv™	Amgen	5/28/2024
		Epysqli	Samsung Bioepis	7/19/2024
Stelara® IV/SC	Johnson & Johnson	Imuldosa IV/SC	Dong-A Pharmaceutical; Intas; Meiji Seika; Accord	10/10/2024
		Otulfi IV/SC	Formycon; Bioeq; Fresenius Kabi	9/27/2024
		Pyzchiva® IV/SC	Samsung Bioepis; Sandoz	6/28/2024
		Selarsdi™ IV/SC	Alvotech; Teva	10/18/2024; 4/16/2024
		Ustekinumab Alvotech IV/SC	Alvotech; Teva	10/18/2024

*As of December 19, 2024. Excludes biosimilars that are FDA approved and have launched.

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

Brand name	Brand manufactuer	Biosimilar name	Biosimilar anufacturer	FDA approval*
Stelara® IV/SC	Johnson & Johnson	Wezlana™ IV/SC	Amgen	10/31/2023
		Yesintek IV/SC	Biocon	12/1/2024
		BAT2206 IV/SC	Bio-Thera Solutions; Hikma	Pending
		Steqeyma IV/SC	Celltrion	12/17/2024
Tysabri® IV	Biogen; Royalty Pharma	Tyruko®	Polpharma; Sandoz	8/24/2023
Xgeva®	Amgen	Wyost®	Sandoz	3/5/2024
		CT-P41-X	Celltrion	Pending
		FKS518	Fresenius Kabi	Pending
		HLX14	Henlius; Organon	Pending
		INTP23	Intas; Accord	Pending
		SB16-X	Samsung Bioepis	Pending
Xolair®	Roche; Genentech; Novartis	CT-P39	Celltrion	Pending

*As of December 19, 2024. 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 one-time 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. 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 and $4 million.[1]

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

Gene therapy/ gene-based therapy	Indication/route	Expected use	Place in therapy	Estimated approval date
Prademagene zamikeracel (Pz-cel; EB-101) Abeona Therapeutics	Dystrophic epidermolysis bullosa (DEB)/ surgically placed skin-graft	One-time surgically placed gene-modified skingraft	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 (refiled)
Vusolimogene oderparepvec (RP- 1) Replimune	Advanced melanoma/injected directing into the tumor	Multiple dosing	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).	09/21/2025 (filed)
Marnetegragene autotemcel (RP-L201) Rocket Pharmaceuticals	Leukocyte adhesion deficiency-I/ intravenous (IV)	One-time dose	First gene therapy for this indication. Uses viral vector (lentivirus).	FDA-denied (plans to refile)
Botaretigene sparoparvovec (AAV-RPGR) Athena Vision; MeiraGTx Ltd.; Janssen Pharma	X-linked retinitis pigmentosa (XLRP)/ subretinal injection	One-time dose	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2025
Cretostimogene grenadenorepvec (CG0070) Novartis	Non-muscle invasive bladder cancer (NMIBC)/intravesical	Multiple dosing	Second gene-based therapeutic; would compete with Adstiladrin®. Uses viral vector (adeno-associated virus).	2025

*As of December 19, 2024

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

Gene therapy/ gene-based therapy	Indication/route	Expected use	Place in therapy	Estimated approval date
Dabocemagene autoficel (D-Fi; FCX- 007) Castle Creek Biosciences	Dystrophic epidermolysis bullosa (DEB)/ intradermal injections	Multiple intradermal injections of gene-modified cells	"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)."	2025
DTX401 Ultragenyx Pharmaceutical	Glycogen storage disease type Ia/IV	One-time dose	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2025
Engensis; donaperminogene seltoplasmid Helixmith	Diabetic peripheral neuropathy and Diabetic foot and other ulcers/ intramuscular injections	Intramuscular injections (multiple doses)	First gene-based therapy for these indications. Uses non-viral vector [plasmid deoxyribonucleic acid (DNA)].	2025
Giroctocogene fitelparvovec (PF- 07055480; SB-525) Pfizer and Sangamo Therapeutics	Hemophilia A/IV	One-time dose	Second gene therapy for hemophilia A; will compete with factor 8 (FVIII) products, Hemlibra, and Roctavian. Uses viral vector (adeno-associated virus).	2025
OTL-201 Orchard	Mucopolysaccharidosis IIIA (Sanfilippo Type A)/IV	One-time dose	Competing with ABO-102 to be first gene therapy for this indication; will compete with hematopoietic cell transplantation (HCT). Uses viral vector (lentivirus).	2025
RGX-121 Regenxbio	Mucopolysaccharidosis II (MPS II; Hunter syndrome)/intracisternal or intracerebroventricular injection	One-time dose	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2025
RP-A501 Rocket Pharmaceuticals	Danon disease/IV	One-time dose	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2025
RP-L102 Rocket Pharmaceuticals	Fanconi anemia (FA)/IV	One-time dose	First gene therapy for this indication. Uses viral vector (lentivirus).	2025
Sonpiretigene isteparvovec (MCO-010) Nanoscope Therapeutics	Retinitis Pigmentosa (RP)/IV	One-time dose	First mutation-agnostic gene therapy for RP. Uses viral vector (adeno-associated virus).	2025

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

Gene therapy/ gene-based therapy	Indication/route	Expected use	Place in therapy	Estimated approval date
UX111 (ABO-102) Abeona Therapeutics	Mucopolysaccharidosis IIIA (Sanfilippo Type A)/IV	One-time dose	Competing with OTL-201 to be first gene therapy for this indication; will compete with HCT. Uses viral vector (adeno-associated virus).	2025
AMT-130 uniQure	Huntington's disease/stereotaxic surgery with infusion into the brain	One-time dose	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2025-2026
DTX301 Ultragenyx Pharmaceutical	Ornithine transcarbamylase (OTC) deficiency/IV	One-time dose	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2025-2026
Generx® (alferminogene tadenovec) Gene Biotherapeutics	Angina/intracoronary infusion	One-time dose	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2025-2026
TAVO (tavokinogene telseplasmid) OncoSec Medical	Metastatic melanoma/ intratumoral injections	Intratumoral injections (multiple doses)	First gene therapy for this indication. Uses non-viral vector (plasmid DNA).	2025-2026
UX701 Ultragenyx	Wilson disease/IV	One-time dose	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2025-2026
Zolgensma® (onasemnogene abeparvovec) Novartis	Spinal muscular atrophy (SMA) Type 2/ intrathecal infusion	One-time dose	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
ABBV-RGX-314 Regenxbio	Neovascular age-related macular degeneration (wet AMD) and diabetic retinopathy/subretinal and/or suprachoroidal injection	One-time dose	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

*As of December 19, 2024

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

Gene therapy/ gene-based therapy	Indication/route	Expected use	Place in therapy	Estimated approval date
Isaralgagene civaparvovec (ST-920) Sangamo	Fabry disease/intravenous infusion	One-time dose	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2026
LX2006 Lexeo Therapeutics	Friedreich's Ataxia Cardiomyopathy/ intravenous infusion	One-time dose	First gene therapy for this indication. Uses viral vector (adeno-associated virus).	2026
RGX-202 Regenxbio	Duchenne muscular dystrophy (DMD)/ intravenous infusion	One-time dose	Second gene therapy for DMD; will compete with Elevidys. Uses viral vector (adeno-associated virus)."	2026
Vyjuvek (beremagene geperpavec-svdt) Krystal Biotech	Dystrophic epidermolysis bullosa (DEB)/ophthalmic	Multiple dosing	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

*As of December 19, 2024

Update: Epinephrine for anaphylaxis product pipeline

Anaphylaxis is the sudden onset of a potentially life-threatening hypersensitivity reaction due to exposure to an allergen including food, medications, or insect stings. Symptoms may affect the skin, tongue, lips, throat, gastrointestinal system, and cardiovascular system. An estimated 1.6% to 5.1% of people in the United States have experienced anaphylaxis.[2]

Epinephrine is used for first-line treatment of anaphylaxis and should be administered immediately. Intramuscular administration into the mid-outer thigh is recommended. Use of an auto-injector is preferred over an ampule, syringe, and needle or prefilled syringe due to ease of use and dosing accuracy.[3] In addition to brand and generic auto-injectors available for anaphylaxis, Neffy® (epinephrine intranasal) was recently approved by the FDA.

Although epinephrine autoinjectors are the mainstay of treatment and are effective if used immediately and properly, there are drawbacks with these products that may lead to reluctance to carry or administer the drug. Key issues with auto-injectors include:[3,4]

- Bulky size of the products make them difficult to carry especially since the recommendation is to have 2 injectors available at all times
- Fear of needles
- Needle-related injuries
- Potentially confusing to administer
- Short shelf life (12 to 18 months)
- Stability and storage issues (recommended to be stored at 68°– 77°F with excursions permitted from 59°– 86°F)

Neffy addresses some of these unmet needs by providing a smaller product with needle-free administration, a 30-month shelf life, and temperature excursions up to 122° F. Additional pipeline agents in late-stage development with potentially favorable attributes are provided in table below.

Epinephrine pipeline: agents in late-stage development*

Drug	Route	Attributes to help address unmet needs	Estimated FDA approval date (stage of development)
Anaphylm™	Sublingual	• Needle-free • Applied under tongue for rapid delivery of epinephrine • No water or swallowing is required • Similar in size to postage stamp and weighs less than one ounce • Designed to withstand temperature excursions • Expected to have longer shelf life than autoinjectors	2025/2026 (Phase 3)
NS-002	Intranasal	• Needle-free • Small size • Stable at room temperature for up to 5 years	2026 (Phase 2)
OX640	Intranasal	• Needle-free • Small size • Stable at a wide range of low to high temperatures • Extended shelf-life	2026 (Phase 1)
BRYN NDS1C	Intranasal	• Needle-free • Small size • Capable of delivering two therapeutic doses of epinephrine	Unknown (Phase 2)

*As of December 19, 2024

Market trends

Immunoglobulin A nephropathy (IgAN) treatment landscape and pipeline

Immunoglobulin A nephropathy (IgAN), also known as Berger's disease, is an autoimmune condition caused by the buildup of immunoglobulin A and other antibodies in the blood vessels of the kidneys, known as glomeruli. It is the leading cause of primary glomerular disease, with an incidence of at least 25 cases per million population per year worldwide.[5] IgAN more commonly affects Asian and Caucasian individuals, and Caucasian males are twice as likely to develop IgAN than females.[6]

IgAN is a chronic, slowly progressive disease with about 40% of individuals progressing to end stage renal disease over 20 years.[5] Kidney Disease: Improving Global Outcomes (KDIGO) guidelines indicate the primary focus of management should be optimized supportive care to slow disease progression.[7] This includes the use of angiotensin-converting enzyme inhibitors (ACEi) and angiotensin II receptor blockers (ARBs) to control blood pressure and reduce protein in the urine (proteinuria), and lifestyle modification. Individuals that remain at high risk of progressive disease can consider a 6-month course of glucocorticoids. Immunosuppressive therapies such as cyclophosphamide and mycophenolate mofetil are reserved for rapidly progressive disease.

Medications with specific indications for IgAN were approved by the Food and Drug Administration (FDA) after the KDIGO guideline was published in 2021. Three oral medications achieved accelerated FDA approval for reducing proteinuria in adults at high risk of progressive disease: Tarpeyo® (budesonide), Filspari® (sparsentan), and Fabhalta® (iptacopan), a medication already approved for use in paroxysmal nocturnal hemoglobinuria. Both Tarpeyo and Filspari recently achieved full FDA-approval for reducing the loss of kidney function in adults with IgAN. Full FDA approval is pending for Fabhalta.

In clinical trials, all three medications were used in combination with maximally tolerated ACEi or ARBs, however, their current place in therapy relative to each other remains unclear. There are limited data regarding second-line and repeat therapy in unresponsive individuals, and it is unknown if these medications can be used in combination. KDIGO is currently working on an updated guideline for IgAN that may address the use of some of these medications.

The IgAN treatment landscape is projected to undergo major changes between 2024 and 2034 with the introduction of several agents with novel mechanisms of action. By 2034, the total market size is expected to reach about $4.1 billion in the United States.[8] CarelonRx is closely monitoring the pipeline and following medications in late-stage development.

IgAN pipeline: agents in late-stage development[4]

Drug or biologic Manufacturer	**Route (frequency)**	**Place in therapy**	**Estimated FDA approval date (stage of development)**
Atrasentan Novartis	Oral (once daily)	• Endothelin A receptor antagonist expected to directly compete with Filspari • Phase 3 ALIGN study initiated; estimated completion 2026	Mid-2025
Sibeprenlimab Otsuka	SC (once every 4 weeks)	• First-in-class humanized IgG2 monoclonal antibody targeting APRIL • First APRIL inhibitor therapy to receive FDA's Breakthrough Therapy designation for IgAN • Phase 3 VISIONARY study initiated; estimated completion Dec 2026	2025 (Phase 3)
Ataticept Vera Therapeutics	SC (once weekly)	• Recombinant fusion protein targeting APRIL and BAFF • Phase 3 ORIGIN 3 study initiated; primary results expected May 2025 with study completion in 2028	2026 (Phase 3)
Povetacicept Vertex	SC (once every 4 weeks)	• Monoclonal antibody targeting APRIL and BAFF • Phase 3 RAINIER study initiated; estimated completion Sept 2028"	2027+ (Phase 3)
Zigakibart Novartis	SC (once every 2 weeks)	• Monoclonal antibody targeting APRIL • Phase 3 BEYOND study initiated; primary results expected Feb 2026 with study completion in 2028	2027+ (Phase 3)
IONIS-FB-LRx Roche	SC (once every 4 weeks)	• Ligand-conjugated antisense therapy aimed at decreasing production of complement factor B • Phase 3 IMAGINATION study initiated; primary results expected Sept 2026 with study completion in 2030	2027+ (Phase 3)
Ultomiris® (ravulizumab) AstraZeneca	IV (once every 8 weeks)	• C5 complement inhibitor already approved for use in PNH • Expected to compete with Fabhalta and IONIS-FB- LRx • Phase 3 ICAN study initiated; primary results expected Feb 2026 with study completion in 2029"	Phase 3

Key

ACEi: angiotensin-converting enzyme inhibitor

APRIL: a proliferation-inducing ligand

ARB: angiotensin II receptor blocker

BAFF: B-cell activating factor

IgAN: immunoglobulin A nephropathy

IV: intravenous injection

PNH: paroxysmal nocturnal hemoglobinuria

SC: subcutaneous injection

Hypertrophic cardiomyopathy treatment landscape and pipeline

Hypertrophic cardiomyopathy (HCM) is a genetic heart condition characterized by the thickening of the heart muscle, disorganized cells, and frequent fibrosis or scarring. This condition may affect the mitral valve, leading to intermittent blood flow obstructions that can result in regurgitation and elevated heart pressures. HCM is relatively common, with a prevalence of around 1 in 500 adults, though many cases go undiagnosed. Most individuals with HCM lead normal lives without significant symptoms, but some experience chest pain, shortness of breath, fatigue, palpitations, and lightheadedness. While rare, there is a risk of sudden death, particularly among younger people.

HCM can be classified into obstructive and nonobstructive forms. In obstructive HCM, typically the thickened septum between the ventricles impedes blood flow from the left ventricle to the aorta, impacting about two-thirds of those with HCM. In nonobstructive HCM, although the heart muscle is thickened, it does not obstruct blood flow.

Treatment is usually reserved for individuals who are symptomatic and can include pharmacological treatment and/or surgical procedures (e.g., septal reduction therapy). Beta-blockers (e.g., nadolol, metoprolol) are most often used as first-line therapy, while non-dihydropyridine calcium channel blockers (e.g., verapamil, diltiazem) may be used in individuals who are unable to take a beta-blocker or for whom they are ineffective.

A newer class of drugs, cardiac myosin inhibitors (CMIs), offer the first targeted treatment of HCM by reducing myocardial hypercontractility. Camzyos™ (mavacamten) was approved in 2022 for symptomatic obstructive HCM based on data showing its use significantly improved exercise capacity and left ventricular outflow tract obstruction. National guidelines from the American Heart Association and American College of Cardiology released in 2024 recommend Camzyos, disopyramide, and SRT as options for individuals with persistent symptoms despite first-line therapy.

Camzyos can cause the heart to become too relaxed, increasing the risk of heart failure. Therefore, the medication is only available through a Risk Evaluation and Mitigation Strategy (REMS) program, which is required by the FDA to monitor the safe use of the medication. Individuals affected may require interruption of treatment followed by continuation at a lower dose or discontinuation.

Aficamten is a second CMI that has submitted for FDA approval with an estimated decision date of September 2025. It would compete with Camzyos, if approved, for use in individuals with obstructive HCM. Use of CMIs for nonobstructive disease is being studied as well as their use as first-line therapy compared with beta-blockers.

Of note, Inpefa® (sotagliflozin), currently approved as a sodium-glucose co-transporter 2 (SGLT2) inhibitor for heart failure, is a new class of agent being studied for both obstructive and nonobstructive HCM.

The introduction of CMIs to the HCM treatment landscape provides a step forward in improving outcomes and quality of life. Progressive developments that address the underlying mechanisms of the disease are promising. CarelonRx will continue to monitor the pipeline and advancements in late-stage development to ensure that individuals receive the most up-to-date and effective treatments available.

Transthyretin-related amyloidosis treatment landscape and pipeline

Transthyretin amyloidosis (ATTR) is a progressive and often underdiagnosed disease caused by the misfolding of the transthyretin (TTR) protein. These misfolded proteins form amyloid deposits that accumulate in various organs, most notably the heart and peripheral nerves, leading to serious health complications. Two types of ATTR include hereditary ATTR (hATTR) and wild-type ATTR (wtATTR).

In hATTR, genetic mutations in the TTR gene lead to amyloid deposits in the heart, nerves, and other organs. Symptoms typically manifest in individuals from 30 to 65 years of age. Conversely, wtATTR occurs without genetic mutations and is not inherited. It primarily affects elderly men and is associated with cardiac symptoms, carpal tunnel syndrome, and peripheral neuropathy.

The buildup of amyloid deposits in the heart leads to ATTR cardiomyopathy (ATTR-CM), which results in heart stiffness, impaired relaxation, and eventual heart failure. Peripheral nerve involvement can lead to ATTR polyneuropathy (ATTR-PN), causing symptoms like numbness, tingling, and pain. Individuals may experience both neurologic and cardiac symptoms.

Until recently, ATTR standard of care relied on supportive therapy and organ transplantation. Advances in medical research have shifted this landscape significantly in recent years, resulting in several FDA-approved medications that are considered disease-modifying.

TTR silencing agents work by inhibiting TTR production in the liver and have largely supplanted the need for liver transplantation. Amvuttra® (subcutaneous vutrisiran), Onpattro® (intravenous patisiran), Tegsedi® (subcutaneous inotersen), and Wainua™ (subcutaneous eplontersen) have each demonstrated the ability to slow the progression of neuropathy in individuals with hATTR-PN. Tegsedi is associated with serious safety risks, requires frequent monitoring, and is available only through a restricted distribution program.

Vyndaqel®/Vyndamax® (oral tafamidis) and Attruby™ (oral acoramidis) are considered TTR stabilizers that help to slow progression of ATTR-CM by preventing the misfolding of the TTR protein. Both agents have demonstrated the ability to reduce cardiovascular death and cardiovascular-related hospitalization in individuals with ATTR-CM.

Historically, ATTR-CM was underdiagnosed due to its overlap with other more common cardiac conditions and a lack of specific treatments. The approval of Vyndaqel/Vyndamax in 2019 has highlighted the importance of diagnosing ATTR-CM accurately and early, encouraging physicians to consider this diagnosis more readily in individuals with heart failure symptoms.

The landscape of treatments for ATTR-CM continues to evolve, with several agents currently in the pipeline.

A second indication approval for Amvuttra would introduce a novel mechanism of action for ATTR-CM treatment, which may appeal to individuals who experience an inadequate response to Vyndaqel/Vyndamax. Additionally, Amvuttra would be the first drug in the broader amyloidosis category to have an indication for both hATTR-PN and ATTR-CM treatment. The dual indication may make Amvuttra the preferred agent for individuals with a mixed phenotype, who exhibit symptoms of neuropathy and cardiomyopathy. Wainua is also being studied in the ATTR-CM population.

ALXN2220 is an investigative therapy targeting the underlying pathology of ATTR-CM, aiming to stabilize transthyretin and prevent amyloid formation. NTLA-2001 uses CRISPR-based gene-editing technology that is designed to offer a one-time treatment by inactivating the TTR gene, thereby halting the production of misfolded transthyretin proteins.

Agents for ATTR-CM in late-stage development

Drug or biologic	Manufacturer	Administration	Mechanism	Approval Status
Amvuttra® (vutrisiran)	Alnylam	Subcutaneous	Small interfering RNA	Pending March 2025
ALXN2220	Neurimmune; AstraZeneca; Alexion	Intravenous	Anti-amyloid fibril antibody	Phase 3
NTLA-2001 (nexiguran)	"Intellia Therapeutics; Regeneron"	Intravenous	CRISPR gene editing	Phase 3
Wainua® (eplontersen)	Akcea	Subcutaneous	Antisense oligonucleotide	Phase 3

Recent approvals and pipeline therapies reflect significant advances in the management of amyloidosis, aiming to improve outcomes and quality of life. CarelonRx is closely monitoring the pipeline and following medications in late-stage development.

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