RxOutlook®

2nd Quarter 2024

Optum Rx®

Welcome to the second quarter RxOutlook Report of 2024. Optum Rx closely monitors and evaluates the drug development pipeline to identify noteworthy upcoming drug approvals and reports the essential findings here.

Recap of First Half 2024 - Where Are We Today?

As of May 20, the FDA's Center for Drug Evaluation and Research (CDER) has approved 16 new molecular entities in 2024. Notable drug approvals included **Rezdiffra™ (resmetirom)**, the first approved treatment for nonalcoholic steatohepatitis (NASH); **Tryvio™ (aprocitentan)**, the first endothelin receptor antagonist approved for hypertension; and **Winrevair™ (sotatercept-csrk)**, a first-in-class treatment for pulmonary arterial hypertension.

In addition to these drugs, the FDA's Center for Biologics Evaluation and Research (CBER) approved two gene therapies: **Lenmeldy™ (atidarsagene autotemcel)**, for treatment of metachromatic leukodystrophy, and **Beqvez™ (fidanacogene elaparvovec-dzkt)**, the second gene therapy for treatment of hemophilia B. Of note, Lenmeldy is $4.25 million for a one-time treatment, the highest cost of any gene therapy approved to date.

Looking Ahead to 3Q 2024

In this edition of RxOutlook, we highlight 10 key products with an approval decision by the end of the 3rd quarter 2024. The first product discussed in the report, Sanofi/Regeneron's **Dupixent® (dupilumab)**, is already on the market and approved across several indications (eg, asthma, atopic dermatitis), but is under review for a new indication for treatment of chronic obstructive pulmonary disease (COPD). If approved, Dupixent would be the first biologic approved for COPD.

The chronic inflammatory disorder category is expected to have two new products: **deuruxolitinib**, potentially the third Janus kinase (JAK) inhibitor for alopecia areata, and **nemolizumab**, a first-in-class interleukin-31 inhibitor for prurigo nodularis and atopic dermatitis. Nemolizumab is expected to compete with existing biologics for both indications, including the aforementioned Dupixent.

Xanomeline/trospium (also referred to as KarXT), would be a novel, non-dopaminergic treatment for schizophrenia and an alternative to atypical antipsychotics. Due to its novel mechanism (M1/M4 muscarinic receptor agonist), xanomeline/trospium can provide a unique side effect profile compared to the existing standard of care.

Genentech's **crovalimab** and Gilead/CymaBay Therapeutics' **seladelpar** would each represent novel treatments for different orphan conditions. Crovalimab is expected to be the first self-administered subcutaneous (SC) complement C5 inhibitor to come to market for paroxysmal nocturnal hemoglobinuria and potentially the third novel drug approved for the disease in the last 12 months. Seladelpar is expected to be the third approved second-line treatment for primary biliary cholangitis, and a competitor to Ocaliva® (obeticholic acid) and potentially another pipeline drug, elafibranor (FDA approval decision expected in June 2024).

A new **SC formulation of Ocrevus® (ocrelizumab)** is under review by the FDA. The IV formulation of Ocrevus is one of the most commonly used medications for multiple sclerosis. The SC formulation will still require healthcare provider administration but reduces the infusion time from 2 hours to 10 minutes.

Tradipitant could be the first treatment approved for gastroparesis in over 40 years. Gastroparesis affects millions of people in the U.S., but it is typically undiagnosed. Currently, generic metoclopramide is the only approved therapy, with other drugs (eg, erythromycin) being used off-label.

Insulin icodec is a novel, once weekly basal insulin that would reduce the injection burden for patients with diabetes (type 1 and type 2) who currently use once daily insulin products. The lingering question for the product, which will be discussed by an upcoming FDA Advisory Committee meeting, is the risk of hypoglycemia relative to other insulins.

Finally, the report will discuss **linvoseltamab**, another BCMA-targeted therapy for multiple myeloma. Treatment for relapsed/refractory multiple myeloma has become a competitive space, driven in part by the incurable nature of multiple myeloma and the need for retreatment with new therapies.

Key pipeline drugs with FDA approval decisions expected by end of the 3rd quarter 2024

Drug Name	Manufacturer	Indication/Use	Expected FDA Decision Date
Dupixent (dupilumab)	Regeneron/Sanofi	Chronic obstructive pulmonary disease	6/27/2024
Crovalimab	Genentech	Paroxysmal nocturnal hemoglobinuria*	7/2024
Deuruxolitinib	Sun Pharmaceuticals	Alopecia areata	7/2024
Nemolizumab	Galderma	Prurigo nodularis (PN) / atopic dermatitis (AD)	8/12/2024 (PN); 12/13/2024 (AD)
Seladelpar	Gilead/CymaBay Therapeutics	Primary biliary cholangitis*	8/14/2024
Linvoseltamab	Regeneron Pharmaceuticals	Multiple myeloma	8/22/2024
Ocrevus SC (ocrelizumab/ hyaluronidase)	Genentech	Multiple sclerosis	9/13/2024
Tradipitant	Vanda Pharmaceuticals	Gastroparesis	9/18/2024
Xanomeline/trospium	Bristol Myers Squibb	Schizophrenia	9/26/2024
Insulin icodec	Novo Nordisk	Diabetes	3Q 2024

* Orphan Drug Designation

Detailed Drug Insights

This section reviews the important characteristics (eg, therapeutic use, clinical profile, competitive environment and regulatory timeline) for key pipeline drugs with potential FDA approvals by the end of the 3rd quarter 2024.

Read more

Extended Brand Pipeline Forecast

This supplemental table provides a summary of developmental drugs, including both traditional and specialty medications that may be approved in the upcoming two years.

Read more

Key Pending Indication Forecast

This supplemental table provides a summary of key new indications that are currently under review by the FDA and may be approved in the upcoming 12 months.

Read more

Extended Generic Pipeline Forecast

This section provides a summary of upcoming first-time generic drugs and biosimilars that may be approved in the upcoming two years.

Please note that RxOutlook highlights select near-term approvals. Some drugs may not appear in this issue because they have been reviewed in previous editions of RxOutlook. Drugs of interest that are earlier in development or with expected approvals beyond 3rd quarter 2024 may appear in future reports; however, for those who need an initial look at the larger pipeline, please refer to the Brand Pipeline Forecast Table found later in this report.

Read more

Getting acquainted with pipeline forecast terms

Clinical trial phases

Phase I trials	Researchers test an experimental drug or treatment in a small group of people for the first time to evaluate its safety, determine a safe dosage range, and identify side effects.
Phase II trials	The experimental study drug or treatment is given to a larger group of people to see if it is effective and to further evaluate its safety.
Phase III trials	The experimental study drug or treatment is given to large groups of people to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the experimental drug or treatment to be used safely.
Phase IV trials	Post marketing studies delineate additional information including the drug's risks, benefits, and optimal use.

Pipeline acronyms

ANDA	Abbreviated New Drug Application
BLA	Biologic License Application
CRL	Complete Response Letter
FDA	Food and Drug Administration
MOA	Mechanism of Action
NME	New Molecular Entity
NDA	New Drug Application
sBLA	Supplemental Biologic License Application
sNDA	Supplemental New Drug Application
OTC Drugs	Over-the-Counter Drugs
PDUFA	Prescription Drug User Fee Act
REMS	Risk Evaluation and Mitigation Strategy

Detailed Drug Insights

Dupilumab (Brand Name: Dupixent®)

Manufacturer: Regeneron/Sanofi
Regulatory designation: Breakthrough Therapy
Expected FDA decision: June 27, 2024

Therapeutic use

Dupixent is under review for a new indication for treatment of moderate-to-severe chronic obstructive pulmonary disease (COPD) with type 2 inflammation (eosinophilic COPD).

Dupixent is currently approved for atopic dermatitis, asthma, chronic rhinosinusitis, eosinophilic esophagitis, and prurigo nodularis.

COPD is a group of lung diseases that cause abnormal limitations in airflow and lead to chronic and progressive breathing-related problems such as shortness of breath, coughing, and increased lung mucous. It includes emphysema and chronic bronchitis. In patients with type 2 inflammation, cytokines and immune cells are commonly elevated including, interleukin-5 (IL-5), IL-4, IL-13, type 2 innate lymphoid cells, and type 2 helper T cells, and increased levels of these cells can cause elevated eosinophil counts.

Chronic lower respiratory disease, primarily COPD, was the fourth leading cause of death in the U.S. in 2018. Almost 15.7 million people (6.4%) in the U.S. reported that they have been diagnosed with COPD. Regeneron/Sanofi estimate that approximately 300,000 people in the U.S. have uncontrolled COPD with evidence of type 2 inflammation.

What you need to know:

Proposed Indication: Treatment of moderate-to-severe COPD with type 2 inflammation

Mechanism: IL-4/IL-13 inhibitor

Efficacy: COPD exacerbations reduced by 30% to 34% vs. placebo

Common AEs: Nasopharyngitis, upper respiratory tract infection, headache

Dosing: SC once every 2 weeks

Why it Matters: Potentially the first biologic approved for COPD and the first treatment specifically for type 2 inflammation, promising efficacy results with significant improvements in COPD exacerbations, favorable safety profile

Important to Note: Eligible population will likely be patients who have exhausted traditional inhalers, potential future competition (eg, Nucala), requires SC administration

Estimated Cost: ~$49,000 per year (based on current cost of Dupixent)

Clinical profile

Dupixent is a monoclonal antibody that inhibits the signaling of the IL-4 and IL-13 pathways. IL-4 and IL-13 are key drivers of type 2 inflammation.

Pivotal trial data:
The efficacy of Dupixent was evaluated in NOTUS and BOREAS, two identical Phase 3, randomized, double-blind, placebo-controlled studies in 1,874 adults with moderate-to-severe COPD with type 2 inflammation, as measured by blood eosinophils ≥ 300 cells/µL. Patients were randomized to Dupixent or placebo added to a maximal standard-of-care inhaled triple therapy of inhaled corticosteroids (ICS), long-acting beta agonists (LABA), and long-acting muscarinic antagonists (LAMA). The primary endpoint was the annualized rate of acute moderate or severe COPD exacerbations over 52 weeks. Moderate exacerbations were defined as those requiring systemic steroids and/or antibiotics. Severe exacerbations were defined as those requiring hospitalization; requiring more than a day of observation in an emergency department or urgent care facility; or resulting in death.

Dupilumab *(continued...)*

In BOREAS, the annualized rate of moderate or severe exacerbations was 0.78 with Dupixent and 1.10 with placebo (rate ratio 0.70; 95% CI: 0.58, 0.86; p < 0.001), representing a 30% reduction in COPD exacerbations.

Similarly, in NOTUS, the annualized rate of moderate or severe exacerbations was reduced by 34% (p = 0.0002).

Safety:
The most common adverse events with Dupixent use were nasopharyngitis, upper respiratory tract infection, and headache.

Dosing:
In the pivotal trials for COPD, Dupixent was administered via subcutaneous (SC) injection every 2 weeks.

Competitive environment

The current standard of care for maintenance treatment of COPD includes inhaled long-acting bronchodilators (LAMAs and LABAs) and corticosteroids. In patients who continue to be symptomatic, there are limited treatment options available and there remains an unmet need.

Dupixent would potentially be the first biologic approved for COPD and the first treatment specifically for type 2 inflammation. In the pivotal studies, Dupixent demonstrated significant improvement in COPD exacerbations when used as an add-on therapy to the existing standard of care. Dupixent was generally well tolerated in the studies and the side effect profile was consistent with the known safety profile of Dupixent in its currently approved indications.

COPD represents a large population but the use of Dupixent will be limited to patients with type 2 inflammation with elevated eosinophil counts and in patients who have exhausted traditional inhaler therapies. In this population, Dupixent may also face future competition, as several other biologics are currently being studied in COPD, including GSK's IL-5 antagonist, Nucala® (mepolizumab).

Finally, SC administration may represent a barrier in for some patients especially since COPD is currently treated with inhaled and oral therapies.

The Wholesale Acquisition Cost (WAC) for Dupixent is approximately $49,000 per year.

Crovalimab (Brand Name: To be determined)

Manufacturer: Genentech
Regulatory designations: Orphan Drug, Breakthrough Therapy
Expected FDA decision: July 2024

Therapeutic use

Crovalimab is under review for the treatment of paroxysmal nocturnal hemoglobinuria (PNH).

PNH is a rare, complement-mediated blood disorder in which an acquired mutation in a patient's hematopoietic stem cells causes the production of defective red blood cells (RBCs). These defective RBCs are susceptible to premature destruction by a patient's own immune system (complement system). This can cause anemia, blood clots, and can lead to kidney disease.

The incidence of clinically significant PNH is estimated to be at least 1 to 10 cases per million in the general population and approximately 6,000 people are living with PNH in the U.S.

Clinical profile

Crovalimab is an anti-C5 monoclonal antibody designed to block the last step of the complement cascade.

Pivotal trial data:
The efficacy of crovalimab was evaluated in COMMODORE 2, a Phase 3, randomized, open-label study in 204 adult patients with PNH who were not treated previously with C5 inhibitors. Patients were randomized to crovalimab or Soliris® (eculizumab) (another C5 inhibitor). The co-primary endpoints were the proportion of patients with hemolysis control (defined as a lactate dehydrogenase [LDH] ≤ 1.5 × upper limit of normal) from Week 5 through Week 25 and the proportion of patients with transfusion avoidance from baseline through Week 25. LDH levels are considered an important clinical marker of hemolysis. Transfusion avoidance was defined as patients who become transfusion-free and did not require transfusion per protocol-specified guidelines.

Hemolysis control was achieved in 79.3% (95% CI: 72.9, 84.5) of patients with crovalimab vs. 79.0% (95% CI: 69.7, 86.0) with Soliris. Additionally, 65.7% (95% CI: 56.9, 73.5) achieved transfusion avoidance with crovalimab vs. 68.1% (95% CI: 55.7, 78.5) with Soliris. Both endpoints met the non-inferiority criteria.

Safety:
The most common adverse event with crovalimab use was infusion-related reactions.

Dosing:
In the pivotal trial, crovalimab was administered with intravenous (IV) and SC loading doses followed by SC maintenance doses every 4 weeks.

What you need to know:

Proposed Indication: Treatment of PNH

Mechanism: Complement C5 inhibitor

Efficacy:

- Hemolysis control: 79.3% vs. 79.0% with Soliris
- Transfusion avoidance: 65.7% vs. 68.1% with Soliris

Common AEs: Infusion-related reactions

Dosing: IV/SC loading doses followed by SC maintenance doses once every 4 weeks

Why it Matters: IV/SC loading doses followed by SC maintenance doses once every 4 weeks

Important to Note: Alternative C5 inhibitors available (Soliris, Ultomiris), other recently approved treatments including in patients with inadequate response to C5 inhibitors (eg, SC Empaveli, oral Fabhalta)

Estimated Cost: ~$460,000 per year (based on pricing for Empaveli)

Crovalimab *(continued...)*

Competitive environment

If approved, crovalimab would provide an additional C5 inhibitor treatment option and it would potentially be the first SC self-administered drug in the class to come to market. Soliris requires IV dosing every 2 weeks and the other C5 inhibitor, Ultomiris® (ravulizumab), requires IV dosing every 4 or 8 weeks. There is an FDA approved SC administered on-body delivery system for Ultomiris, but that product has not yet launched.

Crovalimab is a relatively late market entry in the class and both Soliris and Ultomiris have become well-established treatments for PNH and are approved for indications outside of PNH. Other alternatives to C5 inhibitors have also been approved including SC administered Empaveli® (pegcetacoplan) (C3 inhibitor) and the recently approved oral Fabhalta® (iptacopan) (Factor B inhibitor). Both Empaveli and Fabhalta can be used as monotherapies for the treatment of PNH and have demonstrated efficacy in patients with insufficient response to C5 inhibitors.

For reference, the WAC for Empaveli is approximately $460,000 per year.

Deuruxolitinib (Brand Name: To be determined)

Manufacturer: Sun Pharmaceuticals
Regulatory designations: Breakthrough Therapy, Fast Track
Expected FDA decision: July 2024

Therapeutic use

Deuruxolitinib is under review for the treatment of adult patients with moderate-to-severe alopecia areata.

Alopecia areata is an autoimmune disease in which the immune system attacks hair follicles, resulting in partial or complete loss of hair on the scalp and body. The scalp is the most commonly affected area, but any hair-growing site can be affected alone or together with the scalp. Onset of alopecia areata can be at any age, but often develops during childhood or teenage years and can affect both men and women. Alopecia areata is frequently associated with other autoimmune disorders, as well as emotional and psychosocial distress.

Approximately 300,000 patients have severe alopecia areata defined as at least 50% scalp hair loss.

Clinical profile

Deuruxolitinib is an oral selective Janus kinase 1 and 2 (JAK1/JAK2) inhibitor. JAK-signal transducer and activator of transcription (STAT) signaling leads to a T-cell mediated inflammatory response that attacks hair follicles and is the driving force behind the hair loss. JAK inhibitors block the inflammatory response and help facilitate hair regrowth.

What you need to know:

Proposed Indication: Treatment of adult patients with moderate-to-severe alopecia areata

Mechanism: JAK1/JAK2 inhibitor

Efficacy: SALT score of 20 or less at Week 24:

- THRIVE-AA1 trial: 29.6% (8 mg) and 41.9% (12 mg) vs. 0.8% with placebo
- THRIVE-AA2 trial: 33% (8 mg) and 38.3% (12 mg) vs. 0.8% with placebo

Common AEs: Headache, acne, upper respiratory infection, increased creatine kinase levels, COVID-19 infection, nasopharyngitis

Dosing: Oral twice daily

Why it Matters: Third oral JAK inhibitor for alopecia areata

Important to Note: Alternative treatments available (JAK inhibitors ie, Olumiant and Litfulo), lack of head-to-head trial data vs. standards of care, lack of long-term efficacy and safety data, JAK inhibitor class boxed warnings, not being studied for other indications

Estimated Cost: ~$49,000 (based on pricing of Litfulo)

Pivotal trial data:
The efficacy of deuruxolitinib was studied in two Phase 3, randomized, double-blind, placebo-controlled clinical studies (THRIVE-AA1 and THRIVE-AA2) in 1,223 adult patients aged 18 to 65 years with moderate-to-severe alopecia areata. Patients were randomized to receive either 8 mg or 12 mg of deuruxolitinib or placebo. The key inclusion criterion included having ≥ 50% scalp hair loss due to alopecia areata as measured by the Severity of Alopecia Tool (SALT) at baseline. The SALT score describes the percentage of scalp hair loss and ranges from 0 to 100. For example, a SALT score of 100 means there is complete (or 100%) scalp hair loss. A SALT score of ≥ 50 is generally considered severe disease. The primary endpoint was the percentage of patients achieving a SALT score of 20 or less at Week 24.

In THRIVE-AA1, 29.6%, 41.9%, and 0.8% of patients achieved a SALT score of 20 or less at Week 24 in the 8 mg, 12 mg, and placebo groups, respectively ($p < 0.0001$).

In THRIVE-AA2, 33%, 38.3%, and 0.8% of patients achieved a SALT score of 20 or less at Week 24 in the 8 mg, 12 mg, and placebo groups, respectively ($p < 0.0001$).

Deuruxolitinib *(continued...)*

Safety:
The most common adverse events with deuruxolitinib use were headache, acne, upper respiratory infection, increased creatine kinase levels, COVID-19 infection, and nasopharyngitis.

Dosing:
In the pivotal trials, deuruxolitinib was administered orally twice daily.

Competitive environment

Historically, the standard of care for alopecia areata included off-label use of corticosteroids, immunosuppressants, calcineurin inhibitors, and minoxidil. In June 2022, the FDA approved Eli Lilly's Olumiant® (baricitinib), an oral JAK inhibitor, for treatment of adult patients with severe alopecia areata. In June 2023, the FDA approved another JAK inhibitor, Litfulo™ (ritlecitinib), for the treatment of adult and adolescent patients 12 years and older with severe alopecia areata.

Deuruxolitinib would be the third oral JAK inhibitor approved for treatment of alopecia areata. Compared indirectly to Litfulo, deuruxolitinib demonstrated numerically higher response rates. An indirect comparison between deuruxolitinib and Olumiant is more difficult because both drugs were evaluated with different dosages and their primary endpoints were assessed at different time points. The primary endpoint of SALT score of 20 or less was measured at 36 weeks in the studies for Olumiant, while the same primary endpoint was measured at 24 weeks for Litfulo and deuruxolitinib. Unlike Olumiant and Litfulo which are both dosed once daily, deuruxolitinib is dosed twice daily.

The short-term safety profile of deuruxolitinib appears to be similar to those of Olumiant and Litfulo. The long-term efficacy and safety are still being studied. If approved, it is expected that deuruxolitinib would share the same class boxed warnings as other JAK inhibitors for serious infections, mortality, malignancy, major adverse cardiovascular events, and thrombosis.

Deuruxolitinib is not in development for other indications, which may limit its utilization compared to Litfulo and Olumiant. In addition to alopecia areata, Olumiant holds other indications for rheumatoid arthritis and COVID-19. Litfulo is indicated for the adolescent population for alopecia areata and is being studied for other indications, such as ulcerative colitis and Crohn's disease.

For reference, the WAC for Litfulo is approximately $49,000 per year.

Nemolizumab (Brand Name: To be determined)

Manufacturer: Galderma
Regulatory designation: Breakthrough Therapy (prurigo nodularis)
Expected FDA decisions: August 12, 2024 (prurigo nodularis); December 13, 2024 (atopic dermatitis)

Therapeutic use

Nemolizumab is under review for treatment of adults with prurigo nodularis and for adolescents and adults with moderate-to-severe atopic dermatitis.

Prurigo nodularis is a chronic, debilitating skin disease characterized by the presence of intense itch and thick skin nodules covering large body areas. The intensity of pruritus in prurigo nodularis is considered the highest among several types of chronic pruritic skin diseases. Prurigo nodularis is typically refractory to treatment and may be associated with diabetes, chronic kidney disease, and HIV infection. Estimated prevalence ranges from 36.7 to 43.9 per 100,000 people (about 120,000 to 150,000 people) in the U.S.

Atopic dermatitis is a common, chronic, and flaring inflammatory skin disease characterized by persistent itch and recurrent skin lesions. It is the most common type of eczema, affecting more than 9.6 million children and about 16.5 million adults in the U.S.

Clinical profile

Nemolizumab is a monoclonal antibody directed against the interleukin (IL)-31 receptor that works by blocking signaling from IL-31. IL-31 plays a key role in both atopic dermatitis and prurigo nodularis. IL-31 stimulates sensory neurons related to itch and contributes to inflammation and barrier dysfunction.

Pivotal trial data:
Prurigo nodularis

The efficacy of nemolizumab was evaluated in two Phase 3, randomized, double-blind, placebo-controlled studies (OLYMPIA 1 and OLYMPIA 2) in 560 adult patients with moderate-to-severe prurigo nodularis. Patients were randomized to nemolizumab 30 mg or 60 mg or placebo. The primary endpoints for both studies were the proportion of participants with an improvement of ≥ 4 from baseline in Peak Pruritus Numeric Rating Scale (PP-NRS) at Week 16 and proportion of participants with an Investigator Global Assessment (IGA) success at Week 16. The PP-NRS is a self-reported scale from 0 to 10 to measure itch over the past 24 hours, with 0 being "no itch" and 10 being "worst itch imaginable." The IGA is a 5-point scale used to assess disease severity and the success of treatment for prurigo nodularis. With this endpoint, investigators assessed if patients could achieve a score of 0 ("clear") or 1 ("almost clear") and at least a 2-point improvement from baseline.

What you need to know:

Proposed Indication: Treatment of prurigo nodularis and moderate-to-severe atopic dermatitis

Mechanism: IL-31 receptor antagonist

Efficacy:

Prurigo nodularis

- IGA response: 26.3% to 37.7% vs. 7.3% to 11% with placebo
- PP-NRS response: 56.3% to 58.4% vs. 16.7% to 20.9% with placebo

Atopic dermatitis

- IGA response: 35.6% to 37.7% vs. 24.6% to 26% with placebo
- EASI-75 response: 42.1% to 43.5% vs. 29% to 30.2% with placebo

Common AEs: Headache

Dosing: SC; once every 4 weeks for prurigo nodularis and every 4 or 8 weeks for atopic dermatitis (maintenance)

Why it Matters: Novel mechanism of action, potential competitor to Dupixent (indicated for both atopic dermatitis and prurigo nodularis), potential use for other indications (eg, systemic sclerosis, chronic kidney disease associated pruritis)

Important to Note: Lack of head-to-head trial data vs. standards of care, other treatment options available particularly for atopic dermatitis

Estimated Cost: ~$49,000 per year (based on pricing of Dupixent)

Nemolizumab *(continued...)*

In OLYMPIA 1, 58.4% of nemolizumab-treated patients and 16.7% of placebo-treated patients achieved at least a 4-point reduction in itch ($p < 0.0001$). IGA response was achieved in 26.3% of nemolizumab-treated patients and 7.3% of placebo-treated patients ($p < 0.0001$).

In OLYMPIA 2, 56.3% of nemolizumab-treated patients and 20.9% of placebo-treated patients achieved at least a 4-point improvement in itch intensity ($p < 0.0001$). IGA response was achieved in 37.7% of nemolizumab-treated patients and 11% of placebo-treated patients ($p < 0.0001$).

Atopic dermatitis

The efficacy of nemolizumab was evaluated in two Phase 3, randomized, double-blind, placebo-controlled studies (ARCADIA 1 and ARCADIA 2) in 1,728 adolescent and adult patients 12 years and older with moderate-to-severe atopic dermatitis. Patients were randomized to nemolizumab 30 mg or 60 mg or placebo, with concomitant background topical corticosteroids or topical calcineurin inhibitors. The primary endpoints were the proportion of participants with IGA success at Week 16 and the proportion of patients with a 75% reduction in Eczema Area and Severity Index (EASI-75) from baseline to Week 16. EASI-75 measures severity and body area involvement for atopic dermatitis and ranges from 0 (no disease) to 72 (maximal disease).

In ARCADIA 1 and 2, 35.6% and 37.7% of nemolizumab-treated patients, and 24.6% and 26.0% of placebo-treated patients achieved IGA response ($p < 0.0006$). In the same trials, EASI-75 was achieved by 43.5% and 42.1% of nemolizumab-treated patients, and 29% and 30.2% of placebo-treated patients ($p < 0.0001$).

Safety:
The most common adverse event with nemolizumab use was headache.

Dosing:
In the pivotal trials for prurigo nodularis, nemolizumab was administered via SC injection every four weeks. In the pivotal trials for atopic dermatitis, nemolizumab was administered via SC injection every four or eight weeks for maintenance dosing.

Competitive environment

If approved, nemolizumab offers a first-in-class treatment option in patients with atopic dermatitis and prurigo nodularis. Prior to the approval of Sanofi/Regeneron's Dupixent® (dupilumab) in September 2022, there were no FDA approved treatments for prurigo nodularis. Drugs used off-label for prurigo nodularis include corticosteroids, calcineurin inhibitors, and antihistamines. When compared indirectly, the response rates for Dupixent appear to be numerically higher than those for nemolizumab for prurigo nodularis.

For atopic dermatitis, Dupixent and other oral and injectable treatments are available. When comparing nemolizumab to the other SC injectables, Dupixent and Adbry® (tralokinumab-ldrm), the response rates for nemolizumab appear to be numerically better than those for Adbry, but not as high as those for Dupixent.

Nemolizumab is also being studied for other indications (eg, systemic sclerosis and chronic kidney disease associated pruritis), which could potentially expand its target population.

For reference, the WAC for Dupixent is approximately $49,000 per year.

Seladelpar (Brand Name: To be determined)

Manufacturer: Gilead/CymaBay Therapeutics
Regulatory designations: Orphan Drug, Breakthrough Therapy
Expected FDA decision: August 14, 2024

Therapeutic use

Seladelpar is under review for the second-line treatment of primary biliary cholangitis (PBC).

PBC is a chronic, progressive liver disorder that leads to inflammation and scarring of the small bile ducts. The damage to bile ducts can inhibit the liver's ability to get rid of toxins in the body and can lead to cirrhosis (scarring of liver tissue). The exact cause of PBC is unknown, but it is thought that it is likely due to a combination of factors such as autoimmune, genetic, and environmental factors.

PBC mostly occurs in women over the age of 40, and the overall prevalence in the U.S. is estimated to be about 50,000 people.

Clinical profile

Seladelpar is a selective peroxisome proliferator-activated receptor (PPAR) delta agonist. Seladelpar works by regulating genes involved in bile acid synthesis, inflammation, fibrosis and lipid metabolism, storage, and transport.

Pivotal trial data:
The efficacy of seladelpar was evaluated in RESPONSE, a Phase 3, randomized, double-blind, placebo-controlled study in 193 patients who had an inadequate response to or who had a history of unacceptable side effects with ursodeoxycholic acid (UDCA). Patients received seladelpar 10 mg daily or placebo. The primary endpoint was a biochemical response, which was defined as an alkaline phosphatase level (ALP) less than 1.67 times the upper limit of the normal range, with a decrease of 15% or more from baseline, and a normal total bilirubin level at Month 12. Both ALP and bilirubin are key biomarkers in PBC, and elevated levels are signs of liver damage.

A biochemical response was achieved in 61.7% of patients with seladelpar 10 mg vs. 20.0% with placebo (difference 41.7, 95% CI: 27.7, 53.4; $p < 0.001$).

The efficacy of seladelpar was also evaluated in ENHANCE, a Phase 3, randomized, double-blind, placebo-controlled study in patients with inadequate response or intolerance to UDCA. Patients received seladelpar 5 mg or 10 mg, or placebo once daily. ENHANCE was terminated early following an erroneous safety signal in a concurrent nonalcoholic steatohepatitis trial. While blinded, the primary endpoint (same as RESPONSE) was amended to Month 3. Biochemical response was achieved in 57.1% and 78.2% of patients with seladelpar 5 mg and 10 mg vs. 12.5% with placebo ($p < 0.0001$).

What you need to know:

Proposed Indication: Second-line treatment of PBC

Mechanism: PPAR delta agonist

Efficacy: Biochemical response:

- RESPONSE: 61.7% with seladelpar 10 mg vs. 20.0% with placebo
- ENHANCE: 57.1% to 78.2% with seladelpar 5 mg and 10 mg vs. 12.5% with placebo

Common AEs: Headache, abdominal pain, nausea, abdominal distention

Dosing: Oral once daily

Why it Matters: Promising response rate (numerically higher than competitors), favorable safety profile and significantly reduced rates of pruritus (common symptom associated with PBC)

Important to Note: Alternative available for second-line treatment of PBC (ie, Ocaliva), potential additional competition – elafibranor expected to be approved in June 2024, lack of head-to-head trial data

Estimated Cost: ~$110,000 per year (based on pricing for Ocaliva)

Seladelpar *(continued...)*

Safety:
The most common adverse events with seladelpar use were headache, abdominal pain, nausea, and abdominal distention.

Dosing:
In the pivotal trials, seladelpar was administered orally once daily.

Competitive environment

First-line treatment of PBC is UDCA, which is available as generics. UDCA has been shown to slow disease progression; however, some patients may need additional treatment if liver tests remain high. For second-line treatment, the only approved treatment is Intercept Pharmaceuticals' Ocaliva® (obeticholic acid). Ipsen/Genfit's PPAR alpha/delta agonist, elafibranor, is currently under FDA review for PBC with a decision expected by June 10, 2024.

Seladelpar will likely be the third drug approved for second-line treatment of PBC and a direct competitor to Ocaliva and elafibranor. The primary differentiator for seladelpar is that it was associated with a statistically significant decrease in pruritus, which is a disease manifestation of PBC, whereas pruritus is a common side effect associated with Ocaliva.

The trial results for seladelpar were promising with higher response rates than Ocaliva and elafibranor, but comparing across different trials is challenging and there are no direct head-to-head trial data vs. its competitors.

For reference, the WAC for Ocaliva is approximately $110,000 per year.

Linvoseltamab (Brand Name: To be determined)

Manufacturer: Regeneron Pharmaceuticals
Regulatory designation: Fast Track
Expected FDA decision: August 22, 2024

Therapeutic use

Linvoseltamab is under review for the treatment of patients with relapsed or refractory multiple myeloma who were previously treated with a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

Multiple myeloma is a blood cancer of plasma cells in the bone marrow. In patients with multiple myeloma, plasma cells make an antibody that stimulates overgrowth of plasma cells, leading to severe complications such as renal dysfunction, infections, anemias, and osteoporosis.

As the second most common blood cancer, it is estimated 35,000 people will be diagnosed with multiple myeloma in the U.S. every year. It occurs predominantly in the geriatric population with a median age at diagnosis of about 70 years and is slightly more commonly seen in males than females.

Clinical profile

Linvoseltamab is a B-cell maturation antigen (BCMA) CD3-targeted bispecific antibody. BCMA is highly expressed on the surface of multiple myeloma cells, and CD3 receptors are found on the surface of T-cells. Linvoseltamab bridges T-cells and multiple myeloma cells together and activates the T-cells to kill the myeloma cell.

What you need to know:

Proposed Indication: Treatment of patients with relapsed or refractory multiple myeloma who were previously treated with a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody

Mechanism: BCMA CD3-targeted bispecific antibody

Efficacy: ORR: 71%

Common AEs: CRS, cough, neutropenia, diarrhea, fatigue, infection

Dosing: IV loading doses followed by IV once every 2 or 4 weeks

Why it Matters: Another treatment option in a difficult to treat cancer, potentially better safety profile than CAR T cell therapies, potential use in earlier lines of therapy

Important to Note: Narrow initial indication, alternatives available, lack of robust survival data, IV administration

Estimated Cost: ~$26,000 per month (based on pricing for Elrexfio)

Pivotal trial data:
The efficacy of linvoseltamab was evaluated in LINKER-MM1, a Phase 2, open-label, single-arm study in patients with relapsed or refractory multiple myeloma who progressed on or after at least three lines of therapy including a proteasome inhibitor, an immunomodulatory drug, and an anti-CD38 antibody, or were at least triple class refractory. The primary endpoint was objective response rate (ORR). Key secondary endpoints included progression-free survival (PFS) and overall survival (OS).

As of April 2024, data was available from 117 patients treated with linvoseltamab. The ORR was 71%, with 46% of patients achieving a complete response. Median PFS and median OS were not yet reached.

Safety:
The most common adverse events with linvoseltamab use were cytokine release syndrome (CRS), cough, neutropenia, diarrhea, fatigue, and infection.

Linvoseltamab *(continued...)*

Dosing:
In the pivotal trial, linvoseltamab was administered via intravenous (IV) infusion once weekly for weeks 1 through 14, then once every two weeks for maintenance. Patients who had a very good partial response had their dose reduced to every four weeks.

Competitive environment

According to the National Comprehensive Cancer Network (NCCN) guidelines, the preferred regimens for relapsed or refractory multiple myeloma include chimeric antigen receptor (CAR) T cell therapies and bispecific antibodies. Several agents have been approved for multiple myeloma over the years, but there is still an unmet need because multiple myeloma is generally incurable and associated with a high relapse rate with conventional drugs.

Linvoseltamab would be the fourth BCMA targeted bispecific antibody on the market. Johnson & Johnson's Tecvayli® (teclistamab) and Talvey® (talquetamab), and Pfizer's Elrexfio® (elranatamab) are currently approved and NCCN-recommended after four prior therapies for relapsed or refractory multiple myeloma. CAR T cell therapies are another group of BCMA targeted therapies that have been approved in similar lines of therapy for multiple myeloma. These are one-time, patient-specific genetically modified cellular therapies.

All BCMA targeted therapies share a boxed warning for CRS and neurologic toxicity. Recently, the FDA added a new boxed warning to the CAR T cell therapies for T cell malignancy. Generally, BCMA bispecific antibodies have lower risk of CRS when compared indirectly to CAR T cell therapies. This difference in safety profiles, in addition to the complicated, patient-specific manufacturing process for CAR T cell therapies, can make bispecific antibodies like linvoseltamab a better option for certain patients.

Like other recently approved multiple myeloma drugs, the initial indication for linvoseltamab is expected to be narrow, but Regeneron is evaluating the drug in earlier lines of treatment.

For reference, the WAC for Elrexfio is approximately $26,000 per month.

Ocrelizumab/hyaluronidase (Brand Name: Ocrevus SC)

Manufacturer: Genentech
Expected FDA decision: September 13, 2024

Therapeutic use

Ocrevus SC is under review for the treatment of relapsing and primary progressive forms of multiple sclerosis (MS).

Ocrevus is currently available as an IV infusion.

MS is a chronic disorder of the central nervous system. MS typically starts with a relapsing-remitting course, in which episodes of worsening function (relapses) are followed by recovery periods (remissions). These remissions may not be complete and can leave patients with some degree of residual disability. Primary progressive MS is a more severe form of the disease marked by steadily worsening symptoms but typically without district relapses or periods of remission.

The overall estimated prevalence of MS in the U.S. may be as high as 1 million individuals and about 85% of patients are initially diagnosed with a relapsing form of MS.

What you need to know:

Proposed Indication: Treatment of relapsing and primary progressive forms of MS

Mechanism: CD20-directed cytolytic antibody

Common AEs: Injection reactions, including erythema, pain, swelling, and pruritus

Dosing: SC infusion once every 6 months

Why it Matters: More convenient administration vs. IV administered Ocrevus (10-minute infusion vs. 2-hour), comparable safety and same dosing frequency as IV formulation of Ocrevus

Important to Note: Alternatives available including within the same therapeutic class (Kesimpta and Briumvi), requires healthcare provider administration

Estimated Cost: ~$79,000 per year (based on pricing for Ocrevus IV)

Clinical profile

Ocrevus is a monoclonal antibody that targets CD20-positive B cells, which is a type of immune cell thought to be a key contributor in the pathophysiology of MS.

Pivotal trial data:
Ocrevus SC was evaluated in a randomized study evaluating the pharmacokinetics, safety, and clinical effects of the SC formulation of Ocrevus compared with the IV formulation of Ocrevus in 236 patients with relapsing MS or primary progressive MS. The primary endpoint was serum area under the curve (AUC) of drug levels from day 1 to 12 weeks after SC injection compared to IV infusion. The goal of the study was to examine whether the SC formulation achieves the same blood levels as the IV formulation.

The study met that primary endpoint demonstrating non-inferiority vs. the IV formulation with the SC formulation achieving similar drug levels in the blood compared to the IV formulation.

Genentech recently announced longer-term data showing that SC Ocrevus resulted in near-complete suppression of relapse activity (97.2% had no relapse during the treatment phase) up to 48 weeks with an annualized relapse rate of 0.04.

Safety:
The most common adverse events with Ocrevus SC use were injection-site reactions, including erythema, pain, swelling, and pruritus.

Ocrelizumab/hyaluronidase *(continued...)*

Dosing:
In the pivotal trial, Ocrevus SC was administered via SC infusion once every 6 months.

Competitive environment

The IV formulation of Ocrevus is one of the most commonly used medications for MS, in part because of its high efficacy for both relapsing and progressive forms of MS. A SC formulation would offer a more convenient treatment option that could widen access to the drug compared the current IV formulation. The SC formulation requires a 10-minute infusion vs. a 2-hour infusion with the IV formulation. Like the IV formulation, the SC formulation is expected to require healthcare provider administration but can be administered once every 6 months.

MS is a crowded category and Ocrevus SC will be competing with other CD20 targeted therapies, including Novartis' Kesimpta® (ofatumumab), which can be self-administered via SC injection once every month and TG Therapeutics' Briumvi™ (ublituximab), which is administered as a 1-hour IV infusion every 6 months. Other oral and injectable treatments for MS are also available across different mechanisms of action.

For reference, the WAC for Ocrevus IV is approximately $79,000 per year.

Tradipitant (Brand Name: To be determined)

Manufacturer: Vanda Pharmaceuticals
Expected FDA decision: September 18, 2024

Therapeutic use

Tradipitant is under review for the treatment of symptoms of gastroparesis.

Gastroparesis is a chronic gastrointestinal motility disorder. Symptoms include post-meal fullness, nausea, vomiting, and upper abdominal pain. Gastroparesis can be caused by diabetes, stomach surgery, bacterial and viral infections, and medications that may delay stomach emptying. Some patients with gastroparesis have no clear cause.

The estimated prevalence of gastroparesis in the U.S. is approximately 6 million people, many of whom are undiagnosed.

Clinical profile

Tradipitant is a neurokinin-1 (NK-1) receptor antagonist. NK-1 receptors are located in the gastric neuromuscular junction, where they stimulate smooth muscle contractions.

Pivotal trial data:
The efficacy of tradipitant was evaluated in a Phase 2, double-blind, proof of concept study in 150 adult patients with diabetic or idiopathic gastroparesis. Patients were randomized to receive tradipitant or placebo for 4 weeks. The primary endpoint was change from baseline to Week 4 in average nausea severity, measured by the Gastroparesis Core Symptom Daily Diary (GCS-DD). In the GCS-DD, patients are asked to rate each symptom of gastroparesis in the past 24 hours on scale of a 0 (no symptoms) to 5 (very severe symptoms).

Patients receiving tradipitant had a significant decrease in the GCS-DD nausea score of -1.2 vs. -0.7 with placebo at Week 4 ($p = 0.0099$).

The efficacy of tradipitant was further evaluated in a Phase 3, double-blind, placebo-controlled study in 201 adult patients diagnosed with gastroparesis. Patients were randomized to receive tradipitant or placebo for 12 weeks. The primary endpoint was the change from baseline in daily average nausea severity scores from GCS-DD at Week 12.

Tradipitant did not demonstrate statistical significance in the primary endpoint at Week 12 in the intent-to-treat population ($p = 0.741$). The tradipitant group had an average nausea severity score reduction of -1.55 vs. -1.49 in the placebo group.

Safety:
The most common adverse events with tradipitant use were diarrhea, nausea, abdominal pain, dizziness, and headache.

What you need to know:

Proposed Indication: Treatment of symptoms of gastroparesis

Mechanism: NK-1 receptor antagonist

Efficacy: GCS-DD nausea score:

- Phase 2 trial: -1.2 vs. -0.7 with placebo
- Phase 3 trial: -1.55 vs. -1.49 with placebo (statistical superiority not met)

Common AEs: Diarrhea, nausea, abdominal pain, dizziness, headache

Dosing: Oral twice daily

Why it Matters: First novel drug to be approved for gastroparesis in over 40 years, favorable safety profile, potential use for other indications (eg, motion sickness, atopic dermatitis)

Important to Note: Modest efficacy – Phase 3 trial did not demonstrate statistical significance, current standards of care have generic availability

Tradipitant *(continued...)*

Dosing:
In the pivotal trials, tradipitant was administered orally twice daily.

Competitive environment

If approved, tradipitant would be the first treatment approved for gastroparesis in over 40 years and would be an alternative treatment for the short-term relief of nausea in patients with diabetic and idiopathic gastroparesis. Currently, metoclopramide is the only approved therapy for the treatment of gastroparesis. However, metoclopramide carries a boxed warning for the risk of tardive dyskinesia and treatment is not recommended for longer than 12 weeks. Other drugs, such as erythromycin, botulinum toxin injections, and antiemetics are used off-label to treat symptoms of gastroparesis.

In clinical trials, tradipitant was generally well tolerated and it potentially has a better safety profile than metoclopramide. However, efficacy data appear modest, and in the single Phase 3 trial, tradipitant did not demonstrate statistical superiority vs. placebo. Additionally, the current treatment options (approved and off-label) for gastroparesis are mostly generically available and have been used in practice for decades.

Tradipitant is in development for other indications, including motion sickness and atopic dermatitis, which may expand the eligible patient population for this drug.

Xanomeline/trospium (Brand Name: To be determined)

Manufacturer: Bristol Myers Squibb
Expected FDA decision: September 26, 2024

Therapeutic use

Xanomeline/trospium is under review for the treatment of adult patients with schizophrenia.

Schizophrenia is a mental disorder characterized by disruptions in thought processes, perceptions, emotional responsiveness, and social interactions. Schizophrenia symptoms generally fall into three categories: positive (eg, delusions, hallucinations, disorganized speech, thought and behavior), negative (poor motivation, lack of pleasure and enjoyment, lack of speech, lack of social interaction), and cognitive (eg, impaired executive function, attention, and memory). The underlying cause of schizophrenia is unknown, but it is thought to be due to a combination of genetic and environmental factors.

People with schizophrenia are usually diagnosed between ages 16 and 30. Lifetime prevalence of schizophrenia is higher among men compared to women. The estimated prevalence of schizophrenia in the U.S. is 2.8 million people.

What you need to know:

Proposed Indication: Treatment of adult patients with schizophrenia

Mechanism: M1/M4 muscarinic acetylcholine receptor agonist

Efficacy: Mean change from baseline in PANSS score:

- EMERGENT-2: -21.2 vs. -11.6 with placebo
- EMERGENT-3: -20.6 vs. -12.2 with placebo

Common AEs: Constipation, dyspepsia, headache, nausea, vomiting, hypertension, dizziness, gastroesophageal reflux disease, diarrhea

Dosing: Oral twice daily

Why it Matters: Novel mechanism of action, unique side effect profile (eg, reduced extrapyramidal symptoms, weight gain) vs. atypical antipsychotics, potential use as add-on therapy for schizophrenia and treatment of psychosis with Alzheimer's disease

Important to Note: Well established alternatives available with generic availability, lack of head-to-head trial data vs. standards of care

Estimated Cost: ~$20,000 per year (based on pricing for Caplyta)

Clinical profile

Xanomeline/trospium is a dual M1/M4 muscarinic acetylcholine receptor agonist. Xanomeline is a muscarinic cholinergic receptor agonist that stimulates M1 and M4 receptors, which have been implicated in the pathophysiology of schizophrenia. Trospium is a muscarinic receptor antagonist that does not cross the blood-brain barrier and inhibits M1 through M5 receptors in peripheral tissues, thus limiting systemic absorption of xanomeline. Trospium is intended to mitigate xanomeline-related adverse events associated with peripheral muscarinic receptors.

Pivotal trial data:
The efficacy of xanomeline/trospium was evaluated in EMERGENT-2 (N = 252) and EMERGENT-3 (N = 256), two Phase 3, randomized, double-blind, placebo-controlled studies in acutely psychotic hospitalized adults with schizophrenia. Patients were randomized to receive xanomeline/trospium or placebo. Xanomeline/trospium dosing started at 50 mg/20 mg twice daily and increased to a maximum of 125 mg/30 mg twice daily. The primary endpoint was the change from baseline in Positive and Negative Syndrome Scale (PANSS) total score at Week 5. The PANSS is used to measure symptom severity in patients with schizophrenia. The PANSS consists of 30 items across three scales (positive, negative, and general psychopathology scales), with each item scored from 1 (absent) to 7 (extreme), for a total possible score from 30 to 210. A greater PANSS total score represents greater schizophrenia symptom severity.

Xanomeline/trospium *(continued...)*

In EMERGENT-2, the mean change from baseline to Week 5 in the PANSS total score was -21.2 for xanomeline/trospium and -11.6 points for placebo (difference -9.6, $p < 0.0001$).

In EMERGENT-3, the mean change from baseline to Week 5 in the PANSS total score was -20.6 for xanomeline/trospium and -12.2 points for placebo (difference -8.4, $p < 0.0001$).

Safety:
The most common adverse events with xanomeline/trospium use were constipation, dyspepsia, headache, nausea, vomiting, hypertension, dizziness, gastroesophageal reflux disease, and diarrhea.

Dosing:
In the pivotal trial, xanomeline/trospium was administered orally twice daily.

Competitive environment

The current standard of care for schizophrenia is atypical antipsychotics. These drugs can provide significant benefit, particularly for the positive symptoms associated with schizophrenia. Generally, antipsychotics are associated with adverse events including extrapyramidal symptoms, sedation, weight gain, metabolic disturbances, and hyperprolactinemia due to their mechanisms involving dopaminergic or serotonergic pathways.

Xanomeline/trospium is a first-in-class therapy with a novel mechanism of action for the treatment of schizophrenia. The efficacy of xanomeline/trospium appears comparable to atypical antipsychotics. The primary differentiator is its tolerability profile. Specifically, xanomeline/trospium is associated with less weight gain and extrapyramidal symptoms compared to current treatment options. However, in clinical trials, the discontinuation rate for xanomeline/trospium appears similar when compared indirectly to atypical antipsychotics.

Xanomeline/trospium will be entering a treatment landscape where almost all the well-established, oral atypical antipsychotics are available as generics and long-acting injectable antipsychotics are available for patients who struggle with nonadherence. While xanomeline/trospium may offer some advantages, it has not yet been compared in head-to-head trials against its competitors.

The initial indication for xanomeline/trospium is for monotherapy treatment of schizophrenia but it is in development for adjunctive therapy in schizophrenia and as a treatment for psychosis with Alzheimer's disease. If the results are positive in these uses, that could significantly increase the market potential for xanomeline/trospium.

For reference, the WAC for Caplyta® (lumateperone), a branded atypical antipsychotic, is approximately $20,000 per year.

Insulin icodec (Brand Name: To be determined)

Manufacturer: Novo Nordisk
Expected FDA decision: 3Q 2024

Therapeutic use

Insulin icodec is under review to improve glycemic control in patients with type 1 and type 2 diabetes mellitus (T1DM and T2DM).

T1DM is an autoimmune disease in which the body's immune system destroys the insulin-producing cells in the pancreas. In T2DM, patients do not produce enough insulin, or their cells stop responding to insulin properly. Both T1DM and T2DM cause elevated blood sugar levels, which can result in downstream complications (eg, heart disease, chronic kidney disease, vision loss).

About 38 million people are estimated to have diabetes in the U.S. T2DM accounts for the majority of cases, affecting about 90% to 95% of people with diabetes.

What you need to know:

Proposed Indication: To improve glycemic control in patients with T1DM and T2DM

Mechanism: Long-acting basal insulin

Efficacy: Statistically non-inferior or superior to comparator basal insulins (refer to full text for details)

Safety: Common AEs were comparable to other basal insulins

Dosing: SC once weekly

Why it Matters: First once-weekly basal insulin (fewer injections vs. current basal insulins), comparable or statistically better A1c reduction vs. competitors

Important to Note: Competing against well-established basal insulins (eg, Lantus, Toujeo, Tresiba), basal insulin biosimilars currently available with more expected in the near-term, consistently higher numerical rates of clinically significant or severe hypoglycemia vs. comparators

Estimated Cost: ~$6,000 per year (based on pricing for Tresiba)

Clinical profile

Insulin icodec is an ultra-long-acting basal insulin analog.

Pivotal trial data:
The efficacy of insulin icodec was evaluated in the ONWARDS clinical program (ONWARDS 1 to 6). The studies were Phase 3, randomized, open-label (except ONWARDS 3 which was double-masked), active-controlled trials. ONWARDS 1 to 5 were conducted in patients with T2DM and ONWARDS 6 was conducted in patients with T1DM. The primary endpoint across all six trials was the change in HbA1c.

T2DM

ONWARD 1 was conducted in 984 adults with T2DM who had not previously received insulin. Patients were randomized to once-weekly insulin icodec or once-daily insulin glargine U-100. The mean reduction in HbA1c at 52 weeks was −1.55% with icodec vs. −1.35% with glargine (difference of −0.19, 95% CI: −0.36, −0.03; $p < 0.001$ for non-inferiority and $p = 0.02$ for superiority).

ONWARDS 2 was conducted in 526 adults with T2DM inadequately controlled on once-daily or twice-daily basal insulin. Patients were randomized to once-weekly insulin icodec or once-daily insulin degludec. The mean reduction in HbA1c at 26 weeks was −0.93% with icodec vs. −0.71% with degludec (difference of −0.22, 95% CI: −0.37, −0.08; $p < 0.0001$ for non-inferiority and $p = 0.0028$ for superiority).

ONWARDS 3 was conducted in 588 adults with T2DM who had not previously received insulin. Patients were randomized to once-weekly insulin icodec and once-daily placebo or once-daily insulin degludec and once-weekly placebo. The mean reduction in HbA1c at 26 weeks was −1.57% with icodec vs. −1.36% with degludec (difference of −0.2, 95% CI: −0.3, −0.1; $p < 0.001$ for non-inferiority and $p = 0.002$ for superiority).

Insulin icodec *(continued...)*

ONWARDS 4 was conducted in 582 adults with T2DM inadequately controlled with basal-bolus insulin. Patients were randomized to once-weekly insulin icodec or once-daily insulin glargine U100 combined with 2 to 4 daily bolus insulin aspart injections. The mean reduction in HbA1c at 26 weeks was −1.16% with icodec vs. −1.18% with glargine (difference of 0.02, 95% CI: −0.11, 0.15; $p < 0.0001$ for non-inferiority).

ONWARDS 5 was conducted in 1,085 adults with T2DM who had not previously received insulin. Patients were randomized to once-weekly insulin icodec with a dosing guide application or a once-daily basal insulin dosed as per standard clinical practice. The mean reduction in HbA1c at 52 weeks was −1.68% with icodec vs. −1.31% with basal insulin (difference of −0.38, 95% CI: −0.66, −0.09; $p < 0.001$ for non-inferiority and $p = 0.009$ for superiority).

T1DM

ONWARDS 8 was conducted in 583 adults with T1DM with previous treatment with basal-bolus insulin. Patients were randomized to once-weekly insulin icodec or once-daily insulin degludec, both in combination with insulin aspart (two or more daily injections). The mean reduction in HbA1c at 26 weeks was −0.47% with icodec vs. −0.51% with degludec (difference of 0.05, 95% CI: -0.13, 0.23; $p = 0.0065$ for non-inferiority).

Safety:
The adverse events associated with insulin icodec use were comparable to other basal insulins. However, rates of clinically significant or severe hypoglycemia were generally numerically higher with insulin icodec vs. other basal insulins and in the lone T1DM study, the difference was statistically significant. In ONWARDS 6, the overall rate of combined clinically significant or severe hypoglycemia was 19.9 vs. 10.4 events per patient-year of exposure for insulin icodec vs. insulin degludec, respectively (estimated rate ratio 1.9, 95% CI: 1.5, 2.3; $p < 0.0001$).

Dosing:
In the pivotal trials, insulin icodec was administered SC once weekly.

Competitive environment

If approved, insulin icodec would be the first once weekly basal insulin. The current basal insulins on the market generally require once daily administration. The primary differentiator for insulin icodec would be reducing the injection burden for insulin-dependent diabetes patients, without compromising glycemic control. Across its six pivotal trials, insulin icodec was either statistically superior or non-inferior to comparator basal insulins.

The primary clinical question with insulin icodec use is the risk of hypoglycemia, due to the prolonged dosing interval. The increased risk of severe hypoglycemia was particularly concerning in T1DM patients. Current basal insulins are well-established with patients and providers comfortable with their dosing.

In addition, basal insulin biosimilars are already available and more are expected in the near-term, making this category much more competitive by the time insulin icodec enters the market.

For reference, the WAC for Tresiba is approximately $6,000 per year.

Extended brand pipeline forecast

Optum Rx brand pipeline forecast

Pipeline Drug Name(s)	Generic Name	Company	Mechanism of Action	Disease State	Route	FDA Status	Projected FDA Approval Decision	Specialty Drug	Orphan Drug
2024 Possible launch date									
mRNA-1345	mRNA-1345	Moderna	vaccine	Respiratory syncytial virus	IM	Filed BLA	05/2024	No	No
GFT-505	elafibranor	Ipsen/ Genfit	selective peroxisome proliferator-activated receptor modulator	Primary biliary cholangitis	PO	Filed NDA	06/10/2024	Yes	Yes
BBI-4000	sofpironium bromide	Botanix Pharmaceuticals	anticholinergic	Hyperhidrosis	TOP	Filed NDA	06/10/2024	No	No
GRN-163L	imetelstat	Geron	telomerase inhibitor	Myelodysplastic syndrome	IV	Filed NDA	06/16/2024	Yes	Yes
V-116	pneumococcal conjugate vaccine	Merck	vaccine	Pneumococcal vaccine	IM	Filed BLA	06/17/2024	No	No
RPL-554	ensifentrine	Verona Pharma	phosphodiesterase-3 and phosphodiesterase-4 inhibitor	Chronic obstructive pulmonary disease	INH	Filed NDA	06/26/2024	No	No
HER3-DXd	patritumab deruxtecan	Daiichi Sankyo	antibody drug conjugate	Non-small cell lung cancer	IV	Filed BLA	06/26/2024	Yes	No

Pipeline Drug Name(s)	Generic Name	Company	Mechanism of Action	Disease State	Route	FDA Status	Projected FDA Approval Decision	Specialty Drug	Orphan Drug
ND-0612H	levodopa/ carbidopa	Mitsubishi Tanabe	dopamine precursor/ dopa-decarboxylase inhibitor	Parkinson's disease	SC	Filed NDA	2Q2024	Yes	No
BT-595	immune globulin	Biotest	immune globulin	Primary immunodeficiency	IV	Filed BLA	06/29/2024	Yes	No
RP-L201	marnetegragene autotemcel	Rocket Pharmaceuticals	gene therapy	Leukocyte adhesion deficiency-I	IV	Filed BLA	06/30/2024	Yes	Yes
Lydolyte	lidocaine	MEDRx	anesthetic agent	Neuropathic pain	TOP	CRL	Mid-2024	No	No
RG-6107	crovalimab	Roche	C5 inhibitor	Paroxysmal nocturnal hemoglobinuria	IV/SC	Filed BLA	07/07/2024	Yes	Yes
ALPHA-1062	galantamine prodrug	Alpha Cognition	acetylcholinesterase inhibitor	Alzheimer's disease	PO	Filed NDA	07/27/2024	No	No
LAI-287	insulin icodec	Novo Nordisk	ultra-long-acting basal insulin	Diabetes mellitus	SC	Filed BLA	07/2024	No	No
Dasynoc	dasatinib	Xspray Pharma	kinase inhibitor	Chronic myeloid leukemia	PO	Filed NDA	07/31/2024	Yes	Yes
CTP-543	deuruxolitinib	Sun Pharma	janus kinase inhibitor	Alopecia areata	PO	Filed NDA	07/2024	Yes	No
ADP-A2M4 (MAGE-A4)	afamitresgene autoleucel	Adaptimmune	SPEAR T-cell therapy	Sarcoma	IV	Filed BLA	08/06/2024	Yes	Yes
IPX-203	carbidopa/ levodopa	Amneal	dopamine precursor/ dopa-decarboxylase inhibitor	Parkinson's disease	PO	Filed NDA	08/07/2024	No	No

Pipeline Drug Name(s)	Generic Name	Company	Mechanism of Action	Disease State	Route	FDA Status	Projected FDA Approval Decision	Specialty Drug	Orphan Drug
Humacyl	human acellular vessel	Humacyte	cellular therapy	End-stage renal disease	Implant	Filed BLA	08/10/2024	Yes	No
MDMA	midomafetamine	Lykos Therapeutics	psychoactive drug	Post-traumatic stress disorder	PO	Filed NDA	08/11/2024	No	No
I/Ontak	denileukin diftitox	Citius	CD25-directed cytotoxin	Cutaneous T-cell lymphoma	IV	Filed BLA	08/13/2024	Yes	Yes
nemolizumab	nemolizumab	Galderma	interleukin-31 receptor antagonist	Atopic dermatitis	SC	Filed BLA	08/14/2024	Yes	No
TransCon PTH	palopegteriparatide	Ascendis Pharma	parathyroid hormone	Hypoparathyroidism	SC	Filed NDA	08/14/2024	Yes	Yes
MBX-8025 (RWJ-800025)	seladelpar	CymaBay Therapeutics	peroxisome proliferator-activated receptor delta agonist	Primary biliary cholangitis	PO	Filed NDA	08/14/2024	Yes	Yes
AG-881	vorasidenib	Servier	isocitrate dehydrogenase-1 and -2 inhibitor	Brain cancer	PO	Filed NDA	08/20/2024	Yes	Yes
REGN-5458	linvoseltamab	Regeneron	BCMA and CD3 bispecific antibody inhibitor	Multiple myeloma	IV	Filed BLA	08/22/2024	Yes	No
ZP-1848	glepaglutide	Zealand Pharma	glucagon peptide-2 agonist	Short bowel syndrome	SC	Filed NDA	08/22/2024	Yes	Yes
JNJ-1937	lazertinib	Janssen	kinase inhibitor	Non-small cell lung cancer	PO	Filed NDA	08/22/2024	Yes	No

Pipeline Drug Name(s)	Generic Name	Company	Mechanism of Action	Disease State	Route	FDA Status	Projected FDA Approval Decision	Specialty Drug	Orphan Drug
SNDX-6352	axatilimab	Syndax Pharmaceuticals	colony stimulating factor 1 receptor monoclonal antibody	Graft vs. host disease	IV	Filed BLA	08/28/2024	Yes	Yes
RG-1594	ocrelizumab	Genentech	CD20-directed cytolytic antibody	Multiple sclerosis	SC	Filed BLA	09/13/2024	Yes	No
Tecentriq SC	atezolizumab	Roche	programmed death-ligand 1 blocking antibody	Cancers (mirroring indications to IV formulation)	SC	Filed BLA	09/15/2024	Yes	No
LY-686017	tradipitant	Vanda Pharmaceuticals	neurokinin 1 receptor antagonist	Gastroparesis	PO	Filed NDA	09/18/2024	No	No
arimoclomol	arimoclomol	Zevra Therapeutics	cytoprotectives	Niemann-Pick disease	PO	Filed NDA	09/21/2024	Yes	Yes
IBI-1000	acetylleucine	IntraBio	modified amino acid	Niemann-Pick Disease type C	PO	Filed NDA	09/24/2024	Yes	Yes
SNDX-5613	revumenib	Syndax	Menin-mixed lineage leukemia 1 inhibitor	Acute myelogenous leukemia	PO	Filed NDA	09/26/2024	Yes	Yes
KarXT	xanomeline/ trospium	Karuna Therapeutics	muscarinic acetylcholine receptor agonist/ muscarinic receptor antagonist	Schizophrenia	PO	Filed NDA	09/26/2024	No	No
LY-3002813	donanemab	Eli Lilly	beta-amyloid monoclonal antibody	Alzheimer's disease	IV	Filed BLA	3Q2024	Yes	No

Pipeline Drug Name(s)	Generic Name	Company	Mechanism of Action	Disease State	Route	FDA Status	Projected FDA Approval Decision	Specialty Drug	Orphan Drug
OX-125	nalmefene	Orexo	opioid receptor antagonist	Opioid use disorder	Intranasal	InTrial	3Q2024	No	No
ARS-1	epinephrine	ARS Pharmaceuticals	non-selective alpha/ beta-adrenergic receptor agonist	Anaphylaxis	Intranasal	Filed NDA	10/02/2024	No	No
LY-03010	paliperidone	Luye Pharma	atypical antipsychotic	Schizophrenia	IM	Filed NDA	10/09/2024	No	No
PF-06741086	marstacimab	Pfizer	tissue factor pathway inhibitor	Hemophilia	SC	Filed BLA	10/11/2024	Yes	Yes
CAM-2029	octreotide	Camurus	somatostatin analogue	Acromegaly	SC	Filed NDA	10/21/2024	Yes	Yes
sulopenem	sulopenem	Iterum Therapeutics	carbapenem	Urinary tract infections	PO	Filed NDA	10/29/2024	No	No
MILR-1444A	lebrikizumab	Eli Lilly	interleukin-13 inhibitor	Atopic dermatitis	SC	Filed BLA	10/2024	Yes	No
BH-009	docetaxel	Zhuhai Beihai Biotechnology	microtubule inhibitor	Breast cancer/ non-small cell lung cancer/ prostate cancer/ gastric cancer	IV	Filed NDA	11/03/2024	Yes	No
DFD-29	minocycline	Journey Medical/ Dr. Reddy's	tetracycline	Rosacea	PO	Filed NDA	11/04/2024	No	No
MCLA-128	zenocutuzumab	Merus	neuregulin/HER3 inhibitor	Non-smell cell lung cancer/ pancreatic cancer	IV	Filed BLA	11/06/2024	Yes	No
PTC-AADC	eladocagene exuparvovec	PTC Therapeutics	gene therapy	Aromatic L-amino acid decarboxylase deficiency	Intracerebral	Filed BLA	11/13/2024	Yes	Yes

Pipeline Drug Name(s)	Generic Name	Company	Mechanism of Action	Disease State	Route	FDA Status	Projected FDA Approval Decision	Specialty Drug	Orphan Drug
Obe-cel	obecabtagene autoleucel	Autolus Therapeutics	autologous chimeric antigen receptor T-cells	Acute lymphoblastic leukemia	IV	Filed BLA	11/16/2024	Yes	Yes
AT-007	govorestat	Applied Therapeutics	aldose reductase inhibitor	Galactosemia	PO	Filed NDA	11/28/2024	Yes	Yes
AG-10 (AG10)	acoramidis	BridgeBio	tetrameric transthyretin stabilizer	Transthyretin amyloid cardiomyopathy	PO	Filed NDA	11/29/2024	Yes	No
SH-201	SH-201	Shorla Oncology	Unknown	Leukemias	PO	Filed NDA	11/30/2024	Yes	No
ZW-25	zanidatamab	Jazz Pharmaceuticals	HER2 monoclonal antibody	Biliary tract cancer	IV	Filed BLA	12/02/2024	Yes	Yes
CSL-312	garadacimab	CSL Limited	anti-factor XIIa monoclonal antibody	Hereditary angioedema	SC	Filed BLA	12/14/2024	Yes	Yes
DS-1062	datopotamab deruxtecan	Daiichi Sankyo/ AstraZeneca	trop-2 antibody-drug conjugate	Non-small cell lung cancer	IV	Filed BLA	12/20/2024	Yes	No
X-396	ensartinib	Xcovery	anaplastic lymphoma kinase inhibitor	Non-small cell lung cancer	PO	Filed NDA	12/28/2024	Yes	No
AXS-07	meloxicam/rizatriptan	Axsome Therapeutics	non-steroidal anti-inflammatory drug/triptan	Migraine	PO	CRL	4Q2024	No	No
STS-101	dihydroergotamine	Satsuma Pharmaceuticals	ergotamine	Migraine	Intranasal	CRL	4Q2024	No	No

Pipeline Drug Name(s)	Generic Name	Company	Mechanism of Action	Disease State	Route	FDA Status	Projected FDA Approval Decision	Specialty Drug	Orphan Drug
CK-301	cosibelimab	Checkpoint Therapeutic	anti programmed cell death ligand 1	Cutaneous squamous cell carcinoma	IV	CRL	4Q2024	Yes	No
RG-7433 (ABT-263)	navitoclax	AbbVie	Bcl-2 inhibitor	Myelofibrosis	PO	InTrial	4Q2024	Yes	Yes
IONIS-APOCIII-LRx (ISIS-678354)	olezarsen	Ionis	antisense drug	Familial chylomicronemia syndrome	SC	Filed BLA	4Q2024	Yes	Yes
VX-121/ tezacaftor/ deutivacaftor	vanzacaftor/ tezacaftor/ deutivacaftor	Vertex	CF transmembrane conductance modulators	Cystic fibrosis	PO	Filed NDA	4Q2024	Yes	Yes
iMAB-362	zolbetuximab	Astellas	GC182 monoclonal antibody	Gastric cancer	IV	Filed BLA	2H2024	Yes	Yes
OX-124	naloxone	Orexo	opioid antagonist	Opioid overdose	Intranasal	CRL	2H2024	No	No
Hepcludex	bulevirtide	Gilead	HBV receptor binder	Hepatitis delta virus	SC	CRL	2H2024	Yes	Yes
OMS-721	narsoplimab	Omeros	anti-MASP-2 monoclonal antibody	Hematopoietic stem cell transplant-associated thrombotic microangiopathy	IV	CRL	2H2024	Yes	Yes
ADI-PEG20	pegargiminase	Polaris	pegylated arginine deiminase	Mesothelioma	IM	InTrial	2H2024	Yes	Yes
CUTX-101	copper histidinate	Fortress Biotech	copper replacement	Menkes Disease	SC	InTrial	2H2024	Yes	Yes

Pipeline Drug Name(s)	Generic Name	Company	Mechanism of Action	Disease State	Route	FDA Status	Projected FDA Approval Decision	Specialty Drug	Orphan Drug
XMT-1536	upifitamab rilsodotin	Mersana Therapeutics	antibody-drug conjugate	Ovarian cancer	IV	InTrial	2H2024	Yes	No
TC-002	latanoprost	TearClear	prostaglandin analog	Glaucoma	OPH	InTrial	2H2024	No	No
Opdivo SC	nivolumab/ hyaluronidase	Bristol Myers Squibb	programmed death receptor-1-blocking antibody	Various cancers	SC	Filed BLA	12/29/2024	Yes	No
LIQ-861	treprostinil	Liquidia Technologies	prostacyclin analog	Pulmonary arterial hypertension; interstitial lung disease	INH	Tentative Approval	2024	Yes	No
DS-100	dehydrated alcohol	Eton	undisclosed	Methanol poisoning	SC	CRL	2024	No	Yes
ABBV-951	foscarbidopa/ foslevodopa	AbbVie	aromatic amino acid decarboxylation inhibitor/ aromatic amino acid	Parkinson's disease	SC	CRL	2024	Yes	No
AZD-5156	AZD-5156	AstraZeneca	monoclonal antibody	COVID-19	IM	InTrial	2024	TBD	No
Prochymal	remestemcel-L	Mesoblast	mesenchymal stem cells	Graft vs. host disease	IV	CRL	Late 2024	Yes	Yes
VNRX-5133	cefepime/ taniborbactam	VenatoRx Pharmaceuticals	cephalosporin/ beta-lactamase inhibitor	Bacterial infections	IV	CRL	Late 2024	No	No
RP-L102 (RPL-102)	RP-L102	Rocket Pharmaceuticals	gene therapy	Fanconi anemia	IV	InTrial	Late 2024	Yes	Yes

Pipeline Drug Name(s)	Generic Name	Company	Mechanism of Action	Disease State	Route	FDA Status	Projected FDA Approval Decision	Specialty Drug	Orphan Drug
AEB-1102	pegzilarginase	Aeglea BioTherapeutics	enzyme replacement/ arginase-I stimulator	Arginase 1 deficiency	IV	InTrial	Late 2024	Yes	Yes
NN-7415	concizumab	Novo Nordisk	anti-tissue factor pathway inhibitor	Hemophilia A and hemophilia B	SC	CRL	Late 2024	Yes	Yes
F-901318	olorofim	F2G	orotomide antifungal	Aspergillosis	PO/IV	CRL	Late 2024	No	Yes
UX-111 (ABO-102)	UX-111	Ultragenyx Pharmaceutical	gene therapy	Sanfilippo syndrome type A	IV	InTrial	Late 2024	Yes	Yes
2025 Possible launch date									
Subvenite	lamotrigine	OWP Pharmaceuticals	anticonvulsant	Epilepsy/ bipolar disorder	PO	Filed NDA	01/03/2025	No	No
MTP-131 (SS-31)	elamipretide	Stealth Biotherapeutics	mitochondrial permeability transition pore inhibitor	Barth syndrome	SC	Filed NDA	01/29/2025	Yes	Yes
MenABCWY	meningococcal vaccine	GSK	vaccine	Meningococcal disease	IM	Filed sBLA	02/14/2025	No	No
Hernicore (SI-6603)	condoliase	Seikagaku	glycosaminoglycan-degrading enzyme	Pain	Intrathecal	Filed BLA	03/14/2025	Yes	No
MSP-2017	etripamil	Milestone	calcium channel blocker	Arrhythmia	Intranasal	Filed NDA	03/28/2025	TBD	No
S-217622	ensitrelvir fumaric acid	Shionogi	Protease inhibitor	COVID-19 treatment	PO	InTrial	1Q2025	No	No

Pipeline Drug Name(s)	Generic Name	Company	Mechanism of Action	Disease State	Route	FDA Status	Projected FDA Approval Decision	Specialty Drug	Orphan Drug
Translarna	ataluren	PTC Therapeutics	gene transcription modulator	Duchenne muscular dystrophy	PO	CRL	1Q2025	Yes	Yes
EBV-CTL (ATA-129)	tabelecleucel	Atara Biotherapeutics	cell therapy	Lymphoproliferative disorder	IV	InTrial	1Q2025	Yes	Yes
EB-101	prademagene zamikeracel	Abeona Therapeutics	gene therapy	Epidermolysis Bullosa	TOP	CRL	1Q2025	Yes	Yes
PDP-716	brimonidine	Visiox Pharma	alpha-2 agonist	Glaucoma	OPH	Not Approved	1Q2025	No	No
KVD-900	sebetralstat	KalVista Pharmaceuticals	plasma kallikrein inhibitor	Hereditary angioedema	PO	InTrial	1Q2025	Yes	Yes
PD-0325901	mirdametinib	SpringWorks Therapeutics	MEK 1/2 inhibitor	Neurofibromatosis	PO	InTrial	1Q2025	Yes	Yes
Leqembi SC	lecanemab	Eisai/Biogen	beta-amyloid targeted therapy	Alzheimer's disease	SC	InTrial	1Q2025	Yes	No
UGN-102	mitomycin	UroGen	alkylating drug	Bladder cancer	Intravesical	InTrial	1Q2025	Yes	No
VX-548	suzetrigine	Vertex	selective NaV1.8 inhibitor	Acute pain	PO	InTrial	1Q2025	No	No
NBI-74788	crinecerfont	Neurocrine Biosciences	CRF receptor antagonist	Congenital adrenal hyperplasia	PO	Filed NDA	04/2025	Yes	Yes
AXS-14	S-reboxetine	Axsome Therapeutics	selective noradrenaline reuptake inhibitor	Fibromyalgia	PO	InTrial	2Q2025	No	No

Pipeline Drug Name(s)	Generic Name	Company	Mechanism of Action	Disease State	Route	FDA Status	Projected FDA Approval Decision	Specialty Drug	Orphan Drug
Sarconeos	BIO-101	Biophytis	MAS G-protein coupled receptor agonist	COVID-19 treatment	PO	InTrial	1H2025	No	No
NS-2 (ALDX-1E1, ADX-102)	reproxalap	Aldeyra Therapeutics	aldehyde antagonist	Dry eye disease	OPH	CRL	1H2025	No	No
RTT-01	tiratricol	Egetis Therapeutics	thyroid-stimulating hormone receptor	Monocarboxylate transporter 8 deficiency	PO	InTrial	1H2025	Yes	Yes
Xinlay	atrasentan	Novartis	selective endothelin-A receptor antagonist	IgA nephropathy	PO	InTrial	1H2025	Yes	No
CORT-125134	relacorilant	Corcept Therapeutics	glucocorticoid receptor II antagonist	Cushing's syndrome	PO	InTrial	1H2025	Yes	Yes
DCCR	diazoxide choline controlled-release	Soleno Therapeutics	vasodilator	Prader-Willi syndrome	PO	InTrial	1H2025	Yes	Yes
cytisine	cytisine	Achieve Life Sciences	nicotinic acetylcholine receptor antagonist	Smoking cessation	PO	InTrial	1H2026	No	No
SPI-014	lanthanum dioxycarbonate	Unicycive	phosphate binder	Hyperphosphatemia	PO	InTrial	1H2025	No	No
NRX-100	ketamine	NeuroRx	NMDA antagonist	Depression	PO	InTrial	1H2025	No	No
SLS-001 (WT-1)	galinpepimut-S	Sellas Life Sciences Group	vaccine	Acute myeloid leukemia	SC	InTrial	1H2025	Yes	Yes

Pipeline Drug Name(s)	Generic Name	Company	Mechanism of Action	Disease State	Route	FDA Status	Projected FDA Approval Decision	Specialty Drug	Orphan Drug
Ovastat	treosulfan	Medexus Pharmaceuticals	alkylating agent	Hematopoietic stem cell transplantation	IV	InTrial	1H2025	Yes	Yes
SEL-212	SVP-rapamycin/ pegsiticase	Selecta Biosciences/ 3SBio	synthetic vaccine particle/ enzyme combination	Gout	IV	InTrial	1H2025	Yes	No
YN-96D1	rivoceranib (apatinib)	Elevar Therapeutics	vascular endothelial growth factor receptor antagonist	Hepatocellular carcinoma	PO	CRL	1H2025	Yes	Yes
MT-1621	deoxythymidine/ deoxycytidine	UCB	deoxynucleoside	Thymidine kinase 2 deficiency	PO	InTrial	1H2025	Yes	Yes
LIB-003	lerodalcibep	LIB Therapeutics	PCSK9 inhibitor	Hypocholesteremia	SC	InTrial	1H2025	No	No
REN-001	mavodelpar	Reneo Pharmaceuticals	PPARd agonist	Primary mitochondrial myopathies	PO	InTrial	1H2025	Yes	Yes
SHR-1210	camrelizumab	Elevar Therapeutics	programmed death receptor-1-blocking antibody	Hepatocellular carcinoma	IV	CRL	1H2025	Yes	Yes
DCC-3014	vimseltinib	Deciphera	CSF1R inhibitor	Tenosynovial giant cell tumor	PO	InTrial	1H2025	Yes	No
VS-6063	defactinib	Verastem	focal adhesion kinase inhibitor	Ovarian cancer	PO	InTrial	1H2025	Yes	Yes
VS-6766	avutometinib	Verastem	RAF/MEK clamp	Ovarian cancer	PO	InTrial	1H2025	Yes	No

Pipeline Drug Name(s)	Generic Name	Company	Mechanism of Action	Disease State	Route	FDA Status	Projected FDA Approval Decision	Specialty Drug	Orphan Drug
SDN-037	difluprednate	Visiox	corticosteroid	Ocular inflammation/pain	OPH	InTrial	Mid-2025	No	No
PTC-743	vatiquinone	PTC Therapeutics	undisclosed	Friedreich's ataxia	PO	InTrial	Mid-2025	Yes	Yes
GZ-402671 (SAR-402671)	venglustat (ibiglustat)	Sanofi	glucosylceramide synthase inhibitor	M2 Gangliosidosis	PO	InTrial	Mid-2025	Yes	Yes
K-127	pyridostigmine	Amneal	cholinesterase inhibitor	Myasthenia gravis	PO	InTrial	Mid-2025	No	No
ONS-5010	bevacizumab-vikg	Outlook Therapeutics	anti-VEGF antibody	Wet age-related macular degeneration	Intravitreal	CRL	Mid-2025	Yes	No
AR-15512	AR-15512	Aerie Pharmaceuticals	TRPM8 agonist	Dry eye disease	OPH	InTrial	Mid-2025	No	No
PRN-1008	rilzabrutinib	Sanofi	BTK inhibitor	Chronic immune thrombocytopenia	PO	InTrial	Mid-2025	No	Yes
ALZ-801	valiltramiprosate	Alzheon	amyloid beta-protein inhibitor	Alzheimer's disease	PO	InTrial	Mid-2025	Yes	No
SB-525	giroctocogene fitelparvovec	Pfizer/ Sangamo Therapeutics	gene therapy	Hemophilia A	IV	InTrial	Mid-2025	Yes	Yes
LOU-064	remibrutinib	Novartis	Bruton's tyrosine kinase inhibitor	Chronic spontaneous urticaria	PO	InTrial	Mid-2025	Yes	No
RGX-121	RGX-121	Regenxbio	gene therapy	Mucopolysaccharidosis Type II	Intracisternal	InTrial	Mid-2025	Yes	Yes

Pipeline Drug Name(s)	Generic Name	Company	Mechanism of Action	Disease State	Route	FDA Status	Projected FDA Approval Decision	Specialty Drug	Orphan Drug
PTC-923	sepiapterin	PTC Therapeutics	phenylalanine hydroxylase activator	Phenylketonuria	PO	InTrial	Mid-2025	Yes	Yes
RP-1	vusolimogene oderparepvec	Replimune	oncolytic immunotherapy	Cutaneous skin cell cancer	Intratumoral	InTrial	Mid-2025	Yes	No
AT-527	bemnifosbuvir	Atea Pharmaceuticals	HCV NS5B polymerase inhibitor	Treatment of COVID-19	PO	InTrial	Mid-2025	No	No
AGEN-1181	botensilimab	Agenus	anti-CTLA-4 antibody	Colorectal cancer	IV	InTrial	Mid-2025	Yes	No
ICP-022	orelabrutinib	InnoCare	Bruton's tyrosine kinase inhibitor	Mantle cell lymphoma	PO	InTrial	Mid-2025	Yes	Yes
INO-3107	INO-3107	Inovio Pharmaceuticals	immunotherapy	Recurrent respiratory papillomatosis	IM	InTrial	Mid-2025	Yes	Yes
DZD-9008	sunvozertinib	Dizal	EGFR inhibitor	Non-small cell lung cancer	PO	InTrial	Mid-2025	Yes	No
ANB-019	imsidolimab	AnaptysBio	interleukin-36 receptor antagonist	Generalized pustular psoriasis	IV	InTrial	3Q2025	Yes	Yes
SAR-442168	tolebrutinib	Sanofi	Bruton’s tyrosine kinase inhibitor	Multiple sclerosis	PO	InTrial	4Q2025	Yes	No
ARO-APOC3	plozasiran	Arrowhead Pharmaceuticals	RNAi targeting apolipoprotein C-III	Familial chylomicronemia syndrome	SC	InTrial	4Q2025	Yes	Yes

Pipeline Drug Name(s)	Generic Name	Company	Mechanism of Action	Disease State	Route	FDA Status	Projected FDA Approval Decision	Specialty Drug	Orphan Drug
resiniferatoxin	resiniferatoxin	Sorrento Therapeutics	TRPV-1 inhibitor	Osteoarthritis pain/ cancer pain	Intrathecal/ Intraarticular	InTrial	4Q2025	TBD	Yes
Donesta	estetrol	Mithra Pharmaceuticals	estrogen	Vasomotor symptoms	PO	InTrial	4Q2025	No	No
PAX-101	suramin	PaxMedica	unknown	trypanosomiasis	IV	InTrial	2H2025	No	No
SPR-001	tildacerfont	Spruce Biosciences	corticotropin-releasing factor type-1 receptor antagonist	Congenital adrenal hyperplasia	PO	InTrial	2H2025	Yes	Yes
Tonmya	cyclobenzaprine	Tonix	muscle relaxant	Fibromyalgia	PO	InTrial	2H2025	No	No
ALN-APC (ALN-AT3)	fitusiran	Sanofi/ Alnylam	RNAi therapeutic	Hemophilia A and B	SC	InTrial	2H2025	Yes	Yes
GSK-2140944	gepotidacin	GlaxoSmithKline	bacterial Type II topoisomerase inhibitor	Bacterial infections	PO/IV	InTrial	2H2025	No	No
AXS-12	reboxetine	Axsome Therapeutics	norepinephrine reuptake inhibitor	Narcolepsy	PO	InTrial	2H2025	No	Yes
IdeS (immunoglobulin G-degrading enzyme of Streptococcus pyogenes)	imlifidase	Hansa Medical	bacterial enzyme	Kidney transplant	IV	InTrial	2H2025	Yes	Yes

Pipeline Drug Name(s)	Generic Name	Company	Mechanism of Action	Disease State	Route	FDA Status	Projected FDA Approval Decision	Specialty Drug	Orphan Drug
EB-1020	centanafadine	Otsuka	norepinephrine, dopamine and serotonin reuptake inhibitor	Attention deficit hyperactivity disorder	PO	InTrial	2H2025	No	No
SPK-8011	dirloctocogene samoparvovec	Roche/ Spark Therapeutics	gene therapy	Hemophilia	IV	InTrial	2H2025	Yes	Yes
CF-101	piclidenoson	Can-Fite BioPharma	A3 adenosine receptor agonist	Plaque psoriasis	PO	InTrial	2H2025	Yes	No
RPC-4046 (ABT-308)	cendakimab	Bristol Myers Squibb	interleukin-13 inhibitor	Eosinophilic esophagitis	SC	InTrial	2H2025	Yes	Yes
Revascor (NeoFuse, Replicart, MPC-150-IM, MPC-25, MPC-150, MPC-300, CEP-41750)	rexlemestrocel-L	Mesoblast	allogeneic autologous mesenchymal precursor cell	Heart failure	IV	InTrial	2H2025	Yes	Yes
GSK-3511294	depemokimab	GlaxoSmithKline	interleukin-5 antagonist	Eosinophilic asthma	SC	InTrial	2H2025	Yes	No
BAY-342	elinzanetant	Bayer	neurokinin-1,3 receptor antagonist	Vasomotor symptoms	PO	InTrial	2H2025	No	No
CK-274	aficamten	Cytokinetics	cardiac myosin inhibitor	Obstructive hypertrophic cardiomyopathy	PO	InTrial	2H2025	Yes	Yes
RG-6114	inavolisib	Roche	phosphatidylinositol 3-kinase alpha inhibitor	Breast cancer	PO	InTrial	2H2025	Yes	No

Pipeline Drug Name(s)	Generic Name	Company	Mechanism of Action	Disease State	Route	FDA Status	Projected FDA Approval Decision	Specialty Drug	Orphan Drug
CPI-0610	pelabresib	MorphoSys	BET inhibitor	Myelofibrosis	PO	InTrial	2H2025	Yes	Yes
CTX-1301	dexmethylphenidate	Cingulate	CNS stimulant	Attention deficit hyperactivity disorder	PO	InTrial	2H2025	TBD	No
D-PLEX100	doxycycline	PolyPid	tetracycline	Surgical site infections	IMPLANT	InTrial	2H2025	No	No
XEN-1101	XEN-1101	Xenon Pharmaceuticals	Kv7 potassium channel opener	Focal epilepsy	PO	InTrial	2H2025	TBD	No
CT-041	CT-041	CARsgen Therapeutics	chimeric antigen receptor T cell therapy	Gastric cancer	IV	InTrial	2H2025	Yes	Yes
CRN-00808	paltusotine	Crinetics Pharmaceuticals	somatostatin receptor 2 agonist	Acromegaly	PO	InTrial	2H2025	Yes	Yes
AQST-109	epinephrine	Aquestive Therapeutics	non-selective alpha/ beta-adrenergic receptor agonist	Anaphylaxis	PO	InTrial	2H2025	No	No
Mim8	Mim8	Novo Nordisk	Factor VIII mimetic bispecific antibody	Hemophilia A	SC	InTrial	2H2025	Yes	Yes
LNZ-101	aceclidine	Lenz Therapeutics	acetylcholine receptor agonist	Treatment of presbyopia	OPH	InTrial	2H2025	No	No
DTX-401	pariglasgene brecaparvovec	Ultragenyx Pharmaceutical	gene therapy	Glycogen storage disease type Ia	IV	InTrial	2H2025	Yes	Yes
XS-003	nilotinib	Xspray Pharma	kinase inhibitor	Chronic myeloid leukemia	PO	InTrial	2H2025	Yes	No

Pipeline Drug Name(s)	Generic Name	Company	Mechanism of Action	Disease State	Route	FDA Status	Projected FDA Approval Decision	Specialty Drug	Orphan Drug
TransCon CNP	navepegritide	Ascendis Pharma	C-type natriuretic peptide	Achondroplasia	SC	InTrial	2H2025	Yes	Yes
MCO-010	sonpiretigene Isteparvovec	Nanoscope Therapeutics	Adeno associate virus carried multi characteristic opsin	Retinitis pigmentosa	Intravitreal	InTrial	2H2025	Yes	Yes
HLX-10	serplulimab	Henlius	anti-PD-1	Small cell lung cancer	IV	InTrial	2H2025	Yes	Yes
mRNA-1083	influenza and COVID-19 vaccine	Moderna	mRNA	Prevention of influenza and COVID-19	IM	InTrial	2025	No	No
BNT161+BNT162b2	influenza and COVID-19 vaccine	Pfizer/BioNTech	mRNA	Prevention of influenza and COVID-19 infection	IM	InTrial	2025	No	No
PB-2452	bentracimab	SFJ Pharmaceuticals	antiplatelet monoclonal antibody	Antiplatelet drug toxicity	IV	InTrial	2025	No	No
APN-311	dinutuximab beta	Recordati	anti-GD2 antigen	Neuroblastoma	IV	InTrial	2025	Yes	Yes
M-281	nipocalimab	J&J	FcRn antagonist	Warm autoimmune hemolytic anemia/ generalized myasthenia gravis	IV	InTrial	2025	Yes	Yes
P2B-001	pramipexole/ rasagiline	Pharma Two B	dopamine agonist/ monoamine oxidase B inhibitor	Parkinson's disease	PO	InTrial	2025	No	No

Pipeline Drug Name(s)	Generic Name	Company	Mechanism of Action	Disease State	Route	FDA Status	Projected FDA Approval Decision	Specialty Drug	Orphan Drug
FCX-007 (GM-HDF-COL7, INXN-3002)	dabocemagene autoficel	Castle Creek Pharmaceutical	gene therapy	Epidermolysis bullosa	Intradermal	InTrial	2025	Yes	Yes
pIL-12 (DNA IL-12)	tavokinogene telsaplasmid	OncoSec Medical	gene therapy	Melanoma	Intratumoral	InTrial	2025	Yes	Yes
AGEN-2034	balstilimab	Agenus	PD-1 antagonist	Colorectal cancer	IV	InTrial	2025	Yes	No
NRX-101 (Cyclurad)	d-cycloserine/ lurasidone	NeuroRx	N-methyl-D-aspartate receptor modulator/ 5-HT2A receptor antagonist	Bipolar disorder	PO	InTrial	2025	No	No
PF-06939926	fordadistrogene movaparvovec	Pfizer	gene therapy	Duchenne muscular dystrophy	IV	InTrial	2025	Yes	Yes
MOR-202	felzartamab	I-Mab	anti-CD38 monoclonal antibody	Multiple myeloma	IV	InTrial	2025	Yes	No
ASP-1929 (RM-1929)	ASP-1929	Rakuten	EGFR inhibitor	Head and neck squamous cell carcinoma	IV	InTrial	2025	Yes	No
PXT-3003	baclofen/ naltrexone/ sorbitol	Pharnext	GABA-ergic agonist/ opioid receptor antagonist/ sorbitol combination	Charcot-Marie Tooth disease	PO	InTrial	2025	No	Yes
CNM-Au8	CNM-Au8	Clene	gold nanocrystal	Amyotrophic lateral sclerosis	PO	InTrial	2025	Yes	Yes

Pipeline Drug Name(s)	Generic Name	Company	Mechanism of Action	Disease State	Route	FDA Status	Projected FDA Approval Decision	Specialty Drug	Orphan Drug
KN-035	envafolimab	TRACON Pharmaceuticals	programmed death-ligand 1 inhibitor	Sarcoma	SC	InTrial	2025	Yes	Yes
Mino-Lok	minocycline-EDTA-ETOH	Citrus	tetracyclines	Bacterial infection	Intracatheter	InTrial	2025	No	No
REGN-2477	garetosmab	Regeneron	Activin A antibody	Fibrodysplasia ossificans progressiva	IV/SC	InTrial	2025	Yes	Yes
SPN-830	apomorphine	Supernus Pharmaceuticals	non-ergoline dopamine agonist	Parkinson's disease	SC infusion	CRL	2025	Yes	No
Iomab-B	iodine I 131 monoclonal antibody BC8	Actinium	anti-CD45 monoclonal antibody	Acute myeloid leukemia	IV	InTrial	2025	Yes	Yes
GSK-2330672	linerixibat	GlaxoSmithKline	ileal bile acid transfer inhibitor	Primary biliary cholangitis	PO	InTrial	2025	Yes	Yes
TAK-935	soticlestat	Takeda	cholesterol 24-hydroxylase inhibitor	Lennox-Gastaut syndrome/ Dravet syndrome	PO	InTrial	2025	Yes	Yes
TAVT-45	abiraterone acetate	Tavanta Therapeutics	CYP17 inhibitor	Prostate cancer	PO	InTrial	2025	Yes	No
Dihydroergotamine autoinjector	dihydroergotamine	Amneal Pharmaceuticals	ergot derivative	Migraine	SC	InTrial	2025	No	No
CT-053 (Zevor-cel)	CT-053	CARsgen Therapeutics	B-cell maturation antigen-directed genetically	Multiple myeloma	IV	InTrial	2025	Yes	Yes

Pipeline Drug Name(s)	Generic Name	Company	Mechanism of Action	Disease State	Route	FDA Status	Projected FDA Approval Decision	Specialty Drug	Orphan Drug
			modified autologous T cell immunotherapy						
ABBV-399	telisotuzumab	AbbVie	antibody (anti-c-Met)-drug conjugate	Non-small cell lung cancer	IV	InTrial	2025	Yes	No
MTX-005	MTX-005	Memo Therapeutics	monoclonal antibody	BKV infection	IV	InTrial	2025	TBD	No
PRGN-2012	PRGN-2012	Precigen	immunotherapy	Respiratory papillomatosis	SC	InTrial	2025	Yes	Yes
mRNA-1010	mRNA-1010	Moderna	vaccine	Influenza	IM	InTrial	2025	No	No
FE-203799	apraglutide	Ironwood	glucagon-like peptide-2 analog	Short bowel syndrome	SC	InTrial	2025	Yes	Yes
SY-1425	tamibarotene	Syros Pharmaceuticals	retinoic acid receptor alpha agonist	Myelodysplastic syndrome	PO	InTrial	2025	Yes	Yes
CAP-1002	CAP-1002	Capricor Therapeutics	cellular therapy	Duchenne muscular dystrophy	IV	InTrial	Late 2025	Yes	Yes
RG-6058	tiragolumab	Roche	TIGIT monoclonal antibody	Non-small cell lung cancer/ esophageal cancer	IV	InTrial	Late 2025	Yes	No

IM = intramuscular, INH = inhalation, INJ = injection, IUD = intrauterine device, IV = intravenous, OPH = ophthalmic, PO = oral, SC = subcutaneous, TOP = topical

Key pending indication forecast

Optum Rx key pending indication forecast

Brand Name	Generic Name	Company	Mechanism of Action	Indication Type	Proposed New/Revised Indication	Route	Estimated Approval Date
2024 Possible launch date							
Breyanzi	lisocabtagene maraleucel	Bristol Myers Squibb	CD19-directed genetically modified autologous T cell immunotherapy	New	Treatment of relapsed or refractory mantle cell lymphoma	IV	05/31/2024
Arexvy	respiratory syncytial virus vaccine, adjuvanted	GSK	vaccine	Revised	Active immunization for the prevention of lower respiratory tract disease caused by respiratory syncytial virus in individuals 50 years of age and older	IM	06/07/2024
Kevzara	sarilumab	Sanofi	interleukin-6 receptor monoclonal antibody	New	Treatment of polyarticular juvenile idiopathic arthritis	SC	06/10/2024
Augtyro	repotrectinib	Bristol Myers Squibb	kinase inhibitor	New	Treatment of adult and pediatric patients 12 years of age and older with solid tumors that have a NTRK gene fusion, and are locally advanced or metastatic or where surgical resection is likely to result in severe morbidity	PO	06/15/2024
Krazati	adagrasib	Mirati Therapeutics	RAS GTPase family inhibitor	New	In combination with cetuximab for the treatment of patients with previously treated KRASG12C-mutated locally advanced or metastatic colorectal cancer	PO	06/21/2024

Brand Name	Generic Name	Company	Mechanism of Action	Indication Type	Proposed New/Revised Indication	Route	Estimated Approval Date
Elevidys	delandistrogene moxeparvovec-rokl	Sarepta	gene therapy	Accelerated to Full Approval	Treatment of Duchenne muscular dystrophy patients with a confirmed mutation in the DMD gene	IV	06/21/2024
Wakix	pitolisant	Harmony Biosciences	histamine-3 receptor antagonist/inverse agonist	Revised	Treatment of excessive daytime sleepiness or cataplexy in pediatric patients with narcolepsy	PO	06/21/2024
Vyvgart Hytrulo	efgartigimod alfa/ hyaluronidase	argenx	neonatal Fc receptor blocker/ endoglycosidase	New	Treatment of chronic inflammatory demyelinating polyneuropathy	SC	06/21/2024
Blincyto	blinatumomab	Amgen	bispecific CD19-directed CD3 T-cell engager	Revised	Treatment of early-stage, CD19-positive B-cell precursor acute lymphoblastic leukemia	IV	06/21/2024
Keytruda	pembrolizumab	Merck	programmed death receptor-1-blocking antibody	New	In combination with standard of care chemotherapy (carboplatin and paclitaxel), followed by Keytruda as a single agent for the treatment of patients with primary advanced or recurrent endometrial carcinoma	IV	06/21/2024
Dupixent	dupilumab	Sanofi/ Regeneron	interleukin-4/13 inhibitor	New	Treatment of chronic obstructive pulmonary disease	SC	06/27/2024
Skyrizi	risankizumab-rzaa	AbbVie	interluekin-23 inhibitor	New	Treatment of ulcerative colitis	SC	06/28/2024
Epkinly	epcoritamab-bysp	AbbVie/ Genmab	bispecific CD20-directed CD3 T-cell engager	New	Treatment of adult patients with relapsed or refractory follicular lymphoma after two or more lines of systemic therapy	SC	06/28/2024
Ofev	nintedanib	Boehringer Ingelheim	tyrosine kinase inhibitor	New	Treatment for children and adolescents between 6 to 17 years old with fibrosing interstitial lung disease	PO	2Q2024

Brand Name	Generic Name	Company	Mechanism of Action	Indication Type	Proposed New/Revised Indication	Route	Estimated Approval Date
Sirturo	bedaquiline	Janssen	diarylquinoline antimycobacterial drug	Accelerated to Full Approval	As part of combination therapy in adult and pediatric patients (5 years and older and weighing at least 15 kg) with pulmonary multi-drug resistant tuberculosis (MDR-TB). Reserve SIRTURO for use when an effective treatment regimen cannot otherwise be provided	PO	06/2024
Imfinzi	durvalumab	AstraZeneca	programmed death-ligand 1 blocking antibody	New	Adjuvant treatment of non-small cell lung cancer	IV	1H2024
Imfinzi	durvalumab	AstraZeneca	programmed death-ligand 1 blocking antibody	New	In combination with Lynparza (olaparib), for first-line treatment of endometrial cancer	IV	Mid-2024
Zoryve	roflumilast	Arcutis Biotherapeutics	phosphodiesterase-4 inhibitor	New	Treatment of mild-to-moderate atopic dermatitis in patients 6 years and older	TOP	07/07/2024
Voquezna	vonoprazan	Phathom Pharmaceuticals	potassium-competitive acid blocker	New	Treatment of heartburn associated with non-erosive gastroesophageal reflux disease in adults	PO	07/19/2024
Darzalex Faspro	daratumumab/ hyaluronidase-fihj	J&J	humanized anti-CD38 monoclonal antibody	Revised	In combination with bortezomib, lenalidomide and dexamethasone for induction and consolidation treatment and with lenalidomide for maintenance treatment of adult patients who are newly diagnosed with multiple myeloma (NDMM) and are eligible for autologous stem cell transplant	SC	07/30/2024
Fabhalta	iptacopan	Novartis	complement factor B inhibitor	New	Treatment of IgA nephropathy	PO	08/15/2024

Brand Name	Generic Name	Company	Mechanism of Action	Indication Type	Proposed New/Revised Indication	Route	Estimated Approval Date
Rybrevant	amivantamab-vmjw	Janssen	bispecific EGF receptor-directed and MET receptor-directed antibody	Revised	In combination with lazertinib for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer with epidermal growth factor receptor (EGFR) exon 19 deletions or L858R substitution mutations, as detected by an FDA-approved test	IV	08/22/2024
Filspari	sparsentan	Travere Therapeutics	endothelin/angiotensin II receptor antagonist	Accelerated to Full Approval	To reduce proteinuria in adults with primary IgA nephropathy at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR) ≥1.5 g/g	PO	09/11/2024
Dupixent	dupilumab	Sanofi/ Regeneron	interleukin-4/13 inhibitor	New	Add-on maintenance treatment for adolescents aged 12 to 17 years with inadequately controlled chronic rhinosinusitis with nasal polyposis	SC	09/15/2024
Opdivo	nivolumab	Bristol Myers Squibb	programmed death receptor-1-blocking antibody	New	Neoadjuvant treatment with chemotherapy followed by surgery and adjuvant treatment for the perioperative treatment of resectable stage IIA to IIIB non-small cell lung cancer	IV	10/08/2024
Wegovy	semaglutide	Novo Nordisk	glucagon-like peptide-1 receptor agonist	New	Treatment of adults with heart failure with preserved ejection fraction and obesity	SC	11/2024
Bimzelx	bimekizumab	UCB	interleukin-17A and F antagonist	New	Treatment of hidradenitis suppurativa	SC	12/04/2024
Bimzelx	bimekizumab	UCB	interleukin-17A and F antagonist	New	Treatment of ankylosing spondylitis	SC	12/2024

Brand Name	Generic Name	Company	Mechanism of Action	Indication Type	Proposed New/Revised Indication	Route	Estimated Approval Date
Tevimbra	tislelizumab	BeiGene	programmed death receptor-1–blocking antibody	New	In combination with fluoropyrimidine- and platinum-containing chemotherapy, for the treatment of patients with locally advanced unresectable or metastatic gastric or gastroesophageal junction adenocarcinoma	IV	12/2024
Enhertu	fam-trastuzumab deruxtecan-nxki	AstraZeneca	HER2-directed antibody and topoisomerase inhibitor conjugate	Revised	Third-line treatment of advanced/refractory, metastatic HER2+ breast cancer	IV	2H2024
Fasenra	benralizumab	AstraZeneca	interleukin-5 receptor antibody	New	Treatment of eosinophilic granulomatosis with polyangiitis	SC	2H2024
2025 Possible launch date							
Tremfya	guselkumab	Janssen	interleukin-23 inhibitor	New	Treatment of adults with moderately to severely active ulcerative colitis	IV/SC	01/11/2025
Gemtesa	vibegron	Sumitomo Pharma America	beta-3 adrenergic receptor agonist	Revised	Treatment of men with overactive bladder symptoms receiving pharmacological therapy for benign prostatic hyperplasia	PO	01/13/2025
Rexulti	brexpiprazole	Otsuka/ Lundbeck	atypical antipsychotic	New	In combination with sertraline for the treatment of post-traumatic stress disorder in adults	PO	02/09/2025
Omvoh	mirikizumab-mrkz	Eli Lilly	interleukin-23 antagonist	New	Treatment of adults with moderately to severely active Crohn's disease	IV/SC	1Q2025

Extended generic and biosimilar pipline forecast

Optum Rx generic and biosimilar pipeline forecast

(Bolded fields are Biosimilar products)

Trade Name	Generic Name	Brand Company(ies)	Indications	Route of Administration	Anticipated Availability
2024 Possible launch date					
SANDOSTATIN LAR	octreotide acetate	Novartis	Acromegaly; Carcinoid Tumors; Vasoactive Intestinal Peptide Tumors	Subcutaneous	2024
GIAZO	balsalazide disodium	Bausch Health	Ulcerative Colitis in Male Patients	Oral	2024
TEFLARO	ceftaroline fosamil	Allergan	Community Acquired Pneumonia; Skin and Skin Structure Infections	Intravenous	2024
PROMACTA	eltrombopag	Novartis	Thrombocytopenia	Oral	2024
ISENTRESS	raltegravir	Merck	Human Immunodeficiency Virus-1 Infection	Oral	2024
VESICARE LS	solifenacin	Astellas	Neurogenic Detrusor Overactivity	Oral	1H-2024
NYMALIZE	nimodipine	Arbor	Subarachnoid Hemorrhage	Oral	1H-2024
TYSABRI	natalizumab	Biogen	Multiple Sclerosis; Crohn's Disease	Intravenous	1H-2024
RADICAVA	edaravone	Mitsubishi Tanabe	Amyotrophic Lateral Sclerosis	Intravenous	05-2024
DUAVEE	conjugated estrogens/bazedoxifene acetate	Pfizer/Ligand Pharmaceuticals	Treatment of Moderate to Severe Vasomotor Symptoms Associated with Menopause; Prevention of Postmenopausal Osteoporosis	Oral	05-2024
PROBUPHINE	buprenorphine	Titan Pharmaceuticals/Braeburn Pharmaceuticals	Maintenance Treatment of Opioid Dependence	Subdermal	06-2024
VICTOZA	liraglutide	Novo Nordisk	Type 2 Diabetes Mellitus (T2DM); Reduce the Risks of Cardiovascular Events in T2DM	Subcutaneous	06-2024
OXTELLAR XR	oxcarbazepine	Supernus	Partial Seizures	Oral	09-2024
SPRYCEL	dasatinib	Bristol-Myers Squibb	Chronic Myeloid Leukemia; Acute Lymphoblastic Leukemia	Oral	09-2024
SUSTOL	granisetron	Heron Therapeutics	Chemotherapy-Induced Nausea and Vomiting	Subcutaneous	09-2024
PRIALT	ziconotide acetate	TerSera Therapeutics	Severe Pain	Intrathecal	10-2024

Trade Name	Generic Name	Brand Company(ies)	Indications	Route of Administration	Anticipated Availability
LAZANDA	fentanyl citrate	Depomed	Breakthrough Pain in Cancer Patients	Intranasal	10-2024
VUITY	pilocarpine	AbbVie	Presbyopia	Ophthalmic	10-2024
STENDRA	avanafil	Petros Pharmaceuticals	Erectile Dysfunction	Oral	10-2024
QSYMIA	phentermine/topiramate	Vivus	Chronic Weight Management	Oral	12-2024
SIKLOS	hydroxyurea	Addmedica/Medunik	Sickle Cell Anemia	Oral	12-2024
PRADAXA	dabigatran etexilate mesylate	Boehringer Ingelheim	Venous Thromboembolic Events in Pediatric Patients	Oral	12-2024
NAMZARIC	memantine/donepezil	AbbVie	Moderate to Severe Dementia of the Alzheimer's Type	Oral	01-2025
2025 Possible launch date					
GELNIQUE	oxybutynin	Allergan	Overactive Bladder	External	2025
SIMPONI	golimumab	Janssen	Ankylosing Spondylitis; Psoriatic Arthritis; Rheumatoid Arthritis; Ulcerative Colitis	Subcutaneous	2025
SIMPONI ARIA	golimumab	Janssen	Rheumatoid Arthritis; Psoriatic Arthritis; Ankylosing Spondylitis; Juvenile Idiopathic Arthritis	Intravenous	2025
BOSULIF	bosutinib	Pfizer	Chronic Myelogenous Leukemia	Oral	2025
EYLEA	aflibercept	Regeneron	Wet Age-Related Macular Degeneration; Diabetic Macular Edema; Macular Edema Following Retinal Vein Occlusion; Diabetic Retinopathy in Patients with Diabetic Macular Edema; Retinopathy of Prematurity	Intravitreal	2025
COMPLERA	emtricitabine/rilpivirine/tenofovir disoproxil fumarate	Gilead/Janssen	Human Immunodeficiency Virus-1 Infection	Oral	2025
XOLAIR	omalizumab	Roche/Genentech	Asthma; Idiopathic Urticaria; Nasal Polyps; IgE-Mediated Food Allergy	Subcutaneous	1Q-2025
TRACLEER	bosentan	Actelion/Janssen	Pulmonary Arterial Hypertension	Oral	01-2025
LEXETTE	halobetasol	Mayne	Plaque Psoriasis	External	01-2025
IZBA	travoprost	Alcon	Open-Angle Glaucoma; Ocular Hypertension	Ophthalmic	01-2025
STELARA	ustekinumab	Janssen	Plaque Psoriasis; Psoriatic Arthritis; Ulcerative Colitis; Crohn's Disease	Subcutaneous; intravenous	01-2025
HALAVEN	eribulin	Eisai	Metastatic Breast Cancer; Liposarcoma	Intravenous	01-2025
CORLANOR	ivabradine	Amgen	Heart Failure	Oral	01-2025

Trade Name	Generic Name	Brand Company(ies)	Indications	Route of Administration	Anticipated Availability
PHOSLYRA	calcium acetate	Fresenius	Phosphate Binder	Oral	01-2025
FINACEA	azelaic acid	LEO Pharma	Rosacea	External	01-2025
SANCUSO	granisetron	Kyowa Hakko Kirin/ProStrakan	Prevention of Nausea and Vomiting in Patients Receiving Moderately and/or Highly Emetogenic Chemotherapy	External	01-2025
XARELTO	rivaroxaban	Bayer/Janssen	Reduce the Risk of Stroke, Myocardial Infarction, Cardiovascular Events and Blood Clots; Prevention and Treatment of Deep Vein Thrombosis and Pulmonary Embolism	Oral	03-2025
SOLIRIS	eculizumab	AstraZeneca	Paroxsymal Nocturnal Hemoglobinuria; Hemolytic Uremic Syndrome; Myasthenia Gravis; Neuromyelitis Optica	Intravenous	03-2025
AURYXIA	ferric citrate	Keryx/Akebia Therapeutics	Control of Serum Phosphorus Levels in Chronic Kidney Disease (CKD) on Dialysis; Iron Deficiency Anemia in Adult Patients with CKD Not on Dialysis	Oral	03-2025
HORIZANT	gabapentin enacarbil	Arbor	Restless Legs Syndrome; Postherpetic Neuralgia	Oral	04-2025
JYNARQUE	tolvaptan	Otsuka	Polycystic Kidney Disease	Oral	04-2025
BRILINTA	ticagrelor	AstraZeneca	To Reduce the Risk of Cardiovascular Death, Myocardial Infarction (MI), and Stroke in Patients with Acute Coronary Syndrome, History of MI, Coronary Artery Disease, or Acute Ischemic Stroke or Transient Ischemic Attack	Oral	05-2025
APTIOM	eslicarbazepine	Sunovion/Bial	Partial-Onset Seizures	Oral	05-2025
TIROSINT-SOL	levothyroxine	IBSA Institut Biochemique	Hypothyroidism; Thyrotropin-Dependent Thyroid Cancer	Oral	05-2025
FYCOMPA	perampanel	Catalyst	Partial-Onset Seizures; Primary Generalized Tonic-Clonic Seizures	Oral	05-2025
PROLIA	denosumab	Amgen	Postmenopausal Osteoporosis; Bone Loss in Men and Women at Risk of Fracture	Subcutaneous	05-2025
XGEVA	denosumab	Amgen	Prevention of Fractures in Bone Malignancies and Multiple Myeloma; Giant Cell Tumor in Bone; Hypercalcemia	Subcutaneous	05-2025
TASIGNA	nilotinib	Novartis	Philadelphia Chromosome-Positive Chronic Myeloid Leukemia	Oral	06-2025
NUCYNTA	tapentadol	Collegium	Moderate to Severe Acute Pain	Oral	06-2025

Trade Name	Generic Name	Brand Company(ies)	Indications	Route of Administration	Anticipated Availability
NUCYNTA ER	tapentadol	Collegium	Moderate to Severe Chronic Pain	Oral	06-2025
PERJETA	pertuzumab	Genentech	HER-2 Positive Breast Cancer	Intravenous	2H-2025
RAVICTI	glycerol phenylbutyrate	Amgen	Urea Cycle Disorders	Oral	07-2025
RYANODEX	dantrolene	Eagle Pharmaceuticals	Malignant Hyperthermia	Intravenous	07-2025
CARDENE IV	nicardipine	Chiesi	Short-Term Treatment of Hypertension When Oral Therapy is Not Possible	Intravenous	07-2025
RYTARY	carbidopa/levodopa	Amneal	Parkinson's Disease	Oral	07-2025
DIACOMIT	stiripentol	Biocodex	Dravet Syndrome	Oral	08-2025
ADZENYS XR-ODT	amphetamine polistirex	Neos Therapeutics	Attention Deficit Hyperactivity Disorder	Oral	09-2025
QTERN	dapagliflozin/saxagliptin	AstraZeneca	Type 2 Diabetes Mellitus	Oral	10-2025
FUROSCIX	furosemide	scPharmaceuticals	Chronic Heart Failure	Subcutaneous	10-2025
EDURANT	rilpivirine	Janssen	Human Immunodeficiency Virus-1 Infection	Oral	10-2025
TRADJENTA	linagliptin	Eli Lilly/Boehringer Ingelheim	Type 2 Diabetes Mellitus	Oral	11-2025
JENTADUETO XR	linagliptin/metformin	Boehringer Ingelheim/Eli Lilly	Type 2 Diabetes Mellitus	Oral	11-2025
JENTADUETO	linagliptin/metformin	Boehringer Ingelheim/Eli Lilly	Type 2 Diabetes Mellitus	Oral	11-2025
PICATO	ingenol mebutate	LEO Pharma	Actinic Keratosis	External	12-2025
OPSUMIT	macitentan	Janssen	Pulmonary Arterial Hypertension	Oral	12-2025
2026 Possible launch date					
BRYHALI	halobetasol	Bausch Health	Plaque Psoriasis	External	2026
MAVENCLAD	cladribine	Serono	Multiple Sclerosis	Oral	2026
ABILIFY MAINTENA	aripiprazole	Otsuka/Lundbeck	Schizophrenia; Bipolar Disorder	Intramuscular	2026
POMALYST	pomalidomide	Celgene	Multiple Myeloma; Kaposi Sarcoma	Oral	1Q-2026
YONSA	abiraterone	Sun	Prostate Cancer	Oral	01-2026
VELPHORO	sucroferric oxyhydroxide	Vifor Fresenius Medical Care Renal Pharma (VFMCRP)	Hyperphosphatemia In Patients with Chronic Kidney Disease on Dialysis	Oral	01-2026
BYVALSON	nebivolol/valsartan	AbbVie	Hypertension	Oral	01-2026
LUCEMYRA	lofexidine	US Worldmeds	Opioid Withdrawal Symptoms	Oral	01-2026

Trade Name	Generic Name	Brand Company(ies)	Indications	Route of Administration	Anticipated Availability
JEVTANA KIT	cabazitaxel	Sanofi	Hormone-Refractory Metastatic Prostate Cancer	Intravenous	01-2026
EDARBI	azilsartan kamedoxomil	Arbor	Hypertension	Oral	01-2026
SERNIVO	betamethasone dipropionate	Encore Dermatology	Plaque Psoriasis	External	01-2026
ELLA	ulipristal	Afaxys/Perrigo	Emergency Contraception	Oral	01-2026
TYVASO	treprostinil	United Therapeutics	Pulmonary Arterial Hypertension; Pulmonary Hypertension with Interstitial Lung Disease	Inhalation	01-2026
QBRELIS	lisinopril	Silvergate	Hypertension; Heart Failure; Acute Myocardial Infarction	Oral	01-2026
BRIVIACT	brivaracetam	UCB	Epilepsy	Oral; intravenous	02-2026
XELJANZ XR	tofacitinib	Pfizer	Rheumatoid Arthritis; Psoriatic Arthritis; Ulcerative Colitis; Ankylosing Spondylitis	Oral	2Q-2026
XELJANZ	tofacitinib	Pfizer	Rheumatoid Arthritis; Ulcerative Colitis; Psoriatic Arthritis; Juvenile Idiopathic Arthritis; Ankylosing Spondylitis	Oral	2Q-2026
OFEV	nintedanib	Boehringer Ingelheim	Idiopathic Pulmonary Fibrosis; Systemic Sclerosis-Associated Interstitial Lung Disease (ILD); Chronic Fibrosing ILD	Oral	04-2026
NULOJIX	belatacept	Bristol-Myers Squibb	Prophylaxis of Organ Rejection in Kidney Transplant	Intravenous	04-2026
JANUVIA	sitagliptan	Merck	Type 2 Diabetes Mellitus	Oral	05-2026
JANUMET	sitagliptan/metformin	Merck	Type 2 Diabetes Mellitus	Oral	05-2026
EVOMELA	melphalan	Acrotech/Aurobindo	Multiple Myeloma; Conditioning for Stem Cell Transplant	Intravenous	06-2026
CERDELGA	eliglustat	Sanofi/Genzyme	Gaucher Disease Type 1	Oral	06-2026
SUPPRELIN LA	histrelin	Endo	Central Precocious Puberty	Subcutaneous	06-2026
COTEMPLA XR-ODT	methylphenidate	Neos Therapeutics	Attention Deficit Hyperactivity Disorder	Oral	07-2026
INJECTAFER	ferric carboxymaltose	American Regent/CSL Limited	Iron Deficiency Anemia	Intravenous	07-2026
JANUMET XR	sitagliptin/metformin	Merck	Type 2 Diabetes Mellitus	Oral	07-2026
NUEDEXTA	dextromethorphan/quinidine sulfate	Avanir	Pseudobulbar Affect	Oral	07-2026
COMETRIQ	cabozantinib (S)-malate	Exelixis	Medullary Thyroid Cancer	Oral	08-2026

Trade Name	Generic Name	Brand Company(ies)	Indications	Route of Administration	Anticipated Availability
ADEMPAS	riociguat	Bayer	Pulmonary Arterial Hypertension; Chronic Thromboembolic Pulmonary Hypertension	Oral	4Q-2026
ENTRESTO	sacubitril/valsartan	Novartis	Heart Failure	Oral	4Q-2026
UPTRAVI	selexipag	Janssen	Pulmonary Arterial Hypertension	Oral	10-2026
CYRAMZA	ramucirumab	Eli Lilly	Gastric Cancer; Gastroesophageal Cancer; Metastatic Gastric Cancer; Non-Small Cell Lung Cancer	Intravenous	10-2026
ADASUVE	loxapine	Alexza	Agitation Associated with Schizophrenia or Bipolar Disorder	Inhalation	10-2026
ILARIS	canakinumab	Novartis	Cryopyrin-Associated Periodic Syndromes; Familial Cold Autoinflammatory Syndrome; Muckle-Wells Syndrome; Tumor Necrosis Factor Receptor Associated Periodic Syndrome; Hyperimmunoglobulin D Syndrome/Mevalonate Kinase Deficiency; Familial Mediterranean Fever; Still's Disease; Gout Flares	Subcutaneous	10-2026
IWILFIN	eflornithine	US World Meds	Neuroblastoma	Oral	12-2026
TRINTELLIX	vortioxetine	Takeda/Lundbeck	Major Depressive Disorder	Oral	12-2026
1st Half 2027 Possible launch date					
KYPROLIS	carfilzomib	Amgen	Multiple Myeloma	Intravenous	2027
CIMZIA	certolizumab pegol	UCB/Royalty Pharma	Psoriatic Arthritis; Rheumatoid Arthritis; Ankylosing Spondylitis; Crohn's Disease; Plaque Psoriasis; Axial Spondyloarthritis	Subcutaneous	2027
SAXENDA	liraglutide	Novo Nordisk	Chronic Weight Management	Subcutaneous	2027
IBRANCE	palbociclib	Pfizer	Breast Cancer	Oral	1Q-2027
BONJESTA	doxylamine/pyridoxine	Duchesnay	Nausea and Vomiting Associated with Pregnancy	Oral	01-2027
DIFICID	fidaxomicin	Merck	Treatment of Clostridium difficile-Associated Diarrhea	Oral	01-2027
OSPHENA	ospemifene	Duchesnay	Menopause Symptoms; Dyspareunia	Oral	01-2027
BELEODAQ	belinostat	Acrotech/Aurobindo	Relapsed or Refractory Peripheral T-cell Lymphoma	Intravenous	01-2027
VIBATIV	telavancin	Cumberland	Infections	Intravenous	01-2027
CUBICIN RF	daptomycin	Merck	Complicated Skin and Skin Structure Infections; Staphylococcus aureus Bloodstream Infections	Intravenous	01-2027

Trade Name	Generic Name	Brand Company(ies)	Indications	Route of Administration	Anticipated Availability
ENVARSUS XR	tacrolimus	Veloxis	Prophylaxis of Organ Rejection in Kidney Transplant Patients	Oral	01-2027
RYDAPT	midostaurin	Novartis	Acute Myeloid Leukemia; Systemic Mastocytosis; Mast Cell Leukemia	Oral	01-2027
JUBLIA	efinaconazole	Bausch Health	Onychomycosis of the Toenail	External	01-2027
VALTOCO	diazepam	Neurelis	Epilepsy	Intranasal	01-2027
VIVITROL	naltrexone	Alkermes	Alcohol and/or Opioid Dependence	Intramuscular	01-2027
BELBUCA	buprenorphine	BioDelivery Sciences International	Severe Pain	Oral	01-2027
NATPARA	parathyroid hormone 1-84	Takeda	Hypoparathyroidism	Subcutaneous	01-2027
SUBSYS	fentanyl	BTcP Pharma	Breakthrough Pain in Cancer Patients	Oral	01-2027
NEVANAC	nepafenac	Harrow Health	Pain and Inflammation Associated with Cataract Surgery	Ophthalmic	01-2027
ALTABAX	retapamulin	Aqua Pharmaceuticals/Almirall	Impetigo	External	02-2027
BYDUREON	exenatide	AstraZeneca	Type 2 Diabetes Mellitus	Subcutaneous	02-2027
VITEKTA	elvitegravir	Gilead	Human Immunodeficiency Virus-1 Infection	Oral	02-2027
TUDORZA PRESSAIR	aclidinium	AstraZeneca	Chronic Obstructive Pulmonary Disease	Inhalation	04-2027
DUAKLIR PRESSAIR	aclidinium/formoterol fumarate	AstraZeneca	Chronic Obstructive Pulmonary Disease	Inhalation	04-2027
RAPIVAB	peramivir	BioCryst	Treatment of Acute Uncomplicated Influenza	Intravenous	05-2027
LUMIGAN	bimatoprost	Allergan/AbbVie	Glaucoma; Ocular Hypertension	Ophthalmic	06-2027
ORENITRAM	treprostinil diethanolamine	Supernus/United Therapeutics	Pulmonary Arterial Hypertension	Oral	06-2027

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