RxOutlook®

3rd Quarter 2023

Optum Rx®

Welcome to the third quarterly RxOutlook Report of 2023. Optum Rx closely monitors and evaluates the drug development pipeline to identify noteworthy upcoming drug approvals and reports the essential findings here in RxOutlook.

Recap of 2023

As of August 21st, the FDA has approved 35 new molecular entities in 2023, including 16 drugs with an Orphan Drug designation. Since the previous RxOutlook report, notable novel drug approvals included **Beyfortus™ (nirsevimab)**, the first RSV prevention therapy approved to protect all infants; **Izervay™ (avacincaptad pegol)**, the second approved intravitreal injection for geographic atrophy; and **Zurzuvae™ (zuranolone)**, the first oral drug approved for postpartum depression.

In addition to these drugs, the FDA approved the second vaccine for RSV infection, Pfizer's Abrysvo, for individuals 60 years of age and older, and the first gene therapies for Duchenne muscular dystrophy **(Elevidys [delandistrogene moxeparvovec])** and hemophilia A **(Roctavian™ [valoctocogene roxaparvovec])**.

Looking Ahead to the 4th Quarter 2023

The fourth quarter is expected to be particularly noteworthy from a pipeline perspective, with a large number of drugs expected to be approved, including several high-profile therapies. In this edition of RxOutlook, we highlight 9 key pipeline products with an approval decision in the fourth quarter 2023.

Tirzepatide, which is currently approved under the brand name Mounjaro™ for type 2 diabetes, is under FDA review for chronic weight management (weight loss). Tirzepatide is a glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonist and would be a competing with existing GLP-1 receptor agonists (Wegovy® and Saxenda®) for this use.

Donanemab would potentially be the third beta amyloid targeted therapy approved for Alzheimer's disease and the second with a traditional (full) approval. Leqembi™ (lecanemab) received traditional approval in July 2023. Like the other beta amyloid targeted therapies, similar questions will be asked around the benefit vs. risk profile with donanemab given the modest efficacy and the class-related safety concerns (eg, amyloid related imaging abnormalities [ARIA]).

Exagamglogene autotemcel and **lovotibeglogene autotemcel**, two genetically modified cellular therapies, are under FDA review for sickle cell disease (SCD). Both therapies would be alternatives to hematopoietic stem cell transplant, particularly in patients without a matched donor. Lovotibeglogene autotemcel uses a viral vector to insert a functioning version of the hemoglobin beta gene into the patient's own stem cells whereas exagamglogene autotemcel leverages CRISPR-Cas9 gene editing technology to increase the amount of fetal hemoglobin. If approved, exagamglogene autotemcel would be the first therapy utilizing CRISPR-Cas9 technology.

Two novel oral therapies for Duchenne muscular dystrophy (DMD), **vamorolone** and **givinostat**, could be approved by the end of the year. Vamorolone would be a potential alternative to traditional corticosteroids used for DMD and givinostat would likely be used as an add-on therapy to corticosteroids.

Etrasimod is a S1P receptor modulator and would provide an additional oral treatment option for ulcerative colitis (UC). Etrasimod would primarily be competing with other oral drugs used for UC, including another S1P modulator, Zeposia® (ozanimod), and Janus kinase inhibitors such as Rinvoq® (upadacitinib).

Aprocitentan is an endothelin receptor antagonist (ERA) under review for treatment-resistant hypertension. It would potentially be the first drug in the class approved for this indication. Other ERAs are approved for pulmonary arterial hypertension (PAH).

Finally, **capivasertib** is a novel oral kinase inhibitor that would be a new option for hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer. This is a difficult to treat patient population that has seen growth in targeted treatment options over the last several years.

Approval decisions for other key novel therapies are expected by the end of the fourth quarter 2023 but are not reviewed in this report because they were covered in previous editions of RxOutlook. These include: **lebrikizumab** for atopic dermatitis; **bimekizumab** for plaque psoriasis; **zilucoplan** for myasthenia gravis; and **gefapixant** for chronic cough.

Key pipeline drugs with FDA approval decisions expected by end of the 4th quarter 2023

Drug Name	Manufacturer	Indication/Use	Expected FDA Decision Date
Etrasimod	Pfizer/Everest	Ulcerative colitis	10/21/2023
Vamorolone	Santhera Pharmaceuticals	Duchenne muscular dystrophy*	10/26/2023
Givinostat	Italfarmaco Group	Duchenne muscular dystrophy*	12/21/2023
Tirzepatide	Eli Lilly	Chronic weight management	11/2023 – 12/2023
Donanemab	Eli Lilly	Alzheimer's disease	12/2023
Exagamglogene autotemcel	Vertex Pharmaceuticals/ CRISPR Therapeutics	Sickle cell disease* (SCD) Transfusion-dependent beta thalassemia* (TDT)	12/4/2023 (SCD) / 3/30/2024 (TDT)
Lovotibeglogene autotemcel	bluebird bio	Sickle cell disease*	12/20/2023
Aprocitentan	Idorsia Pharmaceuticals/ Janssen	Treatment-resistant hypertension	12/20/2023
Capivasertib	AstraZeneca	Breast cancer	4Q 2023

* 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 4th quarter 2023.

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.

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

Past and future reviews

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 4th quarter 2023 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.

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

Etrasimod (Brand Name: To be determined)

Manufacturer: Pfizer/Everest
Expected FDA decision: October 21, 2023

Therapeutic use

Etrasimod is under review for the treatment of moderately-to-severely active ulcerative colitis (UC).

UC is a chronic inflammatory condition of the large intestine (colon) and the rectum. Patients develop inflammation and ulcers in the lining of the colon, commonly leading to abdominal pain, bloody stools, persistent diarrhea, weight loss, and fatigue. Patients will experience periods of active inflammation or flareups and periods of remission where they are free of symptoms.

Treatment usually includes induction therapy (for rapid onset of action and achieving disease control) followed by maintenance treatment (for long term disease control).

UC is estimated to affect about 1.8 million people in the U.S.

What you need to know:

Proposed Indication: Treatment of moderately-to-severely active UC

Mechanism: S1P modulator

Efficacy:

- Induction therapy: 24.8% to 27% vs. 7.4% to 15.2% with placebo
- Maintenance therapy: 32.1% vs. 6.7% with placebo

Common AEs: Headache, dizziness, pyrexia, arthralgia, abdominal pain, nausea

Dosing: Oral once daily

Why it Matters: No dose titration required, shorter half-life vs. Zeposia (faster washout period), also in development for other chronic conditions (eg, Crohn's disease, esophagitis, atopic dermatitis)

Important to Note: Alternatives available (eg, Zeposia, JAK inhibitors, injectable biologics), lack of head-to-head trial data vs. existing treatment options

Estimated cost: ~$75,000 per year (based on pricing for Rinvoq)

Clinical profile

Etrasimod is a sphingosine 1-phosphate (S1P) receptor modulator that selectively activates S1P receptor subtypes 1, 4, and 5. S1P modulators block the capacity of lymphocytes to egress from lymph nodes, reducing the number of lymphocytes in peripheral blood. The exact mechanism by which etrasimod exerts therapeutic effects is unknown but may involve the reduction of lymphocyte migration into the intestine.

Pivotal trial data:
The efficacy of etrasimod was evaluated in ELEVATE UC 52, a Phase 3, randomized, double-blind, placebo-controlled study in 433 UC patients who had previously failed or were intolerant to at least one conventional, biologic, or Janus kinase (JAK) inhibitor therapy. The study included a 12-week induction period followed by a 40-week maintenance period with a treat-through design. This design allowed patients to continue with their randomized treatment in the maintenance period independent of whether they reached the objective criteria of clinical response at week 12. The primary endpoints were clinical remission at weeks 12 (induction) and 52 (maintenance). At 12 weeks, 27% of patients achieved clinical remission with etrasimod vs. 7.4% with placebo (treatment difference 19.8, 95% CI: 12.9, 26.6; $p < 0.0001$). At 52 weeks, 32.1% of patients achieved clinical remission with etrasimod vs. 6.7% with placebo (treatment difference 25.4, 95% CI: 18.4, 32.4; $p < 0.0001$).

In addition, etrasimod was evaluated in ELEVATE UC 12, a Phase 3, randomized, double-blind, placebo-controlled study in 354 UC patients who had previously failed or were intolerant to at least one conventional, biologic, or JAK therapy. This study only included a 12-week induction period with no maintenance period. Clinical remission was achieved in 24.8% of patients with etrasimod vs. 15.2% with placebo (treatment difference 9.7, 95% CI: 1.1, 18.2; $p = 0.026$).

Etrasimod (continued...)

Safety:
The most common adverse events with etrasimod use were headache, dizziness, pyrexia, arthralgia, abdominal pain, and nausea.

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

Competitive environment

Etrasimod would provide an additional oral treatment option for UC and would be the second S1P modulator approved for the condition. Bristol Myers Squibb's Zeposia® (ozanimod), the first S1P modulator, was approved for UC in May 2021. Zeposia requires a 7-day dose titration due to the first-dose heart-rate-lowering effects, whereas etrasimod appears to have low risk of bradycardia and did not utilize titration in the clinical trials. Compared to Zeposia, etrasimod has a shorter half-life which allows for a faster washout period if a patient needs to discontinue or temporarily halt treatment (absolute lymphocyte counts returned to normal for ~80% of patients within 2 weeks after cessation of etrasimod treatment).

Etrasimod will be entering a crowded marketplace, competing not only with Zeposia, but injectable biologics and oral JAK inhibitors (eg, Rinvoq® [upadacitinib]). Some of the alternative treatment options have or will have biosimilar or generic competition in the near term (eg, Humira® and Stelara®).

When compared indirectly, the efficacy results for etrasimod appear to be in line with other treatments used for moderately-to-severely active UC, although cross-trial comparisons are difficult to assess. Direct head-to-head trial data assessing the efficacy and safety of etrasimod against its competitors are lacking.

Like other drugs used for chronic inflammatory disorders, etrasimod is in development for other diseases (eg, Crohn's disease, esophagitis, atopic dermatitis). This could potentially expand the target population for etrasimod; however, like UC, there are multiple alternative treatment options available for these other proposed uses.

For reference, the wholesale acquisition cost (WAC) for Rinvoq is approximately $75,000.

Vamorolone (Brand Name: To be determined)

Manufacturer: Santhera Pharmaceuticals
Regulatory designations: Orphan Drug, Fast Track
Expected FDA decision: October 26, 2023

Therapeutic use

Vamorolone is under review for the treatment of ambulatory boys with Duchenne muscular dystrophy (DMD).

DMD is a rare, progressive, neuromuscular disorder characterized by weakness and wasting of the muscles of the pelvic area followed by the involvement of the shoulder muscles. As the disease progresses, muscle weakness and atrophy spread to affect additional muscles of the body. The age of onset is usually between 3 and 5 years and by the early teenage years, patients will typically require a wheelchair and serious life-threatening complications may ultimately develop including cardiomyopathy and respiratory difficulties.

DMD is caused by mutations of the dystrophin gene on the X chromosome. The gene regulates the production of the dystrophin protein, which plays an important role in the functioning of muscle cells.

The birth prevalence is estimated to be 1 in every 3,500 live male births.

What you need to know:

Proposed Indication: Treatment of ambulatory boys with DMD

Mechanism: Dissociative steroidal anti-inflammatory drug

Efficacy: Change from baseline in TTSTAND velocity at Week 24: 0.05 rises/second vs. −0.01 rises/second with placebo

Common AEs: Cushingoid features, vomiting, vitamin D deficiency

Dosing: Oral once daily

Why it Matters: Alternative to traditional corticosteroids with some safety benefits (eg, reduced bone adverse events, improved height trajectory), high unmet need

Important to Note: Lack of efficacy advantage over traditional corticosteroids (available generically), trial data limited to patients 4 to less than 7 years of age

Clinical profile

Vamorolone is a dissociative steroidal anti-inflammatory drug that binds to the same target receptors as the corticosteroid class but has a unique structure and differences in mechanism of action (MOA). Vamorolone shows fewer positive gene transcriptional activity than corticosteroids but retains inhibition of nuclear factor κB proinflammatory pathways. Pre-clinical data indicate that vamorolone may have the potential for fewer bone-related adverse events. Lastly, vamorolone is a potent antagonist of the mineralocorticoid receptor, whereas most corticosteroids are agonists.

Pivotal trial data:
The efficacy of vamorolone was evaluated in VISION-DMD, a Phase 2b, two-part, randomized, double-blind, placebo- and active-controlled study in 121 boys 4 to less than 7 years of age with genetically confirmed DMD not previously treated with corticosteroids. In Part 1, patients were randomized to one of the four arms: vamorolone 2 mg/kg per day, vamorolone 6 mg/kg per day, prednisone 0.75 mg/kg per day, or placebo. The primary endpoint was the mean change from baseline to Week 24 for time to stand from supine (TTSTAND) velocity for vamorolone 6 mg/kg per day vs. placebo.

The trial met the primary endpoint for TTSTAND velocity; the least squares mean (LSM) velocity was 0.05 rises/second for vamorolone 6 mg/kg vs. −0.01 rises/second for placebo (LSM difference 0.06, 95% CI: 0.02, 0.10; p = 0.002).

After Week 24, prednisone- and placebo-treated participants from VISION-DMD were crossed over into one of the vamorolone dose groups (Part 2). Prednisone-treated patients that crossed over to vamorolone showed maintenance of efficacy across all efficacy endpoints for vamorolone 6 mg/kg/day. Annualized rates of adverse events were reduced after the switch from prednisone to vamorolone (all events: 20% reduction, steroid-related events: 40% reduction). Stunting of growth observed with prednisone during Part 1 was reversed during treatment with vamorolone during Part 2. Placebo-treated participants in Part 1 that crossed over to vamorolone in Part 2 (delayed starters) showed an improvement in multiple efficacy outcomes after the switch to vamorolone.

Vamorolone (continued...)

Safety:
The most common adverse events with vamorolone use were cushingoid features, vomiting, and vitamin D deficiency.

In VISION-DMD, height percentile declined in prednisone-treated (not vamorolone-treated) participants (change from baseline: prednisone, -1.88 percentile vs. vamorolone 6 mg/kg per day, +3.86 percentile; p = 0.02). Additionally, bone turnover markers declined with prednisone but not with vamorolone.

Dosing:
In the pivotal trial, vamorolone was administered orally once daily.

Competitive environment

The pharmacologic standard of care for DMD are corticosteroids which have been shown to improve disease progression (eg, improve motor and pulmonary function, delaying loss of ambulation). Corticosteroids used for DMD include generically available drugs like prednisone and Emflaza® (deflazacort), the only FDA approved corticosteroid for DMD. Several disease-modifying, exon-skipping therapies have been approved (eg, Exondys 51®, Vyondys 53®, Amondys 45®) but these treatments can only be used in patients with specific mutations. Exon-skipping therapies provide small improvements in dystrophin expression, but clinical benefit has not been established. In June 2023, the FDA approved the first gene therapy for DMD – Elevidys (delandistrogene moxeparvovec), in ambulatory patients aged 4 through 5 years.

Compared to traditional corticosteroids, the main differentiator for vamorolone is its unique chemical structure which may result in a better safety profile. Of note, vamorolone appears to be associated with reduced bone adverse events, improved height trajectory, and lower rates of behavioral changes.

The pivotal trial included an active control arm (prednisone), but the primary efficacy analysis was comparing vamorolone vs. placebo. Compared numerically, the efficacy of vamorolone appears similar to prednisone. Traditional corticosteroids like prednisone are available generically.

Additionally, vamorolone was only evaluated in patients 4 to less than 7 years of age so it is difficult to extrapolate the results to older DMD patients.

Givinostat (Brand Name: To be determined)

Manufacturer: Italfarmaco Group
Regulatory designations: Orphan Drug, Fast Track
Expected FDA decision: December 21, 2023

Therapeutic use

Givinostat is under review for the treatment of ambulatory boys with DMD.

Clinical profile

Givinostat is a novel inhibitor of histone deacetylases (HDACs). Studies have shown that higher than normal HDAC activity in individuals with DMD may prevent muscle regeneration and triggers inflammation.

Pivotal trial data:
The efficacy of givinostat was evaluated in EPIDYS, a randomized, double-blind, placebo-controlled study in 120 ambulatory boys 6 to less than 18 years of age. Patients were randomized to receive givinostat or placebo for a period of 18 months. Patients were required to be on stable steroids for at least 6 months. The primary endpoint was the mean change from baseline to climb 4 stairs after 18 months of treatment. The time (in seconds) to climb 4 standard-sized stairs is a timed function test that represents stair-climbing ability.

What you need to know:

Proposed Indication: Treatment of ambulatory boys with DMD

Mechanism: HDAC inhibitor

Efficacy: Mean change from baseline to climb 4 stairs after 18 months: Difference vs. placebo of 1.78 seconds

Common AEs: Diarrhea, abdominal pain, thrombocytopenia, hypertriglyceridemia, decreased platelets, increased triglycerides

Dosing: Oral twice daily

Why It Matters: Novel MOA for treatment of DMD, manageable adverse event profile, high unmet need

Important to Note: Modest efficacy results, add-on therapy to corticosteroids (rather than replacement), trial data is limited to pediatric patients 6 years and older

Givinostat demonstrated a slower decline in the time to climb 4 stairs vs. placebo (difference vs. placebo of 1.78 seconds, p = 0.0345).

Safety:
The most common adverse events with givinostat use were diarrhea, abdominal pain, thrombocytopenia, hypertriglyceridemia, decreased platelets, and increased triglycerides.

Dosing:
In the pivotal trial, givinostat was administered orally twice daily.

Competitive environment

Givinostat would offer an oral, novel MOA for the treatment of DMD. While there have been advancements in the treatment of DMD in the last 10 years, there is still a high unmet need as DMD is associated with significant morbidity and mortality at a young age.

In the pivotal study, givinostat demonstrated statistical superiority vs. placebo for a timed function test (time to climb 4 stairs) and givinostat appears to have a manageable adverse event profile. However, the numerical difference vs. placebo for the primary endpoint was modest.

Unlike vamorolone, which is a potential replacement for traditional corticosteroids, givinostat was evaluated as add-on therapy to corticosteroids. Additionally, the pivotal trial data is limited to pediatric patients 6 years and older.

Tirzepatide (Brand Name: To be determined)

Manufacturer: Eli Lilly
Regulatory decision: Fast Track
Expected FDA decision: November 2023 – December 2023

Therapeutic use

Tirzepatide is under review as an adjunct to a reduced calorie diet and increased physical activity for chronic weight management.

The prevalence of obesity in the U.S. in adults is 41.9%. The prevalence of adults with overweight, including obesity, is 73.6%.

Clinical profile

Tirzepatide is a glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonist. GLP-1 is a physiological regulator of appetite and caloric intake, and the GLP-1 receptor is present in several areas of the brain involved in appetite regulation. GIP activation appeared to act synergistically with GLP-1 receptor activation to allow greater weight reduction.

Tirzepatide is currently approved under the brand name Mounjaro™, as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (T2DM). Eli Lilly could market tirzepatide for chronic weight management under a different brand name.

What you need to know:

Proposed Indication: Adjunct to a reduced calorie diet and increased physical activity for chronic weight management

Mechanism: GIP/GLP-1 receptor agonist

Efficacy:

- SURMOUNT-1: Change in body weight from baseline at Week 72: –15% to –20.9% vs. –3.1% with placebo
- SURMOUNT-2: Change in body weight from baseline at Week 72: –12.8% to –14.7% vs. –3.2% with placebo

Common AEs: Nausea, diarrhea, vomiting, constipation

Dosing: SC once weekly

Why It Matters: Best-in-class weight reduction compared indirectly to other GLP-1 receptor agonists

Important to Note: Alternatives available (eg, Wegovy, Saxenda) and potential future competition (eg, oral semaglutide, generic Saxenda), lack of cardiovascular outcomes data

Estimated Cost: ~$17,500 per year (based on pricing for Wegovy)

Pivotal trial data:
The efficacy of tirzepatide was evaluated in the SURMOUNT clinical program, which included four Phase 3, randomized, double-blind, placebo-controlled studies. The primary endpoints were the percentage of body weight reduction from baseline and percentage of participants achieving ≥ 5% body weight reduction.

SURMOUNT-1 included 2,539 adults without T2DM who had obesity, or overweight with at least one of the following co-morbidities: hypertension, dyslipidemia, obstructive sleep apnea or cardiovascular disease. Patients were randomized to receive either tirzepatide 5 mg, 10 mg, 15 mg, or placebo. The mean percentage change in weight at Week 72 was –15.0% with tirzepatide 5 mg, –19.5% with tirzepatide 10 mg, –20.9% with tirzepatide 15 mg, and –3.1% with placebo ($p < 0.001$ for all comparisons vs. placebo). The percentage of participants who had weight reduction of ≥ 5% was 85%, 89%, and 91% with 5 mg, 10 mg, and 15 mg of tirzepatide, respectively vs. 35% with placebo ($p < 0.001$ for all comparisons vs. placebo).

SURMOUNT-2 included 938 adults with obesity or overweight and T2DM. Patients were randomized to receive either tirzepatide 10 mg, 15 mg, or placebo. The mean percentage change in weight at Week 72 with tirzepatide 10 mg and 15 mg was –12.8% and –14.7%, respectively, vs. –3.2% with placebo ($p < 0.0001$ vs. placebo for both doses). More participants met the bodyweight reduction threshold of ≥ 5% with tirzepatide (79 to 83%) than placebo (32%; $p < 0.0001$ vs. placebo for both doses).

Tirzepatide (continued...)

SURMOUNT-3 included 806 adults with obesity or overweight with weight-related comorbidities, excluding T2DM. The trial had a 12-week lead-in period with intensive lifestyle intervention. After 12 weeks, 579 participants achieved at least 5% body weight reduction and were randomized to receive tirzepatide (a maximum tolerated dose of 10 mg or 15 mg) or placebo for 72 weeks. Patients randomized to tirzepatide, on average, lost an additional 18.4% of their body weight from randomization compared to those taking placebo who experienced mean weight regain of 2.5% over 72 weeks. Similarly, 87.5% of those taking tirzepatide achieved an additional ≥ 5% body weight reduction from randomization to week 72 compared with 16.5% in those taking placebo.

SURMOUNT-4 included adults with obesity or overweight with weight-related comorbidities, excluding T2DM. The trial had two periods: a 36-week open-label lead-in period in which all participants took tirzepatide, and a subsequent 52-week double-blind treatment period in which participants were randomized to either continue on tirzepatide or switch to placebo. The trial enrolled 783 participants into the open-label lead-in period and 670 participants were randomized in the 52-week double-blind treatment period to receive tirzepatide or placebo. Patients randomized to continue tirzepatide, on average, lost an additional 5.5% of their body weight from randomization, whereas those taking placebo experienced mean weight regain of 14.0% from randomization at 88 weeks. Participants who remained on tirzepatide after randomization achieved a total of 25.3% mean body weight loss from study entry over the entire 88-week period.

Safety:
The most common adverse events with tirzepatide use were nausea, diarrhea, vomiting, and constipation.

Dosing:
In the pivotal trials, tirzepatide was administered subcutaneously (SC) once weekly.

Competitive environment

Currently, two other drugs in the GLP-1 class, Novo Nordisk's Saxenda® (liraglutide) and Wegovy® (semaglutide), are approved for chronic weight management. Compared indirectly to these drugs, tirzepatide may provide best-in-class reductions in body weight.

However, tirzepatide does not have data supporting improvements in cardiovascular risk in any patient population. In contrast, semaglutide is approved for cardiovascular risk reduction in T2DM patients and Novo Nordisk recently announced positive results from the SELECT-CVOT trial indicated a 20% reduction in major cardiovascular events (MACE) among overweight and obese patients treated with Wegovy. Eli Lily does have a cardiovascular risk trial in process and anticipates sharing top-line results from the Phase 3 SURPASS-CVOT study for tirzepatide in 2024. SURPASS-CVOT is a cardiovascular outcomes study in T2DM patients comparing tirzepatide vs. Lilly's other GLP-1 receptor agonist, Trulicity® (dulaglutide).

In addition to competing with the existing treatment options, other competitors may be available for chronic weight management in 2024, including an oral formulation of semaglutide and potentially generic version(s) of Saxenda.

For reference, the WAC for Wegovy is approximately $17,500 per year.

Donanemab (Brand Name: To be determined)

Manufacturer: Eli Lilly
Regulatory designation: Breakthrough Therapy
Expected FDA decision: December 2023

Therapeutic use

Donanemab is under review for the treatment of mild cognitive impairment (MCI) due to Alzheimer's disease (AD) and mild AD.

Alzheimer's disease is an irreversible, progressive brain disorder that slowly destroys memory and cognition. MCI is usually the first sign of Alzheimer's disease which then progresses to dementia related to Alzheimer's disease (further classified as mild, moderate, or severe dementia). The disease is characterized by changes in the brain, including the abnormal accumulation of toxic amyloid beta plaque.

Alzheimer's disease is the most common form of dementia. It affects about 6.5 million people in the U.S., and it is the 5th leading cause of death among adults aged 65 years or older.

Clinical profile

Donanemab is a monoclonal antibody directed specifically at an N-terminal pyroglutamate A▌ epitope that is present only in established beta amyloid plaques.

Deposition of beta amyloid in the brain is an early event in AD that leads to neurofibrillary tangles composed of tau protein and other characteristic brain changes referred to as the amyloid cascade.

What you need to know:

Proposed Indication: Treatment of MCI due to AD and mild AD

Mechanism: Beta amyloid targeted monoclonal antibody

Efficacy:

- Change in iADRS score from baseline at Week 72 (overall population): −10.2 vs. −13.1 with placebo
- Change in CDR-SB score from baseline at Week 72 (overall population): 1.72 vs. 2.42 with placebo

Common AEs: ARIA, infusion related reactions, hypersensitivity

Dosing: IV once monthly

Why It Matters: Potential competitor to Leqembi with similar efficacy (compared indirectly), administered once every 4 weeks (Leqembi is once every 2 weeks), treatment can be discontinued after amyloid plaque clearance

Important to Note: ARIA safety concern, modest efficacy, lack of long-term data

Estimated Cost: ~$26,500 per year (based on pricing for Leqembi)

Pivotal trial data:
The efficacy of donanemab was evaluated in TRAILBLAZER-ALZ 2, a randomized, double-blind, placebo-controlled study in 1,736 patients with early symptomatic AD (MCI/mild dementia) with amyloid pathology based on positron emission tomography (PET) imaging. Study groups were stratified by tau pathology (low/medium or high) as measured by PET scan. Patients were randomized to receive donanemab or placebo for 72 weeks. If donanemab-treated patients reached low levels of amyloid plaque (assessed at 24 and 52 weeks), they were switched to placebo in a blinded manner. The primary endpoint was change in integrated Alzheimer Disease Rating Scale (iADRS) score from baseline to 76 weeks. iADRS is a validated scale with a range of 0 to 144 with lower scores indicating greater impairment. A key secondary endpoint was change in the sum of boxes of the Clinical Dementia Rating Scale (CDR-SB) score (range, 0 to 18; higher scores indicate greater impairment); the CDR-SB has been used in other trials studying beta amyloid targeted therapies.

Donanemab (continued…)

The least-squares mean (LSM) change in iADRS score at 76 weeks was −6.02 in the donanemab group vs. −9.27 in the placebo group (difference 3.25, 95% CI: 1.88, 4.62; p<0.001) in the low/medium tau population. In the combined population (including high tau pathology), the LSM change was −10.2 with donanemab vs. −13.1 with placebo (difference 2.92, 95% CI: 1.51, 4.33; p<0.001).

LSM change in CDR-SB score at 76 weeks was 1.20 with donanemab vs. 1.88 with placebo (difference −0.67, 95% CI: −0.95, −0.40; p<0.001) in the low/medium tau population. In the combined population, the LSM change was 1.72 with donanemab vs. 2.42 with placebo (difference −0.7, 95% CI: −0.95, −0.45; p<0.001).

Safety:
The most common adverse events with donanemab use were amyloid related imaging abnormalities (ARIA), infusion related reactions, and hypersensitivity.

Dosing:
In the pivotal trial, donanemab was administered via intravenous (IV) infusion once every month.

Competitive environment

There are currently two beta amyloid targeted therapies FDA approved for Alzheimer's disease: Biogen's Aduhelm® (aducanumab-avwa) and Eisai/Biogen's Leqembi® (lecanemab-irmb). Leqembi received accelerated approval in January 2023 and then traditional (full) approval in July 2023. Aduhelm received accelerated approval in 2021 and the timeline for traditional approval is unclear.

Eli Lilly pursued an accelerated approval for donanemab based on Phase 2 data, but the FDA provided a Complete Response Letter (CRL) or rejection in January 2023 due to the limited number of patients with at least 12 months of drug exposure data provided in the submission. The current FDA review for donanemab is for a traditional approval based on the Phase 3 trial data, which was not available for the initial FDA review.

The efficacy for donanemab appears comparable to Leqembi, although the magnitude of change observed with both drugs is the subject of continued debate as experts question if it reaches the level of clinically meaningfulness. The main differentiator for donanemab is the expected dosing. Donanemab is IV administered once every month whereas Leqembi is IV administered once every 2 weeks. Of note, the donanemab pivotal trial allowed patients to discontinue treatment after they met amyloid clearance criteria (as measured by PET imaging).

The recently published Phase 3 trial demonstrated that donanemab reduced clinical decline, but the benefit was small in magnitude and, although statistically significant vs. placebo, less than what would be considered clinically meaningful. Additionally, long-term data is not yet available; however, an extension trial is ongoing.

Like the other drugs in the class, donanemab is associated with ARIA-related side effects, including brain edema and microhemorrhages which would require additional monitoring. In the pivotal trial, ARIA of edema or effusion occurred in 205 participants (24.0%; 52 symptomatic) in the donanemab group vs. 18 (2.1%; 0 symptomatic during study) in the placebo group. Three donanemab-treated patients with serious ARIA subsequently died in the pivotal trial.

Finally, donanemab may face future competition with a self-administered, SC formulation of Leqembi. Eisai/Biogen are expected to file for approval for SC Leqembi by the end of 2023 or first quarter 2024.

For reference, the WAC for Leqembi is approximately $26,500 per year.

Exagamglogene autotemcel (Brand Name: To be determined)

Manufacturer: Vertex Pharmaceuticals/CRISPR Therapeutics
Regulatory designation: Orphan Drug, Fast Track
Expected FDA decisions: December 8, 2023 (SCD); March 30, 2024 (TBT)

Therapeutic use

Exagamglogene autotemcel (Exa-cel) is under review for the treatment of severe sickle cell disease (SCD) and transfusion-dependent beta thalassemia (TDT).

SCD

SCD is an inherited blood disorder caused by mutations in the hemoglobin beta (HBB) gene. These mutations lead to the presence of "sickle", or crescent-shaped, red blood cells. The sickle shaped cells die early, which can cause anemia. Additionally, the red blood cells become stiff and sticky and interact with other cells and the blood clotting system to block blood flow. The blocking of blood flow can lead to painful vaso-occlusive crises (VOCs) and more severe complications, such as severe organ damage or stroke.

SCD affects approximately 100,000 people in the U.S.

TDT

Similar to SCD, beta thalassemia is an inherited blood disorder by mutations in the HBB gene. The disease is characterized by reduced levels of functional hemoglobin and decreased red blood cell production. In severe cases, patients with beta thalassemia depend on life-long regular red blood cell transfusions (TDT) and will additionally need iron chelation therapy to combat the excess levels of iron in the body due to the repeated blood transfusions.

Relative to SCD, beta thalassemia is much rarer; the incidence of symptomatic cases is estimated to be approximately 1 in 100,000 individuals in the general population.

What you need to know:

Proposed Indication: Treatment of severe SCD and TDT

Mechanism: Ex vivo CRISPR/Cas9 gene-edited therapy

Efficacy:

- SCD: 94.1% (16 of 17) achieved freedom from severe VOCs for at least 12 consecutive months
- TDT: 88.9% (24 of 27) achieved transfusion-independence for at least 12 consecutive months

Common AEs: The safety profile of Exa-cel was generally consistent with myeloablative conditioning with busulfan and autologous hematopoietic stem cell transplant

Dosing: IV as a one-time dose

Why it Matters: Alternative to HSCT (not all patients have a matched donor), promising efficacy results for both SCD and TDT with potential for long-term efficacy

Important to Note: Unknown durability of response, small subset of patients will be eligible for therapy, complex patient journey including intensive myeloablative conditioning therapy

Estimated Cost: $2.8 million for a one-time dose (based on pricing for Zynteglo)

Clinical profile

Exa-cel is an autologous ex vivo CRISPR/Cas9 gene-edited therapy. A patient's own hematopoietic stem cells are edited to produce high levels of fetal hemoglobin (HbF) in red blood cells. HbF is the form of the oxygen-carrying hemoglobin that is naturally present during fetal development, which then switches to the adult form of hemoglobin after birth. Elevated levels of HbF are associated with improved morbidity and mortality in patients with TDT and SCD.

Exagamglogene autotemcel (continued…)

Pivotal trial data:

SCD

The efficacy of Exa-cel was evaluated in CLIMB-SCD-121, a Phase 1/2/3, single-arm, open-label study in patients ages 12 to 35 years with severe SCD. Patients received a single dose of Exa-cel. The primary endpoint was the proportion of patients who have not experienced a severe VOC for at least 12 months after the infusion of Exa-cel, starting 60 days after their last red blood cell (RBC) transfusion.

As of a February 2022 data cut off, all patients (31 of 31) were VOC-free (duration of follow-up 2.0 to 32.3 months after Exa-cel infusion). The mean proportion of HbF was >20% by Month 3, with mean total Hb levels >11 g/dL on and after Month 3.

As of a data cut off in June 2023, 17 patients were evaluable for the primary endpoint. Of the 17 patients, 94.1% (16 of 17) achieved the primary endpoint of freedom from VOCs for at least 12 consecutive months (95% CI: 71.3, 99.9; p = 0.0001). Mean duration of VOC-free was 18.7 months, with a maximum of 36.5 months. Additionally, all evaluable patients (17/17) achieved the key secondary endpoint of being free from hospitalizations related to VOCs for at least 12 consecutive months (95% CI: 80.5, 100.0; p < 0.0001).

TDT

The efficacy of Exa-cel was evaluated in CLIMB THAL-111, a Phase 1/2/3, single-arm open-label study in patients ages 12 to 35 years with severe TDT. Patients received a single dose of Exa-cel. The primary endpoint was the proportion of patients achieving a maintained weighted average hemoglobin (Hb) ≥ 9 g/dL without RBC transfusions for at least 12 consecutive months after Exa-cel infusion.

As of a February 2022 data cut off, 44 patients had been infused with Exa-cel. Overall, 95.5% (42 of 44) of patients stopped RBC transfusions. The median time since last transfusion was 9.0 (0.8 to 36.2) months, with 16 patients having at least 12 months since their last transfusion. Two patients had not yet stopped transfusions but had 75% and 89% reductions in transfusion volume. By Month 3, increases in HbF and mean total Hb levels (>9 g/dL) were achieved, with mean total Hb levels increasing to and maintained at >11 g/dL thereafter.

As of a data cut off in June 2023, 27 TDT patients were evaluable for the primary endpoint. Of the 27 patients, 24 (88.9%) achieved the primary endpoint of transfusion-independence for at least 12 consecutive months. Mean duration of transfusion-independence was 20.5 months with a maximum of 40.7 months.

Safety:
The safety profile of Exa-cel was generally consistent with myeloablative conditioning with busulfan and autologous hematopoietic stem cell transplant.

Dosing:
In the pivotal trials, patients CD34+ hematopoietic stem and progenitor cells (HSPCs) were collected by apheresis. Exa-cel was manufactured from these CD34+ cells by editing with CRISPR-Cas9.

Patients received single-agent busulfan myeloablation conditioning therapy before the IV infusion of a single-dose of Exa-cel.

Exagamglogene autotemcel (continued...)

Competitive environment

Historically, the only curative treatment for both SCD and TDT was hematopoietic stem cell transplant (HSCT); however, this is a limited option because not all patients have a compatible donor (particularly a matched related donor). HSCT carries its own risks such as graft failure/rejection and graft-versus-host disease (GVHD). In August 2022, the FDA approved bluebird bio's gene therapy, Zynteglo® (betibeglogene autotemcel), for TDT.

Exa-cel would potentially be the first approved CRISPR/Cas9 gene-edited therapy and a competitor to bluebird bio's gene therapies for TDT (Zynteglo) and SCD (Lovo-cel). Like bluebird bio's products, Exa-cel would be a one-time treatment and an alternative to HSCT, particularly in patients without a compatible donor. The short-term efficacy data for Exa-cel are promising with the primary endpoints being met in approximately 90% of patients in the pivotal trials. From a safety perspective, no secondary malignancies have been reported with Exa-cel, which is a concern with bluebird bio's gene therapies.

Exa-cel, as an ex vivo genetically modified cellular therapy, is complex to prepare and administer. The process from collecting a patients own cells to administering the final genetically modified product will take several months and requires myeloablative conditioning and extensive monitoring. Only a small subset of patients with TDT and particularly SCD would be eligible for treatment given the inclusion criteria in the clinical trials.

Lastly, due to the short follow-up time and small sample size in the pivotal study, the durability of response and long-term safety is unknown.

For reference, the WAC for Zynteglo is $2.8 million for a one-time dose.

Lovotibeglogene autotemcel (Brand Name: To be determined)

Manufacturer: bluebird bio
Regulatory designations: Orphan Drug, Fast Track
Expected FDA decision: December 20, 2023

Therapeutic use

Lovotibeglogene autotemcel (Lovo-cel) is under review for the treatment of sickle cell disease (SCD) in patients ages 12 and older who have a history of vaso-occlusive events (VOEs).

Clinical profile

Lovo-cel is an autologous ex vivo gene therapy. Functional copies of a modified form of the beta globin gene are added into a patient's own hematopoietic stem cells. Once patients have the gene added, their red blood cells (RBCs) can produce anti-sickling hemoglobin that decreases the proportion of sickled hemoglobin, with the goal of reducing sickled RBCs, hemolysis, and other complications.

Pivotal trial data:
The efficacy of Lovo-cel was evaluated in HGB-206, a Phase 1/2, single-arm, open-label study in patients ages 12 to less than 50 years with severe SCD. Patients received a single-dose of Lovo-cel. The primary endpoint was complete resolution of severe VOEs after Lovo-cel infusion.

As of August 2022, 96% (31/32) of patients experienced complete resolution of severe VOE through 24 months of follow-up. A single severe VOE was observed in one adult patient experiencing persistent anemia.

What you need to know:

Proposed Indication: Treatment of SCD in patients ages 12 and older who have a history of VOEs

Mechanism: Gene therapy

Efficacy: 96% (31 of 32) achieved freedom from severe VOCs through 24 months of follow-up

Common AEs: Most common adverse events with Lovo-cel use were known side effects of busulfan conditioning regimen

Dosing: IV as one-time dose

Why it Matters: Alternative to HSCT (not all patients have a matched donor), promising efficacy results for SCD with potential for long-term efficacy

Important to Note: Unknown durability of response, small subset of patients will be eligible for therapy, complex patient journey including intensive myeloablative conditioning therapy, increased risk of insertional oncogenesis

Estimated Cost: $2.8 million for a one-time dose (based on pricing for Zynteglo)

Safety:
The most common adverse events with Lovo-cel use were known side effects of busulfan conditioning regimen.

Dosing:
In the pivotal trial, patients CD34+ hematopoietic stem and progenitor cells (HSPCs) were collected by apheresis. Lovo-cel was manufactured by transducing these cells with the BB305 lentiviral vector encoding a modified beta globin gene.

Patients received single-agent busulfan myeloablation before the IV infusion of a single-dose of Lovo-cel.

Lovotibeglogene autotemcel (continued...)

Competitive environment

Lovo-cel would be a potential competitor to Vertex's Exa-cel and another alternative to HSCT for treatment of severe SCD. Like Exa-cel, the efficacy data for Lovo-cel are promising with almost all patients achieving the primary endpoint. Relative to Exa-cel, the number of patients evaluated after treatment with Lovo-cel is larger and the length of follow-up is longer, but the same overall uncertainties (eg, long term durability of response) are present, and the patient journey is similarly complex.

A potential safety concern unique to Lovo-cel is increased risk of hematologic malignancies. Bluebird bio's currently marketed gene therapy, Zynteglo, which is similar to Lovo-cel, has a warning for increased risk of lentiviral vector-mediated insertional oncogenesis after treatment. The labeling for Zynteglo recommends that all treated patients be monitored lifelong for hematologic malignancies, and a similar recommendation is likely for Lovo-cel.

For reference, the WAC for Zynteglo is $2.8 million for a one-time dose.

Aprocitentan (Brand Name: To be determined)

Manufacturer: Idorsia Pharmaceuticals/Janssen
Expected FDA decision: December 20, 2023

Therapeutic use

Aprocitentan is under review for the treatment of patients with resistant hypertension.

Resistant hypertension is classified as elevated blood pressure while being treated with at least 3 or more antihypertensive medications at optimal doses or when blood pressure is under control but requires at least 4 or more antihypertensive medications. Based on a blood pressure cutoff of 140/90 mm Hg, the prevalence of resistant hypertension is approximately 13% in the adult population.

Clinical profile

Aprocitentan is a dual endothelin receptor antagonist, which potently inhibits the binding of endothelin-1 (ET-1) to endothelin receptor A (ETA) and endothelin receptor B (ETB) receptors. ET-1 is a potent vasoconstrictor that also induces neurohormonal activation, vascular hypertrophy and remodeling, cardiac hypertrophy and fibrosis, and endothelial dysfunction.

What you need to know:

Proposed Indication: Treatment of patients with resistant hypertension

Mechanism: Endothelin receptor antagonist

Efficacy: Change from baseline in SBP at 4 weeks (mm Hg): −15.2 to −15.3 with aprocitentan vs. −11.5 with placebo

Common AE: Edema/fluid retention

Dosing: Oral once daily

Why it Matters: Novel MOA for the treatment of hypertension, large potential target population

Important to Note: Alternatives available (with high generic utilization), lack of head-to-head trial data vs. standards of care, class-related adverse events (eg, edema)

Estimated Cost: ~$7,500 per year (based on pricing for Verquvo)

Pivotal trial data:
The efficacy of aprocitentan was evaluated in the PRECISION study in 730 patients with a sitting systolic blood pressure (SBP) of 140 mm Hg or higher despite taking standardized background therapy consisting of three antihypertensive drugs. The study consisted of 3-sequential parts. Part 1 was the 4-week, randomized, placebo-controlled, double-blind portion of the study, in which patients received aprocitentan 12.5 mg, aprocitentan 25 mg, or placebo once daily; Part 2 was a 32-week single (patient)-blind period, in which all patients received aprocitentan 25 mg; and Part 3 was a 12-week, randomized, placebo-controlled, double-blind, withdrawal period, in which patients were re-randomized to aprocitentan 25 mg or placebo. The primary and key secondary endpoints were changes in unattended office systolic blood pressure from baseline to week 4 and from withdrawal baseline to week 40, respectively.

The least square mean (LSM) change in office SBP at 4 weeks was −15.3 mm Hg for aprocitentan 12.5 mg, −15.2 mm Hg for aprocitentan 25 mg, and −11.5 mm Hg for placebo, for a difference vs. placebo of −3.8 mm Hg (97.5% CI: −6.8, −0.8, p = 0.0042) and −3.7 mm Hg (97.5% CI: −6.7, −0.8; p = 0.0046), respectively. After 4 weeks of withdrawal, office SBP significantly increased with placebo vs. aprocitentan (5.8 mm Hg, 95% CI: 3.7, 7.9, p < 0.0001).

Safety:
The most common adverse event with aprocitentan use was edema or fluid retention.

Dosing:
In the pivotal trial, aprocitentan was administered orally once daily.

Aprocitentan (continued...)

Competitive environment

The standard of care for hypertension currently includes drugs across different MOAs. The primary agents include thiazide diuretics, angiotensin-converting enzyme (ACE) inhibitors/angiotensin II receptor blockers (ARBs), and calcium channel blockers. In patients who need additional blood pressure lowering or have contraindications to the first-line treatments, additional options include mineralocorticoid receptor antagonists, beta blockers, and hydralazine. Despite currently available treatment options, resistant hypertension is still relatively common, affecting over 10% of the population.

Aprocitentan would offer a novel MOA for the treatment of hypertension. The FDA approval of currently available endothelin receptor antagonists is limited to treatment of pulmonary arterial hypertension (PAH). Given the proposed indication and the inclusion criteria for the pivotal study, aprocitentan would likely be used in patients who have failed at least 3 other antihypertensive drugs. However, other drugs used in this setting (eg, spironolactone) are almost all available generically and there are no head-to-head trial data comparing aprocitentan vs. other classes of drugs used for resistant hypertension.

One class-related adverse event associated with endothelin receptor antagonists that was also present in the aprocitentan pivotal study is edema or fluid retention. This may limit some uptake for aprocitentan because heart failure, which is associated with edema, is a common comorbidity with hypertension.

For reference, the WAC for Verquvo® (vericiguat), a recently approved novel cardiovascular drug for backline treatment of heart failure, is approximately $7,500 per year.

Capivasertib (Brand Name: To be determined)

Manufacturer: AstraZeneca
Regulatory designation: Fast Track
Expected FDA decision: 4Q 2023

Therapeutic use

Capivasertib is under review, in combination with fulvestrant, for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer following recurrence or progression on or after an endocrine-based regimen.

An estimated 297,790 new cases of invasive breast cancer will be diagnosed in women in 2023 and about 43,700 women will die from breast cancer. Approximately 70% of breast cancer cases are of the HR+/HER2- subtype. Although less common, breast cancer can also occur in men.

Clinical profile

Capivasertib is an AKT kinase inhibitor. AKT is the key node of the PI3K–AKT–PTEN signaling pathway. Overactivation of the pathway occurs in approximately half of HR+/HER2- breast cancers by means of activating mutations in *PIK3CA* and *AKT1* and inactivating alterations in *PTEN*.

Pivotal trial data:
The efficacy of capivasertib was evaluated in CAPItello-291, a Phase 3, randomized, double-blind study in 708 pre-, peri-, and postmenopausal women and men with HR+/HER2- advanced breast cancer who had had a relapse or disease progression during or after treatment with an aromatase inhibitor, with or without previous cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitor therapy. Patients received capivasertib plus fulvestrant or placebo plus fulvestrant. The dual primary endpoint was progression-free survival (PFS) assessed both in the overall population and among patients with AKT pathway–altered (PIK3CA, AKT1, or PTEN) tumors.

In the overall population, the median PFS was 7.2 months in the capivasertib-fulvestrant group vs. 3.6 months in the placebo-fulvestrant group (hazard ratio [HR] 0.60, 95% CI: 0.51, 0.71; $p < 0.001$). In the AKT pathway–altered population, the median PFS was 7.3 months in the capivasertib-fulvestrant group vs. 3.1 months in the placebo–fulvestrant group (HR 0.50, 95% CI: 0.38, 0.65; $p < 0.001$).

Safety:
The most common adverse events with capivasertib use were diarrhea, nausea, rash, fatigue, and vomiting.

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

What you need to know:

Proposed Indication: In combination with fulvestrant, for the treatment of adult patients with HR+/HER2- locally advanced or metastatic breast cancer following recurrence or progression on or after an endocrine-based regimen

Mechanism: AKT kinase inhibitor

Efficacy: Median PFS (overall population): 7.2 months with capivasertib plus fulvestrant vs. 3.6 months with placebo plus fulvestrant

Common AEs: Diarrhea, nausea, rash, fatigue, vomiting

Dosing: Oral twice daily

Why it Matters: Promising PFS data vs. monotherapy standard of care, manageable safety profile, potential expanded use in earlier breast cancer settings and other cancers

Important to Note: Lack of head-to-head data against standard of care combination regimens, narrow initial use (second- or third-line)

Estimated Cost: ~$19,000 per month (based on pricing for Piqray)

Capivasertib (continued...)

Competitive environment

Endocrine therapy, with either an aromatase inhibitor or fulvestrant, plus a CDK4/6 inhibitor, is the recommended first-line treatment for locally advanced or metastatic HR+/HER2- breast cancer. For patients who fail initial treatment, subsequent regimens that are not biomarker specific include fulvestrant plus CDK4/6 inhibitors or everolimus. Biomarker specific drugs include Piqray® (alpelisib) for patients with a PIK3CA mutation and the recently approved Orserdu™ (elacestrant) for ESR1-mutated advanced or metastatic breast cancer.

Capivasertib would provide an additional treatment option for HR+/HER2- breast cancer. Compared to Piqray, which also targets PIK3CA, capivasertib demonstrated PFS survival benefit in both the overall efficacy population and patients with an alteration in the AKT pathway; Piqray has demonstrated PFS benefit only in patients with PIK3CA-mutated tumors. Based on the data currently available, capivasertib appears to have a more manageable safety profile compared with Piqray.

The results from CAPItello-291 are promising with improved PFS vs. fulvestrant monotherapy, however, the current standard of care in patients who failed initial treatment usually includes a fulvestrant-containing combination regimen. There is a lack of robust data comparing capivasertib combination therapy vs. existing combination regimens.

The initial target population is likely to be limited for capivasertib but its place in therapy could grow if future trials are positive. It is currently in development in earlier settings of breast cancer and other cancers.

For reference, the WAC for Piqray is approximately $19,000 per month.

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
2023 Possible launch date					
FORTEO	teriparatide	Eli Lilly	Osteoporosis	Injection	2023
DYLOJECT	diclofenac	Hospira/Pfizer/Javelin	Mild to Moderate Pain	Intravenous	2023
DULERA	formoterol fumarate/mometasone furoate	Organon	Asthma	Inhalation	2023
NEUPRO	rotigotine	UCB	Parkinson's Disease; Restless Legs Syndrome	External	2023
NASCOBAL	cyanocobalamin	Par/Endo	Pernicious Anemia Patients	Intranasal	2023
TEFLARO	ceftaroline fosamil	Allergan	Community Acquired Pneumonia; Skin and Skin Structure Infections	Intravenous	2023
ONEXTON	clindamycin/benzoyl peroxide	Bausch Health	Acne Vulgaris	External	2023
MYDAYIS	amphetamine mixture/dextroamphetamine mixture	Takeda	Attention Deficit Hyperactivity Disorder	Oral	2023
ALPHAGAN P	brimonidine	Allergan	Glaucoma; Ocular Hypertension	Ophthalmic	2023
THALOMID	thalidomide	Celgene	Multiple Myeloma; Erythema Nodosum Leprosum	Oral	2023
SPIRIVA HANDIHALER	tiotropium	Boehringer Ingelheim	Chronic Obstructive Pulmonary Disease	Inhalation	2023
GATTEX	teduglutide recombinant	Takeda	Short Bowel Syndrome	Subcutaneous	2H-2023
VYVANSE	lisdexamfetamine	Shire/Takeda	Attention Deficit Hyperactivity Disorder; Moderate to Severe Binge Eating Disorder	Oral	08-2023
CAROSPIR	spironolactone	CMP Pharma	Edema in Cirrhotic Patients, Heart Failure and/or Hypertension	Oral	09-2023
LEXETTE	halobetasol	Mayne	Plaque Psoriasis	External	09-2023
PROLENSA	bromfenac	Bausch Health	Postoperative Ocular Inflammation and Ocular Pain Following Cataract Surgery	Ophthalmic	4Q-2023
NEULASTA ONPRO	pegfilgrastim	Amgen/Insulet	Prophylaxis of Neutropenia in Cancer Patients	Subcutaneous	10-2023

Trade Name	Generic Name	Brand Company(ies)	Indications	Route of Administration	Anticipated Availability
VOTRIENT	pazopanib	Novartis	Renal Cell Carcinoma; Soft Tissue Sarcoma	Oral	10-2023
LIVALO	pitavastatin	Eli Lilly/Kowa Pharmaceuticals	Hyperlipidemia	Oral	11-2023
2024 Possible launch date					
VESICARE LS	solifenacin	Astellas	Neurogenic Detrusor Overactivity	Oral	1H-2024
BALCOLTRA	levonorgestrel/ethinyl estradiol/ferrous bisglycinate	Avion/Albion	Pregnancy Prevention	Oral	01-2024
GIAZO	balsalazide disodium	Bausch Health	Ulcerative Colitis in Male Patients	Oral	01-2024
MYRBETRIQ	mirabegron	Astellas	Overactive Bladder; Neurogenic Detrusor Overactivity	Oral	01-2024
GRALISE	gabapentin	Assertio Therapeutics	Postherpetic Neuralgia	Oral	01-2024
CAPLYTA	lumateperone	Intra-Cellular Therapies	Schizophrenia; Bipolar Depression	Oral	01-2024
TASIGNA	nilotinib	Novartis	Philadelphia Chromosome-Positive Chronic Myeloid Leukemia	Oral	01-2024
SIMPONI	golimumab	Janssen	Ankylosing Spondylitis; Psoriatic Arthritis; Rheumatoid Arthritis; Ulcerative Colitis	Subcutaneous	02-2024
SIMPONI ARIA	golimumab	Janssen	Rheumatoid Arthritis; Psoriatic Arthritis; Ankylosing Spondylitis; Juvenile Idiopathic Arthritis	Intravenous	02-2024
NATESTO	testosterone	Acerus	Replacement Therapy in Males with Deficiency of Endogenous Testosterone	Nasal	02-2024
EMFLAZA	deflazacort	PTC Therapeutics	Duchenne Muscular Dystrophy	Oral	02-2024
BYLVAY	odevixibat	Albiero	Pruritus in Progressive Familial Intrahepatic Cholestasis and Alagille Syndrome	Oral	03-2024
ISENTRESS	raltegravir	Merck	Human Immunodeficiency Virus-1 Infection	Oral	04-2024
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
SAXENDA	liraglutide	Novo Nordisk	Chronic Weight Management	Subcutaneous	05-2024
NYMALIZE	nimodipine	Arbor	Subarachnoid Hemorrhage	Oral	05-2024
PROBUPHINE	buprenorphine	Titan Pharmaceuticals/Braeburn Pharmaceuticals	Maintenance Treatment of Opioid Dependence	Subdermal	06-2024

Trade Name	Generic Name	Brand Company(ies)	Indications	Route of Administration	Anticipated Availability
VICTOZA	liraglutide	Novo Nordisk	Type 2 Diabetes Mellitus (T2DM); Reduce the Risks of Cardiovascular Events in T2DM	Subcutaneous	06-2024
VIVITROL	naltrexone	Alkermes	Alcohol and/or Opioid Dependence	Intramuscular	2H-2024
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	2H-2024
TWYNEO	tretinoin/benzoyl peroxide	Galderma	Acne Vulgaris	External	07-2024
SLYND	drospirenone	Exeltis/Insud	Prevention of Pregnancy	Oral	08-2024
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
LAZANDA	fentanyl citrate	Depomed	Breakthrough Pain in Cancer Patients	Intranasal	10-2024
RYDAPT	midostaurin	Novartis	Acute Myeloid Leukemia; Systemic Mastocytosis; Mast Cell Leukemia	Oral	10-2024
VUITY	pilocarpine	AbbVie	Presbyopia	Ophthalmic	10-2024
STENDRA	avanafil	Metuchen 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
2025 Possible launch date					
ACTEMRA	tocilizumab	Roche/Chugai	Juvenile Idiopathic Arthritis; Rheumatoid Arthritis; Giant Cell Arteritis; Cytokine Release Syndrome; Systemic Sclerosis-Associated Interstitial Lung Disease	Intravenous; subcutaneous	2025
BOSULIF	bosutinib	Pfizer	Chronic Myelogenous Leukemia	Oral	2025
DALVANCE	dalbavancin	AbbVie	Acute Bacterial Skin and Skin Structure Infections	Intravenous	2025

Trade Name	Generic Name	Brand Company(ies)	Indications	Route of Administration	Anticipated Availability
TYSABRI	natalizumab	Biogen	Multiple Sclerosis; Crohn's Disease	Intravenous	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	Intravenous	2025
NAMZARIC	memantine/donepezil	Allergan/Adamas	Moderate to Severe Dementia of the Alzheimer's Type	Oral	01-2025
TRACLEER	bosentan	Actelion/Janssen	Pulmonary Arterial Hypertension	Oral	01-2025
RISPERDAL CONSTA	risperidone	Janssen	Psychosis; Schizophrenia	Injection	01-2025
FLOVENT DISKUS	fluticasone propionate	GSK	Asthma	Inhalation	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
PHOSLYRA	calcium acetate	Fresenius	Phosphate Binder	Oral	01-2025
FINACEA Foam	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
PROLIA	denosumab	Amgen	Postmenopausal Osteoporosis; Bone Loss in Men and Women at Risk of Fracture	Subcutaneous	02-2025
XGEVA	denosumab	Amgen	Prevention of Fractures in Bone Malignancies and Multiple Myeloma; Giant Cell Tumor in Bone; Hypercalcemia	Subcutaneous	02-2025
SOLIRIS	eculizumab	Alexion	Paroxsymal Nocturnal Hemoglobinuria; Hemolytic Uremic Syndrome; Myasthenia Gravis; Neuromyelitis Optica	Intravenous	03-2025
BENLYSTA	belimumab	GSK	Systemic Lupus Erythematosus; Lupis Nephritis	Intravenous; subcutaneous	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
YERVOY	ipilimumab	Bristol-Myers Squibb	Melanoma; Renal Cell Cancer; Colorectal Cancer; Hepatocellular Cancer; Non-Small Cell Lung Cancer; Mesothelioma	Intravenous	03-2025

Trade Name	Generic Name	Brand Company(ies)	Indications	Route of Administration	Anticipated Availability
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
EPRONTIA	topiramate	Azurity	Epilepsy; Lennox-Gastaut Syndrome; Migraine Prevention	Oral	05-2025
FYCOMPA	perampanel	Eisai	Partial-Onset Seizures; Primary Generalized Tonic-Clonic Seizures	Oral	05-2025
PERJETA	pertuzumab	Genentech	HER-2 Positive Breast Cancer	Intravenous	06-2025
NULOJIX	belatacept	Bristol-Myers Squibb	Prophylaxis of Organ Rejection in Kidney Transplant	Intravenous	06-2025
NUCYNTA	tapentadol	Collegium	Moderate to Severe Acute Pain	Oral	06-2025
NUCYNTA ER	tapentadol	Collegium	Moderate to Severe Chronic Pain	Oral	06-2025
CARDENE	nicardipine	Chiesi	Short-Term Treatment of Hypertension When Oral Therapy is Not Possible	Intravenous	07-2025
RAVICTI	glycerol phenylbutyrate	Horizon	Urea Cycle Disorders	Oral	07-2025
RYANODEX	dantrolene	Eagle Pharmaceuticals	Malignant Hyperthermia	Intravenous	07-2025
SOLIQUA	insulin glargine/lixisenatide	Sanofi	Type 2 Diabetes Mellitus	Subcutaneous	07-2025
RYTARY	carbidopa/levodopa	Impax/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
OFEV	nintedanib	Boehringer Ingelheim	Idiopathic Pulmonary Fibrosis; Systemic Sclerosis-Associated Interstitial Lung Disease (ILD); Chronic Fibrosing ILD	Oral	10-2025
XIGDUO XR	dapagliflozin/metformin	AstraZeneca	Type 2 Diabetes Mellitus; Reduce the Risk of Hospitalizations with Heart Failure; Chronic Kidney Disease	Oral	10-2025

Trade Name	Generic Name	Brand Company(ies)	Indications	Route of Administration	Anticipated Availability
FARXIGA	dapagliflozin	AstraZeneca	Type 2 Diabetes Mellitus; Reduce the Risk of Hospitalization with Heart Failure; Chronic Kidney Disease	Oral	10-2025
QTERN	dapagliflozin/saxagliptin	AstraZeneca	Type 2 Diabetes Mellitus	Oral	10-2025
FUROSCIX	furosemide	scPharmaceuticals	Chronic Heart Failure	Subcutaneous	10-2025
ELELYSO	taliglucerase alfa	Pfizer	Gaucher Disease	Intravenous	10-2025
EDURANT	rilpivirine	Janssen	Human Immunodeficiency Virus-1 Infection	Oral	10-2025
JENTADUETO XR	linagliptin/metformin	Boehringer Ingelheim/Eli Lilly	Type 2 Diabetes Mellitus	Oral	11-2025
TRADJENTA	linagliptin	Eli Lilly/Boehringer Ingelheim	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					
CIMZIA	certolizumab pegol	UCB/Royalty Pharma	Psoriatic Arthritis; Rheumatoid Arthritis; Ankylosing Spondylitis; Crohn's Disease; Plaque Psoriasis; Axial Spondyloarthritis	Subcutaneous	2026
BRYHALI	halobetasol	Bausch Health	Plaque Psoriasis	External	2026
ABILIFY MAINTENA	aripiprazole	Otsuka/Lundbeck	Schizophrenia; Bipolar Disorder	Intramuscular	2026
POMALYST	pomalidomide	Celgene	Multiple Myeloma; Kaposi Sarcoma	Oral	1Q-2026
MOTEGRITY	prucalopride	Takeda	Chronic Idiopathic Constipation	Oral	01-2026
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
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

Trade Name	Generic Name	Brand Company(ies)	Indications	Route of Administration	Anticipated Availability
BROMSITE	bromfenac	Sun	Treatment of Postoperative Inflammation and Prevention of Ocular Pain in Patients Undergoing Cataract Surgery	Ophthalmic	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
PROMACTA	eltrombopag	Novartis	Thrombocytopenia	Oral	01-2026
CYRAMZA	ramucirumab	Eli Lilly	Gastric Cancer; Gastroesophageal Cancer; Metastatic Gastric Cancer; Non-Small Cell Lung Cancer	Intravenous	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
JANUVIA	sitagliptan	Merck	Type 2 Diabetes Mellitus	Oral	05-2026
JANUMET	sitagliptan/metformin	Merck	Type 2 Diabetes Mellitus	Oral	05-2026
NAYZILAM	midazolam	UCB	Epilepsy	Intranasal	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
TRINTELLIX	vortioxetine	Takeda/Lundbeck	Major Depressive Disorder	Oral	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
ADEMPAS	riociguat	Bayer	Pulmonary Arterial Hypertension; Chronic Thromboembolic Pulmonary Hypertension	Oral	4Q-2026

Trade Name	Generic Name	Brand Company(ies)	Indications	Route of Administration	Anticipated Availability
VEREGEN	sinecatechins	Sandoz	External Genital and Perianal Warts	External	10-2026
UPTRAVI	selexipag	Janssen	Pulmonary Arterial Hypertension	Oral	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	Subcutaneous	10-2026

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
2023 Possible launch date									
SVT-15473	clobetasol	Salvat Laboratories	corticosteroid	Post-ocular surgery	OPH	Filed NDA	08/25/2023	No	No
ONS-5010	bevacizumab-vikg	Outlook Therapeutics	anti-VEGF antibody	Wet age-related macular degeneration	Intravitreal	Filed BLA	08/29/2023	Yes	No
BL-8040 (BKT-140)	motixafortide	BioLineRx	selective chemokine receptor 4 inverse agonist	Stem cell transplant	SC	Filed NDA	09/09/2023	Yes	Yes
RA-101495	zilucoplan	UCB	complement inhibitor	Generalized myasthenia gravis	SC	Filed NDA	09/14/2023	Yes	Yes
Tecentriq SC	atezolizumab	Roche	programmed death-ligand 1 blocking antibody	Cancers (mirroring indications to IV formulation)	SC	Filed BLA	09/15/2023	Yes	No
CYT-387	momelotinib	GlaxoSmithKline	janus kinase inhibitor	Myeloproliferative disorders	PO	Filed NDA	09/16/2023	Yes	Yes
ARS-1	epinephrine	ARS Pharmaceuticals	non-selective alpha/ beta-adrenergic receptor agonist	Anaphylaxis	Intranasal	Filed NDA	09/19/2023	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
ATI-1501	metronidazole	Saptalis	nitroimidazole	Fungal infections, anaerobic bacterial infections	PO	Filed NDA	09/23/2023	No	No
BBI-4000	sofpironium bromide	Brickell	anticholinergic	Hyperhidrosis	TOP	Filed NDA	09/26/2023	No	No
Nyxol	phentolamine	Ocuphire	Alpha-1 and alpha-2 blocker	Mydriasis reversal	OPH	Filed NDA	09/28/2023	No	No
Lydolyte	lidocaine	MEDRx	anesthetic agent	Neuropathic pain	TOP	Filed NDA	09/28/2023	No	No
MILR-1444A	lebrikizumab	Eli Lilly	interleukin-13 inhibitor	Atopic dermatitis	SC	Filed BLA	09/2023	Yes	No
JS-001	toripalimab	Coherus Biosciences	anti-PD-1 monoclonal antibody	Nasopharyngeal carcinoma	IV	Filed BLA	3Q2023	Yes	Yes
UCB-4940 (CDP-4940)	bimekizumab	UCB	interleukin-17 receptor inhibitor	Plaque psoriasis	SC	Filed BLA	3Q2023	Yes	No
DCR-PHXC	nedosiran	Novo Nordisk	glycolate oxidase antagonist	Primary hyperoxaluria	SC	Filed NDA	3Q2023	Yes	Yes
AT-GAA	cipaglucosidase alfa	Amicus	enzyme therapy	Pompe disease	IV	Filed BLA	3Q2023	Yes	Yes
Xphozah	tenapanor	Ardelyx	sodium/hydrogen exchanger 3 inhibitor	Hyperphosphatemia	PO	Filed NDA	10/17/2023	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
ATI-1501	metronidazole	Saptalis	nitroimidazole	Fungal infections, anaerobic bacterial infections	PO	Filed NDA	09/23/2023	No	No
APD-334	etrasimod	Pfizer/ Everest	S1P1 receptor agonist	Ulcerative colitis	PO	Filed NDA	10/21/2023	Yes	No
CT-P13	infliximab	Celltrion	Tumor necrosis factor blocker	Inflammatory bowel disease	SC	Filed BLA	10/22/2023	Yes	No
CSF-1	pilocarpine	Orasis Pharmaceuticals	cholinergic muscarinic receptor agonist	Presbyopia	OPH	Filed NDA	10/22/2023	No	No
VBP-15	vamorolone	Santhera Pharmaceuticals/ Catalyst Pharmaceuticals	dissociative steroidal anti-inflammatory drug	Duchenne muscular dystrophy	PO	Filed NDA	10/26/2023	Yes	Yes
Entyvio (SC formulation)	vedolizumab	Takeda	integrin receptor antagonist	Ulcerative colitis	SC	Filed BLA	10/28/2023	Yes	No
PF-06886992	meningococcal vaccine [A, B, C, Y, W-135]	Pfizer	vaccine	Meningococcal disease	IM	Filed BLA	10/28/2023	No	No
Neutrolin (CRMD-003, CRMD-004)	citrate/ taurolidine/ heparin	CorMedix	antimicrobial agent/ anticoagulant	Catheter-related infections	IV	Filed NDA	11/15/2023	No	No
TAK-755 (SHP-655)	TAK-755	Takeda	ADAMTS13 enzyme	Thrombotic thrombocytopenic purpura	IV	Filed BLA	11/16/2023	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
TAK-438	vonoprazan fumarate	Phathom Pharmaceuticals	potassium-competitive acid blocker	Erosive esophagitis	PO	Filed NDA	11/17/2023	No	No
VLA-1553	VLA-1553	Valneva	vaccine	Chikungunya virus	IM	Filed BLA	11/22/2023	No	No
NS-2 (ALDX-1E1, ADX-102)	reproxalap	Aldeyra Therapeutics	aldehyde antagonist	Dry eye disease	OPH	Filed NDA	11/23/2023	No	No
LN-144	lifileucel	Iovance Biotherapeutics	tumor infiltrating lymphocyte	Melanoma	IV	Filed BLA	11/25/2023	Yes	Yes
TPX-0005	repotrectinib	Bristol Myers Squibb	tyrosine kinase inhibitor	Non-small cell lung cancer	PO	Filed NDA	11/27/2023	Yes	Yes
PF-3084014 (PF-03084014)	nirogacestat	SpringWorks Therapeutics	gamma secretase inhibitor	Desmoid tumors	PO	Filed NDA	11/27/2023	Yes	Yes
fruquintinib	fruquintinib	Hutchison China MediTech	VEGF-R inhibitor	Colorectal cancer	PO	Filed NDA	11/30/2023	Yes	No
Tirzepatide (for weight loss)	tirzepatide	Eli Lilly	glucose-dependent insulinotropic polypeptide receptor and glucagon-like peptide-1 receptor agonist	Chronic weight management	SC	Filed NDA	11/2023 - 12/2023	No	No
OX-124	naloxone	Orexo	opioid antagonist	Opioid overdose	Intranasal	Filed NDA	12/03/2023	No	No
NurOwn	autologous cultured mesenchymal bone marrow	BrainStorm Cell Therapeutics	cellular therapy	Amyotrophic lateral sclerosis	IV	Filed BLA	12/08/2023	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
	stromal cells secreting neurotrophic factors								
CTX-001 (Exa-cel)	exagamglogene autotemcel	CRISPR Therapeutics/ Vertex	gene therapy (gene editing CRISPR-Cas9)	Sickle cell disease/ beta-thalassemia	IV	Filed BLA	12/08/2023	Yes	Yes
AZD-5363	capivasertib	AstraZeneca	selective PKB/Akt inhibitor	Breast cancer	PO	Filed NDA	12/12/2023	Yes	No
ARQ-154	roflumilast	Arcutis Biotherapeutics	phosphodiesterase-4 inhibitor	Seborrheic dermatitis	TOP	Filed NDA	12/16/2023	No	No
ACT-132577	aprocitentan	Idorsia Pharmaceuticals	endothelin receptor antagonist	Hypertension	PO	Filed NDA	12/20/2023	No	No
LentiGlobin	lovotibeglogene autotemcel	bluebird bio	gene therapy	Sickle cell disease	IV	Filed BLA	12/20/2023	Yes	Yes
ITF-2357	givinostat	Italfarmaco S.p.A.	histone deacetylase inhibitor	Duchenne muscular dystrophy	PO	Filed NDA	12/21/2023	Yes	Yes
AKCEA-TTR-LRx	eplontersen	AstraZeneca/ Ionis	antisense oligonucleotide	Hereditary transthyretin-mediated amyloid polyneuropathy	SC	Filed BLA	12/22/2023	Yes	Yes
iDose travoprost	travoprost	Glaukos	prostaglandin analog	Glaucoma/ Ocular hypertension	Intraocular	Filed NDA	12/22/2023	No	No
MK-7264	gefapixant	Merck	P2X3 antagonist	Chronic cough	PO	Filed NDA	12/27/2023	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
LY-3002813	donanemab	Eli Lilly	beta-amyloid monoclonal antibody	Alzheimer's disease	IV	Filed BLA	12/2023	Yes	No
LIQ-861	treprostinil	Liquidia Technologies	prostacyclin analog	Pulmonary arterial hypertension; interstitial lung disease	INH	Tentative Approval	2H2023	Yes	No
NVX-CoV2373	coronavirus vaccine	Novavax	vaccine	Novel coronavirus disease 2019 (COVID-19)	IM	InTrial	Late 2023	No	No
LY-3074828	mirikizumab	Eli Lilly	interleukin-23 antagonist	Ulcerative colitis	IV/SC	Filed BLA	Late 2023	Yes	No
BGB-A317 (BGB-A-317)	tislelizumab	BeiGene	programmed death-1 inhibitor	Esophageal squamous cell carcinoma	IV	Filed BLA	Late 2023	Yes	Yes
ITCA-650 (sustained release exenatide)	exenatide sustained-release	Intarcia	glucagon-like peptide-1 receptor agonist	Diabetes mellitus	SC implant	Filed NDA	Late 2023	No	No
2024 Possible launch date									
CK-301	cosibelimab	Checkpoint Therapeutic	anti programmed cell death ligand 1	Cutaneous squamous cell carcinoma	IV	Filed BLA	01/03/2024	Yes	No
SB-206	berdazimer	Novan Therapeutics	nitric oxide-releasing compound	Molluscum contagiosum	TOP	Filed NDA	01/05/2024	No	No
iMAB-362	zolbetuximab	Astellas	GC182 monoclonal antibody	Gastric adenocarcinoma	IV	Filed BLA	01/12/2024	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
GC-5107	human immunoglobulin	GC Biopharma	human immunoglobulin	Primary immunodeficiencies	IV	Filed BLA	01/13/2024	Yes	No
SHR-1210	camrelizumab	Elevar Therapeutics	programmed death receptor-1-blocking antibody	Hepatocellular carcinoma	IV	Filed BLA	01/17/2024	Yes	Yes
DPI-386	scopolamine	Repurposed Therapeutics	anticholinergic	Motion sickness	Intranasal	Filed NDA	01/26/2024	No	No
NVK-002	atropine	Vyluma	anticholinergic	Myopia	OPH	Filed NDA	01/31/2024	No	No
STS-101	dihydroergotamine	Satsuma Pharmaceuticals	ergotamine	Migraine	Intranasal	Filed NDA	01/2024	No	No
VNRX-5133	cefepime/ taniborbactam	VenatoRx Pharmaceuticals	cephalosporin/ beta-lactamase inhibitor	Bacterial infections	IV	Filed NDA	02/22/2024	Yes	No
MIN-101	roluperidone	Minerva Neurosciences	sigma-2 and 5HT-2A receptor antagonist	Schizophrenia	PO	Filed NDA	02/26/2024	No	No
AAI-101	cefepime/enmetazobactam	Allecra Therapeutics	beta-lactam/b-lactamase inhibitor	Urinary tract infection	IV	Filed NDA	02/27/2024	No	No
APP-13007	clobetasol propionate	Formosa Pharmaceuticals	corticosteroid	Eye inflammation/ pain	OPH	Filed NDA	03/04/2024	No	No
glatiramer acetate depot	glatiramer acetate long-acting	Viatris	immunomodulator	Multiple sclerosis	IM	Filed NDA	03/08/2024	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
MGL-3196	resmetirom	Madrigal Pharmaceuticals	beta-selective thyroid hormone receptor agonist	Nonalcoholic steatohepatitis	PO	Filed NDA	03/17/2024	Yes	No
ACE-011	sotatercept	Merck	activin receptor type IIA-Fc fusion protein	Pulmonary arterial hypertension	SC	Filed BLA	03/2024	Yes	Yes
Opsynvi	macitentan/ tadalafil	Janssen	endothelin receptor antagonist/ phosphodiesterase 5 inhibitor	Pulmonary arterial hypertension	PO	Filed NDA	03/30/2024	Yes	Yes
OTL-200	atidarsagene autotemcel	Orchard Therapeutics	gene therapy	Leukodystrophy	IV	Filed BLA	1Q2024	Yes	Yes
AKB-6548	vadadustat	Otsuka Pharmaceutical	hypoxia-inducible factor-prolyl hydroxylase inhibitor	Chronic kidney disease-related anemia	PO	CRL	1Q2024	Yes	No
LNP-023	iptacopan	Novartis	factor B inhibitor	Paroxysmal nocturnal hemoglobinuria	PO	Filed NDA	1Q2024	Yes	Yes
RP-L201	RP-L201	Rocket Pharmaceuticals	gene therapy	Leukocyte adhesion deficiency-I	IV	InTrial	1Q2024	Yes	Yes
LTX-03	hydrocodone bitartrate/ acetaminophen	Acura Pharmaceuticals	opioid analgesic	Pain	PO	Filed NDA	1Q2024	No	No
Zeftera	ceftobiprole	Basilea	cephalosporin antibiotic	Bacterial infections	IV	Filed NDA	04/04/2024	No	No
PF-06838435 (SPK-9001)	fidanacogene elaparvovec	Pfizer/ Spark Therapeutics	gene therapy	Hemophilia B	IV	Filed BLA	04/27/2024	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
YN-96D1	rivoceranib (apatinib)	Elevar Therapeutics	vascular endothelial growth factor receptor antagonist	Hepatocellular carcinoma	PO	Filed NDA	05/16/2024	Yes	Yes
GRN-163L	imetelstat	Geron	telomerase inhibitor	Myelodysplastic syndrome	IV	Filed NDA	06/16/2024	Yes	Yes
RPL-554	ensifentrine	Verona Pharma	phosphodiesterase-3 and phosphodiesterase-4 inhibitor	Chronic obstructive pulmonary disease	INH	Filed NDA	06/27/2024	No	No
LY-686017	tradipitant	Vanda Pharmaceuticals	neurokinin 1 receptor antagonist	Gastroparesis	PO	InTrial	2Q2024	No	No
PTC-AADC	eladocagene exuparvovec	PTC Therapeutics	gene therapy	Aromatic L-amino acid decarboxylase deficiency	Intracerebral	InTrial	2Q2024	Yes	Yes
EB-101	EB-101	Abeona Therapeutics	gene therapy	Epidermolysis Bullosa	TOP	InTrial	2Q2024	Yes	Yes
SPN-830	apomorphine	Supernus Pharmaceuticals	non-ergoline dopamine agonist	Parkinson’s disease	SC infusion	CRL	2Q2024	Yes	No
LAI-287	insulin icodec	Novo Nordisk	ultra-long-acting basal insulin	Diabetes mellitus	SC	Filed BLA	1H2024	No	No
AXS-07	meloxicam/rizatriptan	Axsome Therapeutics	non-steroidal anti-inflammatory drug/triptan	Migraine	PO	CRL	1H2024	No	No
P2B-001	pramipexole/ rasagiline	Pharma Two B	dopamine agonist/ monoamine oxidase B inhibitor	Parkinson's disease	PO	InTrial	1H2024	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
Hepcludex	bulevirtide	Gilead	HBV receptor binder	Hepatitis delta virus	SC	CRL	1H2024	Yes	Yes
arimoclomol	arimoclomol	Orphazyme	cytoprotectives	Niemann-Pick disease	PO	CRL	1H2024	Yes	Yes
Risvan	risperidone	Laboratorios Farmacéuticos Rovi	atypical antipsychotic	Schizophrenia	IM	CRL	1H2024	Yes	No
DAY-101	DAY-101	Day One Biopharmaceuticals	pan-Raf kinase inhibitor	Brain cancer	PO	InTrial	1H2024	Yes	Yes
ALXN-2040	danicopan	AstraZeneca	complement factor D inhibitor	Paroxysmal nocturnal hemoglobinuria	PO	Filed NDA	1H2024	Yes	Yes
PB-2452	bentracimab	SFJ Pharmaceuticals	antiplatelet monoclonal antibody	Antiplatelet drug toxicity	IV	InTrial	Mid-2024	No	No
X4P-001 (X-4P-001, X4-136, X4P-001-RD)	mavorixafor	X4 Pharma	CXC receptor type 4 inhibitor	WHIM syndrome	PO	InTrial	Mid-2024	Yes	Yes
AT-007	govorestat	Applied Therapeutics	aldose reductase inhibitor	Galactosemia	PO	InTrial	Mid-2024	Yes	Yes
ADP-A2M4 (MAGE-A4)	afamitresgene autoleucel	Adaptimmune	SPEAR T-cell therapy	Sarcoma	IV	InTrial	Mid-2024	Yes	Yes
RP-L102 (RPL-102)	RP-L102	Rocket Pharmaceuticals	gene therapy	Fanconi anemia	IV	InTrial	Mid-2024	Yes	Yes
SPI-014	lanthanum dioxycarbonate	Unicycive	phosphate binder	Hyperphosphatemia	PO	InTrial	Mid-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
PF-06939926	fordadistrogene movaparvovec	Pfizer	gene therapy	Duchenne muscular dystrophy	IV	InTrial	Mid-2024	Yes	Yes
RG-6107	crovalimab	Roche	C5 inhibitor	Paroxysmal nocturnal hemoglobinuria	IV/SC	Filed BLA	Mid-2024	Yes	Yes
Cx-601	darvadstrocel	Takeda	allogeneic stem cell therapy	Crohn's disease	IV	InTrial	Mid-2024	Yes	Yes
RG-6058	tiragolumab	Roche	TIGIT monoclonal antibody	Non-small cell lung cancer/ esophageal cancer	IV	InTrial	Mid-2024	Yes	No
SNDX-5613	revumenib	Syndax	Menin-mixed lineage leukemia 1 inhibitor	Acute myelogenous leukemia	PO	InTrial	Mid-2024	Yes	Yes
SNDX-6352	axatilimab	Syndax Pharmaceuticals	colony stimulating factor 1 receptor monoclonal antibody	Graft vs. host disease	IV	InTrial	Mid-2024	Yes	Yes
Obe-cel	obecabtagene autoleucel	Autolus Therapeutics	autologous chimeric antigen receptor T-cells	Acute lymphoblastic leukemia	IV	InTrial	Mid-2024	Yes	Yes
TC-002	latanoprost	TearClear	prostaglandin analog	Glaucoma	OPH	InTrial	Mid-2024	No	No
mRNA-1345	mRNA-1345	Moderna	vaccine	Respiratory syncytial virus	IM	InTrial	Mid-2024	No	No
UX-111 (ABO-102)	UX-111	Ultragenyx Pharmaceutical	gene therapy	Sanfilippo syndrome type A	IV	InTrial	Mid-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
Oral semaglutide (weight loss)	semaglutide	Novo Nordisk	glucagon-like peptide 1 receptor agonist	Chronic weight management	PO	InTrial	Mid-2024	No	No
Leqembi SC	lecanemab	Eisai/Biogen	beta-amyloid targeted therapy	Alzheimer's disease	SC	InTrial	Mid-2024	Yes	No
ALPHA-1062	galantamine prodrug	Alpha Cognition	acetylcholinesterase inhibitor	Alzheimer's disease	PO	InTrial	3Q2024	No	No
MDMA	midomafetamine	MAPS Public Benefit Corporation	psychoactive drug	Post-traumatic stress disorder	PO	InTrial	3Q2024	Yes	No
MSP-2017	etripamil	Milestone	calcium channel blocker	Arrhythmia	Intranasal	InTrial	3Q2024	No	No
KarXT	xanomeline/ trospium	Karuna Therapeutics	muscarinic acetylcholine receptor agonist/ muscarinic receptor antagonist	Schizophrenia	PO	InTrial	3Q2024	No	No
TAVT-45	abiraterone acetate	Tavanta Therapeutics	CYP17 inhibitor	Prostate cancer	PO	InTrial	3Q2024	Yes	No
OX-125	nalmefene	Orexo	opioid receptor antagonist	Opioid use disorder	Intranasal	InTrial	3Q2024	No	No
AXS-14	S-reboxetine	Axsome Therapeutics	selective noradrenaline reuptake inhibitor	Fibromyalgia	PO	InTrial	4Q2024	No	No
Donesta	estetrol	Mithra Pharmaceuticals	estrogen	Vasomotor symptoms	PO	InTrial	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
nemolizumab	nemolizumab	Galderma	interleukin-31 receptor antagonist	Atopic dermatitis	SC	InTrial	2H2024	Yes	No
REGN-1979	odronextamab	Regeneron	CD20/CD3 monoclonal antibody	Follicular lymphoma/ diffuse large b-cell lymphoma	IV	InTrial	2H2024	Yes	Yes
GFT-505	elafibranor	Genfit	selective peroxisome proliferator-activated receptor modulator	Primary biliary cirrhosis	PO	InTrial	2H2024	Yes	Yes
GSK-2140944	gepotidacin	GlaxoSmithKline	bacterial Type II topoisomerase inhibitor	Bacterial infections	PO/IV	InTrial	2H2024	No	No
AVB-S6-500	batiraxcept	Aravive Biologics	GAS6/AXL inhibitor	Ovarian cancer	IV	InTrial	2H2024	Yes	No
REGN-5458	linvoseltamab	Regeneron	BCMA and CD3 bispecific antibody inhibitor	Multiple myeloma	IV	InTrial	2H2024	Yes	No
AG-10 (AG10)	acoramidis	BridgeBio	tetrameric transthyretin stabilizer	Transthyretin amyloid cardiomyopathy	PO	InTrial	2H2024	Yes	No
SAR-408701	tusamitamab ravtansine	Sanofi	antibody-drug conjugate	Non-small cell lung cancer	IV	InTrial	2H2024	Yes	No
CF-101	piclidenoson	Can-Fite BioPharma	A3 adenosine receptor agonist	Plaque psoriasis	PO	InTrial	2H2024	Yes	No
ZP-1848	glepaglutide	Zealand Pharma	glucagon peptide-2 agonist	Short bowel syndrome	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
Dasynoc	dasatinib	Xspray Pharma	kinase inhibitor	Chronic myeloid leukemia	PO	CRL	2H2024	Yes	Yes
CUTX-101	copper histidinate	Fortress Biotech	copper replacement	Menkes Disease	SC	InTrial	2H2024	Yes	Yes
PF-06741086	marstacimab	Pfizer	tissue factor pathway inhibitor	Hemophilia	IV/SC	InTrial	2H2024	Yes	Yes
CSL-312	garadacimab	CSL Limited	anti-factor XIIa monoclonal antibody	Hereditary angioedema	SC	InTrial	2H2024	Yes	Yes
RG-1594	ocrelizumab	Genentech	CD20-directed cytolytic antibody	Multiple sclerosis	SC	InTrial	2H2024	Yes	No
F-901318	olorofim	F2G	orotomide antifungal	Aspergillosis	PO/IV	CRL	2H2024	No	Yes
XMT-1536	upifitamab rilsodotin	Mersana Therapeutics	antibody-drug conjugate	Ovarian cancer	IV	InTrial	2H2024	Yes	No
HP-5000	diclofenac	Hisamitsu Pharmaceutical	non-steroidal anti-inflammatory drug	Osteoarthritis	Transdermal	InTrial	2H2024	No	No
BBP-305	encaleret	BridgeBio	Ca sensing receptor antagonist	Autosomal dominant hypocalcemia type 1	PO	InTrial	2H2024	Yes	Yes
PTC-923	sepiapterin	PTC Therapeutics	phenylalanine hydroxylase activator	Phenylketonuria	PO	InTrial	2H2024	Yes	Yes
RP-1	vusolimogene oderparepvec	Replimune	oncolytic immunotherapy	Cutaneous skin cell cancer	Intratumoral	InTrial	2H2024	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
ZW-25	zanidatamab	Zymeworks	HER2 monoclonal antibody	Biliary tract cancer	IV	InTrial	2H2024	Yes	Yes
Multikine	leukocyte interleukin (CS-001P3)	CEL-SCI	immunomodulator	Head and Neck cancer	SC	InTrial	2024	Yes	Yes
ND-0612H	levodopa/ carbidopa	NeuroDerm	dopamine precursor/ dopa-decarboxylase inhibitor	Parkinson's disease	SC	InTrial	2024	Yes	No
Translarna	ataluren	PTC Therapeutics	gene transcription modulator	Duchenne muscular dystrophy	PO	CRL	2024	Yes	Yes
SDN-037	difluprednate	Visiox	corticosteroid	Ocular inflammation/pain	OPH	InTrial	2024	No	No
SYD-985	[vic-] trastuzumab duocarmazine	Byondis	HER2-targeting antibody-drug conjugate	Breast cancer	IV	CRL	2024	Yes	No
TransCon PTH	palopegteriparatide	Ascendis Pharma	parathyroid hormone	Hypoparathyroidism	SC	CRL	2024	Yes	Yes
NRX-101 (Cyclurad)	d-cycloserine/ lurasidone	NeuroRx	N-methyl-D-aspartate receptor modulator/ 5-HT2A receptor antagonist	Bipolar disorder	PO	InTrial	2024	No	No
OMS-721	narsoplimab	Omeros	anti-MASP-2 monoclonal antibody	Hematopoietic stem cell transplant-associated thrombotic microangiopathy	IV	CRL	2024	Yes	Yes
MT-7117	dersimelagon	Mitsubishi Tanabe Pharma	Undisclosed	Erythropoietic protoporphyria	PO	InTrial	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
MOR-202	felzartamab	I-Mab	anti-CD38 monoclonal antibody	Multiple myeloma	IV	InTrial	2024	Yes	No
Humacyl	human acellular vessel	Humacyte	cellular therapy	End-stage renal disease	Implant	InTrial	2024	Yes	No
DS-100	dehydrated alcohol	Eton	undisclosed	Methanol poisoning	SC	CRL	2024	No	Yes
Mino-Lok	minocycline-EDTA-ETOH	Citrus	tetracyclines	Bacterial infection	Intracatheter	InTrial	2024	No	No
ABBV-951	foscarbidopa/ foslevodopa	AbbVie	aromatic amino acid decarboxylation inhibitor/ aromatic amino acid	Parkinson's disease	SC	CRL	2024	Yes	No
ALT-803	nogapendekin alfa inbakicept	ImmunityBio	interleukin-15 (IL-15) super agonist/ IL-15R alpha-Fc fusion complex	Bladder cancer	Intravesical	CRL	2024	Yes	No
I/Ontak	denileukin diftitox	Citius	CD25-directed cytotoxin	Cutaneous T-cell lymphoma	IV	CRL	2024	Yes	Yes
RG-7433 (ABT-263)	navitoclax	AbbVie	Bcl-2 inhibitor	Myelofibrosis	PO	InTrial	2024	Yes	Yes
NN-7415	concizumab	Novo Nordisk	anti-tissue factor pathway inhibitor	Hemophilia A and hemophilia B	SC	CRL	2024	Yes	Yes
Dihydroergotamine autoinjector	dihydroergotamine	Amneal Pharmaceuticals	ergot derivative	Migraine	SC	InTrial	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
D-PLEX100	doxycycline	PolyPid	tetracycline	Surgical site infections	IMPLANT	InTrial	2024	No	No
LY-03010	paliperidone	Luye Pharma	atypical antipsychotic	Schizophrenia	IM	InTrial	2024	No	No
AZD-5156	AZD-5156	AstraZeneca	monoclonal antibody	COVID-19	IM	InTrial	2024	No	No
PAX-101	suramin	PaxMedica	unknown	trypanosomiasis	IV	InTrial	Late 2024	No	No
APN-311	dinutuximab beta	Recordati	anti-GD2 antigen	Neuroblastoma	IV	InTrial	Late 2024	Yes	Yes
EBV-CTL (ATA-129)	tabelecleucel	Atara Biotherapeutics	cell therapy	Lymphoproliferative disorder	IV	InTrial	Late 2024	Yes	Yes
Ovastat	treosulfan	Medexus Pharmaceuticals	alkylating agent	Hematopoietic stem cell transplantation	IV	InTrial	Late 2024	Yes	Yes
CTP-543	deuruxolitinib	Sun Pharma	janus kinase inhibitor	Alopecia areata	PO	InTrial	Late 2024	Yes	No
MT-1621	deoxythymidine/ deoxycytidine	UCB	deoxynucleoside	Thymidine kinase 2 deficiency	PO	InTrial	Late 2024	Yes	Yes
MAT-2203	amphotericin B	Matinas BioPharma	fungicidal agent	Cryptococcal meningitis	PO	InTrial	Late 2024	No	Yes
IONIS-APOCIII-LRx (ISIS-678354)	olezarsen	Ionis	antisense drug	Familial chylomicronemia syndrome	SC	InTrial	Late 2024	Yes	No
CAM-2029	octreotide	Camurus	somatostatin analogue	Acromegaly	SC	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
NBI-74788	crinecerfont	Neurocrine Biosciences	CRF receptor antagonist	Congenital adrenal hyperplasia	PO	InTrial	Late 2024	Yes	Yes
ABBV-399	telisotuzumab	AbbVie	antibody (anti-c-Met)-drug conjugate	Non-small cell lung cancer	IV	InTrial	Late 2024	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	Indication Type	New/Revised Indication	Route	Estimated Approval Date
Wilate	von Willebrand factor/coagulation factor VIII complex	Octapharma	von Willebrand Factor	Revised	Routine prophylaxis to reduce the frequency of bleeding episodes in children and adults with any type of von Willebrand disease	IV	08/23/2023
Reblozyl	luspatercept-aamt	Bristol Myers Squibb	erythroid maturation agent	Revised	Treatment of anemia without previous use of erythropoiesis-stimulating agents in adult patients with very low- to intermediate-risk myelodysplastic syndromes who may require red blood cell transfusions	SC	08/28/2023
Cosentyx	secukinumab	Novartis	interleukin-17 receptor antagonist	New	Treatment of hidradenitis suppurativa	SC	08/31/2023
Adbry	tralokinumab-ldrm	Leo Pharma	interleukin-13 antagonist	Revised	Treatment of moderate-to-severe atopic dermatitis in adolescents patients whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable	SC	3Q2023
Onpattro	patisiran	Alnylam	RNAi therapeutic	New	Treatment of transthyretin amyloidosis patients with cardiomyopathy	IV	10/08/2023
Opdivo	nivolumab	Bristol Myers Squibb	programmed death receptor-1-blocking antibody	Revised	Monotherapy in the adjuvant setting for the treatment of patients with completely resected stage IIB or IIC melanoma	IV	10/13/2023

Brand Name	Generic Name	Company	Mechanism	Indication Type	New/Revised Indication	Route	Estimated Approval Date
Keytruda	pembrolizumab	Merck	programmed death receptor-1-blocking antibody	Revised	Treatment of patients with resectable stage II, IIIA, or IIIB non-small cell lung cancer in combination with platinum containing chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment	IV	10/16/2023
Zoryve	roflumilast	Arcutis Biotherapeutics	phosphodiesterase-4 inhibitor	Revised	Treatment of plaque psoriasis in children ages 2 to 11	TOP	10/19/2023
Voxzogo	vosoritide	BioMarin	C type natriuretic peptide analog	Revised	To increase linear growth in pediatric patients with achondroplasia who are under 5 years of age	SC	10/21/2023
Dupixent	dupilumab	Sanofi/ Regeneron	interleukin-4/13 inhibitor	New	Treatment of adults and adolescents aged 12 years and older with chronic spontaneous urticaria that is not adequately controlled with the current standard of care, H1 antihistamine treatment	SC	10/22/2023
Jardiance	empagliflozin	Boehringer Ingelheim/ Eli Lilly	sodium-dependent glucose transporter 2 inhibitor	New	To reduce kidney disease progression and cardiovascular mortality risk in patients with chronic kidney disease	PO	10/2023
Exparel	bupivacaine (liposomal suspension)	Pacira	local anesthetic	New	For sciatic nerve block in the popliteal fossa as well as femoral nerve block in the adductor canal	INJ	11/13/2023
Cresemba	isavuconazonium	Astellas	azole antifungal	Revised	Treatment of invasive aspergillosis and invasive mucormycosis in pediatric patients	PO/IV	12/09/2023
Livmarli	maralixibat	Mirum Pharmaceuticals	ileal bile acid transporter inhibitor	New	Treatment of pruritus in patients 2 years of age and older with progressive familial intrahepatic cholestasis	PO	12/14/2023

Brand Name	Generic Name	Company	Mechanism	Indication Type	New/Revised Indication	Route	Estimated Approval Date
Tibsovo	ivosidenib	Servier	isocitrate dehydrogenase-1 inhibitor	New	Treatment of patients with isocitrate dehydrogenase 1 (IDH1)-mutated relapsed or refractory myelodysplastic syndromes	PO	12/15/2023
Abecma	idecabtagene vicleucel	Bristol Myers Squibb	B-cell maturation antigen-directed genetically modified autologous T cell immunotherapy	Revised	Treatment of adult patients with relapsed and refractory multiple myeloma who have received an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody	IV	12/16/2023
Xhance	fluticasone	Optinose	corticosteroid	New	Treatment of chronic sinusitis	Intranasal	12/16/2023
Keytruda	pembrolizumab	Merck	programmed death receptor-1-blocking antibody	Revised	In combination with fluoropyrimidine- and platinum-containing chemotherapy, for the first-line treatment of patients with locally advanced unresectable or metastatic gastric or gastroesophageal junction adenocarcinoma	IV	12/16/2023
Vabysmo	faricimab	Roche/ Genentech	vascular endothelial growth factor and angiopoietin-2 inhibitor	New	Treatment of macular edema following retinal vein occlusion	Intravitreal	12/22/2023
Xtandi	enzalutamide	Pfizer/ Astellas	androgen receptor inhibitor	Revised	Treatment of non-metastatic castration-sensitive prostate cancer	PO	12/23/2023
Braftovi	encorafenib	Pfizer	kinase inhibitor	New	In combination with Mektovi (binimetinib), for patients with metastatic non-small cell lung cancer with a BRAF V600E mutation, as detected by an FDA-approved test	PO	4Q2023
Mektovi	binimetinib	Pfizer	kinase inhibitor	New	In combination with Braftovi (encorafenib), for patients with metastatic non-small cell	PO	4Q2023

Brand Name	Generic Name	Company	Mechanism	Indication Type	New/Revised Indication	Route	Estimated Approval Date
					lung cancer with a BRAF V600E mutation, as detected by an FDA-approved test		
Carvykti	ciltacabtagene autoleucel	J&J	B-cell maturation antigen-directed genetically modified autologous T cell immunotherapy	Revised	Treatment of relapsed and refractory multiple myeloma in patients with 1 to 3 prior lines of therapy	IV	01/08/2024
Edurant	rilpivirine	Janssen	non-nucleoside reverse transcriptase inhibitor	Revised	In combination with other antiretroviral agents for the treatment of HIV-1 infection in treatment-naïve patients 2 years of age and older and weighing at least 10 kg with HIV-1 RNA less than or equal to 100,000 copies/mL	PO	01/28/2024
Keytruda	pembrolizumab	Merck	programmed death receptor-1-blocking antibody	New	In combination with standard of care chemotherapy (gemcitabine and cisplatin) for the treatment of patients with locally advanced unresectable or metastatic biliary tract cancer	IV	02/07/2024
Onivyde	irinotecan	Ipsen	topoisomerase inhibitor	Revised	In combination with fluorouracil/leucovorin and oxaliplatin as first-line treatment for metastatic pancreatic ductal adenocarcinoma	IV	02/13/2024
Ixinity	coagulation factor IX (recombinant)	Medexus Pharmaceuticals	human blood coagulation factor	Revised	On-demand, prophylactic, and perioperative treatment of pediatric patients under 12 years of age with hemophilia B	IV	02/15/2024
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	03/25/2024

Brand Name	Generic Name	Company	Mechanism	Indication Type	New/Revised Indication	Route	Estimated Approval Date
Brukinsa	zanubrutinib	BeiGene	kinase inhibitor	New	In combination with obinutuzumab for the treatment of adult patients with relapsed or refractory follicular lymphoma after at least two prior lines of therapy	PO	1Q2024
Nexletol	bempedoic acid	Esperion	adenosine triphosphate-citrate lyase inhibitor	New	To reduce the risk of cardiovascular events in statin intolerant patients	PO	04/01/2024
Zegalogue	dasiglucagon	Zealand Pharma	antihypoglycemic agent	New	Prevention and treatment of hypoglycemia in pediatric patients 7 days of age or older with congenital hyperinsulinism	SC	04/30/2024
Gammagard Liquid	immune globulin (human)	Takeda	immune globulin	New	Treatment of chronic inflammatory demyelinating polyneuropathy	IV/SC	1H2024

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