RxOutlook®

4th Quarter 2022

Optum Rx®

In this edition of RxOutlook, we highlight 12 key pipeline drugs with an expected FDA decision in the first quarter of 2023. Next year will kick off with high profile FDA decisions on two drugs for Alzheimer's disease: lecanemab and donanemab. Both drugs, like Aduhelm® (aducanumab), are beta-amyloid targeted antibodies, and are being reviewed via the accelerated approval pathway based on a surrogate endpoint – reductions in beta amyloid in the brain. These initial accelerated approval decisions will generate attention; however, Phase 3 confirmatory trial results and the FDA's review of the data for both products will be critical for not only the success of these products but the perception of the beta-amyloid hypothesis in the treatment of Alzheimer's disease.

The number of gene therapies is expected to grow over the next 6 months as four products are currently under review by the FDA, including two with approval decisions potentially in the first quarter: Vyjuvek for dystrophic epidermolysis bullosa (DEB), a rare dermatologic condition, and Roctavian for hemophilia A. Unlike other traditional gene therapies, Vyjuvek is a redosable topical (intradermal) product that is administered weekly to patients with DEB-associated wounds until they experience would closure. Roctavian is a one-time gene therapy that would represent a potential opportunity to significantly reduce or eliminate the need for chronic prophylactic factor VIII replacement therapy in some patients.

Two additional noteworthy drugs with approvals decisions in the first quarter of next year are fezolinetant and pegcetacoplan. Fezolinetant is a first-in-class, non-hormonal treatment for menopause associated-vasomotor symptoms (VMS) and would represent a potentially better tolerated alternative to the current standard of care (hormone therapy and antidepressants). An intravitreal formulation of pegcetacoplan is under review for the treatment of geographic atrophy, a severe form of dry age-related macular degeneration (AMD). Unlike wet AMD, the other severe form of AMD, there are currently no effective treatments for geographic atrophy.

Other drugs included in the report are daprodustat for anemia associated with chronic kidney disease; elacestrant for breast cancer; efanesoctocog alfa for hemophilia A; omecamtiv mecarbil for heart failure; trofinetide for Rett syndrome; and zavegepant for acute migraine headaches.

Key pipeline drugs with FDA approval decisions expected by end of the 1st quarter 2023

Drug Name	Manufacturer	Indication/Use	Expected FDA Decision Date
Lecanemab	Eisai/Biogen	Alzheimer's disease	1/6/2023
Donanemab	Eli Lilly	Alzheimer's disease	1/2023 – 2/2023
Daprodustat	GlaxoSmithKline	Chronic kidney disease-associated anemia	2/1/2023
Vyjuvek (beremagene geperpavec)	Krystal Biotech	Dystrophic epidermolysis bullosa*	2/17/2023
Elacestrant	Menarini Group/ Radius Health	Breast cancer	2/17/2023
Fezolinetant	Astellas Pharma	Menopause associated-vasomotor symptoms	2/22/2023
Pegcetacoplan	Apellis	Geographic atrophy	2/26/2022

Drug Name	Manufacturer	Indication/Use	Expected FDA Decision Date
Efanesoctocog alfa	Sanofi/Sobi	Hemophilia A*	2/28/2023
Omecamtiv mecarbil	Cytokinetics	Heart failure	2/28/2023
Trofinetide	Acadia Pharmaceuticals	Rett syndrome*	3/12/2023
Roctavian (valoctocogene roxaparvovec)	BioMarin	Hemophilia A*	3/31/2023
Zavegepant	Biohaven Pharmaceutical	Acute migraine	1Q 2023

* Orphan Drug Designation

Optum Rx closely monitors and evaluates the drug development pipeline to identify noteworthy upcoming drug approvals and reports the essential findings here in RxOutlook. The report is organized in the following manner:

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 1st 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 1st quarter 2023 may appear in future reports; however, for those who need an initial look at the full 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

Lecanemab (Brand Name: To be determined)

Manufacturer: Eisai/Biogen
Regulatory designation: Breakthrough Therapy, Fast Track
Expected FDA decision: January 6, 2023

Therapeutic use

Lecanemab is under review for the treatment of mild cognitive impairment (MCI) due to Alzheimer's disease and mild Alzheimer's disease (collectively known as early Alzheimer's disease).

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's the 5th leading cause of death among adults aged 65 years or older.

- Treatment of MCI due to Alzheimer's disease and mild Alzheimer's disease

Lecanemab (continued…)

Clinical profile

Lecanemab is a monoclonal antibody that binds to soluble beta amyloid aggregates (oligomers and protofibrils) with high selectivity.

Pivotal trial data:
The FDA submission for accelerated approval for lecanemab was based on Study 201, a randomized, double-blind, placebo-controlled study in 854 patients with early Alzheimer's disease. The study used response adaptive randomization across placebo and five lecanemab arms (2.5 mg/kg biweekly, 5 mg/kg monthly, 5 mg/kg biweekly, 10 mg/kg monthly, 10 mg/kg biweekly). The primary endpoint was a Bayesian analysis of 12-month clinical change on the Alzheimer's Disease Composite Score (ADCOMS) for the 10 mg/kg biweekly dose, which required an 80% probability of ≥ 25% clinical reduction in decline vs. placebo. A key secondary endpoint was brain amyloid reduction.

At 12 months, the 10 mg/kg biweekly dose showed a 64% probability to be better than placebo by 25% on ADCOMS, which missed the 80% threshold for the primary endpoint. At 18 months, 10 mg/kg biweekly lecanemab reduced brain amyloid while demonstrating trends in favor of lecanemab over placebo for other secondary clinical outcomes.

Additionally, Eisai and Biogen announced topline results from Clarity AD, a confirmatory Phase 3, randomized, placebo-controlled, double-blind study in 1,795 patients with early AD. Patients received lecanemab 10 mg/kg biweekly or placebo. The primary endpoint was the change from baseline in the Clinical Dementia Rating-Sum of Boxes (CDR-SB) score at 18 months. The CDR is an evaluation of a patient's cognitive status across 6 domains of functioning including memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. The CDR-SB score is obtained by summing each of the domain box scores, with scores ranging from 0 to 18.

Lecanemab treatment met the primary endpoint in CLARITY AD and reduced clinical decline on CDR-SB by 27% compared with placebo, which represented a treatment difference in the score change of -0.45 ($p = 0.00005$). All key secondary endpoints were also met with statistically significant results compared with placebo ($p < 0.01$).

- Beta amyloid targeted monoclonal antibody
- IV formulation
- Phase 2 trial: Failed to meet primary clinical outcome endpoint but significantly reduced brain amyloid
- Phase 3 trial: Reduced clinical decline on CDR-SB by 27% (-0.45) vs. placebo
- Common AEs: ARIA-E, ARIA-H
- Dosing: Once every 2 weeks

Lecanemab (continued…)

Safety:
The most common adverse events with lecanemab use were amyloid related imaging abnormalities -edema (ARIA-E) and -hemosiderin deposition (ARIA-H).

Dosing:
In the pivotal trial, lecanemab was administered via intravenous (IV) infusion every 2 weeks.

Competitive environment

There is a high unmet need for treatments for Alzheimer's disease since it is a leading cause of morbidity and mortality among the elderly and existing treatment options have not shown benefit in reducing or slowing cognitive decline. The estimated target population is substantial as Alzheimer's disease affects over 6.5 million people in the U.S. and over 1 million people are estimated to be candidates for treatment with amyloid-beta targeted therapies based on early disease status and confirmed presence of amyloid beta.

Cholinesterase inhibitors (eg, Aricept® [donepezil]) and the NMDA inhibitor Namenda® (memantine) are currently available medications for cognition in patients with Alzheimer's disease but these drugs have limited benefit and are considered symptomatic therapies that do not change the underlying pathophysiology of the disease. In June 2021, the FDA approved Aduhelm® (aducanumab), the first amyloid beta-directed antibody, via the accelerated approval pathway based on reductions in amyloid beta plaques. However, a CMS National Coverage Determination limited Medicare coverage for Aduhelm and other beta-amyloid targeted therapies to patients enrolled in clinical trials because of unknown clinical benefit (eg, improvement in progression of disease).

Lecanemab would potentially be the second drug in the class with the initial accelerated approval expected to be similar to Aduhelm, based on the surrogate of reductions in beta amyloid plaques. The recently announced Phase 3 data demonstrated that lecanemab reduced clinical decline, but the benefit was small in magnitude and, although statistically significant, generally less than what would be considered clinically meaningful. Eisai will present the full Phase 3 study results on November 29, 2022, at the Clinical Trials on Alzheimer's Congress (CTAD) and is planning to discuss this data with the FDA with the aim to file for traditional (full) approval by the end of the first quarter in 2023.

Like Aduhelm, lecanemab is associated with ARIA-related side effects, including edema and microhemorrhages which would require additional provider monitoring. It may also face competition with Eli Lilly's donanemab, another beta-amyloid targeted antibody currently under FDA review via the accelerated approval pathway with a potential decision in January or February 2023. Lilly is expecting confirmatory Phase 3 trial results in the middle of 2023. Unlike Aduhelm and donanemab, lecanemab requires biweekly IV infusions as opposed to monthly dosing.

For reference, the Wholesale Acquisition Cost (WAC) for Aduhelm is approximately $28,000 per year.

- Advantages: Statistically significant reduction in cognitive decline, high unmet need, large potential target population
- Disadvantages: Lack of full clinical outcomes data, ARIA safety concern, biweekly IV infusions
- Reference WAC (Aduhelm): ~$28,000 per year

Donanemab (Brand Name: To be determined)

Manufacturer: Eli Lilly
Regulatory designation: Breakthrough Therapy
Expected FDA decision: January to February 2023

Therapeutic use

Donanemab is under review for the treatment of MCI due to Alzheimer's disease and mild Alzheimer's disease (collectively known as early Alzheimer's disease).

Clinical profile

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

Pivotal trial data:
The FDA submission for accelerated approval for donanemab was based on TRAILBLAZER-ALZ, a Phase 2, randomized, double-blind, placebo-controlled study in 257 patients with early symptomatic Alzheimer's disease. The primary endpoint was the change from baseline in the score on the Integrated Alzheimer's Disease Rating Scale (iADRS; range, 0 to 144, with lower scores indicating greater cognitive and functional impairment) at 76 weeks. Secondary outcomes included the change in scores on the Clinical Dementia Rating Scale-Sum of Boxes (CDR-SB), the 13-item cognitive subscale of the Alzheimer's Disease Assessment Scale (ADAS-Cog13), the Alzheimer's Disease Cooperative Study–Instrumental Activities of Daily Living Inventory (ADCS-iADL), and the Mini–Mental State Examination (MMSE). Biomarkers such as change in amyloid plaque level were also assessed.

The change from baseline in the iADRS score at 76 weeks was −6.86 in the donanemab group and −10.06 in the placebo group (difference 3.20; 95% CI: 0.12, 6.27; p = 0.04), suggesting that donanemab was associated with slower cognitive decline. The results for most secondary outcomes showed no substantial difference but there was a significant reduction in amyloid plaque levels.

Safety:
The most common adverse event with donanemab use were amyloid related imaging abnormalities -edema (ARIA-E) and -hemosiderin deposition (ARIA-H).

Dosing:
In the pivotal trials, donanemab was administered via IV infusion every 4 weeks.

- Treatment of MCI due to Alzheimer's disease and mild Alzheimer's disease
- Beta amyloid targeted monoclonal antibody
- IV formulation
- Phase 2 trial: iADRS score change from baseline: −6.86 vs. −10.06 with placebo
- Phase 3 trial: Results not yet available
- Common AEs: ARIA-E, ARIA-H
- Dosing: Once every 4 weeks

Donanemab (continued…)

Competitive environment

Like lecanemab, donanemab would be another beta-amyloid targeted therapy for the treatment of Alzheimer's disease. As discussed previously, there is a high unmet need for additional treatments for Alzheimer's disease.

Like lecanemab, Eli Lilly is pursuing an accelerated approval for donanemab based on Phase 2 data demonstrating improvements in the surrogate marker of amyloid plaque levels. Eli Lilly expects data from the Phase 3 TRAILBLAZER-ALZ-2 study by the middle of 2023. If positive, the Phase 3 study could serve as the confirmatory trial for a traditional (full) approval. Until this data is available, the clinical benefit with donanemab is uncertain.

Like the other drugs in the class, donanemab is associated with ARIA-related side effects which would require additional provider monitoring and it must be administered via IV infusion.

For reference, the WAC for Aduhelm is approximately $28,000 per year.

- Advantages: High unmet need, large potential target population
- Disadvantages: Uncertain clinical outcomes benefit, ARIA safety concerns, IV infusions
- Reference WAC (Aduhelm): ~$28,000 per year

Daprodustat (Brand Name: To be determined)

Manufacturer: GlaxoSmithKline
Expected FDA decision: February 1, 2023

Therapeutic use

Daprodustat is under review for the treatment of anemia of chronic kidney disease (CKD) in dialysis and non-dialysis patients.

Anemia is a common complication of CKD and occurs because patients with the disease do not produce enough erythropoietin, a hormone that helps regulate production of red blood cells. More than 37 million American adults may have CKD and it is estimated that more than 1 out of every 7 people with kidney disease have anemia. The risk of anemia increases as kidney function declines.

- Treatment of anemia of CKD in dialysis and non-dialysis patients

Clinical profile

Daprodustat is a hypoxia-inducible factor prolyl hydroxylase (HIF-PH) inhibitor designed to mimic the physiologic effect of altitude on oxygen availability. At higher altitudes, the body responds to lower oxygen availability with stabilization of hypoxia-inducible factor, which can increase red blood cell production and improve oxygen delivery to tissues.

- HIF-PH inhibitor
- Oral formulation
- Change in hemoglobin: Noninferiority met vs. ESAs in dialysis-dependent and dialysis-independent CKD patients
- Common AEs: Hypertension, diarrhea, dialysis hypotension, peripheral edema, urinary tract infection
- Dosing: Once daily

Pivotal trial data:
The efficacy of daprodustat was evaluated in two large Phase 3 trials (ASCEND-D and ASCEND-ND). ASCEND-D was a randomized, open-label study in 2,964 dialysis patients with anemia of CKD who were on standard of care erythropoiesis-stimulating agents (ESA). Patients were randomized to switch to daprodustat or an injectable ESA (epoetin alfa if they were receiving hemodialysis or darbepoetin alfa if they were receiving peritoneal dialysis). The two primary outcomes were the mean change in the hemoglobin level from baseline to weeks 28 through 52 (noninferiority margin, -0.75 g/dL) and the first occurrence of a major adverse cardiovascular event (MACE) (a composite of death from any cause, non-fatal myocardial infarction, or non-fatal stroke) (noninferiority margin of 1.25 for the hazard ratio [HR]).

The mean change in the hemoglobin level from baseline to weeks 28 through 52 was 0.28 g/dL in the daprodustat group and 0.10 g/dL in the ESA group (difference 0.18 g/dL; 95% CI: 0.12, 0.24), which met the prespecified noninferiority margin. During a median follow-up of 2.5 years, a MACE occurred in 25.2% of patients in the daprodustat group and in 26.7% in the ESA group (HR 0.93; 95% CI: 0.81, 1.07), which also met the prespecified noninferiority margin for daprodustat.

ASCEND-ND was a randomized, open-label study in 3,872 non-dialysis dependent patients with anemia associated with CKD who were either switched from standard of care (ESA) or not currently receiving ESA therapy to receive daprodustat or ESA control (darbepoetin alfa). Primary outcomes were the same as in ASCEND-D.

Daprodustat (continued...)

The mean change in the hemoglobin level from baseline to weeks 28 through 52 was 0.74 g/dL in the daprodustat group and 0.66 g/dL in the darbepoetin alfa group (difference 0.08 g/dL; 95% CI: 0.03, 0.13), which met the prespecified noninferiority margin. During a median follow-up of 1.9 years, a first MACE occurred in 19.5% of patients in the daprodustat group and in 19.2% of patients in the darbepoetin alfa group (HR 1.03; 95% CI 0.89, 1.19), which met the prespecified noninferiority margin.

Safety:
The most common adverse events with daprodustat use were hypertension, diarrhea, dialysis hypotension, peripheral edema, and urinary tract infection.

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

Competitive environment

If approved, daprodustat would potentially be the first novel therapy for the treatment of CKD-related anemia since the introduction of ESAs and would offer an oral alternative to injectable products. In the head-to-head trials vs. an ESA, daprodustat provided similar improvements in hemoglobin in both dialysis and non-dialysis dependent patients.

Daprodustat is the third drug in the HIF-PH inhibitor class reviewed by the FDA. Roxadustat and vadadustat both received Complete Response Letters from the FDA with the primary reason cited for the rejections being cardiovascular safety.

An FDA Advisory Committee was convened to review daprodustat on October 26. The Committee voted 13 to 3 that the benefits outweighed the risks in adults on dialysis. The negative votes were primarily driven by safety concerns such as hospitalization for heart failure and bleeding gastric erosions. However, the Committee voted 11 to 5 that the benefits of daprodustat do not outweigh its risks for adults not on dialysis. In non-dialysis patients, daprodustat appears to have several other important risks in addition to the risks of heart failure and bleeding gastric erosions. The FDA found elevated risks for MACE based on several analyses (eg, when evaluated using a supportive on-treatment analysis; when analyzed in the U.S. subgroup of patients; and when analyzed using cardiovascular death instead of all-cause mortality in the MACE composite). Compared to ESAs, the FDA review also noted elevated estimated risks for cardiovascular mortality, myocardial infarction, stroke, thromboembolic disease, and vascular access thrombosis. Since ESAs already carry some of these risks, a further increase in these risks beyond that seen with the ESAs was concerning.

If daprodustat does get FDA approval but use is limited to dialysis patients, this would significantly reduce the target population for the drug as only a fraction of the CKD population is dialysis-dependent. Of the millions of people in the U.S. with anemia-associated CKD, approximately 550,000 are estimated to be on dialysis. Additionally, dialysis-dependent patients usually receive ESA treatment at the time of dialysis, so there is less of an unmet need for an oral alternative to injectables in these patients.

- Advantages: Novel MOA, oral alternative to injectable ESAs
- Disadvantages: Competing with ESAs – with biosimilars available, safety concerns (eg, cardiovascular and GI bleeds/erosions), indication may be limited to dialysis patients only

Beremagene geperpavec (Brand Name: Vyjuvek)

Manufacturer: Krystal Biotech
Regulatory designations: Orphan Drug, Fast Track
Expected FDA decision: February 17, 2023

Therapeutic use

- Treatment of DEB

Beremagene geperpavec is under review for the treatment of dystrophic epidermolysis bullosa (DEB).

DEB is a genetic disorder characterized by fragile skin that blisters easily from friction or trauma. It's caused by mutations in the COL7A1 gene which encodes for type VII collagen. Patients with DEB can suffer from pain, open wounds, fibrosis which can cause fusion of fingers and toes, and it is associated with an increased risk of squamous cell carcinoma. While the severity can vary depending on the patient, severe cases of DEB can be disabling and potentially fatal.

Krystal Biotech estimates that there are 3,000 people affected with DEB in the U.S.

Clinical profile

- Gene therapy delivering *COL7A1* gene
- Topical (intradermal) formulation
- Complete wound closure: 67.4% vs. 21.6% with placebo
- Dosing: Once weekly until wound closure

Beremagene geperpavec is a topical, redosable gene therapy designed to deliver two copies of the COL7A1 gene when applied directly to DEB wounds. Unlike typical gene therapies, which are one-time doses, beremagene geperpavec is applied repeatedly until wounds are healed.

Pivotal trial data:
The efficacy of beremagene geperpavec was evaluated in GEM-3, a Phase 3, intra-patient, randomized, double-blind, placebo-controlled study in 31 DEB patients with confirmed *COL7A1* mutations. Each patient contributed 1 primary wound pair, randomized to weekly treatment with beremagene geperpavec or placebo for 26 weeks. The primary endpoint was complete wound healing at 6 months. Complete wound healing defined as 100% wound closure from exact wound area at baseline, specified as skin re-epithelialization without drainage.

Complete wound closure at month 6 occurred in 67.4% of patients with beremagene geperpavec vs. 21.6% for placebo (difference 45.8, 95% CI: 23.6, 68.0; $p < 0.005$).

Safety:
Beremagene geperpavec was well tolerated; there were no adverse events leading to treatment discontinuation or death.

Dosing:
In the pivotal trial, beremagene geperpavec was administered topically (intradermal) once weekly until wound closure.

Beremagene geperpavec (continued…)

Competitive environment

Beremagene geperpavec would potentially be the first approved treatment for DEB. There is a high unmet need for treatments as even light friction or trauma can cause the skin of a patient with DEB to tear or blister. The current standard of care is supportive treatment with wound care and prevention of infection. The efficacy results for beremagene geperpavec were promising and the gene therapy appears to be well tolerated.

However, unlike one-time gene therapies, beremagene geperpavec requires redosing and is not intended to be curative. Patients could require retreatment when new wounds develop and while beremagene geperpavec is a topical product, it must be administered by a healthcare provider. The expected target population is small given the overall rare nature of EB and that beremagene geperpavec is an option in patients with the DEB subtype. There is the potential for future competition as well, particularly with Abeona Therapeutics' EB-101, an autologous, gene-corrected cell therapy. Abeona intends to submit an application to the FDA in the second quarter of 2023.

- Advantages: Potentially the first approved treatment for DEB, high unmet need, promising efficacy and tolerability
- Disadvantages: Not curative, small target population, other pipeline therapies in development for EB (including Abeona Therapeutics' gene therapy, EB-101)

Elacestrant (Brand Name: To be determined)

Manufacturer: Menarini Group/Radius Health
Regulatory designations: Fast Track
Expected FDA decision: February 17, 2023

Therapeutic use

Elacestrant is under review for the treatment of estrogen receptor positive (ER+), human epidermal growth factor receptor 2 negative (HER2-) advanced or metastatic breast cancer.

Breast cancer is the second most common cancer in women in the U.S., behind only skin cancers. In 2022, about 287,850 new cases of invasive breast cancer will be diagnosed in women and about 43,250 women will die from breast cancer. Nearly 70% of all breast cancer cases are of the ER+/HER2- subtype.

- Treatment of ER+/HER2- advanced or metastatic breast cancer

Clinical profile

Elacestrant is a selective estrogen receptor degrader (SERD) that works by degrading the ER alpha and inhibiting estradiol-dependent ER-directed gene transcription and tumor growth.

- SERD
- Oral formulation
- 12-month PFS rate: 22.3% vs. 9.4% with standard of care
- Common AEs: Nausea, vomiting, fatigue, decreased appetite, arthralgia
- Dosing: Once daily

Pivotal trial data:
The efficacy of elacestrant was evaluated in EMERALD, a Phase 3, randomized, open-label, active-controlled study in 477 ER+/HER2- advanced or metastatic breast cancer patients. Patients had disease progression during or within 1 month following 1 or 2 lines of endocrine therapy and a cyclin-dependent kinase (CDK) 4/6 inhibitor. Patients could also have received 1 line of chemotherapy. Patients were randomized to receive elacestrant or standard of care (SOC) choice of Faslodex® (fulvestrant) (currently available injectable SERD) or an aromatase inhibitor. The primary endpoints were progression-free survival (PFS) in all patients and patients with detectable *estrogen receptor 1 (ESR1)* mutations.

PFS was prolonged in all patients (HR 0.70, 95% CI: 0.55, 0.88; p = 0.002) and patients with *ESR1* mutation (HR = 0.55, 95% CI: 0.39, 0.77; p = 0.0005). The PFS rate at 12 months with elacestrant was 22.3% vs. 9.4% with SOC in the overall population, and 26.8% vs. 8.2% in the *ESR1* mutation population. The median PFS was extended by 2.9 months with elacestrant vs 1.91 months with SOC in the overall population, and 3.78 months vs 1.87 months in the ESR1 mutation population.

Safety:
The most common adverse events with elacestrant use were nausea, vomiting, fatigue, decreased appetite, and arthralgia.

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

Elacestrant (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 ER+/HER2- breast cancer. Some patients develop endocrine therapy resistance after initial treatment, with mutations in the ESR1 gene being one contributor. This is an area of unmet need as ESR1 mutations are primarily associated with resistance to aromatase inhibitor therapy. A backbone of treatment in these patients usually includes fulvestrant, which is the only SERD currently approved. In contrast to elacestrant which is administered orally, fulvestrant requires monthly intramuscular (IM) injections.

The results from EMERALD 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. These regimens include fulvestrant plus a CDK4/6 inhibitor, fulvestrant plus everolimus, or in patients with a PIK3CA mutation, fulvestrant plus Piqray® (alpelisib).

The initial target population is likely to be limited for elacestrant but its place in therapy could grow if future trials are positive in earlier settings of breast cancer or if elacestrant demonstrates improves outcomes as part of combination regimens.

For reference, the WAC for brand Faslodex is approximately $24,000 per year.

- Advantages: Promising PFS data vs. monotherapy standard of care, first oral SERD, potential future use in earlier breast cancer settings
- Disadvantages: Lack of head-to-head data against standard of care combination regimens, narrow initial use (second- or third-line and potentially in patients with ESR1 mutations)
- Reference WAC (brand Faslodex): ~$24,000 per year

Fezolinetant (Brand Name: To be determined)

Manufacturer: Astellas Pharma
Expected FDA decision: February 22, 2023

Therapeutic use

Fezolinetant is under review for the treatment of moderate-to-severe vasomotor symptoms (VMS) associated with menopause.

VMS are a common complaint associated with menopause and characterized by hot flashes (also called hot flushes) and/or night sweats. A hot flash is a sudden warm feeling over the face, neck, and chest. These symptoms may range from an average of less than one each day to as many as one per hour during the day and night.

In the U.S., about 60% to 80% of women experience these symptoms during or after the menopausal transition.

- Treatment of moderate-to-severe VMS associated with menopause

Clinical profile

Fezolinetant is a neurokinin B (NKB) antagonist that binds to the kisspeptin/neurokinin/dynorphin (KNDy) neuron to moderate neuronal activity in the thermoregulatory center of the brain (the hypothalamus). After menopause, estrogen declines and NKB signaling is increased. It has been proposed that this results in unregulated KNDy neuron activation and vasomotor symptoms.

- NKB antagonist
- Oral formulation
- Change in daily frequency of VMS: Reduced by 1.86 to 2.55 with fezolinetant vs. placebo
- Change in daily severity of VMS: Reduced by 0.16 to 0.29 with fezolinetant vs. placebo
- Common AE: Headache
- Dosing: Once daily

Pivotal trial data:
The efficacy of fezolinetant was evaluated in two Phase 3, randomized, double-blind, placebo-controlled studies (SKYLIGHT 1 and SKYLIGHT 2) in 1,028 women aged 40 to 65 years with moderate-to-severe VMS (≥ 7 hot flashes/day). In both studies, patients were randomized to once daily fezolinetant 30 mg, fezolinetant 45 mg, or placebo. The co-primary endpoints were mean change from baseline to week 4 and 12 in frequency and severity of moderate-to-severe VMS.

In SKYLIGHT 1, daily mean frequency of VMS was reduced by -1.87 ($p < 0.001$) and -2.39 ($p < 0.001$) with fezolinetant 30 mg vs. placebo, at weeks 4 and 12, respectively. At the 45 mg dose, fezolinetant showed a -2.07 ($p < 0.001$) and -2.55 ($p < 0.001$) mean change at weeks 4 and 12, respectively. For the reduction in daily mean severity of moderate to severe VMS vs. placebo, fezolinetant 30 mg demonstrated a -0.15 ($p = 0.012$) and -0.24 ($p = 0.002$) mean change at weeks 4 and 12, respectively. The 45 mg dose of fezolinetant showed a -0.19 ($p = 0.002$) and -0.20 ($p = 0.007$) mean change vs. placebo at weeks 4 and 12, respectively.

In SKYLIGHT 2, fezolinetant 30 mg demonstrated a -1.82 ($p < 0.001$) and -1.86 ($p < 0.001$) mean change in VMS per day vs. placebo, at weeks 4 and 12, respectively. At the 45 mg dose, fezolinetant showed a -2.55 ($p < 0.001$) and -2.53 ($p < 0.001$) mean change per day in VMS frequency vs. placebo at weeks 4 and 12, respectively. Additionally, for the co-primary endpoint of reduction in mean severity of moderate to severe VMS vs. placebo, fezolinetant 30 mg demonstrated a -0.15 ($p = 0.021$) and -0.16 ($p = 0.049$) mean change per day at weeks 4 and 12, respectively. The 45 mg dose of fezolinetant showed a -0.29 ($p < 0.001$) mean change in severity per day vs. placebo at both weeks 4 and 12.

Fezolinetant (continued…)

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

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

Competitive environment

If approved, fezolinetant would provide an additional non-hormonal treatment for VMS that appears to be well tolerated. VMS is a very common symptom associated with menopause and represents a large potential target population. The current standard of care is usually hormone therapy which is very effective but may not be an appropriate option in some women due to risks associated with breast cancer, heart disease, or stroke. Historically, the most used alternative to hormone therapy are antidepressants such as selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs).

While fezolinetant provides an alternative, potentially well tolerated treatment option for VMS, there are no head-to-head trials comparing it to existing standards of care, which are mostly available generically. Fezolinetant may also face future competition as Bayer's elinzanetant, a dual neurokinin-1,3 receptor antagonist, is currently being reviewed across three Phase 3 trials.

For reference, the WAC for Osphena® (ospemifene), a branded drug used for severe dyspareunia and vaginal atrophy associated with menopause, is approximately $3,000 per year.

- Advantages: Novel nonhormonal treatment for VMS, large target population, well tolerated
- Disadvantages: Alternatives available with high generic penetration, lack of head-to-head trial data vs. standards of care (eg, hormone therapy, SSRI/SNRIs), potential future competition (elinzanetant)
- Reference WAC (Osphena): ~$3,000 per year

Intravitreal pegcetacoplan (Brand Name: To be determined)

Manufacturer: Apellis Pharmaceuticals
Regulatory designation: Fast Track
Expected FDA decision: February 26, 2022

Therapeutic use

Pegcetacoplan is under review for the treatment of geographic atrophy secondary to age-related macular degeneration (AMD).

Geographic atrophy is an advanced form of dry AMD caused by destruction of retinal cells through irreversible lesion growth. Geographic atrophy is a progressive disease that typically starts in the perifoveal region and expands to involve the fovea with time, leading to permanent loss of visual acuity.

It's estimated that about 1 million people are affected with geographic atrophy in the U.S., and it is one of the leading causes of blindness.

- Treatment of geographic atrophy secondary to AMD

Clinical profile

Pegcetacoplan is a complement C3 inhibitor designed to regulate excessive activation of the complement cascade, part of the body's immune system. Lesion growth in geographic atrophy is driven in part by excessive complement activation.

A subcutaneous formulation of pegcetacoplan is currently available (Empaveli®) for the treatment of paroxysmal nocturnal hemoglobinuria.

Pivotal trial data:
The efficacy of pegcetacoplan was evaluated in DERBY and OAKS, two Phase 3, randomized, double-masked, sham-controlled studies in 1,258 patients with geographic atrophy secondary to AMD. Patients were randomized to intravitreal injections of pegcetacoplan monthly, pegcetacoplan every other month, or sham. The primary endpoint was the change in total area of geographic atrophy lesion(s) based on fundus autofluorescence imaging at 12 months.

While one of the pivotal trials failed to meet the primary endpoint, in a pooled analysis of the combined DERBY and OAKS studies, monthly and every-other-month treatment with pegcetacoplan reduced geographic lesion growth by 17% ($p < 0.0001$) and 14% ($p = 0.0012$), respectively, compared to pooled sham at 12 months. In a prespecified analysis of the primary endpoint, pegcetacoplan demonstrated a greater effect in patients with extrafoveal lesions at baseline.

Patients in DERBY and OAKS continued to receive masked treatment for 24 months. In a pre-specified analysis, both monthly and every-other-month pegcetacoplan showed a reduction in lesion growth from baseline compared to sham (all p-values are nominal) at month 24: DERBY: 19% monthly ($p = 0.0004$) and 16% every-other-month ($p = 0.0030$); OAKS: 22% monthly ($p < 0.0001$) and 18% every-other-month ($p = 0.0002$).

- Complement C3 inhibitor
- Intravitreal formulation
- Reduction in geographic atrophy lesion growth at month 12: 17% with monthly and 14% with every other month dosing vs. sham
- Common AEs: Infectious endophthalmitis, intraocular inflammation
- Dosing: Once every month or once every other month

Intravitreal pegcetacoplan (continued…)

Safety:
The most common adverse events with pegcetacoplan use were infectious endophthalmitis and intraocular inflammation.

Dosing:
In the pivotal trials, pegcetacoplan was administered as an intravitreal injection once every month to every other month.

Competitive environment

If approved, pegcetacoplan would be the first treatment for geographic atrophy. There is a high unmet need for treatments as existing vascular endothelial growth factor (VEGF) inhibitors (eg, Eylea®, Lucentis®) used for "wet" or neovascular AMD are ineffective for geographic atrophy due to differences in pathophysiology. Since geographic atrophy is one of the leading causes of blindness and due to the lack of alternative treatments, the target population for pegcetacoplan is large.

Pegcetacoplan failed to meet its primary endpoint at month 12 in one of the two pivotal trials, but a pre-specified pooled analysis of the studies showed significant benefit in reduced lesion growth vs. a sham injection. Furthermore, benefit was sustained in an analysis at month 24 and between months 18 to 24, the pegcetacoplan treatment effect accelerated compared to previous six-month periods. However, the combined rate of new-onset exudations (ie, wet AMD) at month 24 was 11.9%, 6.7%, and 3.1% in the pegcetacoplan monthly, every-other-month, and sham groups, respectively. A higher rate of exudations with patients treated with pegcetacoplan could result in more patients needing to be treated with VEGF inhibitors.

Due to the nature of geographic atrophy, patients with significant baseline disease progression (eg, significant foveal involvement) may not be ideal candidates for treatment with pegcetacoplan as it does not reverse vision loss.

Apellis will likely be the first to market for geographic atrophy, but IVERIC bio has also reported positive topline results for Zimura® (avacincaptad pegol), a complement C5 inhibitor for geographic atrophy. IVERIC bio is expecting to file an application with the FDA in the first quarter of 2023.

For reference, the WAC for Eylea is approximately $1,900 per dose.

- Advantages: Potentially the first approved treatment for geographic atrophy, high unmet need, large potential target population
- Disadvantages: Increased risk of new-onset exudations (ie, wet AMD), patients with significant baseline disease progression may not be ideal candidates for treatment, potential future competition with IVERIC bio's avacincaptad pegol
- Reference WAC (Eylea): ~$1,900 per dose

Efanesoctocog alfa (Brand Name: To be determined)

Manufacturer: Sanofi/Swedish Orphan Biovitrum AB
Regulatory designations: Orphan Drug, Breakthrough Therapy, Fast Track
Expected FDA decision: February 28, 2023

Therapeutic use

Efanesoctocog alfa is under review in patients with hemophilia A for routine prophylaxis to reduce the frequency of bleeding episodes and for on-demand treatment and control of bleeding episodes.

Hemophilia A is a genetic blood clotting disorder caused by deficiencies in factor VIII (FVIII). People with hemophilia can experience bleeding episodes that can cause pain, irreversible joint damage and life-threatening hemorrhages. Hemophilia A occurs in about one in 5,000 male births annually, and more rarely in females.

- In patients with hemophilia A for routine prophylaxis to reduce the frequency of bleeding episodes and for on-demand treatment and control of bleeding episodes

Clinical profile

Efanesoctocog alfa is a long-acting recombinant FVIII replacement therapy that provides a patient the missing coagulation FVIII protein needed for effective hemostasis.

Pivotal trial data:
The efficacy of efanesoctocog alfa was evaluated in XTEND-1, an open-label, non-randomized study in 159 patients 12 years of age or older with severe hemophilia A who were previously treated with FVIII replacement therapy. The study consisted of two parallel treatments arms. In the prophylaxis Arm A (n = 133), patients who had received prior FVIII prophylaxis began receiving once-weekly efanesoctocog alfa prophylaxis for 52 weeks. In the on-demand Arm B (n = 26), patients who had received prior on-demand FVIII therapy began 26 weeks of on-demand efanesoctocog alfa, then switched to once-weekly prophylaxis for an additional 26 weeks. The primary endpoint was the annualized bleeding rate (ABR) in Arm A, and the key secondary endpoint was an intra-patient comparison of ABR during the efanesoctocog alfa weekly prophylaxis treatment period vs. the prior FVIII prophylaxis ABR for participants in Arm A who had participated in a previous observational study.

The median and mean ABR were 0.00 (interquartile range: 0.00, 1.04) and 0.71 (standard deviation: 1.43), respectively. The study also met the key secondary endpoint, demonstrating superior bleed protection over prior FVIII prophylaxis with an estimated ABR reduction of 77% and a mean ABR of 0.69 compared to 2.96 on prior prophylaxis ($p < 0.0001$), based on an intra-patient comparison.

Additionally efanesoctocog alfa was effective at treating bleeds, including in target joints; 96.7% of bleeds were resolved with a single 50 IU/kg dose.

- FVIII replacement therapy
- IV formulation
- Mean annualized bleeding rate: 0.71
- Annualized bleeding rate reduction: 77% compared to prior prophylaxis treatment in an observational study (intra-patient comparison)
- Common AEs: Headache, arthralgia, fall, back pain
- Dosing: Once weekly (prophylaxis dosing)

Efanesoctocog alfa (continued…)

Safety:
The most common adverse events with efanesoctocog alfa use were headache, arthralgia, fall, and back pain.

Dosing:
In the pivotal trial, efanesoctocog alfa was administered via IV infusion once weekly for prophylaxis and on-demand for treatment of active bleeds.

Competitive environment

The current standard of care for hemophilia A includes existing FVIII replacement therapies and Hemlibra® (emicizumab), a bispecific FIXa- and FX-directed antibody. Compared to other FVIII replacement therapies which generally require at least two doses per week when used for prophylaxis of bleeds, efanesoctocog alfa would offer a once-weekly alternative. While not compared in a head-to-head trial directly, the secondary analysis demonstrating improved bleeding rates with efanesoctocog alfa compared to prior prophylaxis treatment were promising.

However, Hemlibra has become a major alternative to FVIII replacement therapies for treatment of hemophilia A due to its more convenient subcutaneous (SC) administration and because it can be dosed from once weekly to once every 4 weeks. The initial indication for efanesoctocog alfa is expected to be limited to patients 12 years and older. A Phase 3 trial in pediatric patients under 12 years is ongoing with results expected in 2023.

In addition to existing to treatment options, several novel pipeline agents are in development for hemophilia A. These range from gene therapies (eg, BioMarin's valoctocogene roxaparvovec) to Novo Nordisk's concizumab, a novel SC administered anti-tissue factor pathway inhibitor.

- Advantages: Once weekly administration, promising improvements in bleeding rates vs. prior prophylaxis treatment
- Disadvantages: Alternatives available (including other FVIII replacement therapies and Hemlibra), IV administration, potential future competition (eg, gene therapies, anti-tissue factor pathway inhibitors)

Valoctocogene roxaparvovec (Brand Name: Roctavian)

Manufacturer: BioMarin
Regulatory designations: Orphan Drug, Breakthrough Therapy
Expected FDA decision: March 31, 2023

Therapeutic use

Valoctocogene roxaparvovec is under review for the treatment of adults with severe hemophilia A.

- Treatment of adults with severe hemophilia A

Clinical profile

Valoctocogene roxaparvovec is an adeno-associated virus (AAV)–mediated gene therapy delivering a functional FVIII gene.

- Gene therapy delivering FVIII gene
- IV formulation
- Reduction in treated bleeds: 83.8%
- Reduction in FVIII concentrate use: 98.6%
- Common AEs: Liver enzyme elevation, nausea, headache, fatigue
- Dosing: One-time dose

Pivotal trial data:
The efficacy of valoctocogene roxaparvovec was evaluated in a Phase 3, single-arm, open-label study in 134 patients with severe hemophilia A (FVIII ≤ 1 IU/dL) who had been treated continuously with prophylactic FVIII replacement therapy for a minimum of 1 year prior to enrollment. The study evaluated outcomes at 24 months post valoctocogene roxaparvovec infusion. Among the 112 participants enrolled, the mean annualized rates of FVIII concentrate use and treated bleeding after week 4 had decreased after infusion by 98.6% and 83.8%, respectively ($p < 0.001$ for both comparisons).

Additionally, BioMarin has also continued to collect data up to 5 to 6 years from a smaller Phase 1/2 study. In the follow-up period, valoctocogene roxaparvovec has continued to demonstrate sustained hemostatic efficacy.

Safety:
The most common adverse events with valoctocogene roxaparvovec use were liver enzyme elevation, nausea, headache, and fatigue.

Dosing:
In the pivotal trials, valoctocogene roxaparvovec was administered via IV infusion as a one-time dose.

Valoctocogene roxaparvovec (continued…)

Competitive environment

If approved, valoctocogene roxaparvovec would be the first gene therapy for hemophilia A and it would reduce, and in some cases eliminate, the need for chronic and as-needed factor replacement therapy. Factor replacement therapy has a high treatment burden and can be very costly particularly in severe patients requiring high doses or prophylactic use of FVIII.

Treatment will be limited to patients who have severe hemophilia A which is about 50% of patients. However, patients who have baseline factor inhibitors or autoantibodies to the viral vector would not be candidates for treatment.

Like other gene therapies, particularly for hemophilia, the primary limitation or question is the unknown durability of response. Sustained efficacy is especially important with gene therapies because of the high projected cost for a one-time dose.

Other gene therapies for hemophilia A are in development but are not expected to reach the market in the next 2 years. There may be some patients that are eligible and willing to be treated with gene therapy but who could wait until data is available for these competitors rather than choosing to be early adopters for valoctocogene roxaparvovec.

The projected WAC for valoctocogene roxaparvovec is $2 to $3 million for a one-time dose.

- Advantages: Potentially the first gene therapy for hemophilia A, eliminates or reduces the need for chronic and as-needed FVIII replacement therapy
- Disadvantages: Reserved for patients with severe hemophilia A, lack of data in patients with factor inhibitors, full durability of response not yet known, potential future competition
- Projected WAC: $2 to $3 million for one-time dose

Omecamtiv mecarbil (Brand Name: To be determined)

Manufacturer: Cytokinetics
Regulatory designations: Fast Track
Expected FDA decision: February 28, 2023 *(FDA Advisory Committee scheduled for December 13, 2022)*

Therapeutic use

Omecamtiv mecarbil is under review treatment of heart failure with reduced ejection fraction (HFrEF).

Heart failure occurs when the heart cannot pump enough blood and oxygen to support other organs. HFrEF, or systolic heart failure, is a category of heart failure in which the heart is unable to eject blood sufficiently during its contraction phase.

Of the estimated 6.2 million people in the U.S. with heart failure, approximately 50% have HFrEF.

- Treatment of HFrEF

Clinical profile

Omecamtiv mecarbil is a selective cardiac myosin activator. Omecamtiv mecarbil directly targets the contractile mechanisms of the heart, binding to and recruiting more cardiac myosin heads to interact with actin during systole. Omecamtiv mecarbil is designed to increase the number of active actin-myosin cross bridges during each cardiac cycle and consequently augment the impaired contractility that is associated with heart failure.

- Selective cardiac myosin activator
- Oral formulation
- Primary-outcome event (first heart-failure event or death from cardiovascular causes): 37.0% vs. 39.1% with placebo
- Dosing: Twice daily

Pivotal trial data:
The efficacy of omecamtiv mecarbil was evaluated in GALACTIC-HF, a Phase 3, randomized, double-blind, placebo-controlled study in 8,256 patients with New York Heart Association (NYHA) functional class II, III, or IV symptoms and a left ventricular ejection fraction of 35% or less. The patients were hospitalized for heart failure or had either made an urgent visit to the emergency department or been hospitalized for heart failure within 1 year before screening. Patients received omecamtiv mecarbil or placebo, in addition to standard heart-failure therapy. The primary outcome was a composite of a first heart-failure event (hospitalization or urgent visit for heart failure) or death from cardiovascular causes.

During a median of 21.8 months, a primary-outcome event occurred in 1,523 of 4,120 patients (37.0%) in the omecamtiv mecarbil group vs. 1,607 of 4,112 patients (39.1%) in the placebo group (HR 0.92, 95% CI: 0.86, 0.99; p = 0.03). A total of 808 patients (19.6%) and 798 patients (19.4%), respectively, died from cardiovascular causes (HR 1.01, 95% CI: 0.92, 1.11). There was no significant difference between groups in the change from baseline on the Kansas City Cardiomyopathy Questionnaire total symptom score.

Omecamtiv mecarbil (continued…)

Safety:
The rates of adverse events were similar between omecamtiv mecarbil and placebo.

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

Competitive environment

Omecamtiv mecarbil is a first-in-class, oral cardiac myosin activator and if approved, would offer an additional treatment option in the treatment of chronic heart failure. Despite the availability of existing treatment options, there is still a high unmet need for better treatments for heart failure. Based on data from the CDC, heart failure was mentioned on 379,800 death certificates in 2018 and heart failure costs an estimated $30.7 billion in the U.S.

While omecamtiv mecarbil met the primary composite endpoint in the pivotal study, the results were modest and there were no improvements in the secondary endpoints. Compared indirectly to Entresto® (sacubitril/valsartan) and sodium glucose co-transporter 2 (SGLT2) inhibitors like Farxiga® (dapagliflozin), the results for omecamtiv mecarbil appear less robust, but comparing across different trials is challenging.

Given the results of the pivotal trial and the availability of other treatment options that have been on the market longer, omecamtiv mecarbil is likely to be used later in the treatment algorithm, with initial use potentially limited to high-risk or symptomatic patients or patients who experience adverse events with existing therapies.

For reference, the WAC for Verquvo® (vericiguat), another recently approved novel drug for HFrEF, is approximately $7,500 per year.

- Advantages: Novel mechanism of action, large potential target population, appears well tolerated
- Disadvantages: Alternatives available (eg, Entresto, SGLT2 inhibitors), lack of data for cardiovascular death and all-cause mortality benefit, twice daily administration
- Reference WAC (Verquvo): ~$7,500 per year

Trofinetide (Brand Name: To be determined)

Manufacturer: Acadia Pharmaceuticals
Regulatory designations: Orphan Drug, Fast Track
Expected FDA decision: March 12, 2023

Therapeutic use

- Treatment of Rett syndrome

Trofinetide is under review for the treatment of Rett syndrome.

Rett syndrome is a rare, progressive neurodevelopmental disorder that almost exclusively affects females. Infants with Rett syndrome generally develop normally up until about 7 to 18 months, however after this point, they begin to lose previously acquired skills such as purposeful hand movements and the ability to communicate. Affected children often develop autistic-like behaviors, breathing irregularities, feeding and swallowing difficulties, growth retardation, and seizures. Most Rett syndrome cases are caused by identifiable mutations of the MECP2 gene on the X chromosome and can present with a wide range of disability ranging from mild to severe.

Rett syndrome is often undiagnosed or misdiagnosed, but the incidence is estimated to be 1 in 10,000 girls by age 12 in the U.S. Rett syndrome is the second most common cause of severe intellectual disability after Down syndrome.

Clinical profile

- IGF-1 analog
- Oral formulation
- Change from baseline in RSBQ score: -5.1 vs. -1.7 with placebo
- CGI-I: 3.5 vs. 3.8 with placebo
- Common AEs: Diarrhea, vomiting
- Dosing: Twice daily

Trofinetide is a synthetic analog of the amino-terminal tripeptide of insulin-like growth factor-1 receptor (IGF-1). In the central nervous system, IGF-1 is produced by brain cells. IGF-1 in the brain is critical for both normal development and for response to injury and disease. Trofinetide has been shown to inhibit the production of inflammatory cytokines, inhibit the overactivation of microglia and astrocytes, and increase the amount of available IGF-1 that can bind to IGF-1 receptors.

Pivotal trial data:
The efficacy of trofinetide was evaluated in LAVENDER, a Phase 3, double-blind, randomized, placebo-controlled study in 187 girls and young women aged 5 to 20 years with Rett syndrome. The co-primary endpoints included Rett Syndrome Behavior Questionnaire (RSBQ) and Clinical Global Impression-Improvement (CGI-I) assessment. RSBQ is a caregiver completed, 45-item rating scale assessing core symptoms of Rett syndrome (score ranges from 0 to 90). CGI-I is a global physician assessment of worsening or improving of Rett syndrome (score ranges from 1 to 7).

On the RSBQ, change from baseline to week 12 was -5.1 with trofinetide vs. -1.7 with placebo ($p = 0.0175$). The CGI-I score at week 12 was 3.5 for trofinetide vs. 3.8 for placebo ($p = 0.0030$).

Safety:
The most common adverse events with trofinetide use were diarrhea and vomiting.

Dosing:
In the pivotal trial, trofinetide was administered orally twice daily by mouth or gastrostomy tube (G-tube).

Trofinetide (continued...)

Competitive environment

Trofinetide would offer the first approved treatment for Rett syndrome, a condition with a high unmet need. The current standard of care is generally limited to supportive and symptomatic treatment. Drugs may be used to treat a variety of disease manifestations associated with Rett syndrome including seizures, anxiety, sleep disturbances, breathing problems, and certain gastrointestinal abnormalities.

The efficacy results from the pivotal trial of trofinetide were promising with both caregiver and physician-assessed rating scales showing improvements vs. placebo. There were substantially higher rates of diarrhea and vomiting with trofinetide compared to placebo, but these were mostly mild-to-moderate in severity. However, treatment discontinuation rates related to treatment emergent adverse events were 17.2% in the trofinetide group compared to just 2.1% in the placebo group.

- Advantages: Potentially the first approved treatment for Rett syndrome, high unmet need, may be administered orally or via G-tube
- Disadvantages: Substantially higher rates of diarrhea and vomiting (higher discontinuation rates in the pivotal study)

Zavegepant (Brand Name: To be determined)

Manufacturer: Biohaven Pharmaceutical
Expected FDA decision: 1Q 2023

Therapeutic use

Zavegepant is under review for the acute treatment of migraine headache in adults.

Migraine is characterized by debilitating attacks lasting 4 to 72 hours with multiple symptoms, including pulsating headaches of moderate to severe pain intensity. Patients suffering a migraine headache often also have nausea or vomiting, and/or sensitivity to sound (phonophobia) and sensitivity to light (photophobia). Approximately 39 million individuals in the U.S. are affected by migraines.

- Treatment of acute treatment of migraine in adults

Clinical profile

Zavegepant is a calcitonin gene-related peptide (CGRP) receptor antagonist. CGRP receptor antagonists are believed to relieve migraine by blocking neurogenic inflammation, decreasing artery dilation, and inhibiting pain transmission.

- CGRP receptor antagonist
- Intranasal formulation
- Freedom from pain at 2 hours: 23.6% vs. 14.9% with placebo
- Freedom from most bothersome symptom at 2 hours: 39.6% vs. 31.1% with placebo
- Common AEs: Dysgeusia, nasal discomfort, nausea
- Dosing: As-needed

Pivotal trial data:
The efficacy of zavegepant was evaluated in a Phase 3, randomized, double-blind, placebo-controlled study in 1,405 adults with a history of migraine attacks. Patients received one dose of zavegepant 10 mg nasal spray or placebo to treat one migraine attack. The co-primary efficacy endpoints were freedom from pain and freedom from the most bothersome symptom (nausea, phonophobia, or photophobia) at 2 hours post-dose. Zavegepant was statistically superior to placebo on the co-primary endpoints of pain freedom (23.6% vs. 14.9%, $p < 0.0001$) and freedom from most bothersome symptom (MBS) (39.6% vs. 31.1%, $p = 0.0012$) at 2 hours. Secondary endpoints such as pain relief at 15 minutes and return to normalcy at 30 minutes also favored zavegepant.

In addition, zavegepant was evaluated in a Phase 2/3, dose ranging, randomized, double-blind, placebo-controlled study in 1,673 adults with a history of migraine attacks. Patients received one dose of zavegepant 5 mg, 10 mg, or 20 mg vs. placebo to treat one migraine attack. The co-primary endpoints were the same as the Phase 3 study. Zavegepant 10 mg and 20 mg demonstrated statistical superiority to placebo on the co-primary endpoints of pain freedom (placebo: 15.5%; 10 mg: 22.5% [$p = 0.0113$]; 20 mg: 23.1% [$p = 0.0055$]) and MBS freedom (placebo: 33.7%; 10 mg: 41.9% [$p = 0.0155$]; 20 mg: 42.5% [$p = 0.0094$]). The 5 mg strength was not shown to be superior to placebo.

Safety:
The most common adverse events with zavegepant use were dysgeusia (taste disturbances), nasal discomfort, and nausea.

Dosing:
In the pivotal trials, zavegepant was administered as one dose intranasally as needed to treat an acute migraine headache.

Zavegepant (continued…)

Competitive environment

Zavegepant would provide the first intranasal CGRP antagonist for the acute treatment of migraine headaches. Zavegepant was well tolerated and could be a treatment option in patients who either have contraindications or are non-responders to triptan therapy, the current standard of care. Oral CGRP antagonists are currently available for acute migraine treatment, but an intranasal formulation would provide a potential convenience benefit in this population, as migraine sufferers often report nausea. Compared indirectly to other drugs in the class, zavegepant also appears to have a more rapid onset of action with pain relief demonstrated as early as 15 minutes.

Like other CGRP antagonists, zavegepant would likely be reserved as a second- or third-line agent due to the availability of generic triptan alternatives and a lack of head-to-head data. While zavegepant would be the first intranasal CGRP antagonist, triptan drugs like sumatriptan and zolmitriptan are available in intranasal formulations as well.

For reference, the WAC for Nurtec® ODT (rimegepant), Biohaven's oral CGRP antagonist, is $115 per dose.

- Advantages: Potentially the first intranasal CGRP antagonist, alternative formulation in migraine sufferers with difficulty taking oral medications
- Disadvantages: Alternatives available (including other CGRP antagonists and triptans), lack of head-to-head trial data
- Reference WAC (Nurtec ODT): $115 per dose

Extended generic pipline forecast

Optum Rx generic pipeline forecast

Trade Name	Generic Name	Brand Company(ies)	Route of Administration	Strength(s)	Anticipated Generic Availability
2022 Possible launch date					
NEUPRO	rotigotine	UCB	External	All	2022
ONEXTON	clindamycin/benzoyl peroxide	Bausch Health	External	All	2022
XYREM	sodium oxybate	Jazz	Oral	All	2H-2022
OXAYDO	oxycodone	Egalet	Oral	All	2H-2022
IXEMPRA Kit	ixabepilone	R-Pharm	Intravenous	All	2H-2022
IRESSA	gefitinib	AstraZeneca	Oral	All	4Q-2022
XERESE	acyclovir/hydrocortisone	Bausch Health	External	All	11-2022
FOLOTYN	pralatrexate	Acrotech/Aurobindo	Intravenous	All	11-2022
TREANDA	bendamustine	Cephalon/Teva	Intravenous	All	12-2022
ZIOPTAN	tafluprost	Akorn	Ophthalmic	All	12-2022
RAYOS	prednisone	Horizon	Oral	All	12-2022
2023 Possible launch date					
PREZISTA	darunavir	Janssen	Oral	All	2023
PROLENSA	bromfenac	Bausch Health	Ophthalmic	All	2023
ALPHAGAN P	brimonidine	Allergan	Ophthalmic	All	2023
FORTEO	teriparatide	Eli Lilly	Injection	All	1H-2023
ONGLYZA	saxagliptin	Bristol-Myers Squibb/Astra Zeneca	Oral	All	1H-2023
FIRVANQ KIT	vancomycin	Azurity	Oral	All	1H-2023
KOMBIGLYZE XR	saxagliptin/metformin	Bristol-Myers Squibb/Astra Zeneca	Oral	All	1H-2023
SPIRIVA HANDIHALER	tiotropium	Boehringer Ingelheim	Inhalation	All	01-2023
DYLOJECT	diclofenac	Hospira/Pfizer/Javelin	Intravenous	All	01-2023
DULERA	formoterol fumarate/mometasone furoate	Organon	Inhalation	All	01-2023
NASCOBAL	cyanocobalamin	Par/Endo	Intranasal	All	01-2023
TEFLARO	ceftaroline fosamil	Allergan	Intravenous	All	01-2023
CAMBIA	diclofenac potassium	Assertio	Oral	All	01-2023
LEXISCAN	regadenoson	Astellas	Intravenous	All	01-2023
TROKENDI XR	topiramate	Supernus	Oral	All	01-2023
NOXAFIL	posaconazole	Merck	Intravenous	All	01-2023

Trade Name	Generic Name	Brand Company(ies)	Route of Administration	Strength(s)	Anticipated Generic Availability
BALCOLTRA	levonorgestrel/ethinyl estradiol/ferrous bisglycinate	Avion	Oral	All	01-2023
DUOBRII	halobetasol propionate/tazarotene	Bausch Health	External	All	01-2023
HUMIRA	adalimumab	AbbVie	Subcutaneous	All	01-2023
LATUDA	lurasidone	Sunovion	Oral	All	02-2023
AGGRASTAT	tirofiban	Medicure	Intravenous	All	03-2023
AUBAGIO	teriflunomide	Sanofi/Genzyme	Oral	All	03-2023
GATTEX	teduglutide recombinant	Takeda	Subcutaneous	All	03-2023
ACTEMRA	tocilizumab	Roche/Chugai	Intravenous; subcutaneous	All	2Q-2023
PROVAYBLUE	methylene blue	Provepharm/American Regent	Intravenous	All	04-2023
CLINDESSE	clindamycin phosphate	Perrigo	Vaginal	All	04-2023
TYSABRI	natalizumab	Biogen	Intravenous	All	05-2023
LIVALO	pitavastatin	Eli Lilly/Kowa Pharmaceuticals	Oral	All	05-2023
NEULASTA ONPRO	pegfilgrastim	Amgen/Insulet	Subcutaneous	All	2H-2023
XURIDEN	uridine	Wellstat Therapeutics	Oral	All	07-2023
TOLAK	fluorouracil	Pierre Fabre	External	All	07-2023
MOZOBIL	plerixafor	Sanofi/Genzyme	Subcutaneous	All	07-2023
EGRIFTA	tesamorelin	Theratechnologies	Subcutaneous	All	08-2023
CYSTADROPS	cysteamine	Recordati	Ophthalmic	All	08-2023
KATERZIA	amlodipine	Azurity	Oral	All	08-2023
VYVANSE	lisdexamfetamine	Shire/Takeda	Oral	All	08-2023
CAROSPIR	spironolactone	CMP Pharma	Oral	All	09-2023
VIBATIV	telavancin	Theravance	Intravenous	All	09-2023
LEXETTE	halobetasol	Mayne	External	All	09-2023
VOTRIENT	pazopanib	Novartis	Oral	All	10-2023
OZURDEX	dexamethasone	Allergan	Ophthalmic	All	11-2023
AMTURNIDE	aliskiren/amlodipine/hydrochlorothiazide	Novartis	Oral	All	11-2023
KOGENATE FS	octocog alpha	Bayer	Intravenous	All	11-2023
HELIXATE FS	antihemophilic factor VIII	CSL Behring/Bayer	Intravenous	All	11-2023
KALBITOR	ecallantide	Dyax	Subcutaneous	All	12-2023
2024 Possible launch date					
EYLEA	aflibercept	Regeneron	Intravitreal	All	2024
STELARA	ustekinumab	Janssen	Subcutaneous; intravenous	All	2024
VESICARE LS	solifenacin	Astellas	Oral	All	1H-2024

Trade Name	Generic Name	Brand Company(ies)	Route of Administration	Strength(s)	Anticipated Generic Availability
GIAZO	balsalazide disodium	Bausch Health	Oral	All	01-2024
GRALISE	gabapentin	Assertio Therapeutics	Oral	All	01-2024
MYRBETRIQ	mirabegron	Astellas	Oral	All	01-2024
TASIGNA	nilotinib	Novartis	Oral	All	01-2024
SIMPONI	golimumab	Janssen	Subcutaneous	All	02-2024
SIMPONI ARIA	golimumab	Janssen	Intravenous	All	02-2024
NATESTO	testosterone	Acerus	Nasal	All	02-2024
CIMZIA	certolizumab pegol	UCB/Royalty Pharma	Subcutaneous	All	02-2024
SYMPAZAN	clobazam	Aquestive	Oral	All	02-2024
ISENTRESS	raltegravir	Merck	Oral	All	04-2024
DUTREBIS	lamivudine/raltegravir	Merck	Oral	All	04-2024
PROBUPHINE	buprenorphine	Titan Pharmaceuticals/Braeburn Pharmaceuticals	Subdermal	All	04-2024
RADICAVA	edaravone	Mitsubishi Tanabe	Intravenous	All	05-2024
DUAVEE	conjugated estrogens/bazedoxifene acetate	Pfizer/Ligand Pharmaceuticals	Oral	All	05-2024
SAXENDA	liraglutide	Novo Nordisk	Subcutaneous	All	05-2024
ARANESP	darbepoetin alfa	Amgen/Kirin	Intravenous; subcutaneous	All	05-2024
NYMALIZE	nimodipine	Arbor	Oral	All	05-2024
HAEGARDA	C1 esterase inhibitor	CSL Behring	Subcutaneous	All	06-2024
VICTOZA	liraglutide recombinant	Novo Nordisk	Subcutaneous	All	06-2024
TWYNEO	tretinoin/benzoyl peroxide	Galderma	External	All	07-2024
SLYND	drospirenone	Exeltis/Insud	Oral	All	08-2024
SPRYCEL	dasatinib	Bristol-Myers Squibb	Oral	All	09-2024
SUSTOL	granisetron	Heron Therapeutics	Subcutaneous	All	09-2024
PRIALT	ziconotide acetate	TerSera Therapeutics	Intrathecal	All	10-2024
LAZANDA	fentanyl citrate	Depomed	Intranasal	All	10-2024
RYDAPT	midostaurin	Novartis	Oral	All	10-2024
VUITY	pilocarpine	AbbVie	Ophthalmic	All	10-2024
STENDRA	avanafil	Metuchen Pharmaceuticals	Oral	All	10-2024
QSYMIA	phentermine/topiramate	Vivus	Oral	All	12-2024
SIKLOS	hydroxyurea	Addmedica/Medunik	Oral	All	12-2024
2025 Possible launch date					
BOSULIF	bosutinib	Pfizer	Oral	All	2025
DALVANCE	dalbavancin	AbbVie	Intravenous	All	2025

Trade Name	Generic Name	Brand Company(ies)	Route of Administration	Strength(s)	Anticipated Generic Availability
COMPLERA	emtricitabine/rilpivirine/tenofovir disoproxil fumarate	Gilead/Janssen	Oral	All	2025
NAMZARIC	memantine/donepezil	Allergan/Adamas	Oral	All	01-2025
TRACLEER	bosentan	Actelion/Janssen	Oral	All	01-2025
RISPERDAL CONSTA	risperidone	Janssen	Injection	All	01-2025
HALAVEN	eribulin	Eisai	Intravenous	All	01-2025
MYDAYIS	amphetamine/dextroamphetamine mixture	Takeda	Oral	All	01-2025
CORLANOR	ivabradine	Amgen	Oral	All	01-2025
PHOSLYRA	calcium acetate	Fresenius	Oral	All	01-2025
FINACEA Foam	azelaic acid	LEO Pharma	External	All	01-2025
SANCUSO	granisetron	Kyowa Hakko Kirin/ProStrakan	External	All	01-2025
PROLIA	denosumab	Amgen	Subcutnaeous	All	02-2025
SOLIRIS	eculizumab	Alexion	Intravenous	All	03-2025
BENLYSTA	belimumab	GSK	Intravenous; subcutaneous	All	03-2025
AURYXIA	ferric citrate	Keryx/Akebia Therapeutics	Oral	All	03-2025
YERVOY	ipilimumab	Bristol-Myers Squibb	Intravenous	All	03-2025
HORIZANT	gabapentin enacarbil	Arbor	Oral	All	04-2025
JYNARQUE	tolvaptan	Otsuka	Oral	All	04-2025
BRILINTA	ticagrelor	AstraZeneca	Oral	All	05-2025
TRADJENTA	linagliptin	Eli Lilly/Boehringer Ingelheim	Oral	All	05-2025
JENTADUETO XR	linagliptin/metformin	Boehringer Ingelheim/Eli Lilly	Oral	All	05-2025
JENTADUETO	linagliptin/metformin	Boehringer Ingelheim/Eli Lilly	Oral	All	05-2025
APTIOM	eslicarbazepine	Sunovion/Bial	Oral	All	05-2025
PERJETA	pertuzumab	Genentech	Intravenous	All	06-2025
NULOJIX	belatacept	Bristol-Myers Squibb	Intravenous	All	06-2025
NUCYNTA	tapentadol	Collegium	Oral	All	06-2025
NUCYNTA ER	tapentadol	Collegium	Oral	All	06-2025
RAVICTI	glycerol phenylbutyrate	Horizon	Oral	All	07-2025
RYANODEX	dantrolene	Eagle Pharmaceuticals	Intravenous	All	07-2025
SOLIQUA	insulin glargine/lixisenatide	Sanofi	Subcutaneous	All	07-2025
RYTARY	carbidopa/levodopa	Impax/Amneal	Oral	All	07-2025
ADZENYS XR-ODT	amphetamine polistirex	Neos Therapeutics	Oral	All	09-2025
FYCOMPA	perampanel	Eisai	Oral	All	09-2025

Trade Name	Generic Name	Brand Company(ies)	Route of Administration	Strength(s)	Anticipated Generic Availability
OFEV	nintedanib	Boehringer Ingelheim	Oral	All	10-2025
XIGDUO XR	dapagliflozin/metformin	AstraZeneca	Oral	All	10-2025
FARXIGA	dapagliflozin	AstraZeneca	Oral	All	10-2025
QTERN	dapagliflozin/saxagliptin	AstraZeneca	Oral	All	10-2025
FUROSCIX	furosemide	scPharmaceuticals	Subcutaneous	All	10-2025
ELELYSO	taliglucerase alfa	Pfizer	Intravenous	All	10-2025
EDURANT	rilpivirine	Janssen	Oral	All	10-2025
PICATO	ingenol mebutate	LEO Pharma	External	All	12-2025
OPSUMIT	macitentan	Janssen	Oral	All	12-2025

Extended brand pipeline forecast

Optum Rx brand pipeline forecast

Drug name	Generic name	Company	Mechanism of Action	Disease State	Route	FDA Status	Estimated release date	Specialty drug	Orphan drug
2022 Possible launch date									
PRV-031	teplizumab	Provention Bio	CD3 antigen inhibitor	Diabetes mellitus	IV	Filed BLA	11/17/2022	Yes	No
AMT-061	etranacogene dezaparvovec	CSL Behring/ uniQure	gene therapy	Hemophilia B	IV	Filed BLA	11/24/2022	Yes	Yes
HM781-36B	poziotinib	Spectrum Pharmaceuticals	pan-HER inhibitor	Non-small cell lung cancer	PO	Filed NDA	11/24/2022	Yes	No
RBX-2660	RBX-2660	Rebiotix	microbiota suspension	Clostridium difficile infection	Rectal	Filed BLA	11/30/2022	No	Yes
131I-8H9	omburtamab	Y-mAbs Therapeutics	B7-H3 antagonist	Brain cancer	Intrathecal	Filed BLA	11/30/2022	Yes	Yes
LIQ-861	treprostinil	Liquidia Technologies	prostacyclin analog	Pulmonary arterial hypertension	INH	Tentative Approval	11/2022	Yes	No
MRTX-849	adagrasib	Mirati Therapeutics	KRAS inhibitor	Non-small cell lung cancer	PO	Filed NDA	12/14/2022	Yes	No
JS-001	toripalimab	Coherus Biosciences	anti-PD-1 monoclonal antibody	Nasopharyngeal carcinoma	IV	Filed BLA	12/23/2022	Yes	Yes

Drug name	Generic name	Company	Mechanism of Action	Disease State	Route	FDA Status	Estimated release date	Specialty drug	Orphan drug
GS-CA1 (GS-6207)	lenacapavir	Gilead	HIV capsid inhibitor	HIV-1	SC	Filed NDA	12/27/2022	Yes	No
ublituximab	ublituximab	TG Therapeutics	anti-CD-20 monoclonal antibody	Multiple sclerosis	IV	Filed BLA	12/28/2022	Yes	No
AT-GAA	cipaglucosidase alfa	Amicus	enzyme therapy	Pompe disease	IV	Filed BLA	4Q2022	Yes	Yes
Ovastat	treosulfan	Medexus Pharmaceuticals	alkylating agent	Hematopoietic stem cell transplantation	IV	Filed BLA	4Q2022	Yes	Yes
R-667 (RG-667)	palovarotene	Ipsen	selective retinoic acid receptor agonist	Fibrodysplasia ossificans progressiva	PO	Filed NDA	12/29/2022	Yes	Yes
RG-7828	mosunetuzumab	Genentech	anti-CD20/CD3 monoclonal antibody	Follicular lymphoma	IV/SC	Filed BLA	12/29/2022	Yes	Yes
BGB-A317 (BGB-A-317)	tislelizumab	BeiGene	programmed death-1 inhibitor	Esophageal squamous cell carcinoma	IV	Filed BLA	2H2022	Yes	Yes
2023 Possible launch date									
NexoBrid	bromelain	MediWound	peptide hydrolase replacement agent	Burns/ Skin injury	TOP	Filed BLA	01/01/2023	No	Yes
BAN-2401	lecanemab	Eisai/Biogen	beta-amyloid monoclonal antibody	Alzheimer's disease	IV	Filed BLA	01/06/2023	Yes	No
TAK-438	vonoprazan fumarate	Phantom Pharmaceuticals	potassium-competitive acid blocker	Erosive esophagitis	PO	Filed NDA	01/11/2023	No	No

Drug name	Generic name	Company	Mechanism of Action	Disease State	Route	FDA Status	Estimated release date	Specialty drug	Orphan drug
ACER-001	sodium phenylbutyrate	Acer Therapeutics	nitrogen-binding agent	Urea cycle disorders	PO	Filed NDA	01/15/2023	Yes	No
NiCord	omidubicel	Gamida	stem cell therapy	Hematological cancers	IV	Filed BLA	01/30/2023	Yes	Yes
PT-027	budesonide/albuterol	AstraZeneca/ Avillion	glucocorticoid/short acting beta agonist	Asthma	INH	Filed NDA	01/31/2023	No	No
GSK-1278863	daprodustat	GlaxoSmithKline	hypoxia-inducible factor-prolyl hydroxylase inhibitor	Anemia	PO	Filed NDA	02/01/2023	Yes	No
LY-3527727	pirtobrutinib	Eli Lilly	Bruton's tyrosine kinase inhibitor	Mantle cell lymphoma	PO	Filed NDA	02/04/2023	Yes	No
LY-3002813	donanemab	Eli Lilly	beta-amyloid monoclonal antibody	Alzheimer's disease	IV	Filed BLA	02/04/2023	Yes	No
FT-2102	olutasidenib	Forma Therapeutics	dehydrogenase 1 inhibitor	Acute myeloid leukemia	PO	Filed NDA	02/15/2023	Yes	Yes
PS-433540 (RE-021; DARA)	sparsentan	Travere Therapeutics	dual endothelin angiotensin receptor antagonist	IgA nephropathy	PO	Filed NDA	02/17/2023	Yes	Yes
RAD-1901	elacestrant	Radius Health	selective estrogen receptor degrader	Breast cancer	PO	Filed NDA	02/17/2023	Yes	No
KB-103	beremagene geperpavec	Krystal Biotech	gene therapy	Epidermolysis bullosa	Topical	Filed BLA	02/17/2023	Yes	Yes
ESN-364	fezolinetant	Astellas	NK3 receptor antagonist	Menopause	PO	Filed NDA	02/22/2023	No	No
PF-07321332	nirmatrelvir/ ritonavir	Pfizer	protease inhibitor	COVID-19	PO	Filed NDA	02/25/2023	No	No

Drug name	Generic name	Company	Mechanism of Action	Disease State	Route	FDA Status	Estimated release date	Specialty drug	Orphan drug
pegcetacoplan (intravitreal)	pegcetacoplan	Apellis	compliment C3 inhibitor	Geographic atrophy	Intravitreal	Filed BLA	02/26/2023	Yes	No
BIVV-001	efanesoctocog alfa	Sanofi	recombinant Factor VIII	Hemophilia A	IV	Filed BLA	02/28/2023	Yes	Yes
RTA-408	omaveloxolone	Reata Pharmaceuticals	Nrf2 activator	Friedreich's ataxia	PO	Filed NDA	02/28/2023	Yes	Yes
omecamtiv mecarbil	omecamtiv mecarbil	Cytokinetics	cardiac myosin activator	Heart failure	PO	Filed NDA	02/28/2023	No	No
NNZ-2566	trofinetide	Acadia Pharmaceuticals	insulin-like growth factor 1 derivative	Rett syndrome	PO	Filed NDA	03/12/2023	Yes	Yes
CD-101	rezafungin	Cidara Therapeutics	echinocandin	Fungal infections	IV	Filed NDA	03/22/2023	No	Yes
BHV-3500	zavegepant	Biohaven	calcitonin gene-related peptide receptor antagonist	Migraine	Intranasal	Filed NDA	03/24/2023	No	No
CDZ-173	leniolisib	Pharming/ Novartis	phosphatidylinositol-3-4-5-trisphosphate inhibitor	Primary immunodeficiencies	PO	Filed NDA	03/29/2023	Yes	Yes
Roctavian	valoctocogene roxaparvovec	BioMarin	gene therapy	Hemophilia A	IV	Filed BLA	03/31/2023	Yes	Yes
Botulax	letibotulinumtoxinA	Hugel Pharma	botulinum toxins	Wrinkles	IM	Filed BLA	04/06/2023	Yes	No
Rizaport (VersaFilm)	rizatriptan	IntelGenx	triptans	Acute migraines	PO	Filed NDA	04/18/2023	No	No

Drug name	Generic name	Company	Mechanism of Action	Disease State	Route	FDA Status	Estimated release date	Specialty drug	Orphan drug
quizartinib	quizartinib	Daiichi Sankyo	FLT-3 receptor tyrosine kinase inhibitor	Acute myeloid leukemia	PO	Filed NDA	04/24/2023	Yes	Yes
BIIB-067 (ISIS-333611)	tofersen	Biogen/ Ionis	antisense oligonucleotide targeting SOD1	Amyotrophic lateral sclerosis	Intrathecal	Filed NDA	04/25/2023	Yes	Yes
SER-109	SER-109	Seres Therapeutics	ecobiotic agent	Clostridium difficile infection	PO	Filed BLA	04/26/2023	No	Yes
LY-3074828	mirikizumab	Eli Lilly	IL-23 inhibitor	Ulcerative colitis	SC	Filed BLA	04/28/2023	Yes	No
TransCon PTH	palopegteriparatide	Ascendis Pharma	parathyroid hormone	Hypoparathyroidism	SC	Filed BLA	04/30/2023	Yes	Yes
AV-7909 (CPG 7909)	anthrax vaccine adsorbed	Emergent Biosolutions	vaccine/ oligodeoxynucleotide	Anthrax	IM	Filed BLA	04/30/2023	No	No
TV-46000	risperidone	Teva Pharmaceuticals/ MedinCell	atypical antipsychotic	Schizophrenia	SC	Filed NDA	05/03/2023	No	No
GSK-3844766A	GSK-3844766A	GlaxoSmithKline	vaccine	Respiratory syncytial virus	IM	Filed BLA	05/03/2023	No	No
SYD-985	[vic-] trastuzumab duocarmazine	Byondis	HER2-targeting antibody-drug conjugate	Breast cancer	IV	Filed BLA	05/12/2023	Yes	No
Lamazym	velmanase alfa	Chiesi	enzyme replacement therapy	Alpha-mannosidosis	IV	Filed BLA	05/12/2023	Yes	Yes

Drug name	Generic name	Company	Mechanism of Action	Disease State	Route	FDA Status	Estimated release date	Specialty drug	Orphan drug
Aripiprazole 2-month	aripiprazole	Lundbeck/ Otsuka Pharmaceutical	atypical antipsychotic	Schizophrenia/ bipolar disorder	IM	Filed NDA	05/13/2023	No	No
PRX-102	pegunigalsidase alfa	Protalix	enzyme replacement	Fabry disease	IV	Filed BLA	05/14/2023	Yes	No
ABBV-951	foscarbidopa/ foslevodopa	AbbVie	aromatic amino acid decarboxylation inhibitor/ aromatic amino acid	Parkinson's disease	SC	Filed NDA	05/20/2023	Yes	No
ALT-803	nogapendekin alfa inbakicept	ImmunityBio	interleukin-15 (IL-15) super agonist/ IL-15R alpha-Fc fusion complex	Bladder cancer	Intravesical	Filed BLA	05/23/2023	Yes	No
SRP-9001 (RG-6356)	delandistrogene moxeparvovec	Sarepta/ Roche	gene therapy	Duchenne muscular dystrophy	IV	Filed BLA	05/29/2023	Yes	Yes
Zynquista	sotagliflozin	Lexicon	sodium-dependent glucose transporter 1 (SGLT-1) and SGLT-2 inhibitor	Diabetes mellitus	PO	Filed NDA	05/31/2023	No	No
AOP-200704	landiolol	Eagle Pharmaceuticals	cardio-selective beta-1 adrenergic blocker	Dysrhythmia	IV	Filed NDA	06/01/2023	No	No
CyclASol	cyclosporine	Novaliq	immunosuppressant	Dry eye disease	OPH	Filed NDA	06/08/2023	No	No
CYT-387	momelotinib	GlaxoSmithKline	janus kinase inhibitor	Myeloproliferative disorders	PO	Filed NDA	06/16/2023	Yes	Yes
FT-218	sodium oxybate extended-release	Avadel	dopamine receptor agonist	Narcolepsy	PO	Tentative Approval	06/17/2023	Yes	Yes

Drug name	Generic name	Company	Mechanism of Action	Disease State	Route	FDA Status	Estimated release date	Specialty drug	Orphan drug
VBP-15	vamorolone	Santhera Pharmaceuticals	corticosteroid	Duchenne muscular dystrophy	PO	Filed NDA	06/27/2023	Yes	Yes
NOV-03	perfluorohexyloctane	Bausch/ Novaliq	tear film stabilizer	Dry eye disease	OPH	Filed NDA	06/28/2023	No	No
UCB-4940 (CDP-4940)	bimekizumab	UCB	interleukin-17 receptor inhibitor	Plaque psoriasis	SC	CRL	2Q2023	Yes	No
ritlecitinib	ritlecitinib	Pfizer	janus kinase inhibitor	Alopecia areata	PO	Filed NDA	2Q2023	Yes	No
IPX-203	carbidopa/ levodopa	Amneal	dopamine precursor/ dopa-decarboxylase inhibitor	Parkinson's disease	PO	Filed NDA	06/30/2023	No	No
CUTX-101	copper histidinate	Fortress Biotech	copper replacement	Menkes Disease	SC	InTrial	1H2023	Yes	Yes
OPNT-003	nalmefene	Opiant Pharmaceuticals	opioid receptor antagonist	Opioid overdose	Intranasal	InTrial	Mid-2023	No	No
TAK-003	Dengue fever vaccine	Takeda	vaccine	Dengue fever	SC	InTrial	Mid-2023	Yes	No
obeticholic acid	obeticholic acid	Intercept Pharmaceuticals	farnesoid X receptor agonist	Nonalcoholic steatohepatitis	PO	CRL	Mid-2023	Yes	No
MEDI-8897	nirsevimab	AstraZeneca/ Sanofi	anti-RSV monoclonal antibody D25	Respiratory syncytial virus	IM	InTrial	Mid-2023	No	No
PF-3084014 (PF-03084014)	nirogacestat	SpringWorks Therapeutics	gamma secretase inhibitor	Desmoid tumors	PO	InTrial	Mid-2023	Yes	Yes

Drug name	Generic name	Company	Mechanism of Action	Disease State	Route	FDA Status	Estimated release date	Specialty drug	Orphan drug
LN-144	lifileucel	Iovance Biotherapeutics	tumor infiltrating lymphocyte	Melanoma	IV	InTrial	Mid-2023	Yes	Yes
Neutrolin (CRMD-003, CRMD-004)	citrate/ taurolidine/ heparin	CorMedix	antimicrobial agent/ anticoagulant	Catheter-related infections	IV	CRL	Mid-2023	No	No
SGX-301	synthetic hypericin	Soligenix	synthetic hypericin	Cutaneous T-cell lymphoma	TOP	InTrial	Mid-2023	Yes	Yes
AKCEA-TTR-LRx	eplontersen	AstraZeneca/ Ionis	antisense oligonucleotide	Hereditary transthyretin-mediated amyloid polyneuropathy	SC	InTrial	Mid-2023	Yes	Yes
MT-1621	deoxythymidine/ deoxycytidine	Zogenix	deoxynucleoside	Thymidine kinase 2 deficiency	PO	InTrial	Mid-2023	Yes	Yes
RG-7440 (GDC-0068)	ipatasertib	Roche	pan-Akt inhibitor	Prostate cancer	PO	InTrial	Mid-2023	Yes	No
NN-7415	concizumab	Novo Nordisk	anti-tissue factor pathway inhibitor	Hemophilia A and hemophilia B	SC	InTrial	Mid-2023	Yes	Yes
PF-06928316 (RSVpreF)	PF-06928316	Pfizer	vaccine	Respiratory syncytial virus	IM	InTrial	Mid-2023	No	No
ARS-1	epinephrine	ARS Pharmaceuticals	non-selective alpha/ beta-adrenergic receptor agonist	Anaphylaxis	Intranasal	Filed NDA	Mid-2023	No	No
Melblez Kit	melphalan	Delcath	phenylalanine mustard	Hepatocellular cancer/ melanoma	INJ	InTrial	Mid-2023	Yes	Yes

Drug name	Generic name	Company	Mechanism of Action	Disease State	Route	FDA Status	Estimated release date	Specialty drug	Orphan drug
efgartigimod SC	efgartigimod-PH20	argenx/ Halozyme	neonatal Fc receptor antibody	Generalized myasthenia gravis	SC	Filed BLA	07/21/2023	Yes	Yes
I/Ontak	denileukin diftitox	Citius	CD25-directed cytotoxin	Cutaneous T-cell lymphoma	IV	Filed BLA	07/28/2023	Yes	Yes
PDP-716	brimonidine	Visiox Pharma	alpha-2 agonist	Glaucoma	OPH	Filed NDA	08/05/2023	No	No
ONS-5010	bevacizumab-vikg	Outlook Therapeutics	anti-VEGF antibody	Wet age-related macular degeneration	Intravitreal	Filed BLA	08/29/2023	Yes	No
TP-03	lotilaner	Tarsus Pharmaceuticals	antagonist of insect and arachnid GABA-Cl channels	Demodex blepharitis	TOP	Filed NDA	09/07/2023	No	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
BBI-4000	sofpironium bromide	Brickell	anticholinergic	Hyperhidrosis	TOP	Filed NDA	09/26/2023	No	No
PTC-AADC	eladocagene exuparvovec	PTC Therapeutics	gene therapy	Aromatic L-amino acid decarboxylase deficiency	Intracerebral	InTrial	3Q2023	Yes	Yes
arimoclomol	arimoclomol	Orphazyme	cytoprotectives	Niemann-Pick disease	PO	CRL	3Q2023	Yes	Yes
MILR-1444A	lebrikizumab	Eli Lilly	interleukin-13 inhibitor	Atopic dermatitis	SC	Filed BLA	3Q2023	Yes	No

Drug name	Generic name	Company	Mechanism of Action	Disease State	Route	FDA Status	Estimated release date	Specialty drug	Orphan drug
ETX-2514 (SUL-DUR)	durlobactam/ sulbactam	Entasis Therapeutics	broad-spectrum β-lactamase inhibitor/ beta-lactam antimicrobial	Bacterial infections	IV	InTrial	3Q2023	No	No
UCB-7665	rozanolixizumab	UCB	neonatal Fc receptor inhibitor	Generalized myasthenia gravis	SC	InTrial	3Q2023	Yes	Yes
VLA-1553	VLA-1553	Valneva	vaccine	Chikungunya virus	IM	InTrial	3Q2023	No	No
GC-4419	avasopasem manganese	Galera Therapeutics	dismutase mimetic	Radiotherapy-induced oral mucositis	IV	InTrial	3Q2023	Yes	No
GEN-3013	epcoritamab	AbbVie	CD3/CD20 monoclonal antibody	Diffuse large B-cell lymphoma	SC	Filed BLA	10/28/2023	Yes	No
NS-2 (ALDX-1E1, ADX-102)	reproxalap	Aldeyra Therapeutics	aldehyde antagonist	Dry eye disease	OP	InTrial	4Q2023	No	No
RG-1450	gantenerumab	Roche	beta-amyloid monoclonal antibody	Alzheimer's disease	SC	InTrial	4Q2023	Yes	No
OTL-200	atidarsagene autotemcel	Orchard Therapeutics	gene therapy	Leukodystrophy	IV	InTrial	4Q2023	Yes	Yes
TRC-101	veverimer	Tricida	carrier protein modulator	Chronic kidney disease	PO	CRL	4Q2023	Yes	No
SDN-037	difluprednate	Visiox	corticosteroid	Ocular inflammation/pain	OPH	InTrial	4Q2023	No	No
CTX-001 (Exa-cel)	exagamglogene autotemcel	CRISPR Therapeutics/ Vertex	gene editing (CRISPR)	Beta-thalassemia; sickle cell anemia	IV	InTrial	4Q2023	Yes	Yes

Drug name	Generic name	Company	Mechanism of Action	Disease State	Route	FDA Status	Estimated release date	Specialty drug	Orphan drug
OX-124	naloxone	Orexo	opioid antagonist	Opioid overdose	Intranasal	InTrial	4Q2023	No	No
MBG-453	sabatolimab	Novartis	anti-TIM-3	Myelodysplastic syndrome	IV	InTrial	4Q2023	Yes	No
IDP-126	IDP-126	Bausch Health	retinoid/ antibiotic	Acne	TOP	InTrial	4Q2023	No	No
SAGE-217	zuranolone	Sage Therapeutics/ Biogen	GABA-A receptor allosteric modulator	Major depressive disorder	PO	InTrial	4Q2023	No	No
iDose travoprost	travoprost	Glaukos	prostaglandin analog	Glaucoma/ Ocular hypertension	Intraocular	InTrial	4Q2023	No	No
LentiGlobin	lovotibeglogene autotemcel	bluebird bio	gene therapy	Sickle cell disease	IV	InTrial	4Q2023	Yes	Yes
X4P-001 (X-4P-001, X4-136, X4P-001-RD)	mavorixafor	X4 Pharma	CXC receptor type 4 inhibitor	WHIM syndrome	PO	InTrial	4Q2023	Yes	Yes
FMXIN-001	naloxone	Nasus Pharma	opioid antagonist	Opioid overdose	Intranasal	InTrial	4Q2023	No	No
SPI-014	lanthanum dioxycarbonate	Unicycive	phosphate binder	Hyperphosphatemia	PO	InTrial	4Q2023	No	No
RG-6026	glofitamab	Roche	anti-CD20/CD3 T cell monoclonal antibody	Diffuse large B cell lymphoma	IV	InTrial	2H2023	Yes	No
PB-2452	bentracimab	PhaseBio	antiplatelet monoclonal antibody	Antiplatelet drug toxicity	IV	InTrial	2H2023	No	No

Drug name	Generic name	Company	Mechanism of Action	Disease State	Route	FDA Status	Estimated release date	Specialty drug	Orphan drug
Zeftera	ceftobiprole	Basilea	cephalosporin antibiotic	Bacterial infections	IV	InTrial	2H2023	No	No
Translarna	ataluren	PTC Therapeutics	gene transcription modulator	Duchenne muscular dystrophy	PO	CRL	2H2023	Yes	Yes
REGN-1979	odronextamab	Regeneron	CD20/CD3 monoclonal antibody	Follicular lymphoma/ diffuse large b-cell lymphoma	IV	InTrial	2H2023	Yes	Yes
NVX-CoV2373	coronavirus vaccine	Novavax	vaccine	Novel coronavirus disease 2019 (COVID-19)	IM	InTrial	2H2023	No	No
ATI-1501	metronidazole	Saptalis	nitroimidazole	Fungal infections, anaerobic bacterial infections	PO	InTrial	2H2023	No	No
DCR-PHXC	nedosiran	Novo Nordisk	glycolate oxidase antagonist	hyperoxaluria	SC	InTrial	2H2023	Yes	Yes
EBV-CTL (ATA-129)	tabelecleucel	Atara Biotherapeutics	cell therapy	Lymphoproliferative disorder	IV	InTrial	2H2023	Yes	Yes
SB-206	SB-206	Novan Therapeutics	nitric oxide-releasing compound	Molluscum contagiosum	TOP	InTrial	2H2023	No	No
REGN-3918	pozelimab	Regeneron	C5a receptor inhibitor	CHAPLE disorder	IV/SC	InTrial	2H2023	Yes	Yes
CK-301	cosibelimab	Checkpoint Therapeutic	anti programmed cell death ligand 1	Cutaneous squamous cell carcinoma	IV	InTrial	2H2023	Yes	No

Drug name	Generic name	Company	Mechanism of Action	Disease State	Route	FDA Status	Estimated release date	Specialty drug	Orphan drug
SPN-830	apomorphine	Supernus Pharmaceuticals	non-ergoline dopamine agonist	Parkinson's disease	SC infusion	CRL	2H2023	Yes	No
ALXN-1840 (WTX-101)	bis-choline tetrathiomolybdate	AstraZeneca	chelating agent	Wilson's disease	PO	InTrial	2H2023	Yes	Yes
RG-7433 (ABT-263)	navitoclax	AbbVie	Bcl-2 inhibitor	Myelofibrosis	PO	InTrial	2H2023	Yes	Yes
YN-96D1	rivoceranib (apatinib)	Elevar Therapeutics	vascular endothelial growth factor receptor antagonist	Gastric cancer	PO	InTrial	2H2023	Yes	Yes
Adstiladrin	nadofaragene firadenovec	FerGene	gene therapy	Bladder cancer	Intravesical	CRL	2H2023	Yes	No
LN-145	LN-145	Iovance Biotherapeutics	tumor infiltrating lymphocyte	Cervical Cancer	IV	InTrial	2H2023	Yes	No
F-901318	olorofim	F2G	orotomide antifungal	Aspergillosis	PO/IV	InTrial	2H2023	No	Yes
ADP-A2M4 (MAGE-A4)	afamitresgene autoleucel	Adaptimmune	SPEAR T-cell therapy	Sarcoma	IV	InTrial	2H2023	Yes	Yes
CNM-Au8	CNM-Au8	Clene	gold nanocrystal	Amyotrophic lateral sclerosis	PO	InTrial	2H2023	Yes	Yes
APD-334	etrasimod	Pfizer/ Arena Pharmaceuticals	S1P1 receptor agonist	Ulcerative colitis	PO	InTrial	2H2023	Yes	No
Prochymal	remestemcel-L	Mesoblast	mesenchymal stem cells	Graft vs. Host disease	IV	CRL	2023	Yes	Yes

Drug name	Generic name	Company	Mechanism of Action	Disease State	Route	FDA Status	Estimated release date	Specialty drug	Orphan drug
pivmecillinam	pivmecillinam	Utility Therapeutics	amidinopenicillin	Urinary tract infections	PO	InTrial	2023	No	No
VP-102	cantharidin	Verrica	vesicant (blistering agent)	Molluscum	TOP	CRL	2023	No	No
Hepcludex	bulevirtide	Gilead	HBV receptor binder	Hepatitis delta virus	SC	CRL	2023	Yes	Yes
OMS-721	narsoplimab	Omeros	anti-MASP-2 monoclonal antibody	Hematopoietic stem cell transplant-associated thrombotic microangiopathy	IV	CRL	2023	Yes	Yes
GC-5107	human immunoglobulin	GC Pharma	human immunoglobulin	Primary immunodeficiencies	IV	CRL	2023	Yes	No
Qtrypta	zolmitriptan	Zosano	triptans	Acute migraines	TOP	CRL	2023	No	No
Doria	risperidone	Laboratorios Farmacéuticos Rovi	atypical antipsychotic	Schizophrenia	IM	CRL	2023	Yes	No
CAM-2038	buprenorphine	Braeburn	opioid receptor agonist (partial)	Opioid use disorder	SC	CRL	2023	Yes	No
Dihydroergotamine autoinjector	dihydroergotamine	Amneal Pharmaceuticals	ergot derivative	Migraine	SC	InTrial	2023	No	No
R-1646 (RO-4926219, AF-219, MK-7264)	gefapixant	Merck/ Roche	P2X3 antagonist	Chronic cough	PO	CRL	Late 2023	No	No

Drug name	Generic name	Company	Mechanism of Action	Disease State	Route	FDA Status	Estimated release date	Specialty drug	Orphan drug
ACT-132577	aprocitentan	Johnson & Johnson/ Idorsia	endothelin receptor antagonist	Hypertension	PO	InTrial	Late 2023	No	No
ADX-2191	methotrexate	Aldeyra Therapeutics	dihydrofolate reductase inhibitor	Proliferative vitreoretinopathy	Intravitreal	InTrial	Late 2023	Yes	Yes
ADV-7103	tripotassium citrate monohydrate/ potassium hydrogen carbonate	Advicenne	potassium	Distal rental tubular acidosis	PO	InTrial	Late 2023	Yes	No
P-2B001 (P2-B001, P2B-001, P2B001)	pramipexole/ rasagiline	Pharma Two B	dopamine agonist/ monoamine oxidase B inhibitor	Parkinson's disease	PO	InTrial	Late 2023	No	No
TAK-755 (SHP-655)	TAK-755	Takeda	ADAMTS13 enzyme	Thrombotic thrombocytopenic purpura	IV	InTrial	Late 2023	Yes	Yes
PSD-502	lidocaine/ prilocaine	Plethora/ Recordati	sodium channel blocker	Premature ejaculation	TOP	InTrial	Late 2023	No	No
LY-686017	tradipitant	Vanda Pharmaceuticals	neurokinin 1 receptor antagonist	Gastroparesis	PO	InTrial	Late 2023	No	No
MT-7117	dersimelagon	Mitsubishi Tanabe Pharma	Undisclosed	Erythropoietic protoporphyria	PO	InTrial	Late 2023	Yes	No
MOR-202	felzartamab	I-Mab	anti-CD38 monoclonal antibody	Multiple myeloma	IV	InTrial	Late 2023	Yes	No
SAR-408701	SAR-408701	Sanofi	antibody-drug conjugate	Non-small cell lung cancer	IV	InTrial	Late 2023	Yes	No

Drug name	Generic name	Company	Mechanism of Action	Disease State	Route	FDA Status	Estimated release date	Specialty drug	Orphan drug
MGL-3196 (VIA-3196)	resmetirom	Madrigal	beta-selective thyroid hormone receptor agonist	Nonalcoholic steatohepatitis	PO	InTrial	Late 2023	Yes	No
RG-6171	giredestrant	Roche	selective estrogen receptor degrader	Breast cancer	PO	InTrial	Late 2023	Yes	No
Iomab-B	iodine I 131 monoclonal antibody BC8	Actinium	anti-CD45 monoclonal antibody	Acute myeloid leukemia	IV	InTrial	Late 2023	Yes	Yes
Nyxol	phentolamine	Ocuphire	Alpha-1 and alpha-2 blocker	Mydriasis reversal	OPH	InTrial	Late 2023	No	No
CPN-301	clobetasol propionate	Formosa Pharmaceuticals/ AimMax Therapeutics	corticosteroid	Eye inflammation/ pain	OPH	InTrial	Late 2023	No	No
Tirzepatide (for weight loss)	tirzepatide	Eli Lilly	glucose-dependent insulinotropic polypeptide receptor and glucagon-like peptide-1 receptor agonist	Chronic weight management	SC	InTrial	Late 2023	No	No

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

Key pending indication forecast

Optum Rx key pending indication forecast

Brand name	Generic name	Company	Mechanism of Action	Therapeutic use	Proposed New Indication	Route of administration	Estimated approval date
Brexafemme	ibrexafungerp	Scynexis	triterpenoid antifungal	Recurrent vulvovaginal candidiasis (prevention)	Prevention of recurrent vulvovaginal candidiasis	PO	11/30/2022
Lynparza	olaparib	AstraZeneca/ Merck	poly (ADP-ribose) polymerase inhibitor	Prostate cancer	In combination with abiraterone and prednisone or prednisolone, for treatment of adult patients with metastatic castration-resistant prostate cancer	PO	4Q2022
Vraylar	cariprazine	AbbVie	dopamine D3-preferring D3/D2 receptor partial agonist	Major depressive disorder	Adjunctive treatment of patients with major depressive disorder	PO	12/22/2022
Injectafer	ferric carboxymaltose	Daiichi Sankyo	iron replacement product	Chronic heart failure - anemia	Treatment of heart failure and iron deficiency, either with or without anemia	IV	1Q2023
Tymlos	abaloparatide	Radius Health	human parathyroid hormone related peptide analog	Osteoporosis (men)	Treatment of men with osteoporosis at high risk for fracture	SC	01/01/2023
Tukysa	tucatinib	Seagen	kinase inhibitor	Colorectal cancer	In combination with trastuzumab in patients with previously treated HER2-positive metastatic colorectal cancer	PO	01/19/2023
Brukinsa	zanubrutinib	BeiGene	kinase inhibitor	Chronic lymphocytic leukemia/ small lymphocytic lymphoma	Treatment of adult patients with chronic lymphocytic leukemia or small lymphocytic lymphoma	PO	01/20/2023

Brand name	Generic name	Company	Mechanism of Action	Therapeutic use	Proposed New Indication	Route of administration	Estimated approval date
Keytruda	pembrolizumab	Merck	programmed death receptor-1-blocking antibody	Non-small cell lung cancer	Adjuvant treatment of patients with stage IB (≥4 centimeters), II or IIIA non-small cell lung cancer following complete surgical resection	IV	1Q2023
Takhzyro	lanadelumab-flyo	Takeda	plasma kallikrein inhibitor	Hereditary angioedema	Prophylaxis to prevent attacks of hereditary angioedema in adult and pediatric patients 2 years and older	SC	1H2023
Trodelvy	sacituzumab govitecan-hziy	Gilead	Trop-2-directed antibody and topoisomerase inhibitor conjugate	Breast cancer (HR+/HER- metastatic)	Treatment of adult patients with unresectable locally advanced or metastatic hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative (IHC 0, IHC 1+ or IHC 2+/ISH–) breast cancer who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting	IV	02/11/2023
Eylea	aflibercept	Regeneron	vascular endothelial growth factor inhibitor	Retinopathy of prematurity	Treatment of retinopathy of prematurity in preterm infants	Intravitreal	02/11/2023
Eylea	aflibercept	Regeneron	vascular endothelial growth factor inhibitor	Diabetic retinopathy (16-week dosing)	New dosing regimen: Every-16-weeks dosing regimen for treatment of non-proliferative diabetic retinopathy	Intravitreal	02/28/2023
Polivy	polatuzumab vedotin-piiq	Genentech	CD79b-directed antibody-drug conjugate	Diffuse large B-cell lymphoma	In combination with Rituxan (rituximab) plus cyclophosphamide, doxorubicin and prednisone (R-CHP) for the treatment of people with previously untreated diffuse large B-cell lymphoma	IV	04/02/2023

Brand name	Generic name	Company	Mechanism of Action	Therapeutic use	Proposed New Indication	Route of administration	Estimated approval date
Qulipta	atogepant	AbbVie	calcitonin gene-related peptide receptor antagonist	Chronic migraine prophylaxis	Preventive treatment of chronic migraine in adults	PO	04/21/2023
Sogroya	somapacitan-beco	Novo Nordisk	growth hormone analog	Pediatric growth hormone deficiency	Treatment of pediatric growth hormone deficiency	SC	04/28/2023
Tecentriq	atezolizumab	Roche	programmed death-ligand 1 blocking antibody	Sarcoma	Treatment of alveolar soft part sarcoma	IV	04/2023
Padcev	enfortumab vedotin-ejfv	Seagen	Nectin-4-directed antibody and microtubule inhibitor conjugate	Urothelial cancer (with Keytruda)	In combination with Keytruda (pembrolizumab), as first-Line Treatment for advanced urothelial cancer	IV	04/2023
Trikafta	elexacaftor/tezacaftor/ivacaftor; ivacaftor	Vertex	cystic fibrosis transmembrane conductance regulator modulators	Cystic fibrosis (pediatric)	Treatment of cystic fibrosis in patients aged 2 years and older who have at least one F508del mutation in the CFTR gene or a mutation in the CFTR gene that is responsive based on in vitro data	PO	05/03/2023
Rinvoq	upadacitinib	AbbVie	Janus kinase inhibitor	Crohn's disease	Treatment of Crohn's disease	PO	05/26/2023
Camzyos	mavacamten	Bristol Myers Squibb	cardiac myosin inhibitor	Reduce septal reduction therapy	To reduce the need for septal reduction therapy in adults with symptomatic New York Heart Association (NYHA) class II-III obstructive hypertrophic cardiomyopathy	PO	06/16/2023
Rubraca	rucaparib	Clovis Oncology	poly (ADP-ribose) polymerase inhibitor	Ovarian cancer	First-line maintenance treatment for women with advanced ovarian cancer regardless of biomarker status who have responded to first-line platinum-based chemotherapy	PO	07/13/2023

Brand name	Generic name	Company	Mechanism of Action	Therapeutic use	Proposed New Indication	Route of administration	Estimated approval date
Daxxify	daxibotulinumtoxinA-lanm	Revance Therapeutics	acetylcholine release inhibitor/ neuromuscular blocking agent	Cervical dystonia	Treatment of cervical dystonia	IM	08/20/2023
Cosentyx	secukinumab	Novartis	IL-17 receptor antagonist	Hidradenitis suppurativa	Treatment of hidradenitis suppurativa	SC	08/31/2023
Prevnar 20	pneumococcal 20-valent conjugate	Pfizer	vaccine	Pneumococcal disease (pediatric)	Active immunization for the prevention of pneumonia and invasive disease in pediatric patients	IM	08/31/2023

References:

Acadia Pharmaceuticals Press Release. Acadia Pharmaceuticals Web site. Acadia Pharmaceuticals announces positive top-line results from the pivotal Phase 3 Lavender trial of trofinetide in Rett syndrome. https://acadia.com/media/news-releases/acadia-pharmaceuticals-announces-positive-top-line-results-from-the-pivotal-phase-3-lavender-trial-of-trofinetide-in-rett-syndrome. December 6, 2021. Accessed September 23, 2022.

Acadia Pharmaceuticals Press Release. Acadia Pharmaceuticals Web site. Acadia Pharmaceuticals announces trofinetide New Drug Application for the treatment of Rett syndrome has been accepted for filing and review by U.S. FDA. https://acadia.com/media/news-releases/acadia-pharmaceuticals-announces-trofinetide-new-drug-application-for-the-treatment-of-rett-syndrome-has-been-accepted-for-filing-and-review-by-u-s-fda. September 12, 2023. Accessed September 23, 2022.

American Cancer Society. Breast Cancer. American Cancer Society Web site. https://www.cancer.org/cancer/breast-cancer.html. Accessed August 31, 2022.

Apellis Pharmaceuticals Press Release. Apellis Pharmaceuticals Web site. Apellis announces 24-month results showing increased effects over time with pegcetacoplan in Phase 3 DERBY and OAKS studies in geographic atrophy (GA). https://investors.apellis.com/news-releases/news-release-details/apellis-announces-24-month-results-showing-increased-effects. August 24, 2022. Accessed September 6, 2022.

Apellis Pharmaceuticals Press Release. Apellis Pharmaceuticals Web site. Apellis announces FDA acceptance and Priority Review of the New Drug Application for pegcetacoplan for the treatment of geographic atrophy (GA). https://investors.apellis.com/news-releases/news-release-details/apellis-announces-fda-acceptance-and-priority-review-new-drug-0. July 19, 2022. Accessed September 6, 2022.

Apellis Pharmaceuticals Press Release. Apellis Pharmaceuticals Web site. Apellis announces top-line results from Phase 3 DERBY and OAKS studies in geographic atrophy (GA) and plans to submit NDA to FDA in the first half of 2022. https://investors.apellis.com/news-releases/news-release-details/apellis-announces-top-line-results-phase-3-derby-and-oaks. September 9, 2021. Accessed September 6, 2022.

Astellas Pharma Press Release. Astellas Pharma Web site. Astellas to present fezolinetant 12-week findings from Phase 3 SKYLIGHT 2™ trial in oral session at The North American Menopause Society 2021 Annual Meeting. https://www.astellas.com/en/system/files/news/2021-09/20210922_en_1.pdf. September 22, 2021. Accessed August 22, 2022.

Astellas Pharma Press Release. Astellas Pharma Web site. Astellas to present 12-week data from pivotal Phase 3 SKYLIGHT 1™ trial of fezolinetant in oral session at the American College of Obstetricians and Gynecologists Annual Meeting. https://www.astellas.com/en/system/files/news/2022-05/20220506_en_1_1.pdf. May 6, 2022. Accessed August 22, 2022.

Astellas Pharma Press Release. Astellas Pharma Web site. U.S. FDA accepts Astellas' New Drug Application for fezolinetant. https://www.astellas.com/en/news/26126. August 18, 2022. Accessed August 22, 2022.

Bidard FC, Kaklamani VG, Neven P, et al. Elacestrant (oral selective estrogen receptor degrader) versus standard endocrine therapy for estrogen receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer: results from the randomized Phase III EMERALD trial. *J Clin Oncol*. 2022:JCO2200338. Epub ahead of print.

Biogen Press Release. Biogen Web site. Biogen announces topline results from the tofersen Phase 3 study and its open-label extension in SOD1-ALS. https://investors.biogen.com/news-releases/news-release-details/biogen-announces-topline-results-tofersen-phase-3-study-and-its. October 17, 2021. Accessed August 31, 2022.

Biogen Press Release. Biogen Web site. FDA accepts Biogen's New Drug Application and grants priority review of tofersen for a rare, genetic form of ALS. https://investors.biogen.com/news-releases/news-release-details/fda-accepts-biogens-new-drug-application-and-grants-priority. July 26, 2022. Accessed August 31, 2022.

Biogen Press Release. Biogen Web site. New 12-month tofersen data presented at ENCALS Meeting show clinically meaningful benefit in people with SOD1-ALS. https://investors.biogen.com/news-releases/news-release-details/new-12-month-tofersen-data-presented-encals-meeting-show. June 3, 2022. Accessed August 31, 2022.

Biohaven Pharmaceutical Press Release. Biohaven Pharmaceutical Web site. Biohaven achieves positive topline results in pivotal Phase 2/3 study of vazegepant, the first and only intranasal CGRP receptor antagonist in clinical development for the acute treatment of migraine. https://www.biohavenpharma.com/investors/news-events/press-releases/12-17-2019. December 17, 2019. Accessed August 29, 2022.

Biohaven Pharmaceutical Press Release. Biohaven Pharmaceutical Web site. Biohaven reports positive topline results from pivotal migraine trial of intranasal zavegepant demonstrating ultra-rapid pain relief by 15 minutes; prepares for submission of New Drug Application. https://www.biohavenpharma.com/investors/news-events/press-releases/12-06-2021-0. December 6, 2021. Accessed August 29, 2022.

Biohaven Pharmaceutical Press Release. Biohaven Pharmaceutical Web site. US FDA accepted for review Biohaven's New Drug Application (NDA) filing of intranasal zavegepant for the acute treatment of migraine. https://www.biohavenpharma.com/investors/news-events/press-releases/05-23-2022-0. May 23, 2022. Accessed August 29, 2022.

BioMarin Press Release. BioMarin Web site. FDA accepts BioMarin's Biologics License Application (BLA) for valoctocogene roxaparvovec AAV gene therapy for adults with severe hemophilia A. https://investors.biomarin.com/2022-10-12-FDA-Accepts-BioMarins-Biologics-License-Application-BLA-for-Valoctocogene-Roxaparvovec-AAV-Gene-Therapy-for-Adults-with-Severe-Hemophilia-A. October 12, 2022. Accessed October 28, 2022.

BioMedTracker Drug Intelligence Platform. BioMedTracker Web site. http://www.biomedtracker.com.

Centers for Disease Control and Prevention (CDC). Alzheimer's disease and related dementias. CDC Web site. https://www.cdc.gov/aging/aginginfo/alzheimers.htm. Last reviewed October 26, 2020. Accessed September 9, 2022.

Centers for Disease Control and Prevention (CDC). Heart failure. CDC Web site. https://www.cdc.gov/heartdisease/heart_failure.htm. Last reviewed September 8, 2020. Accessed August 30, 2022.

Centers for Disease Control and Prevention (CDC). Hemophilia. CDC Web site. https://www.cdc.gov/ncbddd/hemophilia. Last reviewed August 1, 2022. Accessed August 30, 2022.

Cytokinetics Press Release. Cytokinetics Web site. Cytokinetics announces date for FDA Advisory Committee Meeting to review New Drug Application for omecamtiv mecarbil. https://ir.cytokinetics.com/news-releases/news-release-details/cytokinetics-announces-date-fda-advisory-committee-meeting. Accessed June 24, 2022.

Eisai Press Release. Eisai Web site. Lecanemab confirmatory Phase 3 Clarity AD study met primary endpoint, showing highly statistically significant reduction of clinical decline in large global clinical study of 1,795 participants with early Alzheimer's disease. https://www.eisai.com/news/2022/news202271.html. September 28, 2022. Accessed October 4, 2022.

Eisai Press Release. Eisai Web site. The U.S. FDA accepted and grants Priority Review for Eisai's Biologics License Application of lecanemab for early Alzheimer's disease under the accelerated approval pathway. https://www.eisai.com/news/2022/news202254.html. July 6, 2022. Accessed October 4, 2022.

GlaxoSmithKline Press Release. GlaxoSmithKline Web site. US Food and Drug Administration accepts New Drug Application for daprodustat. https://www.gsk.com/en-gb/media/press-releases/us-food-and-drug-administration-accepts-new-drug-application-for-daprodustat. April 19, 2022. Accessed August 26, 2022.

Krystal Biotech Press Release. Krystal Biotech Web site. FDA accepts Krystal Biotech's Biologics License Application for dystrophic epidermolysis bullosa. https://ir.krystalbio.com/news-releases/news-release-details/fda-accepts-krystal-biotechs-biologics-license-application. August 18, 2022. Accessed August 26, 2022.

Krystal Biotech Press Release. Krystal Biotech Web site. New GEM-3 Phase 3 results for B-VEC presented at 2022 American Academy of Dermatology Annual Meeting. https://ir.krystalbio.com/news-releases/news-release-details/new-gem-3-phase-3-results-b-vec-presented-2022-american-academy. March 26, 2022. Accessed August 29, 2022.

Menarini Group Press Release. Menarini Group Web site. Menarini Group's elacestrant granted priority review by the U.S. FDA for patients with ER+/HER2- advanced or metastatic breast cancer. https://www.menarini.com/en-us/news/news-detail/menarini-groups-elacestrant-granted-priority-review-by-the-us-fda-for-patients-with-erher2-advanced-or-metastatic-breast-cancer. August 11, 2022. Accessed August 31, 2022.

Mintun MA, Lo AC, Duggan Evans C, et al. Donanemab in early Alzheimer's disease. *N Engl J Med*. 2021;384(18):1691-1704.

National Cancer Institute. Cancer stat facts: female breast cancer subtypes. National Cancer Institute Web site. https://seer.cancer.gov/statfacts/html/breast-subtypes.html. Accessed August 31, 2022.

National Organization for Rare Disorders (NORD). Amyotrophic lateral sclerosis. NORD Web site. https://rarediseases.org/rare-diseases/amyotrophic-lateral-sclerosis. Accessed August 31, 2022.

National Organization for Rare Disorders (NORD). Epidermolysis bullosa. NORD Web site. https://rarediseases.org/rare-diseases/epidermolysis-bullosa. Accessed August 29, 2022.

National Organization for Rare Disorders (NORD). Rett syndrome. NORD Web site. https://rarediseases.org/rare-diseases/rett-syndrome. Accessed September 23, 2022.

Ozelo MC, Mahlangu J, Pasi KJ, et al; GENEr8-1 Trial Group. valoctocogene roxaparvovec gene therapy for hemophilia A. N Engl J Med. 2022;386(11):1013-1025.

Sanofi Press Release. Sanofi Web site. FDA grants priority review to efanesoctocog alfa for people with hemophilia A. https://www.sanofi.com/en/media-room/press-releases/2022/2022-08-30-05-30-00-2506359. August 30, 2022. Accessed August 30, 2022.

Sanofi Press Release. Sanofi Web site. Pivotal data demonstrate once-weekly efanesoctocog alfa provides superior bleed protection compared to prior factor prophylaxis. https://www.sanofi.com/en/media-room/press-releases/2022/2022-07-10-13-45-00-2476897. July 10, 2022. Accessed August 30, 2022.

Singh AK, Carroll K, McMurray JJV; ASCEND-ND Study Group. Daprodustat for the treatment of anemia in patients not undergoing dialysis. *N Engl J Med*. 2021;385(25):2313-2324.

Singh AK, Carroll K, Perkovic V; ASCEND-D Study Group. Daprodustat for the treatment of anemia in patients undergoing dialysis. *N Engl J Med*. 2021;385(25):2325-2335.

Swanson CJ, Zhang Y, Dhadda S, et al. A randomized, double-blind, phase 2b proof-of-concept clinical trial in early Alzheimer's disease with lecanemab, an anti-Aβ protofibril antibody. *Alzheimers Res Ther*. 2021 Apr 17;13(1):80.

Teerlink JR, Diaz R, Felker GM, et al; GALACTIC-HF Investigators. Cardiac myosin activation with omecamtiv mecarbil in systolic heart failure. *N Engl J Med*. 2021;384(2):105-116.

UpToDate Database. https://www.uptodate.com.

Optum

optum.com/optumrx

RxOutlook® is published by the OptumRx Clinical Services Department.