OPTUMRx®

RxOutlook®

4th Quarter 2021

In this edition of RxOutlook, we highlight 12 key pipeline drugs with an expected FDA decision by the end of the first quarter 2022. Of note, two long-acting injectable HIV-1 antivirals could be approved in the next quarter. This includes cabotegravir for HIV infection pre-exposure prophylaxis (PrEP). Cabotegravir is administered intramuscularly every 2 months when used for PrEP and would be a competitor to daily oral medications currently used for PrEP (Truvada®, Descovy®). Lenacapavir is a novel HIV-1 capsid inhibitor that is administered subcutaneously once every 6 months for the treatment of multidrug resistant HIV-1 infection. Lenacapavir is also in development for HIV PrEP so these two products could eventually compete with one another for this use.

Tezepelumab is a first-in-class thymic stromal lymphopoietin (TSLP) monoclonal antibody for the treatment of severe asthma. It will be competing with other biologics used for severe asthma such as Nucala® (mepolizumab) and Dupixent® (dupilumab). Like those drugs, tezepelumab is also in development for several other uses outside of asthma, including nasal polyps, chronic spontaneous urticaria, and chronic obstructive pulmonary disease. Vadadustat is a potential first-in-class hypoxia-inducible factor prolyl hydroxylase (HIF-PH) inhibitor for the treatment of anemia associated with chronic kidney disease (CKD). It is the second HIF-PH inhibitor reviewed by the FDA with roxadustat being rejected by the agency back in August 2021. If approved, vadadustat would be an oral alternative to injectable erythropoiesis-stimulating agents (ESAs) for treatment of CKD-associated anemia; however lingering questions about the cardiovascular safety of HIF-PH inhibitors remain.

Continuing recent trends, a significant proportion of drugs with potential approval in the first quarter 2022 have been granted orphan drug designation and would be used for rare conditions. Of the 12 drugs discussed below, 6 have an orphan drug designation. Several of these would be first-in-class treatments for their indications, including mavacamten for obstructive hypertrophic cardiomyopathy, bardoxolone methyl for Alport syndrome, and mitapivat for pyruvate kinase deficiency. Notably, all 6 of the orphan drugs discussed in this review are administered orally and would be expected to be high-cost pharmacy benefit drugs.

Approval decisions for other key novel therapies are expected in late 2021 or first quarter 2022 but are not reviewed in this report because they were covered in previous editions of RxOutlook. These include: efgartigimod for myasthenia gravis; bimekizumab for plaque psoriasis; dextromethorphan/bupropion for major depressive disorder; abrocitinib for atopic dermatitis; inclisiran for hypercholesterolemia; and gefapixant for chronic cough. Several of these drugs have experienced regulatory delays in their approval decisions.

Finally, while not discussed in detail in this report, we expect the FDA to announce authorizations, full approvals, and additional uses for COVID-19 vaccines and treatments. This will be headlined by potential full approval for Moderna's mRNA vaccine and potential emergency use authorization for Merck's oral drug, molnupiravir, for treatment of COVID-19 infection. We recognize the importance of the anti-COVID-19 drugs but due to the rapidly changing nature of the pandemic, these drugs are out of scope for this report.

Key pipeline drugs with FDA approval decisions expected by end of the 1st quarter 2022

Drug Name	Manufacturer	Indication/Use	Expected FDA Decision Date
Tezepelumab	Amgen/AstraZeneca	Severe asthma	1Q 2022
Levoketoconazole	Xeris Biopharma	Endogenous Cushing's syndrome*	1/1/2022
Cabotegravir	ViiV Healthcare	HIV-1 infection pre-exposure prophylaxis	1/24/2022
Lenacapavir	Gilead	HIV-1 infection	2/28/2022

Drug Name	Manufacturer	Indication/Use	Expected FDA Decision Date
Oteseconazole	Mycovia Pharmaceuticals	Vulvovaginal candidiasis	1/27/2022
Mavacamten	Bristol Myers Squibb	Obstructive hypertrophic cardiomyopathy*	1/28/2022
Faricimab	Roche	Neovascular age-related macular degeneration and diabetic macular edema	1/31/2022
Mitapivat	Agios Pharmaceuticals	Pyruvate kinase deficiency*	2/17/2022
Bardoxolone methyl	Reata Pharmaceuticals	Alport syndrome*	2/25/2022
Ganaxolone	Marinus Pharmaceuticals	CDKL5 deficiency disorder*	3/20/2022
Ublituximab	TG Therapeutics	Chronic lymphocytic leukemia/ small lymphocytic lymphoma*	3/25/2022
Vadadustat	Akebia Therapeutics/ Otsuka Pharmaceutical	Anemia due to chronic kidney disease	3/29/2022

* Orphan Drug Designation

OptumRx 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 2022.

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 2022 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 insights on key drugs

Tezepelumab (Brand Name: To be determined)

Manufacturer: Amgen/AstraZeneca
Regulatory designations: Breakthrough Therapy
Expected FDA decision: 1Q 2022

Therapeutic use

- Treatment of patients with severe asthma

Tezepelumab is in development for treatment of patients with severe asthma.

There is an estimated 1 million people in the U.S. with severe, uncontrolled asthma. Uncontrolled asthma occurs when symptoms persist despite conventional asthma therapy (eg, inhaled corticosteroids). Severe, uncontrolled asthma is debilitating with patients experiencing frequent exacerbations, significant limitations on lung function and a reduced quality of life.

Clinical profile

- Anti-TSLP monoclonal antibody
- SC formulation
- Annualized rate of asthma exacerbations: 0.93 vs. 2.10 with placebo
- Common AEs: Nasopharyngitis, upper respiratory tract infection, headache
- Dosing: Once every 4 weeks

Tezepelumab is a human monoclonal antibody targeting thymic stromal lymphopoietin (TSLP), a key epithelial cytokine. TSLP is released in response to multiple triggers associated with asthma exacerbations, including allergens, viruses and other airborne particles. Expression of TSLP is increased in the airways of patients with asthma and has been correlated with disease severity. Blocking TSLP may prevent the release of pro-inflammatory cytokines by immune cells, resulting in the prevention of asthma exacerbations and improved asthma control.

Pivotal trial data:
The efficacy of tezepelumab was evaluated in two Phase 3 studies: NAVIGATOR and SOURCE.

The NAVIGATOR study was a randomized, double-blinded, placebo-controlled trial in 1,061 adults and adolescents (12 to 17 years old) with severe, uncontrolled asthma, who were receiving treatment with medium- or high-dose inhaled corticosteroids (ICS) plus at least one additional controller medication with or without oral corticosteroids (OCS). The primary endpoint was the annualized rate of asthma exacerbations over a period of 52 weeks. This endpoint was also assessed in patients with baseline blood eosinophil counts of less than 300 cells/μL. In the overall population, the annualized rate of asthma exacerbations was 0.93 with tezepelumab and 2.10 with placebo (rate ratio [RR] 0.44; 95% CI: 0.37, 0.53; $p < 0.001$). In patients with a blood eosinophil count of less than 300 cells/μL, the annualized rate was 1.02 with tezepelumab and 1.73 with placebo (RR 0.59; 95% CI: 0.46, 0.75; $p < 0.001$).

Tezepelumab (continued...)

SOURCE was a randomized, double-blinded, placebo-controlled study in 150 adult patients with severe asthma who required continuous treatment with ICS plus long-acting beta2-agonists (LABA), and chronic treatment with maintenance OCS therapy. The primary endpoint was the percentage reduction from baseline in maintenance daily OCS dose at week 48, while not losing asthma control. This was also evaluated in patients grouped by baseline blood eosinophil count. The key secondary endpoint was the annualized asthma exacerbation rate over 48 weeks. The cumulative odds of achieving greater percentage reduction in maintenance OCS dose at week 48 were numerically higher with tezepelumab than placebo (odds ratio 1.28, 95% CI: 0.69, 2.35; p = 0.43); however, the difference was not statistically significant. In patients with a baseline blood eosinophil count ≥ 150 cells/μL and ≥ 300 cells/μL, the cumulative odds of achieving a category of greater percentage reduction in maintenance OCS dose at week 48 were 2.58 (95% CI: 1.16, 5.75) and 3.49 (95% CI: 1.16, 10.49) times higher with tezepelumab than placebo, respectively. No effects of tezepelumab vs. placebo on OCS dose reduction were observed in patients with low baseline blood eosinophil counts (< 300 cells/μL and < 150 cells/μL).

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

Dosing:
In the pivotal trials, tezepelumab was administered subcutaneously (SC) once every 4 weeks.

Competitive environment

If approved, tezepelumab would offer a first-in-class biologic treatment for patients with severe, uncontrolled asthma. In these patients, several biologic treatment options are currently available with the drug of choice depending on asthma subtype. Tezepelumab would compete with anti-interleukin (IL)-5 targeted therapies (eg, Nucala®, Cinqair®, Fasenra®), which are approved in patients with eosinophilic asthma and Dupixent (dupilumab), an IL-4 receptor antagonist, which is approved in patients with eosinophilic or OCS dependent asthma. The primary differentiator for tezepelumab is the potential for a broad indication in severe asthma, regardless of eosinophil levels. Tezepelumab reduced asthma exacerbations, irrespective of baseline blood eosinophil counts.

Tezepelumab would be a relatively late market entry in the severe asthma category and will be competing with well-established treatments. A novel mechanism of action (MOA) and broad indication means it could be used in a large target population; however, eosinophilia is the leading cause of severe asthma and in patients with this subtype, there are no head-to-head data comparing tezepelumab vs. the IL-5 targeted therapies or Dupixent.

Finally, tezepelumab is also in Phase 2 and 3 trials for the treatment of nasal polyps, chronic spontaneous urticaria, and chronic obstructive pulmonary disease (COPD).

For reference, the wholesale acquisition cost (WAC) for Dupixent is approximately $41,000 per year.

- Advantages: First-in-class treatment for severe asthma, potential for broad indication in severe asthma, also in development for other indications (ie, nasal polyps, urticaria, COPD)
- Disadvantages: Alternative biologics available (eg, Nucala, Dupixent), late market entry, lack of head-to-head trial data
- Reference WAC (Dupixent): ~$41,000 per year

Levoketoconazole (Brand Name: Recorlev®)

Manufacturer: Xeris Biopharma
Regulatory designations: Orphan Drug
Expected FDA decision: January 1, 2022

Therapeutic use

Levoketoconazole is in development for treatment of endogenous Cushing's syndrome.

Cushing's syndrome is a rare endocrine disorder resulting from excessive amounts of the hormone cortisol. The most common cause of endogenous Cushing's syndrome is benign tumors of the pituitary gland. Symptoms can include weight gain, hypertension, diabetes, osteoporosis, and psychologic disturbances such as depression, anxiety, and insomnia.

The estimated incidence of endogenous Cushing's syndrome is approximately 13 per million people annually. Symptoms commonly begin between 25 to 40 years of age.

- Treatment of endogenous Cushing's syndrome

Clinical profile

Levoketoconazole is an enantiomer of ketoconazole and works as a cortisol synthesis inhibitor.

- Cortisol synthesis inhibitor
- Oral formulation

<u>Pivotal trial data:</u>
The efficacy of levoketoconazole was evaluated in two Phase 3 studies: SONICS and LOGICS.

SONICS was an open-label, single-arm study in 94 patients with endogenous Cushing's syndrome. The primary endpoint was the proportion of patients with mean 24-h urinary free cortisol (mUFC) normalization at the end of maintenance, without dose increase during the maintenance phase. The SONICS study met its primary endpoint, with 30% of patients achieving mUFC normalization at the end of the maintenance phase, without a dose increase ($p = 0.015$ vs. null hypothesis of $\leq 20\%$).

- Single-arm study: Proportion with mean urinary free cortisol (mUFC) normalization: 30%

LOGICS was a double-blind, placebo-controlled, randomized-withdrawal study in Cushing's syndrome patients with baseline mUFC at least 1.5 times the upper limit of normal following completion of a single-arm, open-label treatment phase of approximately 14 to 19 weeks, with levoketoconazole individually titrated according to mUFC response. Of the 84 patients dosed in LOGICS, 79 were titrated and 44 patients were randomized to receive levoketoconazole at an individualized therapeutic dose or a matching placebo regimen. The primary endpoint was the proportion of patients with loss of mUFC response during the randomized withdrawal period. At the end of the randomized-withdrawal phase, 95.5% of patients who were withdrawn to placebo had a loss of mUFC response vs. 40.9% for those who remained on levoketoconazole ($p = 0.0002$). The key secondary endpoint of mUFC normalization at the end of the randomized-withdrawal phase was also statistically significant with 45.5% more patients treated with levoketoconazole maintaining mUFC normalization than the placebo arm ($p = 0.0015$).

- Randomized-withdrawal study (loss of mUFC response): 54.5% more patients who were withdrawn to placebo had a loss of mUFC response vs. those who remained on levoketoconazole
- Common AEs: Nausea, hypokalemia, headache, hypertension, diarrhea
- Dosing: Once to twice daily

Levoketoconazole (continued...)

Safety:
The most common adverse events with levoketoconazole use were nausea, hypokalemia, headache, hypertension, and diarrhea.

Dosing:
In the pivotal trials, levoketoconazole was administered orally up to twice daily.

Competitive environment

Levoketoconazole would provide an additional treatment option for the treatment of Cushing's syndrome. The current standard of care starts with pituitary surgery. If additional medical therapy is needed or patients are ineligible for surgery, cortisol synthesis inhibitors and cortisol receptor blockers are commonly used, including ketoconazole (off-label), Korlym® (mifepristone) and Isturisa® (osilodrostat). An additional FDA approved treatment is the somatostatin analog, Signifor® (pasireotide).

The potential advantages of levoketoconazole over ketoconazole are an improved tolerability profile and reduced drug interactions. Levoketoconazole is a more potent enzyme inhibitor allowing for a lower dose to achieve the same efficacy as ketoconazole. However, levoketoconazole does not eliminate some of the known safety issues of ketoconazole. For instance, levoketoconazole was associated with elevated liver function tests and QT prolongation (liver toxicity and QT prolongation are both boxed warnings for ketoconazole).

There are no head-to-head trial data comparing levoketoconazole vs. ketoconazole or other alternatives used for Cushing's syndrome.

- Advantages: Potential to improve tolerability and drug interaction profile vs. ketoconazole
- Disadvantages: Alternatives available, potential for boxed warnings (ie, liver toxicity, QT prolongation), lack of head-to-head trial data

Cabotegravir (Brand Name: To be determined)

Manufacturer: ViiV Healthcare
Regulatory designations: Breakthrough Therapy
Expected FDA decision: January 24, 2022

Therapeutic use

Cabotegravir is in development for pre-exposure prophylaxis (PrEP) of HIV-1 infection in at risk individuals.

There are an estimated 200,000 people in the U.S. using PrEP therapy to prevent possible HIV infection.

- PrEP of HIV-1 infection in at risk individuals

Clinical profile

Cabotegravir is an HIV-1 integrase strand transfer inhibitor (INSTI) formulated as an extended-release injection. It is currently approved as part of a combination regimen with rilpivirine for the treatment of HIV-1 infection (under the brand name Cabenuva®).

- HIV-1 INSTI
- IM formulation

Pivotal trial data:
The efficacy of cabotegravir was evaluated in Phase 2/3, randomized, double-blind study in 4,500 cisgender men who have sex with men and transgender women who have sex with men. Patients were randomized to receive PrEP therapy using intramuscular (IM) cabotegravir every 8 weeks (after an oral lead-in) or oral daily Truvada® (emtricitabine/tenofovir disoproxil fumarate), a current standard of care treatment option. The primary endpoint was the HIV incidence rate. Overall, the HIV incidence rate was 0.41% with cabotegravir vs. 1.22% with Truvada. Cabotegravir was 69% (95% CI: 41, 84) more effective than Truvada in preventing HIV acquisition in the study population.

- Cisgender men and transgender women study: HIV incidence rate: 0.41% vs. 1.22% with Truvada
- Cisgender women: HIV incidence rate: 0.21% vs. 1.86% with Truvada

Cabotegravir was also evaluated in a Phase 3, randomized, double-blind study in 3,223 cisgender women. The study included participants from seven countries in sub-Saharan Africa. Like the previous study, patients were randomized to receive PrEP therapy with either cabotegravir or Truvada and the primary endpoint was the HIV incidence rate. Overall, the HIV incidence rate was 0.21% with cabotegravir vs. 1.86% with Truvada. Cabotegravir was 89% (95% CI: 68, 96) more effective than Truvada.

Safety:
The most common adverse events with cabotegravir use were injection site reactions, diarrhea, headache, pyrexia, fatigue, sleep disorders, nausea, dizziness, flatulence, and abdominal pain.

- Common AEs: Injection site reactions, diarrhea, headache, pyrexia, fatigue, sleep disorders, nausea, dizziness, flatulence, abdominal pain

Dosing:
In the pivotal trials, patients received cabotegravir orally for 5 weeks and then IM once every 2 months.

- Dosing: Once every 2 months

Cabotegravir (continued...)

Competitive environment

If approved, cabotegravir would be the first long-acting PrEP for HIV infection in at risk individuals. The current standard of care includes daily oral administration of Truvada or Descovy® (emtricitabine/tenofovir alafenamide). Cabotegravir demonstrated superiority vs. a standard of care option in Truvada and this was due to a higher rate of compliance with cabotegravir vs. Truvada in the trials. The primary differentiator for cabotegravir is maintenance dosing once every 2 months instead of daily oral administration of Truvada and Descovy.

However, Truvada and Descovy are well-established PrEP treatments that are still highly effective when taken as directed. Truvada is also now available generically as of 2020. Cabotegravir provides an alternative with infrequent administration, but it must be administered via IM injection in the gluteal muscle by a healthcare provider.

For reference, the WAC for Descovy is approximately $23,000 per year.

- Advantages: Superiority vs. standard of care treatment option (Truvada), dosed once every 2 months vs. daily oral administration for current PrEP treatment options
- Disadvantages: Well-established oral alternatives (Truvada available generically), requires IM injection by a healthcare provider
- Reference WAC (Descovy): ~$23,000 per year

Lenacapavir (Brand Name: To be determined)

Manufacturer: Gilead
Regulatory designations: Breakthrough Therapy
Expected FDA decision: 2/28/2022

Therapeutic use

Lenacapavir is in development for treatment of HIV-1 infection in heavily treatment-experienced patients with multi-drug resistant (MDR) HIV-1 infection.

As of 2019, an estimated 1.2 million people aged 13 and older had HIV infection in the U.S., including an estimated 158,500 (13%) people whose infections had not been diagnosed. While many antiretroviral therapies are currently available for HIV-1 infection, patients may develop MDR.

- Treatment of HIV-1 infection in heavily treatment-experienced patients with MDR HIV-1 infection

Clinical profile

Lenacapavir is a long-acting HIV-1 capsid inhibitor. While most antivirals act on just one stage of viral replication, lenacapavir is designed to inhibit HIV-1 at multiple stages of its lifecycle and has no known cross resistance to other existing drug classes.

- HIV-1 capsid inhibitor
- SC formulation

Pivotal trial data:
The efficacy of lenacapavir was evaluated in CAPELLA, a Phase 2/3, double-blind, placebo-controlled study in 36 heavily treatment-experienced patients with MDR HIV-1 infection. Patients were randomized to receive oral lenacapavir or placebo for 14 days, in addition to continuing their failing regimen (functional monotherapy). An additional 36 participants were enrolled in a separate treatment cohort (non-randomized). Following the 14-day period, participants in the randomized cohort started open-label lenacapavir and an optimized background regimen, while those enrolled in the separate treatment cohort received open-label lenacapavir and an optimized background regimen on day 1. In the maintenance period of the study, all patients received subcutaneous lenacapavir administered every 6 months. The primary endpoint was the proportion of participants randomly allocated to receive lenacapavir or placebo for 14 days, in addition to continuing their failing regimen, achieving ≥ 0.5 log10 copies/mL reduction from baseline in HIV-1 RNA at the end of the functional monotherapy period.

A significantly higher proportion of participants randomly allocated to receive lenacapavir achieved a clinically meaningful viral load reduction of at least 0.5 log10 copies/mL from baseline compared with those randomly allocated to receive placebo during the 14-day functional monotherapy period (88% vs. 17%; $p < 0.0001$). At week 26, 81% of patients from the original randomized cohort had viral load < 50 copies/mL.

- Viral load reduction at 14-days (≥ 0.5 log10 copies/mL reduction from baseline): 88% vs. 17% with placebo
- Week 26: 81% of patients with viral load < 50 copies/mL

Safety:
The most common adverse event with lenacapavir use was injection site reactions, which were mostly mild in severity.

- Common AE: Injection site reactions

Dosing:
In the pivotal trial, patients received lenacapavir orally for 14 days and then were administered the drug SC every 6 months.

- Dosing: Every 6 months (following 14-day oral lead-in)

Lenacapavir (continued...)

Competitive environment

If approved, lenacapavir would be a first-in-class antiretroviral for treatment of MDR HIV-1 infection. While a small percentage of HIV-1 patients develop MDR, there is an unmet need in this population given limited treatment options.

In the MDR HIV-1 subpopulation, lenacapavir will be competing with drugs such as Trogarzo® (ibalizumab-uiyk) and Rukobia® (fostemsavir). These drugs differ in MOA and route of administration. Trogarzo is administered intravenously (IV) every 2 weeks while Rukobia is dosed orally twice daily. Lenacapavir is a long-acting treatment option that can be dosed SC every 6 months.

The initial target population for lenacapavir will be small given that MDR HIV constitutes less than 5% of the overall HIV population. However, lenacapavir is also in development for pre-exposure prophylaxis (PrEP) for HIV-1. A Phase 3 trial is currently ongoing in adolescent girls and young women.

For reference, the WAC for Rukobia is approximately $93,000 per year.

- Advantages: Novel MOA, promising trial results, infrequent dosing schedule (every 6 months), potential future use for HIV PrEP
- Disadvantages: Narrow initial target population, competing with Trogarzo and Rukobia, SC administration
- Reference WAC (Rukobia): ~$93,000 per year

Oteseconazole (Brand Name: To be determined)

Manufacturer: Mycovia Pharmaceuticals
Regulatory designations: Fast Track
Expected FDA decision: January 27, 2022

Therapeutic use

- Treatment of RVVC

Oteseconazole is in development for treatment of recurrent vulvovaginal candidiasis (RVVC).

Vulvovaginal candidiasis (VVC), commonly known as vaginal yeast infection, is usually caused by *Candida albicans* (C. albicans). RVVC, usually defined as three or more episodes of symptomatic VVC in < 1 year, affects < 5% of women. Most women with RVVC have no apparent predisposing or underlying conditions. Most cases of RVVC caused by *C. albicans* respond well to existing treatments (eg, fluconazole) but azole resistance is increasing. Additionally, non-albicans Candida species are observed in 10% to 20% of women with RVVC, and conventional antimycotic therapies are not as effective against these non-albicans yeasts as against *C. albicans*.

Clinical profile

- CYP51 inhibitor
- Oral formulation
- Prevention of recurring infection: 93% to 96% vs. ~40% with placebo
- Limited safety data available
- Dosing: Once weekly (for prevention of RVVC)

Oteseconazole is an inhibitor of lanosterol demethylase (CYP51), an enzyme involved in the synthesis of fungal cell wall sterols. CYP51 is the molecular target of the azole antifungal class of drugs.

Pivotal trial data:
The efficacy of oteseconazole was evaluated in two Phase 3, randomized, double-blind, placebo-controlled studies (VIOLET clinical program) in more than 650 women with RVVC. In part 1 of these studies, patients were treated for their current VVC episode with three doses of fluconazole for a 2-week period. In part 2, patients were randomized to treatment with oteseconazole or placebo for 12 weeks (daily administration for 7 days, then once weekly for 11 weeks) with a follow-up period of 36 weeks. The primary endpoint was the proportion of patients with one or more culture verified acute VVC episodes during the maintenance phase (post-randomization through week 48). Oteseconazole met the primary endpoint ($p < 0.001$) in both VIOLET studies. Topline results showed that oteseconazole prevented a recurring infection over the course of these 48-week studies in 96% and 93% of patients.

In addition to the VIOLET studies, oteseconazole was also evaluated in ultraVIOLET, a Phase 3, randomized, double-blind study in 220 patients with RVVC. In part 1 of this study, patients were randomized to be treated for their current VVC episode with either fluconazole administered as 3 sequential doses (every 72 hours) or oteseconazole daily for 2 days. In part 2 of the study, patients received either oteseconazole or placebo weekly for 11 weeks and then a 37-week follow-up period. The primary endpoint was culture-verified recurrence from randomization through week 50. The recurrence rate was 5.1% with oteseconazole vs. 42.2% in the fluconazole/placebo group ($p < 0.001$). Oteseconazole was also non-inferior to fluconazole in the resolution of signs and symptoms at day 14 for the acute VVC episode.

Oteseconazole (continued...)

Safety:
There is limited safety data for oteseconazole, but topline safety results indicated similar adverse events between oteseconazole and the comparator groups.

Dosing:
In the pivotal trials, oteseconazole was administered once weekly for RVVC.

Competitive environment

Oteseconazole could potentially be the first antifungal approved for RVVC. The current standard of care is maintenance therapy with oral fluconazole weekly for 6 months. However, azole resistance has become increasingly common and there are limited treatment options in these patients.

While similar in mechanism to currently available azoles, oteseconazole's proposed mechanism is thought to be more selective for CYP51 which could potentially avoid off-target interactions and toxicity. The reductions in recurrence of VVC were promising across the pivotal studies.

The use of oteseconazole in acute treatment of VVC is likely limited given the lack of superiority data vs. generically available fluconazole. Additionally, oteseconazole was not compared against fluconazole in the maintenance phases of the pivotal studies for RVVC.

Scynexis' Brexafemme® (ibrexafungerp) is a novel antifungal recently approved for treatment of VVC. It is also currently being evaluated for prevention of RVVC with a filing expected in the first half of 2022. If data is positive in this setting and the drug is approved, it would be competing with oteseconazole for RVVC in patients who are not candidates for fluconazole.

- Advantages: Potentially first antifungal approved for RVVC, unmet need
- Disadvantages: Use likely limited for prevention or treatment of RVVC, lack of robust head-to-head data vs. fluconazole, potential future competition with Brexafemme

Mavacamten (Brand Name: To be determined)

Manufacturer: Bristol Myers Squibb
Regulatory designations: Orphan Drug, Breakthrough Therapy
Expected FDA decision: January 28, 2022

Therapeutic use

- Treatment of symptomatic HCM

Mavacamten is in development for treatment of symptomatic obstructive hypertrophic cardiomyopathy (HCM).

HCM is a chronic, progressive disease in which excessive contraction of the heart muscle and reduced ability of the left ventricle to fill can lead to the development of debilitating symptoms and cardiac dysfunction. The most frequent cause of HCM is mutations in the heart muscle proteins of the sarcomere. In obstructive HCM, the wall (septum) between the two bottom chambers of the heart thickens. The walls of the pumping chamber can also become stiff. It may block or reduce the blood flow from the left ventricle to the aorta. People with HCM are at higher risk for developing atrial fibrillation and may also lead to heart failure.

It's estimated that 1 in every 500 people have HCM, but a large percentage of patients are undiagnosed. Of those diagnosed, two-thirds have obstructive HCM.

Clinical profile

- Cardiac myosin modulator
- Oral formulation
- Composite symptom and functional response: 37% vs. 17% with placebo
- Dosing: Once daily

Mavacamten is an allosteric modulator of cardiac myosin. It is thought to work by reducing cardiac muscle contractility by inhibiting excessive myosin-actin cross-bridge formation that results in hypercontractility, left ventricular hypertrophy and reduced compliance.

Pivotal trial data:
The efficacy of mavacamten was evaluated in EXPLORER-HCM, a Phase 3, randomized, double-blind, placebo-controlled study in 251 adults with symptomatic obstructive HCM. The primary endpoint was a composite of both symptoms and function, consisting of achievement of a ≥ 1.5 mL/kg/min improvement in peak VO2 accompanied by an improvement of ≥ 1 New York Heart Association (NYHA) functional class, or the achievement of a ≥ 3.0 mL/kg/min improvement of peak VO2 with no worsening in NYHA functional class.

Overall, 37% patients on mavacamten vs. 17% on placebo met the primary composite endpoint ($p = 0.0005$). Additionally, 34% more patients in the mavacamten group improved by at least one NYHA class ($p < 0.0001$).

Safety:
The safety and tolerability of mavacamten was similar to placebo in the pivotal trial.

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

Mavacamten (continued...)

Competitive environment

Mavacamten would offer a novel MOA for the treatment of HCM and would potentially be the first disease-specific medication approved for the condition. The current standard of care includes off-label use of beta-blockers, calcium channel blockers and diuretics, which offer limited and varying relief of symptoms. Surgical and nonsurgical procedures, such as septal myectomy, alcohol septal ablation (nonsurgical procedure), and surgically implanted devices (eg, pacemakers) can also be used. Patients who receive these procedures can continue to experience hypertrophy.

The results for mavacamten were promising with improvements in symptom and functional status vs. placebo while having a good safety profile based on available data. However, there is a lack of long-term data around improvements in cardiovascular death or all-cause mortality.

HCM is the most common genetic cause of heart disease but the use of mavacamten will be limited to patients with symptomatic, obstructive forms of the disease and potentially it could be reserved for patients who have tried generically available treatment options such as beta blockers given the lack of long-term cardiovascular clinical outcomes data.

- Advantages: Potentially first approved treatment for HCM, novel MOA, unmet need, well tolerated
- Disadvantages: Lack of long-term cardiovascular outcomes (eg, reduced cardiovascular death or all-cause mortality), use limited to symptomatic and obstructive forms of HCM

Faricimab (Brand Name: To be determined)

Manufacturer: Roche
Expected FDA decision: January 31, 2022

Therapeutic use

- Treatment of nAMD and DME

Faricimab is in development for the treatment of neovascular or wet age-related macular degeneration (nAMD) and diabetic macular edema (DME).

nAMD

AMD is an eye disease that can blur central vision. Wet AMD or nAMD is an advanced form of AMD that usually causes faster vision loss. It develops when new and abnormal blood vessels grow uncontrolled under the macula, causing swelling, bleeding and/or fibrosis.

AMD is the leading cause of vision loss in people over the age of 60. The prevalence of AMD is approximately 11 million in the U.S. with nAMD accounting for about 10 to 15% of all cases.

DME

DME is a potential complication of diabetic retinopathy. Diabetic retinopathy occurs when damage to blood vessels and the formation of new blood vessels cause blood and/or fluid to leak into the retina. DME happens when blood vessels in the retina leak fluid into the macula, which can cause blurry vision. Over time, about 1 in 15 people with diabetes will develop DME.

Clinical profile

- Bispecific antibody targeting Ang-2 and VEGF-A
- Intravitreal formulation
- Non-inferior for visual acuity gains vs. Eylea
- Common AE: Intraocular inflammation
- Dosing: Every two, three, or four months (depending on disease activity)

Faricimab is a bispecific antibody that targets two distinct pathways: angiopoietin-2 (Ang-2) and vascular endothelial growth factor-A (VEGF-A). Ang-2 and VEGF-A contribute to vision loss by destabilizing blood vessels, causing new leaky blood vessels to form and increasing inflammation. Faricimab blocks both the Ang-2 and VEGF-A pathways, thereby stabilizing blood vessels, and potentially improving vision outcomes.

Pivotal trial data:

nAMD

The efficacy of faricimab was evaluated in two identical Phase 3, randomized, double-masked, active comparator studies (TENAYA and LUCERNE) in 1,329 patients with nAMD. The studies each had two treatment arms: faricimab administered once every 4 weeks for 12 weeks followed by administration at fixed intervals of every two, three, or four months, selected based on objective assessment of disease activity at weeks 20 and 24; and Eylea® (aflibercept) administered once every 4 weeks for 8 weeks followed by administration at fixed two-month intervals. The primary endpoint was the average change in best-corrected visual acuity (BCVA) score from baseline through week 48.

Both the TENAYA and LUCERNE studies met their primary endpoint, with faricimab shown to offer non-inferior visual acuity gains to Eylea ($p < 0.05$ for all treatment arms vs. Eylea). In TENAYA and LUCERNE, the average vision gains from baseline in the faricimab arms were +5.8 and +6.6 letters, respectively, compared to +5.1 and +6.6 letters in the Eylea arms. In terms of dosing, 45.7% of patients in TENAYA and 44.9% in LUCERNE were able to be treated every four months in the first year. An additional 34% of patients in TENAYA and 32.9% in LUCERNE were able to be treated every three months.

Faricimab (continued...)

DME
Similar to nAMD, the efficacy of faricimab was evaluated in two identical, Phase 3, randomized, double-masked, active comparator studies (YOSEMITE and RHINE) in 1,891 patients with DME. The studies each had three treatment arms: faricimab administered at personalized dosing intervals of up to four months; faricimab administered at fixed two-month intervals; and Eylea administered at fixed two-month intervals. The primary endpoint was the average change in BCVA score from baseline at one year.

Both the YOSEMITE and RHINE studies met their primary endpoint with faricimab shown to be non-inferior to Eylea ($p < 0.05$ for all treatment arms vs. Eylea). In YOSEMITE, the average vision gains from baseline were +11.6 in the faricimab personalized dosing interval, +10.7 letters in the two-month arm, and +10.9 letters in the Eylea arm. In RHINE, the average vision gains from baseline were +10.8 in the faricimab personalized dosing interval, +11.8 letters in the two-month arm, and +10.3 letters in the Eylea arm. In terms of dosing, 52.8% of faricimab personalized dosing interval patients in YOSEMITE and 51% in RHINE achieved four-month dosing at one year. An additional 21% of patients in YOSEMITE and 20.1% in RHINE achieved three-month dosing.

Safety:
The most common adverse event with faricimab use was intraocular inflammation.

Dosing:
In the pivotal trials, faricimab was administered via intravitreal injection every two, three, or four months.

Competitive environment

Faricimab would offer a novel dual MOA for the treatment of both nAMD and DME. The current standard of care for both conditions are anti-VEGF drugs like Eylea. Faricimab demonstrated statistical non-inferiority vs. Eylea and had numerically favorable results. The primary differentiator for faricimab vs. anti-VEGF therapies is the frequency of injections. A majority of patients were treated every 3 to 4 months with faricimab across the pivotal studies and both indications while Eylea is generally administered every 2 months. Another commonly used anti-VEGF therapy, Lucentis® (ranibizumab), is generally administered every month for DME and nAMD, with efficacy being reduced when dosing is extended to every 3 months (for nAMD).

Faricimab appeared to be relatively well tolerated although it was associated with slightly higher rates of intraocular inflammation vs. Eylea. Additional details around the safety and the final product labeling will likely play a factor in patient and provider acceptance given the availability of well-established alternatives. A biosimilar for Lucentis was also recently approved (Byooviz™) and is expected to launch in June 2022.

For reference, the WAC for Eylea is $1,850 per 2 mg syringe.

- Advantages: Novel MOA, potential for fewer injections vs. competitors for nAMD and DME
- Disadvantages: Well established alternatives available, higher rates of intraocular inflammation vs. Eylea
- Reference WAC (Eylea): $1,850 per 2 mg syringe

Mitapivat (Brand Name: To be determined)

Manufacturer: Agios Pharmaceuticals
Regulatory designations: Orphan Drug, Fast Track
Expected FDA decision: February 17, 2022

Therapeutic use

Mitapivat is in development for treatment of adults with pyruvate kinase deficiency (PKD).

PKD is an ultra-rare genetic disorder characterized by the premature destruction of red bloods and development of hemolytic anemia. PKD is caused by mutations in the PKLR gene, which lead to a deficiency of the enzyme pyruvate kinase. Aside from anemia, symptoms of the condition are highly variable but serious potential complications include gallstones, pulmonary hypertension, extramedullary hematopoiesis, osteoporosis, and iron overload (can occur both in individuals who receive blood transfusions for treatment of anemia and in those who have never been transfused).

The exact prevalence of the disorder is unknown, but Agios Pharmaceuticals estimates there are 3,000 to 8,000 patients in the U.S. and EU5 (France, Germany, Italy, Spain, U.K).

- Treatment of adults with PKD

Clinical profile

Mitapivat is an activator of PKR. PKR is the isoform of pyruvate kinase which is present in red blood cells. Pyruvate kinase is an enzyme involved in the second to last reaction in glycolysis and it is critical for the survival of these cells.

- PKR activator
- Oral formulation

<u>Pivotal trial data:</u>
The efficacy of mitapivat was evaluated in two Phase 3 studies: ACTIVATE and ACTIVATE-T. The ACTIVATE study was a double-blind, placebo-controlled trial in 80 adults with PKD who were transfusion independent (did not receive regular blood transfusions). Patients were required to have a hemoglobin concentration less than or equal to 10.0 g/dL. The primary endpoint was hemoglobin response, defined as a ≥ 1.5 g/dL increase in hemoglobin concentration from baseline that is sustained at two or more scheduled assessments at weeks 16, 20 and 24. Overall, 40% of patients randomized to mitapivat achieved a hemoglobin response, compared to 0 patients randomized to placebo ($p < 0.0001$). The increase in hemoglobin occurred early and was sustained, with an average change from baseline of 1.67 g/dL for mitapivat vs. -0.15 g/dL for placebo ($p < 0.0001$) at weeks 16, 20 and 24.

- ACTIVATE study (transfusion independent): hemoglobin response: 40% vs. 0% with placebo
- ACTIVATE-T study (transfusion dependent): 37% achieved a transfusion reduction and 22% were transfusion-free

ACTIVATE-T was an open-label study in 27 adults with PKD who were transfusion dependent (regularly transfused), defined as receiving six or more blood transfusions in the past 52 weeks. The primary endpoint was reduction in transfusion burden, defined as a reduction of ≥ 33% in the number of red blood cell units transfused during the 24-week fixed dose period compared with the historical transfusion burden standardized to 24 weeks. Overall, 37% of patients achieved a transfusion reduction response and 22% of patients were transfusion-free during the fixed-dose period.

- Common AEs: Increased ALT/AST, headache, fatigue, nausea
- Dosing: Twice daily

Mitapivat (continued...)

Safety:
The most common adverse events with mitapivat use were increased alanine aminotransferase (ALT), increased aspartate aminotransferase (AST), headache, fatigue, and nausea.

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

Competitive environment

Mitapivat would be the first FDA approved treatment for PKD, a condition for which there is a high unmet need, particularly in transfusion-dependent patients. The current standard of care for PKD is blood transfusions and in severe cases, splenectomy. Like many other hematologic conditions, the only curative treatment is allogeneic stem cell transplantation (HSCT).

Mitapivat demonstrated positive findings in both transfusion-independent and dependent patients with PKD. The target population will be small due to the rare nature of PKD and the fact that not all patients develop severe symptoms needing treatment. An additional limitation is that the drug was only evaluated in adult patients, but the condition presents often in childhood.

Mitapivat is in development for the treatment of pediatric PKD patients, as well as other hematologic conditions like thalassemia and sickle cell disease.

- Advantages: Novel MOA, potentially first approved treatment for PKD, high unmet need, also in development for other hematologic conditions (eg, thalassemia, sickle cell disease)
- Disadvantages: Lack of data in pediatric patients, small initial target population

Bardoxolone methyl (Brand Name: To be determined)

Manufacturer: Reata Pharmaceuticals
Regulatory designations: Orphan Drug
Expected FDA decision: February 25, 2022 *(FDA Advisory Committee meeting scheduled for December 8, 2021)*

Therapeutic use

- Treatment of patients with CKD caused by Alport syndrome

Bardoxolone methyl is in development for the treatment of patients with chronic kidney disease (CKD) caused by Alport syndrome.

Alport syndrome is a rare genetic disorder of the kidneys caused by mutations in the genes encoding type IV collagen. The disease is characterized by the presence of blood in the urine (hematuria) early in life, with progressive decline in kidney function that ultimately results in kidney failure, especially in males. X-linked Alport syndrome (XLAS) is the most common form of the disease and about 50% of untreated males with XLAS develop kidney failure by age 25, increasing to 90% by age 40 and nearly 100% by age 60.

Alport syndrome is estimated to affect approximately 1 in 5,000 to 10,000 people in the general population in the U.S., which means that approximately 30,000 to 60,000 people in the U.S. have the disorder.

Clinical profile

- Nrf2 activator
- Oral formulation
- Change in eGFR: -0.8 mL/min/1.73 m^2 vs. -8.5 mL/min/1.73 m^2 with placebo
- Common AEs: Muscle spasms, increases in aminotransferases
- Dosing: Once daily

Bardoxolone is an activator of Nrf2, a transcription factor that induces molecular pathways that promote the resolution of inflammation by restoring mitochondrial function, reducing oxidative stress, and inhibiting pro-inflammatory signaling. Chronic inflammation in the kidney cells leads to a reduction in kidney function.

<u>Pivotal trial data:</u>
The efficacy of bardoxolone methyl was evaluated in CARDINAL, a Phase 3, randomized, double-blind, placebo-controlled study in 157 patients with CKD caused by Alport syndrome. Patients were randomized to bardoxolone or placebo. The primary endpoint for year 2 of the study was the change from baseline in estimated glomerular filtration rate (eGFR) after 100 weeks of treatment. The key secondary endpoint for year 2 of the study was the change from baseline in eGFR at week 104 (four weeks after the last dose in the second year of treatment).

At week 100, patients treated with bardoxolone had a statistically significant improvement compared to placebo in mean change from baseline in eGFR of 7.7 mL/min/1.73 m^2 (p = 0.0005). The change from baseline was -8.5 mL/min/1.73 m^2 with placebo and -0.8 mL/min/1.73 m^2 with bardoxolone. At week 104 (four weeks after last dose in second year of treatment), patients treated with bardoxolone had a statistically significant improvement compared to placebo in mean change from baseline in eGFR of 4.3 mL/min/1.73 m^2 (p = 0.023).

<u>Safety:</u>
The most common adverse events with bardoxolone methyl use were muscle spasms and increases in aminotransferases.

<u>Dosing:</u>
In the pivotal trial, bardoxolone methyl was administered orally once daily.

Bardoxolone methyl (continued...)

Competitive environment

Bardoxolone methyl would be the first FDA approved treatment option for Alport syndrome and there is a high unmet need for treatments for the condition. The current standard of care for Alport syndrome is off-label use of angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs). Historical data strongly suggests that early treatment with these drugs can delays progression to end-stage renal disease. While these treatments may slow the progression of kidney disease, there is no cure for the disorder and no treatment has thus far been shown to completely stop kidney decline.

The slowing of kidney function decline appears to be sustained with continued use of bardoxolone for up to 2 years; however, a couple questions remain about the efficacy and safety of the drug. First, upon discontinuing the drug, there is a sizable decrease in renal function as measured by eGFR, highlighting that much of the benefit with use of bardoxolone is acute or transient. In addition, the drug is associated with increases in albuminuria (normally a sign of kidney damage) as well as elevated liver function tests. Both effects appear to be reversible but the increases in liver enzymes resulted in higher discontinuation rates with bardoxolone vs. placebo. An FDA Advisory Committee is scheduled to convene in December 2021 and these concerns will likely be addressed by the panelists.

Given the generic availability of ACE inhibitors and ARBs, lack of long-term kidney outcomes, and questions about safety, bardoxolone may likely be reserved as a second-line treatment option in patients with Alport syndrome.

Finally, bardoxolone is also currently being studied for several other kidney conditions, such as autosomal dominant polycystic kidney disease (ADPKD), IgA nephropathy, and focal segmental glomerulosclerosis (FSGS). While a submission to the FDA is not imminent for any of these indications, they could significantly expand the market potential for the drug in the future given the high unmet need for these conditions.

- Advantages: Potentially first approved treatment for Alport syndrome, high unmet need, oral and once daily administration, also in development for several other kidney conditions (eg, ADPKD, IgA nephropathy, FSGS)
- Disadvantages: Safety concerns (albuminuria and elevated liver function tests), does not reverse existing kidney damage, potentially reserved as a second-line treatment option

Ganaxolone (Brand Name: To be determined)

Manufacturer: Marinus Pharmaceuticals
Regulatory designations: Orphan Drug
Expected FDA decision: March 20, 2022

Therapeutic use

- Treatment of seizures associated with CDKL5 deficiency disorder

Ganaxolone is in development for treatment of seizures associated with CDKL5 deficiency disorder (CDD).

CDD is a rare genetic disorder caused by mutations in the cyclin-dependent kinase-like 5 (CDKL5) gene located on the X chromosome. CDD is characterized by early onset, difficult to control seizures and severe impairment of development (impacting cognitive, motor, speech, and visual function).

The incidence of CDD is between 1 in 40,000 to 60,000 live births and predominantly affects females.

Clinical profile

- Allosteric modulator of GABA-A receptors
- Oral formulation
- Percentage change in 28-day frequency of major motor seizures: 30.7% median reduction with ganaxolone vs. 6.9% with placebo
- Common AEs: Somnolence, pyrexia, upper respiratory tract infection, salivary hypersecretion
- Dosing: Three times daily

Ganaxolone is a positive allosteric modulator of GABA-A receptors. Ganaxolone exhibits antiseizure activity via its effects on synaptic and extrasynaptic GABA-A receptors.

Pivotal trial data:
The efficacy of ganaxolone was evaluated in MARIGOLD, a Phase 3, randomized, double-blind, placebo-controlled study in 101 children and young adults ages 2 to 21 years with a confirmed, disease-related CDKL5 gene variant. Following a 6-week baseline period, participants were randomized to receive either oral ganaxolone or placebo for 17 weeks, in addition to their existing antiseizure treatment. The primary endpoint was the percentage change in 28-day frequency of major motor seizures during the double-blind phase relative to the 6-week prospective baseline period.

Patients treated with ganaxolone showed a 30.7% median reduction in 28-day major motor seizure frequency vs. 6.9% reduction for those receiving placebo ($p = 0.0036$). Patients in the open-label extension study treated with ganaxolone for at least 12 months ($N = 48$) experienced a median 49.6% reduction in major motor seizure frequency.

Safety:
The most common adverse events with ganaxolone use were somnolence, pyrexia, upper respiratory tract infection, and salivary hypersecretion.

Dosing:
In the pivotal trial, ganaxolone was administered orally three times a day.

Ganaxolone (continued...)

Competitive environment

Ganaxolone would be the first therapy approved for CDD and there is a high unmet need for treatments. Seizure control is often the most challenging aspect of the disease to manage and no one anticonvulsant has been found to be uniformly effective. In the pivotal trial for ganaxolone, the baseline median number of antiepileptic drugs used in patients was seven. The trial results for ganaxolone were promising although patients will likely have to remain on their existing antiepileptic treatments.

The initial target population for ganaxolone will be small given the rare nature of CDD. The oral formulation of ganaxolone is being evaluated in a Phase 3 study for tuberous sclerosis complex, another rare condition associated with epilepsy. Additionally, an IV formulation of the drug is currently in Phase 3 for status epilepticus..

- Advantages: Potentially first approved therapy for CDD, high unmet need, promising trial results, also in development for other epilepsy indications
- Disadvantages: Small initial target population, does not eliminate the need for other antiepileptic treatments

Ublituximab (Brand Name: To be determined)

Manufacturer: TG Therapeutics
Regulatory designations: Orphan Drug, Fast Track
Expected FDA decision: March 25, 2021

Therapeutic use

- Treatment of CLL and SLL

Ublituximab is in development for use in combination with Ukoniq® (umbralisib), for treatment for patients with chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL).

CLL is a type of cancer that starts in the cells that become lymphocytes in the bone marrow. In CLL, the leukemia cells often build up slowly. Many people do not have any symptoms for at least a few years but over time, the cells grow and spread to other parts of the body, including the lymph nodes, liver, and spleen.

CLL is the most common leukemia in adults and there are about 21,250 new cases annually. The average age of people when they are diagnosed is around 70 years. It's rarely seen in people under age 40 and is extremely rare in children.

Clinical profile

- Anti-CD20 monoclonal antibody
- IV formulation
- Median PFS: 31.9 months with ublituximab plus Ukoniq vs. 17.9 months with Gazyva plus chlorambucil
- Common AEs: Neutropenia, thrombocytopenia, diarrhea, infusion-related reaction, elevated liver enzymes, colitis, pneumonitis
- Dosing: Refer to the clinical profile section

Ublituximab is monoclonal antibody that targets a unique epitope on CD20-expressing B-cells. When ublituximab binds to the B-cell it triggers a series of immunological reactions (including antibody-dependent cellular cytotoxicity and complement dependent cytotoxicity), leading to destruction of the cell.

Pivotal trial data:
The efficacy of ublituximab was evaluated in UNITY-CLL, a Phase 3, randomized study in 421 patients with treatment-naïve or relapsed/refractory CLL. Patients were randomized to ublituximab plus Ukoniq or Gazyva® (obinutuzumab) plus chlorambucil. The primary endpoint was progression-free survival (PFS).

At a median follow-up of 36.2 months, ublituximab plus Ukoniq significantly prolonged PFS vs. Gazyva plus chlorambucil (median 31.9 months vs. 17.9 months, respectively; hazard ratio 0.546; $p < 0.0001$). PFS improvement was consistent across all subgroups examined including treatment-naïve patients and relapsed/refractory patients. Additionally, the overall response rate (ORR) was significantly higher with ublituximab plus Ukoniq (83.3% vs. 68.7%; $p < 0.001$).

Safety:
The most common adverse events with ublituximab plus Ukoniq use were neutropenia, thrombocytopenia, diarrhea, infusion-related reaction, elevated liver enzymes, colitis, and pneumonitis.

Dosing:
In the pivotal trial, ublituximab was administered via IV infusion on days 1, 2, 8, and 15 of cycle 1, day 1 of cycles 2 through 6, and on day 1 every 3 cycles after cycle 6.

Ublituximab (continued...)

Competitive environment

If approved, ublituximab would offer an additional treatment regimen (in combination with Ukoniq) for CLL. The combination of ublituximab plus Ukoniq did demonstrate superiority in a head-to-head trial vs. an existing treatment regimen for CLL and appears to have a reasonable safety profile; however, Gazyva plus chlorambucil is no longer a preferred regimen in the first- or second-line setting for CLL. CLL is also now a fairly competitive market with many options available in both treatment-naïve and relapsed/refractory settings. This includes monotherapy with drugs such as Imbruvica® (ibrutinib) and Calquence® (acalabrutinib).

Finally, ublituximab is also in development as part of other treatment regimens for CLL, additional cancers, and multiple sclerosis (MS). For MS, it would potentially be the third approved anti-CD20 targeted therapy. The other drugs in the class approved for MS are Roche's Ocrevus® (ocrelizumab) and Novartis' Kesimpta® (ofatumumab).

- Advantages: Potential safety and tolerability advantages vs. some alternative backline regimens for CLL, also in development for other cancers and MS
- Disadvantages: Alternatives available, lack of head-to-head data vs. preferred CLL regimens, IV administration

Vadadustat (Brand Name: To be determined)

Manufacturer: Akebia Therapeutics/Otsuka Pharmaceutical
Expected FDA decision: March 29, 2022

Therapeutic use

- Treatment of anemia due to CKD

Vadadustat is in development for treatment of anemia due to chronic kidney disease (CKD) in both adult patients on dialysis and adult patients not on dialysis.

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.

The current therapeutic options for the anemia of CKD include iron, erythropoiesis-stimulating agents (ESAs), and, if necessary, red blood cell transfusions.

Clinical profile

- HIF-PH inhibitor
- Oral formulation
- Change in hemoglobin from baseline: Noninferiority met vs. darbepoetin alfa in dialysis-dependent and dialysis-independent CKD patients
- Similar AEs as darbepoetin alfa
- Dosing: Once daily

Vadadustat 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 lead to increased red blood cell production and improved oxygen delivery to tissues.

<u>Pivotal trial data:</u>
The efficacy of vadadustat was evaluated in two Phase 3, randomized, open-label, noninferiority studies in patients with anemia and dialysis-dependent CKD (DD-CKD). The trials included 369 patients with incident DD-CKD (initiated dialysis within 16 weeks before screening and limited prior exposure to ESAs) and 3,554 with prevalent DD-CKD (undergoing maintenance dialysis for at least 12 weeks before screening and receiving prior treatment with an ESA). Patients were randomized to vadadustat or the ESA, darbepoetin alfa. The primary and secondary efficacy endpoints were the mean change in hemoglobin from baseline to weeks 24 to 36 and from baseline to weeks 40 to 52, respectively, in each study (noninferiority margin, -0.75 g/dL). Vadadustat demonstrated noninferiority to darbepoetin alfa in both DD-CKD studies. The mean differences between the groups in the change in hemoglobin concentration were -0.31 g/dL (95% CI: -0.53, -0.10) at weeks 24 to 36 and -0.07 g/dL (95% CI: -0.34, 0.19) at weeks 40 to 52 in the incident DD-CKD study. In the prevalent DD-CKD study, the mean differences between the groups in the change in hemoglobin concentration were -0.17 g/dL (95% CI: -0.23, -0.10) and -0.18 g/dL (95% CI: -0.25, -0.12) at weeks 24 to 36 and at weeks 40 to 52, respectively.

The efficacy of vadadustat was also evaluated in two Phase 3, randomized, open-label, noninferiority studies in patients with anemia and non-dialysis-dependent CKD (NDD-CKD). The studies included 1,751 patients not previously treated with an ESA who had a hemoglobin concentration of < 10 g/dL and 1,725 patients with ESA-treated NDD-CKD and a hemoglobin concentration of 8 to 11 g/dL (in the U.S.) or 9 to 12 g/dL (in other countries). Patients were randomized to vadadustat or darbepoetin alfa. The primary and secondary efficacy endpoints (and the noninferiority margin) were the same as in the DD-CKD studies. Vadadustat demonstrated noninferiority to darbepoetin alfa in both NDD-CKD studies. The mean between-group differences in the change in the hemoglobin concentration at weeks 24 through 36 were 0.05 g/dL (95% CI: -0.04, 0.15) in the study involving ESA-untreated patients and -0.01 g/dL (95% CI: -0.09, 0.07) in the study involving ESA-treated patients.

Vadadustat (continued...)

Safety:
The most common adverse events with vadadustat use were similar to darbepoetin alfa.

Due to the cardiovascular safety concerns surrounding drugs used for CKD-associated anemia (including both ESAs and HIF-PH inhibitors), a primary safety endpoint across the pivotal studies for vadadustat was a time-to-event analysis of the first occurrence of a major adverse cardiovascular event (MACE, a composite of death from any cause, a nonfatal myocardial infarction, or a nonfatal stroke).

In the DD-CKD pooled analysis, the prespecified noninferiority margin of 1.25 was met for vadadustat. A first MACE occurred in 355 patients (18.2%) in the vadadustat group and in 377 patients (19.3%) in the darbepoetin alfa group (HR 0.96; 95% CI: 0.83 to 1.11).

In the NDD-CKD pooled analysis, the prespecified noninferiority margin of 1.25 was not met for vadadustat. A first MACE occurred in 382 patients (22.0%) in the vadadustat group and in 344 patients (19.9%) in the darbepoetin alfa group (HR 1.17; 95% CI: 1.01, 1.36).

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

Competitive environment

If approved, vadadustat 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, vadadustat provided similar improvements in hemoglobin in both dialysis and non-dialysis dependent patients.

Vadadustat is the second drug in the class reviewed by the FDA. FibroGen and AstraZeneca's roxadustat received a Complete Response Letter in August 2021, following a negative FDA Advisory Committee meeting. The primary reason for roxadustat's rejection was concern around cardiovascular safety. This concern could potentially jeopardize the approval of vadadustat, particularly in the NDD-CKD population where vadadustat was associated with a higher rate of MACE events vs. darbepoetin alfa.

If vadadustat does get approved but use is limited to DD-CKD, this would significantly impact the market potential for the drug as only a fraction of the CKD population is dialysis-dependent. Of the nearly 6 million people in the U.S. with anemia-associated CKD, approximately 550,000 are estimated to be on dialysis. It would also be entering the market at a time when multiple biosimilars are now available for ESAs.

Finally, vadadustat may also face future competition as GlaxoSmithKline's HIF-PH inhibitor is in late-stage development with a filing expected in the first half of 2022.

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- Advantages: Novel MOA, oral alternative to injectable ESAs
- Disadvantages: Competing with ESAs – with biosimilars available, cardiovascular safety concerns particularly in non-dialysis patients, potential future competition (ie, GlaxoSmithKline's daprodustat)

4th Quarter 2021

Extended generic pipeline forecast

OptumRx generic pipeline forecast

Trade Name	Generic Name	Brand Company(ies)	Route of Administration	Strength(s)	Anticipated Generic Availability
2021 Possible launch date					
DALIRESP	roflumilast	AstraZeneca	Oral	All	2021
RESTASIS	cyclosporine	Allergan	Ophthalmic	All	2021
BYETTA	exenatide	AstraZeneca	Subcutaneous	All	2021
TOVIAZ	fesoterodine	Pfizer	Oral	All	2021
SYNDROS	dronabinol	Insys Therapeutics	Oral	All	2021
CUVPOSA	glycopyrrolate	Merz	Oral	All	2021
RESCULA	unoprostone isopropyl	R-Tech Ueno	Ophthalmic	All	2021
FORTEO	teriparatide	Eli Lilly	Injection	All	2H-2021
EPIDUO FORTE	adapalene/benzoyl peroxide	Galderma	External	All	2H-2021
NARCAN	naloxone	Emergent BioSolutions	Intranasal	All	2H-2021
LEVEMIR	insulin detemir recombinant	Novo Nordisk	Subcutaneous	All	2H-2021
TRESIBA FLEXTOUCH	insulin degludec	Novo Nordisk	Subcutaneous	All	2H-2021
JEVTANA KIT	cabazitaxel	Sanofi	Intravenous	All	4Q-2021
BROMSITE	bromfenac	Sun	Ophthalmic	All	4Q-2021
VASOSTRICT	vasopressin	Par Sterile	Intravenous	All	4Q-2021
INNOPRAN XL	propranolol	Ani Pharmaceuticals	Oral	All	10-2021
CAYSTON	aztreonam lysine	Gilead	Inhalation	All	12-2021
DEXILANT	dexlansoprazole	Takeda	Oral	All	12-2021
2022 Possible launch date					
DULERA	formoterol fumarate/mometasone furoate	Organon	Inhalation	All	2022
FLOVENT HFA	fluticasone propionate	GlaxoSmithKline	Inhalation	All	2022
POMALYST	pomalidomide	Celgene	Oral	All	2022
THALOMID	thalidomide	Celgene	Oral	All	2022
IXEMPRA Kit	ixabepilone	R-Pharm	Intravenous	All	1H-2022
OXAYDO	oxycodone	Egalet	Oral	All	01-2022
ONEXTON	clindamycin/benzoyl peroxide	Bausch Health	External	All	01-2022

Trade Name	Generic Name	Brand Company(ies)	Route of Administration	Strength(s)	Anticipated Generic Availability
NEUPRO	rotigotine	UCB	External	All	01-2022
BALCOLTRA	levonorgestrel/ethinyl estradiol/ferrous bisglycinate	Avion	Oral	All	01-2022
SELZENTRY	maraviroc	ViiV Healthcare	Oral	All	02-2022
VIMPAT	lacosamide	UCB	Oral; intravenous	All	03-2022
ZIPSOR	diclofenac potassium	Depomed	Oral	All	03-2022
CHOLBAM	cholic acid	Retrophin	Oral	All	03-2022
ABRAXANE	paclitaxel	Celgene/Abraxis	Injection	All	03-2022
REVLIMID	lenalidomide	Bristol-Myers Squibb/Celgene	Oral	All	03-2022
ARESTIN	minocycline hydrochloride	Bausch Health	Subgingival	All	03-2022
PRADAXA	dabigatran etexilate mesylate	Boehringer Ingelheim	Oral	All	2Q-2022
LEXISCAN	regadenoson	Astellas	Intravenous	All	04-2022
COMBIGAN	brimonidine/timolol	Allergan	Ophthalmic	All	04-2022
ZOLADEX	goserelin	TerSera Therapeutics	Subcutaneous	All	04-2022
ALIMTA	pemetrexed disodium	Eli Lilly	Intravenous	All	05-2022
VELCADE	bortezomib	Takeda	Intravenous	All	05-2022
TARGINIQ ER	oxycodone/naloxone	Purdue	Oral	All	05-2022
CAPRELSA	vandetanib	Genzyme/Sanofi	Oral	All	06-2022
VIIBRYD	vilazodone	Forest/Allergan	Oral	All	06-2022
ELESTRIN	estradiol	Mylan	External	All	06-2022
LUCENTIS	ranibizumab	Roche	Intravitreal	All	06-2022
IRESSA	gefitinib	AstraZeneca	Oral	All	07-2022
EVAMIST	estradiol	Perrigo/Elan	External	All	07-2022
KEVEYIS	dichlorphenamide	Strongbridge Biopharma	Oral	All	08-2022
ORAVIG	miconazole	Galt Pharmaceuticals	Oral	All	09-2022
AMZEEQ	minocycline	Foamix	External	All	10-2022
XERESE	acyclovir/hydrocortisone	Bausch Health	External	All	11-2022
FOLOTYN	pralatrexate	Acrotech/Aurobindo	Intravenous	All	11-2022
RAYOS	prednisone	Horizon	Oral	All	12-2022
TREANDA	bendamustine	Cephalon/Teva	Intravenous	All	12-2022
ZIOPTAN	tafluprost	Akorn	Ophthalmic	All	12-2022
ARAZLO	tazarotene	Ortho Dermatologics	External	All	12-2022

Trade Name	Generic Name	Brand Company(ies)	Route of Administration	Strength(s)	Anticipated Generic Availability
2023 Possible launch date					
PREZISTA	darunavir	Janssen	Oral	75 mg, 150 mg, 300 mg	2023
PROLENSA	bromfenac	Bausch Health	Ophthalmic	All	2023
ALPHAGAN P	brimonidine	Allergan	Ophthalmic	All	2023
MYRBETRIQ	mirabegron	Astellas	Oral	All	2023
EYLEA	aflibercept	Regeneron	Intravitreal	All	2023
NEULASTA ONPRO	pegfilgrastim	Amgen/Insulet	Subcutaneous	All	2023
KOMBIGLYZE XR	saxagliptin/metformin	Astra Zeneca	Oral	All	1H-2023
ONGLYZA	saxagliptin	AstraZeneca	Oral	All	1H-2023
NOXAFIL	posaconazole	Merck	Intravenous	All	01-2023
HUMIRA	adalimumab	AbbVie	Subcutaneous	All	01-2023
XYREM	sodium oxybate	Jazz	Oral	All	01-2023
CAMBIA	diclofenac potassium	Assertio	Oral	All	01-2023
TROKENDI XR	topiramate	Supernus	Oral	All	01-2023
DUOBRII	halobetasol propionate/tazarotene	Bausch Health	External	All	01-2023
NASCOBAL	cyanocobalamin	Par/Endo	Intranasal	All	01-2023
DYLOJECT	diclofenac	Hospira/Pfizer/Javelin	Intravenous	All	01-2023
TEFLARO	ceftaroline fosamil	Allergan	Intravenous	All	01-2023
GLOPERBA	colchicine	Avion Pharmaceuticals	Oral	All	01-2023
FIRVANQ KIT	vancomycin	Azurity	Oral	All	01-2023
SUPREP BOWEL PREP KIT	magnesium sulfate anhydrous/ potassium sulfate/sodium sulfate	Braintree	Oral	All	01-2023
LATUDA	lurasidone	Sunovion	Oral	All	02-2023
GATTEX	teduglutide recombinant	Takeda	Subcutaneous	All	03-2023
AGGRASTAT	tirofiban	Medicure	Intravenous	All	03-2023
AUBAGIO	teriflunomide	Sanofi/Genzyme	Oral	All	03-2023
PROVAYBLUE	methylene blue	Provepharm/American Regent	Intravenous	All	04-2023
CLINDESSE	clindamycin phosphate	Perrigo	Vaginal	All	04-2023
CORLANOR	ivabradine	Amgen	Oral	All	04-2023
LIVALO	pitavastatin	Eli Lilly/Kowa Pharmaceuticals	Oral	All	05-2023
KYNMOBI	apomorphine	Sunovion	Sublingual	All	05-2023

Trade Name	Generic Name	Brand Company(ies)	Route of Administration	Strength(s)	Anticipated Generic Availability
BIJUVA	estradiol/progesterone	TherapeuticsMD	Oral	All	06-2023
ACTEMRA	tocilizumab	Roche/Chugai	Intravenous; subcutaneous	All	1H-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
CYSTADROPS	cysteamine	Recordati	Ophthalmic	All	08-2023
VYVANSE	lisdexamfetamine	Shire/Takeda	Oral	All	08-2023
KATERZIA	amlodipine	Azurity	Oral	All	08-2023
STELARA	ustekinumab	Janssen	Subcutaneous	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

Extended brand pipeline forecast

OptumRx Brand Pipeline Forecast

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
2021 Possible launch date									
DE-117	omidenepag isopropyl	Santen Pharmaceutical	Prostaglandin E Receptor 2 agonist	Glaucoma	OPH	Filed NDA	11/19/2021	No	No
BMN-111	vosoritide	BioMarin	C-type natriuretic peptide analog	Achondroplasia	SC	Filed NDA	11/20/2021	Yes	Yes
SHP-620	maribavir	Shire	benzimidazole	Cytomegalovirus	PO	Filed NDA	11/23/2021	No	Yes
ABI-009	sirolimus and albumin	Aadi Bioscience	mTOR kinase inhibitor	Epithelioid cell carcinoma	IV	Filed NDA	11/26/2021	Yes	Yes
Pedmark (STS)	sodium thiosulfate	Fennec	reducing agent	Ototoxicity	IV	Filed NDA	11/27/2021	Yes	Yes
Sci-B-Vac	hepatitis B vaccine	VBI Vaccines	vaccine	Hepatitis B	IM	Filed BLA	11/30/2021	No	No
pacritinib	pacritinib	CTI BioPharma	janus associated kinase-2 inhibitor	Myelofibrosis	PO	Filed NDA	11/30/2021	Yes	Yes
NPI-2358	plinabulin	BeyondSpring	Selective immunomodulating microtubule-binding agent	Chemotherapy-induced neutropenia	IV	Filed BLA	11/30/2021	Yes	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
Filsuvez (AP-101)	episalvan	Amryt Pharma	triterpene	Epidermolysis bullosa	TOP	Filed NDA	11/30/2021	No	Yes
SH-111	SH-111	Shorla Pharma	unknown	T-cell leukemia	undisclosed	Filed NDA	11/2021	Yes	No
DARE-BV1	clindamycin	Daré Bioscience	lincosamide	Bacterial vaginosis	Intravaginal	Filed NDA	12/07/2021	No	No
CAM-2038	buprenorphine	Braeburn	opioid receptor agonist (partial)	Opioid use disorder	SC	Filed NDA	12/15/2021	Yes	No
PL-56	budesonide	Calliditas	corticosteroid	Nephropathy	PO	Filed NDA	12/15/2021	No	Yes
ARGX-113	efgartigimod	Argenx	neonatal Fc receptor antibody	Myasthenia gravis	IV	Filed BLA	12/17/2021	Yes	Yes
dextroamphetamine transdermal system	dextroamphetamine	Noven Pharmaceuticals	CNS stimulant	Attention deficit hyperactivity disorder	TOP	Filed NDA	12/22/2021	No	No
Libervant	diazepam	Aquestive Therapeutics	benzodiazepine	Seizures	PO	Filed NDA	12/23/2021	No	Yes
TadFin	tadalafil and finasteride	Veru	phosphodiesterase type 5 inhibitor/5-alpha-reductase inhibitor	Benign prostatic hyperplasia	PO	Filed NDA	12/23/2021	No	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
UCB-4940	bimekizumab	UCB	interleukin-17 receptor inhibitor	Plaque psoriasis	SC	Filed BLA	4Q2021	Yes	No
AXS-05	dextromethorphan/ bupropion	Axsome	N-methyl-D-aspartate antagonist/ antidepressant	Major depressive disorder	PO	Filed NDA	4Q2021	No	No
FT-218	sodium oxybate extended-release	Avadel	dopamine receptor agonist	Narcolepsy	PO	Filed NDA	4Q2021	Yes	Yes
PF-04965842	abrocitinib	Pfizer	janus kinase 1 inhibitor	Atopic dermatitis	PO	Filed NDA	4Q2021	Yes	No
TAK-721	budesonide	Takeda	corticosteroid	Eosinophilic esophagitis	PO	Filed NDA	2H2021	Yes	Yes
dapivirine ring	dapivirine	International Partnership for Microbicides/ Johnson & Johnson	non-nucleoside reverse transcriptase inhibitor	HIV-1 infection	Intravaginally	Filed NDA	Late 2021	No	No
mRNA-1273	coronavirus vaccine	Moderna	vaccine	Novel coronavirus disease 2019 (COVID-19)	IM	Filed BLA	Late 2021/1Q2022	No	No
2022 Possible launch dates									
COR-003	levoketoconazole	Strongbridge Biopharma	cortisol synthesis inhibitor	Cushing's syndrome	PO	Filed NDA	01/01/2022	No	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
ALN-PCSsc	inclisiran	Novartis	RNA interfering therapeutic targeting PCSK9	Hyperlipidemia	SC	Filed NDA	01/01/2022	Yes	Yes
BXCL-501	dexmedetomidine	BioXcel Therapeutics	selective alpha 2a receptor agonist	Schizophrenia and bipolar disorder	PO	Filed NDA	01/05/2022	No	No
ACT-541468	daridorexant	Idorsia Pharmaceuticals	orexin receptor antagonist	Insomnia	PO	Filed NDA	01/08/2022	No	No
AMG-157 (MEDI-9929)	tezepelumab	AstraZeneca/ Amgen	thymic stromal lymphopoietin antagonist	Severe asthma	SC	Filed BLA	01/10/2022	Yes	No
cabotegravir	cabotegravir	ViiV Healthcare	HIV integrase inhibitor	HIV pre-exposure prophylaxis	IM	Filed NDA	01/24/2022	No	No
AK-105	penpulimab	Akeso	anti-PD-1 monoclonal antibody	Nasopharyngeal carcinoma	IV	Filed BLA	01/24/2022	Yes	Yes
VT-1161	oteseconazole	Mycovia Pharmaceuticals	lanosterol demethylase inhibitor	Vulvovaginal candidiasis	PO	Filed NDA	01/27/2022	No	No
MYK-461	mavacamten	Bristol Myers Squibb	cardiac myosin allosteric modulator	Obstructive hypertrophic cardiomyopathy	PO	Filed NDA	01/28/2022	Yes	Yes
MOD-401	somatrogon	Pfizer/ Opko	human growth hormone	Growth hormone deficiency	SC	Filed BLA	01/30/2022	Yes	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
RG-7716 (RO-6867461)	faricimab	Roche/ Chugai	bispecific VEGF-A/ angiopoietin-2 antagonist	Diabetic macular edema; age-related macular degeneration	Intravitreal	Filed BLA	01/31/2022	Yes	No
BIVV-009 (TNT-009)	sutimlimab	Sanofi	complement C1s subcomponent inhibitor	Cold agglutinin disease	IV	Filed BLA	02/05/2022	Yes	Yes
AG-348	mitapivat	Agios	pyruvate kinase-R activator	Pyruvate kinase deficiency	PO	Filed NDA	02/17/2022	Yes	Yes
IMC-gp100	tebentafusp	Immunocore	anti-CD3 antibody	Uveal melanoma	IV	Filed BLA	02/23/2022	Yes	Yes
RTA-402	bardoxolone methyl	Reata Pharmaceuticals	Nrf2 activator	Alport syndrome	PO	Filed NDA	02/25/2022	Yes	Yes
GC-5107	human immunoglobulin	GC Pharma	human immunoglobulin	Primary immunodeficiencies	IV	Filed BLA	02/25/2022	Yes	No
JNJ-4528 (LCAR-B38M)	ciltacabtagene autoleucel	Legend Biotech/ Janssen	chimeric antigen receptor (CAR) T cell therapy	Multiple myeloma	IV	Filed BLA	02/28/2022	Yes	Yes
GS-CA1 (GS-6207)	lenacapavir	Gilead	HIV capsid inhibitor	HIV-1	SC	Filed NDA	02/28/2022	No	No
LV-101	carbetocin	Levo Therapeutics	oxytocin receptor agonist	Prader-Willi Syndrome	Intranasal	Filed NDA	03/06/2022	Yes	Yes
Corplex donepezil	donepezil	Corium International	acetylcholinesterase inhibitor	Alzheimer's disease	TOP	Filed NDA	03/11/2022	No	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
BMS-986213	relatlimab/ nivolumab	Bristol Myers Squibb	lymphocyte-activation gene 3 blocking antibody/PD-1 immune checkpoint inhibitor	Melanoma	IV	Filed BLA	03/19/2022	Yes	No
CCD-1042	ganaxolone	Marinus Pharmaceuticals	allosteric modulator of GABA(a) receptors	Seizures	PO	Filed NDA	03/20/2022	No	Yes
R-1646 (RO-4926219, AF-219, MK-7264)	gefapixant	Merck/ Roche	P2X3 antagonist	Chronic cough	PO	Filed NDA	03/21/2022	No	No
TG-1303	ublituximab	TG Therapeutics	anti-CD-20 monoclonal antibody	Chronic lymphocytic leukemia	IV	Filed NDA	03/25/2022	Yes	Yes
Zydena	udenafil	Mezzion Pharma	phosphodiesterase type 5 (PDE5) inhibitor	Congenital single ventricle heart disease	PO	Filed NDA	03/26/2022	No	Yes
Tlando	testosterone	Lipocine	androgen	Hypogonadism	PO	Tentative Approval	3/27/2022	No	No
AKB-6548	vadadustat	Otsuka Pharmaceutical	hypoxia-inducible factor-prolyl hydroxylase inhibitor	Chronic kidney disease-related anemia	PO	Filed NDA	03/29/2022	Yes	No
IBI-308	sintilimab	Eli Lilly	programmed death-1 receptor inhibitor	Non-small cell lung cancer	IV	Filed BLA	03/2022	Yes	No
F-627	benegrastim	Evive Biotech	granulocyte colony-stimulating factor	Chemotherapy-induced neutropenia	SC	Filed BLA	03/31/2022	Yes	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
Botulax	letibotulinumtoxinA	Hugel Pharma	botulinum toxins	Wrinkles	IM	Filed BLA	03/31/2022	Yes	No
REGEN-COV	casirivimab/ imdevimab	Regeneron/Roche	monoclonal antibody	COVID-19	IV/IM/SC	Filed BLA	04/13/2022	No	No
ALN-TTRsc02	vutrisiran	Alnylam	siRNA/RNAi	Transthyretin-mediated amyloidosis	SC	Filed BLA	04/14/2022	Yes	Yes
AXS-07	meloxicam/rizatriptan	Axsome Therapeutics	non-steroidal anti-inflammatory drug/triptan	Migraine	PO	Filed NDA	04/30/2022	No	No
HMPL-012	surufatinib	Hutchison China MediTech	angio-immunokinase inhibitor	Neuroendocrine tumors	PO	Filed NDA	04/30/2022	Yes	Yes
INCB-050465	parsaclisib	Incyte	PI3K-delta inhibitor	Follicular lymphoma/ mantle cell lymphoma/ marginal zone lymphoma	PO	Filed NDA	04/30/2022	Yes	Yes
TV-46000	risperidone	Teva Pharmaceuticals/ MedinCell	atypical antipsychotic	Schizophrenia	SC	Filed NDA	04/30/2022	No	No
JS-001	toripalimab	Shanghai Junshi Biosciences/ Coherus Biosciences	anti-PD-1 monoclonal antibody	Nasopharyngeal carcinoma	IV	Filed BLA	05/01/2022	Yes	Yes
Takecab	vonoprazan fumarate	Phathom Pharmaceuticals	potassium-competitive acid blocker	H. pylori infection	PO	Filed NDA	05/08/2022	No	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
Zynteglo (LentiGlobin)	betibeglogene autotemcel	Bluebird Bio	gene therapy	Beta thalassemia	IV	Filed BLA	05/21/2022	Yes	Yes
GSK-2894512 (WBI-1001)	tapinarof	Dermavant Sciences	therapeutic aryl hydrocarbon receptor modulating agent	Plaque psoriasis	TOP	Filed NDA	05/26/2022	Yes	No
LY-3298176	tirzepatide	Eli Lilly	glucose-dependent insulinotropic polypeptide/glucagon-like peptide-1 receptor agonist	Diabetes mellitus	SC	Filed NDA	05/30/2022	No	No
ACER-001	sodium phenylbutyrate	Acer Therapeutics	BCKDC kinase inhibitor	Urea cycle disorders	PO	Filed NDA	06/05/2022	No	No
Furoscix	furosemide	scPharmaceuticals	diuretic	Heart failure	SC	CRL	2Q2022	Yes	No
VP-102	cantharidin	Verrica	antiviral	Molluscum	TOP	CRL	1H2022	No	No
ET-105	lamotrigine	Eton	anticonvulsant	Epilepsy	PO	CRL	1H2022	No	No
SPR-994	tebipenem	Spero Therapeutics	carbapenem	Urinary tract infections	PO	Filed NDA	06/2022	No	No
ERY-ASP (ERY-001)	L-asparaginase (eryaspase)	Erytech/ Recordati	L-asparaginase	Pancreatic cancer	IV	InTrial	Mid-2022	Yes	Yes
AT-007	AT-007	Applied Therapeutics	aldose reductase inhibitor	Galactosemia	PO	InTrial	Mid-2022	Yes	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
Adstiladrin	nadofaragene firadenovec	FerGene	gene therapy	Bladder cancer	Intravesical	CRL	Mid-2022	Yes	No
Tyvaso DPI	treprostinil	United Therapeutics	prostacyclin mimetic	Pulmonary arterial hypertension/ pulmonary hypertension	INH	CRL	Mid-2022	Yes	No
NVX-CoV2373	coronavirus vaccine	Novavax	vaccine	Novel coronavirus disease 2019 (COVID-19)	IM	InTrial	Mid-2022	No	No
Cuprior	trientine tetrahydrochloride	Orphalan	chelating agent	Wilson's disease	PO	Filed NDA	06/2022 - 07/2022	Yes	Yes
BGB-A317 (BGB-A-317)	tislelizumab	BeiGene	anti-programmed death-1 inhibitor	Esophageal squamous cell carcinoma	IV	Filed BLA	07/12/2022	Yes	No
AT-GAA	cipaglucosidase alfa	Amicus	enzyme therapy	Pompe disease	IV	Filed BLA	07/29/2022	Yes	Yes
Priorix	measles/mumps/rubella	GlaxoSmithKline	Vaccine	measles/mumps/rubella vaccine	IM/SQ	Filed BLA	08/02/2022	No	No
ARQ-151	roflumilast	Arcutis Biotherapeutics	phosphodiesterase-4 inhibitor	Plaque psoriasis	TOP	Filed NDA	08/04/2022	Yes	No
OBE-2109 (KLH-2109)	linzagolix	ObsEva	gonadotropin-releasing hormone antagonist	Uterine fibroids	PO	Filed NDA	09/15/2022	No	No
GZ-402665	olipudase alfa	Sanofi	enzyme replacement therapy	Acid sphingomyelinase deficiency	IV	InTrial	3Q2022	Yes	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
ALXN-1840 (WTX-101)	bis-choline tetrathiomolybdate (TTM)	AstraZeneca/ Alexion	chelating agent	Wilson's disease	PO	InTrial	3Q2022	Yes	Yes
AGIL-AADC	eladocagene exuparvovec	PTC Therapeutics	gene therapy	Aromatic L-amino acid decarboxylase deficiency	Intracerebral	InTrial	3Q2022	Yes	Yes
SYD-985	[vic-] trastuzumab duocarmazine	Synthon	HER2-targeting antibody-drug conjugate	Breast cancer	IV	InTrial	3Q2022	Yes	No
Ultomiris SC	ravulizumab-cwvz	Alexion	C5 complement inhibitor	paroxysmal nocturnal hemoglobinuria; Hemolytic uremic syndrome	SC	InTrial	3Q2022	Yes	Yes
CUTX-101	copper histidinate	Fortress Biotech	copper replacement	Menkes Disease	SC	InTrial	3Q2022	Yes	Yes
MRTX-849	adagrasib	Mirati Therapeutics	KRAS inhibitor	Non-small cell lung cancer	PO	InTrial	3Q2022	Yes	No
LY-3002813	donanemab	Eli Lilly	beta-amyloid monoclonal antibody	Alzheimer’s disease	IV	InTrial	3Q2022	Yes	No
DCR-PHXC	nedosiran	Dicerna/ Alnylam	glycolate oxidase antagonist	hyperoxaluria	SC	InTrial	3Q2022	Yes	Yes
RG-7828	mosunetuzumab	Roche	anti-CD20/CD3 monoclonal antibody	Follicular lymphoma	IV/SC	InTrial	3Q2021	Yes	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
ublituximab	ublituximab	TG Therapeutics	anti-CD-20 monoclonal antibody	Multiple sclerosis	IV	Filed BLA	09/30/2022	Yes	No
LIQ-861	treprostinil	Liquidia Technologies	prostacyclin analog	Pulmonary arterial hypertension	INH	Tentative Approval	10/27/2022	Yes	No
AMX-0035	tauroursodeoxycholic acid/ sodium phenylbutyrate	Amylyx Pharmaceuticals	histone deacetylase inhibitor	Amyotrophic lateral sclerosis	PO	Filed NDA	11/02/2022	Yes	Yes
NX-1207 (NYM-4805, REC 0482)	fexapotide triflutate	Nymox	pro-apoptotic	Benign prostatic hyperplasia	Intratumoral	InTrial	4Q2022	Yes	No
omecamtiv mecarbil	omecamtiv mecarbil	Amgen	mysoin activator	Heart failure	PO	InTrial	4Q2022	No	No
Zynquista	sotagliflozin	Lexicon	sodium-dependent glucose transporter 1 (SGLT-1) and SGLT-2 inhibitor	Diabetes mellitus	PO	CRL	4Q2022	No	No
EBV-CTL (ATA-129)	tabelecleucel	Atara Biotherapeutics	cell therapy	Lymphoproliferative disorder	IV	InTrial	4Q2022	Yes	Yes
131I-8H9	omburtamab	Y-mAbs Therapeutics	B7-H3 antagonist	Brain cancer	Intrathecal	InTrial	4Q2022	Yes	Yes
GLPG-0634	filgotinib	Gilead/ Galapagos	janus associated kinase-1 inhibitor	Ulcerative colitis	PO	CRL	4Q2022	Yes	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
BMS-986165	deucravacitinib	Bristol-Myers Squibb	tyrosine kinase 2 inhibitor	Plaque psoriasis	PO	InTrial	4Q2022	Yes	No
VBP-15	vamorolone	Santhera	corticosteroid	Duchenne muscular dystrophy	PO	InTrial	4Q2022	Yes	Yes
RTA-408	omaveloxolone	Reata Pharmaceuticals	Nrf2 activator	Friedreich's ataxia	PO	InTrial	4Q2022	Yes	Yes
PAX-101	suramin	PaxMedica	unknown	trypanosomiasis	IV	InTrial	4Q2022	No	No
FMXIN-001	naloxone	Nasus Pharma	opioid antagonist	Opioid overdose	Intranasal	InTrial	4Q2022	No	No
magrolimab	magrolimab	Gilead	CD47 monoclonal antibody	Myelodysplastic syndrome	IV	InTrial	4Q2022	Yes	Yes
pivmecillinam	pivmecillinam	Utility Therapeutics	amidinopenicillin	Urinary tract infections	PO	InTrial	4Q2022	No	No
MOR-202	felzartamab	MorphoSys/ I-Mab Biopharma	anti-CD38 monoclonal antibody	Multiple myeloma	IV	InTrial	4Q2022	Yes	No
REGN-475 (SAR-164877)	fasinumab	Regeneron/ Sanofi-Aventis/ Teva	selective anti-nerve growth factor monoclonal antibody	Osteoarthritis	SC	InTrial	4Q2022	Yes	No
CDZ-173	leniolisib	Pharming/ Novartis	phosphatidylinositol-3-4-5-trisphosphate inhibitor	Primary immunodeficiencies	PO	InTrial	4Q2022	Yes	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
AAI-101	cefepime/enmetazobactam	Allecra	beta-lactam/ b-lactamase inhibitor	Urinary tract infection	IV	InTrial	2H2022	No	No
BHV-3500	vazegepant	Biohaven	calcitonin gene-related peptide receptor antagonist	Migraine	Intranasal	InTrial	4Q2022	No	No
ABBV-951	levodopa/carbidopa	AbbVie	aromatic amino acid/aromatic amino acid decarboxylation inhibitor	Parkinson's disease	SC	InTrial	4Q2022	Yes	No
PRV-031	teplizumab	Provention Bio/ MacroGenics	CD3 antigen inhibitor	Diabetes mellitus	IV	CRL	2H2022	Yes	No
dovitinib	dovitinib	Allarity Therapeutics	fibroblast growth factor receptor 3 inhibitor	Renal cell carcinoma	PO	InTrial	2H2022	Yes	No
CAT-354	tralokinumab	Leo Pharma	interleukin-13 inhibitor	Atopic dermatitis	SC	CRL	2H2022	Yes	No
SPI-2012	eflapegrastim	Spectrum	granulocyte colony-stimulating factor	Chemotherapy-induced neutropenia	SC	CRL	2H2022	Yes	No
PRO-140	leronlimab	CytoDyn	C-C chemokine receptor 5 antagonist	HIV	SC	InTrial	2H2022	Yes	No
TAK-609	idursulfase-IT	Takeda	enzyme replacement	Hunter syndrome	Intrathecal	InTrial	2H2022	Yes	Yes
Contepo	fosfomycin	Nabriva Therapeutics	cell wall inhibitor	Bacterial infections	IV	CRL	2H2022	Yes	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
Qtrypta	zolmitriptan	Zosano	triptans	Acute migraines	TOP	CRL	2H2022	No	No
CPP-1X/ sulindac (DFMO)	eflornithine/ sulindac	Cancer Prevention Pharma	ornithine decarboxylase inhibitor/ non-steroidal anti-inflammatory drug	Familial adenomatous polyposis	PO	CRL	2H2022	Yes	Yes
DS-100	dehydrated alcohol	Eton	undisclosed	Methanol poisoning	SC	CRL	2H2022	No	Yes
pIL-12 (DNA IL-12)	tavokinogene telsaplasmid	OncoSec Medical	gene therapy	Melanoma	Intratumoral	InTrial	2H2022	Yes	Yes
TAK-003	Dengue fever vaccine	Takeda	vaccine	Dengue fever	SC	InTrial	2H2022	Yes	No
177Lu-PSMA-617	Lutetium	Novartis	radiopharmaceutical	Prostate cancer	IV	Filed BLA	2H2022	Yes	No
BAN-2401	lecanemab	Biogen/ Eisai	beta-amyloid monoclonal antibody	Alzheimer's disease	IV	InTrial	2H2022	Yes	No
HM781-36B	poziotinib	Spectrum Pharmaceuticals	pan-HER inhibitor	Non-small cell lung cancer	PO	InTrial	2H2022	Yes	No
Hepcludex	bulevirtide	Gilead	HBV receptor binder	Hepatitis delta virus	SC	InTrial	2H2022	No	Yes
SPN-830	apomorphine	Supernus Pharmaceuticals	non-ergoline dopamine agonist	Parkinson's disease	SC infusion	InTrial	2H2022	Yes	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
MGA-012	retifanlimab	Incyte	anti-PD-L1 inhibitor	Anal cancer	IV	CRL	2H2022	Yes	Yes
Ovastat	treosulfan	Medexus Pharmaceuticals	alkylating agent	Hematopoietic stem cell transplantation	IV	CRL	2H2022	Yes	Yes
CS-1001	sugemalimab	EQRx/ CStone Pharmaceuticals	anti-PD-L1 inhibitor	Non-small cell lung cancer	IV	InTrial	2H2022	Yes	No
ALPHA-1062	galantamine prodrug	Alpha Cognition	acetylcholinesterase inhibitor	Alzheimer's disease	PO	InTrial	2H2022	No	No
ALT-803	nogapendekin alfa inbakicept	ImmunityBio	interleukin-15 (IL-15) super agonist/ IL-15R alpha-Fc fusion complex	Bladder cancer	Intravesical	InTrial	2H2022	Yes	No
Rizaport (VersaFilm)	rizatriptan	IntelGenx	triptans	Acute migraines	PO	CRL	2022	No	No
RT-002 (Daxi)	daxibotulinumtoxinA	Revance Therapeutics	botulinum toxins	Glabellar lines (frown lines)	IM	CRL	2022	Yes	No
S5G4T-1 (DER-45-EV)	benzoyl peroxide	Sol-Gel Technologies	benzoyl peroxide	Rosacea	TOP	Filed NDA	2022	No	No
Doria	risperidone	Laboratorios Farmacéuticos Rovi	atypical antipsychotic	Schizophrenia	IM	CRL	2022	Yes	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
Leukotac	inolimomab	ElsaLys Biotech	IL-2 monoclonal antibody	Graft vs. host disease	IM	CRL	2022	Yes	Yes
ET-104	zonisamide	Eton	anticonvulsant	Seizures	PO	CRL	2022	No	No
NuThrax	anthrax vaccine adsorbed/ CPG-7909	Emergent Biosolutions	vaccine/ oligodeoxynucleotide	Anthrax	IM	InTrial	Late 2022	Yes	No
MT-7117	MT-7117	Mitsubishi Tanabe Pharma	Undisclosed	Erythropoietic protoporphyria	PO	InTrial	Late 2022	Yes	No
PS-433540 (RE-021; DARA)	sparsentan	Travere Therapeutics	dual-acting angiotensin/endothelin receptor antagonist	IgA nephropathy; focal segmental glomerulosclerosis	PO	InTrial	Late 2022	No	Yes
Vicineum	oportuzumab monatox	Sesen Bio	anti-ECAM exotoxin A fusion protein	Bladder cancer	Intravesical	CRL	Late 2022	Yes	No
Neutrolin (CRMD-003, CRMD-004)	citrate/ taurolidine/ heparin	CorMedix	antimicrobial agent/ anticoagulant	Catheter-related infections	IV	CRL	Late 2022	No	No
NexoBrid	bromelain	Vericel	peptide hydrolase replacement agent	Burns/ Skin injury	TOP	CRL	Late 2022	No	Yes
PRX-102	pegunigalsidase alfa	Protalix	enzyme replacement	Fabry disease	IV	CRL	Late 2022	Yes	No
IMGN-853 (M-9346A-sulfo-SPDB-DM4)	mirvetuximab soravtansine	ImmunoGen	folate receptor-1 antagonist	Ovarian cancer	IV	InTrial	Late 2022	Yes	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
Roctavian	valoctocogene roxaparvovec	BioMarin	gene therapy	Hemophilia A	IV	CRL	Late 2022	Yes	Yes
LN-145	LN-145	Iovance Biotherapeutics	tumor infiltrating lymphocyte	Cervical Cancer	IV	InTrial	Late 2022	Yes	No
PTX-022	rapamycin	Palvella Therapeutics	mTOR kinase inhibitor	Pachyonychia congenita	TOP	InTrial	Late 2022	No	Yes
obeticholic acid	obeticholic acid	Intercept Pharmaceuticals	farnesoid X receptor agonist	Nonalcoholic steatohepatitis	PO	CRL	Late 2022	Yes	No
IDP-120	tretinoin/ benzoyl peroxide	Bausch	retinoid	Acne	TOP	InTrial	Late 2022	No	No
KB-103	beremagene geperpavec	Krystal Biotech	gene therapy	Epidermolysis bullosa	Topical	InTrial	Late 2022	Yes	Yes
OPNT-003	nalmefene	Opiant	opioid receptor antagonist	Opioid overdose	Intranasal	InTrial	Late 2022	No	No
AGEN-1884	zalifrelimab	Agenus	immune checkpoint modulator antibody	Cervical cancer	IV	InTrial	Late 2022	Yes	No
iMAB-362	zolbetuximab	Astellas	GC182 monoclonal antibody	Gastric adenocarcinoma	IV	InTrial	Late 2022	Yes	Yes

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

Key pending indication forecast

OptumRx Key Pending Indication Forecast

Brand name	Generic name	Company	Drug class	Therapeutic use	New Proposed Indication Use	Route of administration	Estimated approval date
Keytruda	pembrolizumab	Merck	anti-PD-1 inhibitor	Melanoma	Adjuvant treatment of adult and pediatric (12 years and older) patients with stage IIB or IIC melanoma following complete resection	IV	12/04/2021
Keytruda	pembrolizumab	Merck	PD-1 blocking antibody	Renal cell carcinoma	Adjuvant treatment of patients with renal cell carcinoma (RCC) at intermediate-high or high risk of recurrence following nephrectomy (surgical removal of a kidney), or following nephrectomy and resection of metastatic lesions	IV	12/10/2021
Caplyta	lumateperone	Intra-Cellular Therapies	antipsychotic	Bipolar I or II disorder	Treatment of bipolar depression in patients with bipolar I or II disorder as monotherapy and adjunctive therapy (with lithium or valproate)	PO	12/17/2021
Otezla	apremilast	Amgen	phosphodieasterase 4 inhibitor	Plaque psoriasis (mild-to-moderate)	Treatment of adults with mild-to-moderate plaque psoriasis who are candidates for phototherapy or systemic therapy	PO	12/19/2021
Aliqopa	copanlisib	Bayer	kinase inhibitor	B-cell non-Hodgkin's Lymphoma	In combination with rituximab, Treatment of patients with relapsed indolent B-cell non-Hodgkin's Lymphoma (iNHL)	IV	12/21/2021
Xarelto	rivaroxaban	Janssen	factor Xa inhibitor	Venous thromboembolism	Treatment of venous thromboembolism (VTE, or blood clots) and reduction in the risk of recurrent VTE in patients aged birth to less than 18 years of age after at least	PO	12/23/2021

Brand name	Generic name	Company	Drug class	Therapeutic use	New Proposed Indication Use	Route of administration	Estimated approval date
					five days of initial parenteral anticoagulant treatment; and thromboprophylaxis (prevention of blood clots) in patients aged 2 years and older with congenital heart disease who have undergone the Fontan procedure		
Orencia	abatacept	Bristol Myers Squibb	selective T cell costimulation modulator	Acute graft versus host disease	Prevention of moderate to severe acute graft versus host disease (aGvHD) in patients 6 years of age and older receiving unrelated donor hematopoietic stem cell transplantation (HSCT)	IV/SC	12/23/2021
Cabenuva	cabotegravir, rilpivirine	ViiV/ Janssen	integrase strand transfer inhibitor/ non-nucleoside reverse transcriptase inhibitor	HIV-1 infection	Dosing update: every 2 month administration (currently approved every month)	IM	12/24/2021
Oxbryta	voxelotor	Global Blood Therapeutics	hemoglobin S polymerization	Sickle cell disease	Treatment of sickle cell disease (SCD) in children ages 4 to 11 years	PO	12/25/2021
Rexulti	brexpiprazole	Otsuka/ Lundbeck	serotonin-dopamine activity modulator	Schizophrenia (adolescents)	Treatment of schizophrenia in adolescents	PO	12/27/2021
Xeljanz	tofacitinib	Pfizer	janus associated kinase inhibitor	Axial spondyloarthritis	Treatment of axial spondyloarthritis	PO	12/28/2021
Rinvoq	upadacitinib	AbbVie	janus associated kinase inhibitor	Psoriatic arthritis	Treatment of adult patients with active psoriatic arthritis	PO	12/31/2021
Rinvoq	upadacitinib	AbbVie	janus associated kinase inhibitor	Atopic dermatitis	Treatment of adults and adolescents with moderate to severe atopic dermatitis	PO	12/31/2021

Brand name	Generic name	Company	Drug class	Therapeutic use	New Proposed Indication Use	Route of administration	Estimated approval date
Rinvoq	upadacitinib	AbbVie	janus associated kinase inhibitor	Ankylosing spondylitis	Treatment of adult patients with active ankylosing spondylitis	PO	12/31/2021
Olumiant	baricitinib	Eli Lilly	janus associated kinase 1/2 inhibitor	Atopic dermatitis	Treatment of adults with moderate-to-severe atopic dermatitis	PO	12/31/2021
Vonvendi	von Willebrand factor (recombinant)	Takeda	von Willebrand factor	von Willebrand disease	Prophylaxis therapy in von Willebrand disease	IV	01/28/2022
Libtayo	cemiplimab-rwlc	Sanofi	programmed death ligand-1 inhibitor	Cervical cancer	Treatment of patients with recurrent or metastatic cervical cancer whose disease progressed on or after chemotherapy	IV	01/30/2022
Skyrizi	risankizumab-rzaa	AbbVie	interleukin-23 antagonist	Psoriatic arthritis	Treatment of psoriatic arthritis	SC	02/06/2022
Rinvoq	upadacitinib	AbbVie	janus associated kinase inhibitor	Ulcerative colitis	Treatment of adults with moderately to severely active ulcerative colitis	PO	03/16/2022
Imcivree	setmelanotide	Rhythm Pharmaceuticals	MC4R agonist	Bardet-Biedl syndrome/ Alström syndrome	Treatment of obesity and control of hunger in adult and pediatric patients 6 years of age and older with Bardet-Biedl syndrome (BBS) or Alström syndrome	SC	03/20/2022
Ukoniq	umbralisib	TG Therapeutics	phosphoinositide-3 kinase delta inhibitor	Chronic lymphocytic leukemia and small lymphocytic lymphoma	Treatment for patients with chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL)	IV	03/26/2022

Brand name	Generic name	Company	Drug class	Therapeutic use	New Proposed Indication Use	Route of administration	Estimated approval date
Fintepla	fenfluramine	Zogenix	serotonin receptor agonist	Lennox Gastaut Syndrome	Adjunctive treatment for seizures in adults and children with Lennox Gastaut Syndrome (LGS)	PO	03/28/2022
Keytruda	pembrolizumab	Merck	programmed death receptor-1-blocking antibody	Endometrial carcinoma	Treatment of patients with advanced endometrial carcinoma that is microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation	IV	03/28/2022
Jardiance	empagliflozin	Boehringer Ingelheim/ Eli Lilly	sodium-dependent glucose transporter 2 inhibitor	Heart failure	Treatment of people with chronic heart failure in patients with preserved ejection fraction	PO	03/30/2022
Yescarta	axicabtagene ciloleucel	Kite/ Gilead	chimeric antigen receptor (CAR) T cell therapy	Large B-cell lymphoma	Treatment of adults with relapsed or refractory large B-cell lymphoma in the second-line setting	IV	03/30/2022
Kymriah	tisagenlecleucel	Novartis	chimeric antigen receptor (CAR) T cell therapy	Follicular lymphoma	Treatment of adult patients with relapsed or refractory follicular lymphoma (FL) after two prior lines of treatment	IV	04/27/2022
Cosentyx	secukinumab	Novartis	interleukin-17 receptor antagonist	Juvenile idiopathic arthritis	Treatment of juvenile idiopathic arthritis	SC	04/29/2022
Qelbree	viloxazine	Supernus	selective norepinephrine reuptake inhibitor	Attention deficit hyperactivity disorder (adults)	Treatment of adults with attention deficit hyperactivity disorder (ADHD)	PO	04/29/2022
Fasenra	benralizumab	AstraZeneca	interleukin-5 receptor alpha inhibitor	Nasal polyposis	Treatment of nasal polyposis	SC	04/30/2022

Brand name	Generic name	Company	Drug class	Therapeutic use	New Proposed Indication Use	Route of administration	Estimated approval date
Myfembree	relugolix/ estradiol/ norethindrone acetate	Myovant	gonadotropin-releasing hormone receptor antagonist/ estrogen/ progestin	Endometriosis	Management of moderate to severe pain associated with endometriosis	PO	05/07/2022
Opdivo	nivolumab	Bristol Myers Squibb	PD-1-blocking antibody	Esophageal squamous cell carcinoma	In combination with Yervoy (ipilimumab) and Opdivo in combination with fluoropyrimidine- and platinum-containing chemotherapy, for first-line treatments for adult patients with unresectable advanced, recurrent or metastatic esophageal squamous cell carcinoma	IV	05/28/2022
Beovu	brolucizumab	Novartis	anti-VEGF antibody	Diabetic macular edema	Treatment of diabetic macular edema	Intravitreal	06/13/2022
Skyrizi	risankizumab-rzaa	AbbVie	interleukin-23 antagonist	Crohn's disease	Treatment of patients 16 years and older with moderate to severe Crohn's disease	SC	07/20/2022
Stelara	ustekinumab	Janssen	human interleukin-12 and -23 antagonist	Juvenile psoriatic arthritis (5 years and older)	Treatment of pediatric patients ages 5 years and older with juvenile psoriatic arthritis	SC/IV	08/08/2022

IM = intramuscular, INH = inhaled, IV = intravenous, OPH = ophthalmic, PO = oral, SC = subcutaneous, TOP = topical

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