OPTUMRx®

RxOutlook®

3rd Quarter 2021

In this edition of RxOutlook, we highlight 12 key pipeline drugs with an expected FDA decision by the end of 2021. Of the products discussed below, one has already been approved by the FDA – AstraZeneca's Saphnelo® (anifrolumab) for the treatment of systemic lupus erythematosus (SLE). Saphnelo is one of the few novel therapies approved for SLE over the last several decades and it would provide an additional treatment option in patients that have failed standard therapy (eg, hydroxychloroquine).

Bimekizumab, an injectable interleukin (IL)-17 monoclonal antibody, is the first of a series of novel drugs that could potentially be approved in the next 18 months for plaque psoriasis. While this is already a highly competitive therapeutic category, bimekizumab demonstrated superiority in head-to-head trials vs. several biologic treatment options for the condition. Plinabulin is a first-in-class treatment for chemotherapy-induced neutropenia (CIN) and would potentially be the first change in the treatment paradigm for management of CIN since the development of granulocyte colony stimulating factors (eg, Neulasta®, Neupogen®).

Consistent with recent pipeline trends, a significant proportion of drugs remaining this year have been granted orphan drug designation and would be used for rare conditions. Of the 12 drugs discussed below, 7 have an orphan drug designation. In some cases, these treatments will represent the first FDA approved therapies for their conditions. This includes narsoplimab for transplant-associated thrombotic microangiopathy and vosoritide for achondroplasia. Other orphan drugs included will be entering more competitive landscapes where alternative treatment options are available, but they may provide advantages in certain subsets of patients (pacritinib in patients with myelofibrosis and severe thrombocytopenia). Overall, individual orphan drugs are unlikely to be significantly impactful from a budgetary perspective for payers; however, collectively they pose a challenge as they represent an increasingly larger proportion of overall drug spend.

Approval decisions for other key novel therapies are expected in the second half of 2021 but are not reviewed in this report because they were covered in previous editions of RxOutlook. These include: abrocitinib and topical ruxolitinib for atopic dermatitis; atogepant for migraine prophylaxis; maralixibat for Alagille syndrome; and avacopan for ANCA-associated vasculitis.

Key pipeline drugs with FDA approval decisions expected by end of the 4th 2021

Drug Name	Manufacturer	Indication/Use	Expected FDA Decision Date
Saphnelo® (anifrolumab)	AstraZeneca	Systemic lupus erythematosus	7/30/2021 (Approved)
Dextromethorphan/ bupropion	Axsome Therapeutics	Major depressive disorder	4Q 2021
Bimekizumab	UCB	Plaque psoriasis	10/15/2021
Varenicline (nasal spray)	Oyster Point Pharma	Dry eye disease	10/17/2021
Narsoplimab	Omeros	Hematopoietic stem cell transplant-associated thrombotic microangiopathy*	10/17/2021
Mobocertinib	Takeda	Non-small cell lung cancer*	10/26/2021
Ropeginterferon alfa-2b	PharmaEssentia	Polycythemia vera*	11/13/2021

Drug Name	Manufacturer	Indication/Use	Expected FDA Decision Date
Vosoritide	BioMarin	Achondroplasia*	11/20/2021
Ciltacabtagene autoleucel	Janssen/ Legend Biotech	Multiple myeloma*	11/29/2021
Plinabulin	BeyondSpring	Chemotherapy-induced neutropenia	11/30/2021
Pacritinib	CTI BioPharma	Myelofibrosis*	11/30/2021
Efgartigimod	Argenx	Generalized myasthenia gravis*	12/17/2021

* 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 4th Quarter 2021.

Read more

Extended Generic Pipeline Forecast

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

Read more

Extended Brand Pipeline Forecast

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

Read more

Key Pending Indication Forecast

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

Read more

Past and future reviews

Please note that RxOutlook highlights select near-term approvals. Some drugs may not appear in this issue because they have been reviewed in previous editions of RxOutlook. Drugs of interest that are earlier in development or with expected approvals beyond 4th quarter 2021 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

Anifrolumab-fnia (Brand Name: Saphnelo®)

Manufacturer: AstraZeneca
Regulatory designations: Fast Track
Approval decision: 7/30/2021

Therapeutic use

Anifrolumab is was approved for the treatment of adult patients with moderate to severe systemic lupus erythematosus (SLE), who are receiving standard therapy.

SLE is a chronic, autoimmune disorder that can affect different organs in the body. Common symptoms include fatigue, skin rashes, fevers, and pain or swelling in the joints. Causes of premature death associated by SLE are mainly active disease, organ failure (eg, kidneys), infection, or cardiovascular disease from accelerated atherosclerosis.

The prevalence of SLE varies widely due to differences in case definitions and study methods. A conservative estimate on prevalence from the Center for Disease Control and Prevention (CDC) is 161,000 with definite SLE and 322,000 with definite or probable SLE.

- Treatment of adult patients with moderate to severe SLE, who are receiving standard therapy

Clinical profile

Anifrolumab is human monoclonal antibody that binds to subunit 1 of the type I interferon (IFN) receptor, blocking the activity of all type I interferons including IFN-alpha, IFN-beta and IFN-omega. Type I interferons are cytokines involved in the inflammatory pathways. Between 60% and 80% of adults with SLE have an increased type I interferon gene signature.

Pivotal trial data:
The safety and efficacy of anifrolumab were evaluated in three randomized, double-blind, placebo-controlled studies. All patients had moderate to severe disease despite receiving standard therapy. Efficacy of anifrolumab was established based on assessment of clinical response using the composite endpoints, the British Isles Lupus Assessment Group based Composite Lupus Assessment (BICLA) and the SLE Responder Index (SRI-4).

Study 1 randomized 305 patients. The primary endpoint was a combined assessment of the SRI-4 and the sustained reduction in oral corticosteroids (OCS). SRI-4 response was 62.8% in the anifrolumab treated patients vs. 38.8% in placebo patients (treatment difference: 24.0; 95% CI: 10.9, 37.2). Consistent trends in favor of anifrolumab vs. placebo, on effect of reduction of OCS use, were observed, but the difference was not statistically significant.

Study 2 randomized 457 patients. The primary endpoint was improvement in disease activity evaluated at 52 weeks, measured by SRI-4. SRI-4 response was 49% in the anifrolumab treated patients vs. 43% in placebo patients (treatment difference: 6.0; 95% CI: -4.2, 16.2). This was not a statistically significant improvement.

Study 3 randomized 362 patients. The primary endpoint was improvement in disease activity evaluated at 52 weeks, measured by BICLA. BICLA response was 47.8% in the anifrolumab treated patients vs. 31.5% in the placebo patients (treatment difference: 16.3; 95% CI: 6.3, 26.3; p = 0.001).

- Monoclonal antibody targeting type 1 IFN receptors
- IV formulation
- For efficacy results, refer to the complete pivotal trial data
- Common AEs: Nasopharyngitis, upper respiratory tract infections, bronchitis, infusion related reactions, herpes zoster, cough
- Dosing: Every 4 weeks

Anifrolumab-fnia (continued...)

Safety:
The most common adverse events with anifrolumab use were nasopharyngitis, upper respiratory tract infections, bronchitis, infusion related reactions, herpes zoster, and cough.

Dosing:
The recommended dose of anifrolumab is 300 mg administered via intravenous (IV) infusion every 4 weeks.

Competitive environment

Anifrolumab represents a novel MOA for treatment of SLE. There is an unmet need for new therapies in SLE as few have been approved by the FDA. The current standard of care includes use of immunosuppressants, with hydroxychloroquine being the most used first line pharmacotherapy. Other immunosuppressants including corticosteroids can be used depending on severity. Benlysta® (belimumab), an injectable B-lymphocyte stimulator-specific inhibitor, was approved for SLE in patients already on standard of care back in 2011.

However, anifrolumab did not meet its primary endpoint in one of its pivotal trials and anifrolumab will likely be reserved for use in patients that fail conventional standard of care, like Benlysta. In terms of dosing, anifrolumab requires IV administration whereas Benlysta is also available via SC injection. Benlysta is also approved for lupus nephritis, a common and serious downstream consequence of SLE.

The wholesale acquisition cost (WAC) for anifrolumab is approximately $60,000 per year.

- Advantages: Novel MOA for treatment of SLE, unmet need
- Disadvantages: Failed to achieve primary endpoint in a pivotal study, reserved for patients who have failed standard of care, IV administration (Benlysta can be administered via SC injection)
- WAC: ~$60,000 per year

Dextromethorphan/bupropion (Brand Name: To be determined)

Manufacturer: Axsome Therapeutics
Regulatory designations: Breakthrough Therapy, Fast Track
Expected FDA decision: 4Q 2021; original PDUFA date of August 22, 2021 was not met due to application deficiencies.

Therapeutic use

Dextromethorphan/bupropion (AXS-05) is in development for treatment of adult patients with major depressive disorder (MDD).

MDD is one of the most common mental health disorders in the U.S. affecting approximately 7% of adults each year.

Clinical profile

The dextromethorphan component of AXS-05 is an uncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist. NMDA receptors have been viewed as a potential target for psychiatric conditions, particularly depression. Dextromethorphan also works as an antagonist the ionotropic glutamate receptor and as a sigma-1 receptor agonist. The bupropion component of AXS-05 serves to increase the bioavailability of dextromethorphan and is a norepinephrine and dopamine reuptake inhibitor.

Dextromethorphan is currently available over-the-counter in various cough and cold medications as a cough suppressant. Bupropion is currently available as a prescription (eg, Wellbutrin®) drug for MDD.

<u>Pivotal trial data:</u>
The efficacy of AXS-05 was evaluated in GEMINI, a Phase 3, randomized, double-blind, placebo-controlled study in 327 adult patients with moderate-to-severe MDD. Patients received AXS-05 or placebo for 6 weeks. The primary endpoint was change from baseline in the Montgomery-Åsberg Depression Rating Scale (MADRS) total score at week 6. The MADRS total score ranges from 0 to 60 with a higher number representing higher severity of depression. There was a statistically significant mean reduction from baseline in the MADRS total score of 16.6 points vs. 11.9 for placebo ($p = 0.002$) after 6 weeks of treatment. AXS-05 also demonstrated a statistically significant improvement vs. placebo on the key secondary endpoint of change from baseline in the MADRS total score at week 1, the earliest time point measured ($p = 0.007$), and at all timepoints thereafter.

AXS-05 was also evaluated in ASCEND, a Phase 2, randomized, double-blind, active-controlled study in 80 adults with a diagnosis of moderate-to-severe MDD. Patients received AXS-05 or bupropion monotherapy for 6 weeks. The primary endpoint was MADRS total score. At week 6, AXS-05 demonstrated a 17.2 point reduction in the MADRS total score compared to a 12.1 point reduction for bupropion ($p = 0.013$). Starting at week 1, AXS-05 achieved superiority over bupropion on the MADRS total score, with statistical significance achieved at week 2 and maintained at all time points thereafter.

- Treatment of adult patients with MDD
- NMDA receptor antagonist/ norepinephrine and dopamine reuptake inhibitor
- Oral formulation
- Change from baseline in the MADRS total score at week 6 (GEMINI trial): 16.6 points vs. 11.9 points with placebo
- Change from baseline in the MADRS total score at week 6 (ASCEND trial): 17.2 points vs. 12.1 points with bupropion
- Common AEs: Dizziness, nausea, headache, diarrhea, somnolence, dry mouth
- Dosing: Twice daily

Dextromethorphan/bupropion (continued...)

Safety:
The most common adverse events with AXS-05 use were dizziness, nausea, headache, diarrhea, somnolence, and dry mouth.

Dosing:
In the pivotal trials, AXS-05 was administered orally twice daily.

Competitive environment

AXS-05 is a novel combination therapy for MDD. Several classes of medications are currently used to treat MDD, with serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and atypical antidepressants (eg, bupropion, mirtazapine) typically used in the first line setting. The choice of antidepressant is based upon multiple factors including side effect profile, comorbid illnesses, and patient preference. While many options are currently available, including generics, treatment failure is high in MDD. Dextromethorphan, the NMDA antagonist component of AXS-05, would be the second drug with this mechanism approved for MDD. Spravato® (esketamine) nasal spray is the other NMDA antagonist and it is approved for treatment-resistant depression and MDD with acute suicidal ideation or behavior. Spravato is a schedule III controlled substance.

The primary differentiator for AXS-05 is that it appears to have a more rapid onset of action, with benefit demonstrated as early as one week. Most antidepressants take several weeks before providing clinical benefit to patients. Nevertheless, AXS-05 would be entering a crowded marketplace with high generic penetration from well-established standards of care. AXS-05 did have the small Phase 2 head-to-head trial vs. monotherapy bupropion, but there is limited data comparing this product vs. other standards of care.

AXS-05 is also in Phase 3 development for agitation in patients with Alzheimer's disease and results are expected in the second half of 2022. There is a high unmet need for treatments in this space, with a lack of FDA approved treatments.

- Advantages: Novel combination for MDD, large potential target population, also in development for Alzheimer's disease-related agitation
- Disadvantages: Alternatives available including many generic options, limited head-to-head trial data

Bimekizumab (Brand Name: To be determined)

Manufacturer: UCB
Expected FDA decision: October 15, 2021

Therapeutic use

Bimekizumab is in development for the treatment of adults 18 years or older with moderate-to-severe plaque psoriasis.

Psoriasis is a common chronic inflammatory condition that primarily affects the skin. The most common subtype is plaque psoriasis, which represents 80-90% of cases. Plaque psoriasis is characterized by thick red patches of skin covered with silvery scales or dry, cracked skin that may bleed. The scalp, elbows, knees and gluteal cleft are common affected areas.

Psoriasis occurs in children and adults, with symptoms usually beginning in adulthood. It affects an estimated 8 million individuals in the U.S.

- Treatment of adults with moderate-to-severe plaque psoriasis in patients 18 years of age or older

Clinical profile

Bimekizumab is a humanized monoclonal IgG1 antibody that selectively inhibits both interleukin (IL)-17A and IL-17F. IL-17A and IL-17F are cytokines that modulate the pathophysiology of psoriasis via independent inflammatory pathways. Inhibition of both pathways is thought to suppress inflammation to a greater extent than inhibition of one pathway alone.

- Interleukin (IL)-17A and IL-17F monoclonal antibody
- SC formulation

<u>Pivotal trial data:</u>
The efficacy of bimekizumab was evaluated in four clinical studies: BE VIVID, BE SURE, BE RADIANT, and BE READY. All were Phase 3, randomized, double-blind studies in patients 18 years or older with moderate-to severe plaque psoriasis.

In BE VIVID (N = 567), patients were randomized to bimekizumab, Stelara® (ustekinumab), or placebo. PASI90 response rates at week 16 (co-primary endpoint) were 85% with bimekizumab ($p < 0.0001$ vs. Stelara and placebo), 50% with Stelara, and 5% with placebo. IGA response rates at week 16 (co-primary endpoint) were 84% with bimekizumab ($p < 0.0001$ vs. Stelara and placebo), 53% with Stelara, and 5% with placebo. PASI100 response rates at week 16 were 59% with bimekizumab ($p < 0.0001$ vs. Stelara and placebo), 21% with Stelara, and 0% with placebo.

- PASI90 response: 85% to 91% with bimekizumab vs. 74% with Cosentyx vs. 50% with Stelara vs. 47% with Humira vs. 1% to 5% with placebo
- PASI100 response: 59% to 68% with bimekizumab vs. 49% with Cosentyx vs. 21% with Stelara vs. 24% with Humira vs. 0% to 1% with placebo

In BE SURE (N = 478), patients were randomized to bimekizumab or Humira® (adalimumab). PASI90 response rates at week 16 (co-primary endpoint) were 86% with bimekizumab and 47% with Humira ($p < 0.0001$). PASI100 response rates at week 16 were 61% with bimekizumab and 24% with Humira ($p < 0.0001$). IGA response rates at week 16 (co-primary endpoint) were 85% with bimekizumab and 57% with Humira ($p < 0.0001$).

- IGA response: 84% to 93% with bimekizumab vs. 79% with Cosentyx vs. 53% with Stelara vs. 57% with Humira vs. 1% to 5% with placebo
- Common AEs: Nasopharyngitis, oral candidiasis, upper respiratory tract infection
- Dosing: Every 4 weeks

Bimekizumab (continued...)

In BE RADIANT (N = 743), patients were randomized to bimekizumab or Cosentyx® (secukinumab). PASI90 response rates at week 16 were 86% with bimekizumab and 74% with Cosentyx ($p < 0.0001$). PASI100 response rates at week 16 (primary endpoint) were 62% with bimekizumab and 49% with Cosentyx ($p < 0.0001$). IGA response rates at week 16 were 86% with bimekizumab and 79% with Cosentyx ($p < 0.0001$).

In BE READY (N = 435), patients were randomized to bimekizumab or placebo. PASI90 response rates at week 16 (co-primary endpoint) were 91% with bimekizumab and 1% with placebo ($p < 0.0001$). PASI100 response rates at week 16 were 68% with bimekizumab and 1% with placebo ($p < 0.0001$). IGA response rates at week 16 (co-primary endpoint) were 93% with bimekizumab and 1% with placebo ($p < 0.0001$).

Safety:
The most common adverse events with bimekizumab use were nasopharyngitis, oral candidiasis, and upper respiratory tract infection. In clinical trials, there were increased rates of oral candidiasis with bimekizumab compared to Cosentyx, Humira, Stelara and placebo. However, almost all cases were of mild or moderate in severity.

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

Competitive environment

If approved, bimekizumab would be the first immunomodulator to target both the IL-17A and IL-17F pathways. In addition, bimekizumab demonstrated superiority in direct head-to-head trials vs. existing standards of care options such as Stelara, Humira, and Cosentyx. Like its competitors which have been approved for other indications, bimekizumab is also being studied for psoriatic arthritis, axial spondyloarthritis, and hidradenitis suppurativa.

Bimekizumab is entering a crowded market and represents yet another SC treatment option for moderate-to-severe plaque psoriasis. Current pharmacotherapy options for plaque psoriasis include topical treatments (eg, corticosteroids, vitamin D analogues, tazarotene), systemic oral therapies (eg, Otezla® [apremilast], cyclosporine, methotrexate, systemic steroids) and several injectable biologic agents. Bimekizumab would compete with these well-established biologic agents for moderate-to-severe plaque psoriasis.

Clinical guidelines recommend biologic agents for the treatment of moderate-to-severe plaque psoriasis but do not recommend a specific biologic agent. Side-effect profile, route of administration, dosing frequency and other factors are often considered when choosing a specific agent.

There were increased rates of oral candidiasis with bimekizumab, as compared to Stelara, Humira, Cosentyx and placebo. Moreover, there are other biologic agents that are dosed less frequently (eg, Skyrizi, Stelara), have indications that bimekizumab is not currently being studied for, or can be used in pediatric populations for plaque psoriasis (eg, Stelara). Finally, biosimilars for Humira are expected to enter the market in 2023.

For reference, the WAC for Cosentyx and Humira are approximately $71,000 and $77,500 per year, respectively.

- Advantages: Head-to-head trial data demonstrating statistical superiority vs. market leaders, unique mechanism of action, also in development for other rheumatologic conditions (eg, psoriatic arthritis, axial spondyloarthritis and hidradenitis suppurativa)
- Disadvantages: Many alternatives currently available and in the pipeline, initial indication limited to adults, Humira biosimilar will launch in 2023
- Reference WAC (Cosentyx): ~$71,000 per year
- Reference WAC (Humira): ~$77,500 per year

Varenicline nasal spray (Brand Name: Tyrvaya™)

Manufacturer: Oyster Point Pharma
Expected FDA decision: October 17, 2021

Therapeutic use

Varenicline nasal spray is in development for treatment of signs and symptoms of dry eye disease.

Dry eye disease is a multifactorial condition characterized by disruption of the tear film. Tear film instability and hyperosmolarity can cause persistent stinging, scratching, burning sensations, sensitivity to light, blurred vision, and eye fatigue.

An estimated 16 million adults in the U.S. have been diagnosed with dry eye disease.

- Treatment of signs and symptoms of dry eye disease

Clinical profile

Varenicline is a selective cholinergic agonist. The parasympathetic nervous system controls tear film homeostasis partially via the trigeminal nerve, which is accessible within the nose. Activation of the trigeminal parasympathetic pathway in the nasal cavity by varenicline is believed to stimulate natural tear film production.

- Selective cholinergic agonist
- Intranasal formulation
- Improvement in tear production (using Schirmer's score): 47% to 54% vs. 14% to 28% with placebo
- Common AEs: Sneeze, cough, throat irritation, instillation site irritation
- Dosing: Twice daily

<u>Pivotal trial data:</u>
The efficacy of varenicline nasal spray was evaluated in ONSET-2 and ONSET-1. ONSET-2 was a Phase 3, randomized, double-masked, vehicle-controlled study in 758 patients with dry eye disease. The study evaluated a 0.6 mg/mL and 1.2 mg/mL dose of varenicline nasal spray vs. a vehicle control. The primary endpoint was improvement in Schirmer's scores at week 4 (defined as gaining ≥ 10 mm in Schirmer's score). Schirmer's test is assessed by quantifying the number of tears produced by each eye. Small strips of paper are placed in the lower eyelids of each eye and the results are measured in millimeters of tears collected over a five-minute time period.

The percentage of eyes showing improvement in Schirmer's scores in the 0.6 mg/mL, 1.2 mg/mL, and vehicle groups were: 47.3% ($p < 0.0001$ vs. vehicle), 49.2% ($p < 0.0001$ vs. vehicle) and 27.8%, respectively. Mean change in Schirmer test scores was 11.3 mm ($p < 0.0001$), 11.5 mm ($p < 0.0001$), and 6.3 mm, respectively.

ONSET-1 was a Phase 2b, dose-ranging, randomized, double-masked, vehicle-controlled study in 182 patients with dry eye disease. The primary endpoint was the change in Schirmer's score at week 4. The mean change from baseline in Schirmer's score in the 0.6 mg/mL, 1.2 mg/mL, and vehicle groups were: 11.4 mm ($p < 0.001$ vs. vehicle), 11.1 mm ($p < 0.001$ vs. vehicle), and 3.7 mm, respectfully. The proportion of patients who had a change ≥ 10 mm in Schirmer's score from baseline at week 4 was statistically significantly higher (vehicle nasal spray: 14%) in the 0.6 mg/ml (54%; $p < 0.001$) and 1.2 mg/ml (48%; $p = 0.001$) varenicline dose groups.

<u>Safety:</u>
The most common adverse events with varenicline nasal spray use were sneeze, cough, throat irritation, and instillation site irritation.

<u>Dosing:</u>
In the pivotal trials, varenicline was administered intranasally twice daily.

Varenicline nasal spray (continued...)

Competitive environment

If approved, intranasal varenicline would provide a non-ocular alternative for dry eye disease. Initial treatment for dry eye is typically artificial tears and lifestyle modifications. In terms of pharmacotherapies, ophthalmic formulations of cyclosporine (Restasis® and Cequa®) and Xiidra® (lifitegrast) are approved treatment options. These products are currently only available as brand products but a generic version of Restasis could be available in the second half of 2021.

In addition to the novel route of administration for treatment of dry eye disease, varenicline also offers a novel mechanism of action (MOA) for treating the condition. Current treatment options are only modestly effective in some patients and given the high prevalence of the disease, there is a large potential target population.

However, intranasal varenicline was not compared head-to-head against existing treatment options and when compared indirectly, the efficacy appears similar. High rates of nasopharyngeal side effects were reported with varenicline in the pivotal trials which could discourage its use as an alternative to the ophthalmic options, although these events were generally mild.

For reference, the WAC for Xiidra is approximately $6,600 per year.

- Advantages: Non-ocular treatment alternative for dry eye disease, large potential target population
- Disadvantages: Alternatives available (Restasis, Cequa, Xiidra), lack of head-to-head trial data, efficacy appears comparable to other options, high rates of non-ocular side effects
- Reference WAC (Xiidra): ~$6,600 per year

Narsoplimab (Brand Name: To be determined)

Manufacturer: Omeros
Regulatory designations: Orphan Drug, Breakthrough Therapy
Expected FDA decision: October 17, 2021

Therapeutic use

- Treatment of HSCT-TMA

Narsoplimab is in development for treatment of hematopoietic stem cell transplant-associated thrombotic microangiopathy (HSCT-TMA).

TMA is one of the most serious complications that can occur in transplant recipients. It is characterized by hemolytic anemia, renal dysfunction and neurological symptoms (eg, seizures, weakness). TMA is caused by endothelial cell damage, induced by a variety of factors, including human leukocyte antigen (HLA) mismatch, conditioning and immunosuppressive regimens, presence of graft vs. host disease (GvHD), and infectious complications.

About 20,000 HSCTs occur annually in the U.S. HSCT-TMA is more common in allogeneic transplants although the exact incidence is unclear. In high risk and severe cases, mortality rates can exceed 90%.

Clinical profile

- Monoclonal antibody targeting MASP-2
- IV formulation
- CRR: 61%
- 100-day survival: 68%
- Common AEs: Nausea, vomiting, diarrhea, hypokalemia, neutropenia, fever
- Dosing: Once weekly for up to 8 weeks

Narsoplimab is a monoclonal antibody targeting mannan-binding lectin-associated serine protease-2 (MASP-2), a pro-inflammatory protein target and the effector enzyme of the lectin pathway of complement. The lectin pathway is one of the principal pathways of complement and is activated primarily by tissue damage and microbial infection.

Pivotal trial data:
The efficacy of narsoplimab was evaluated in one Phase 3, single-arm, open-label study in 28 patients with high-risk HSCT-TMA. Treatment consisted of narsoplimab administered for up to 8 weeks with an extended follow-up period. The primary endpoint was complete response rate (CRR), defined as clinical improvement in TMA markers (platelet count and lactate dehydrogenase [LDH]) and in organ function (renal, pulmonary, gastrointestinal or neurological) or freedom from transfusion. Secondary endpoints included 100-day and overall survival (OS).

The CRR was 61% (95% CI: 40.6, 78.5; $p < 0.0001$ vs. 15% pre-specified efficacy threshold agreed with by the FDA) in the full analysis set (FAS; patients receiving at least one dose of narsoplimab). Additionally, 100-day survival was 68% in the FAS and 94% in complete responders. Median OS was 274 days in the FAS and for complete responders, was not estimable (more than half of the responders were alive at last follow-up).

Safety:
The most common adverse events with narsoplimab use were nausea, vomiting, diarrhea, hypokalemia, neutropenia, and fever. Six deaths occurred in the study, although all from causes common in HSCT.

Dosing:
In the pivotal trial, narsoplimab was administered via IV infusion once weekly for up to 8 weeks.

Narsoplimab (continued...)

Competitive environment

Narsoplimab could potentially be the first FDA approved treatment for HSCT-TMA. The standard of care for treatment of HSCT-TMA includes discontinuation or alteration of a patient's immunosuppressive regimen, treatment of co-existing infections and GvHD, aggressive hypertension control, and supportive therapy. In the absence of other approved therapies, drugs such as Soliris® (eculizumab) and Rituxan® (rituximab) have been used off-label with efficacy being demonstrated in case reports and observational studies.

While the pivotal study did not have a comparator arm, the expected mortality rate in these patients is very high and so the potential impact on overall survival for narsoplimab is promising. The drug also appears to be well tolerated, with reported adverse events being consistent with what is commonly seen in a post-transplant population.

Narsoplimab was only evaluated in a small 28-patient trial that was single-arm. Although this is not uncommon with investigational drugs treating very rare conditions, it highlights that the evidence base, while positive, is very small. Overall, the expected initial impact is likely to be small due to the rarity of the condition and that it would be limited to patients with high risk TMA whose symptoms have not resolved with more conventional strategies (eg, alterations in a patient's immunosuppressive therapy).

Narsoplimab is also being studied for IgA nephropathy and atypical hemolytic uremic syndrome (aHUS). These are rare diseases but could potentially expand the drugs future market potential.

- Advantages: Potentially first approved treatment for HSCT-TMA, unmet need, well tolerated, also in development for IgA nephropathy and aHUS
- Disadvantages: Study design limitations (single-arm trial, 28 patients), narrow initial indication, IV administration

Mobocertinib (Brand Name: To be determined)

Manufacturer: Takeda
Regulatory designations: Orphan Drug, Breakthrough Therapy
Expected FDA decision: October 26, 2021 *(submitted under the FDA's accelerated approval pathway)*

Therapeutic use

Mobocertinib is in development for treatment of adult patients with epidermal growth factor receptor (EGFR) exon 20 insertion mutation-positive metastatic non-small cell lung cancer (NSCLC), as detected by an FDA-approved test, who have received prior platinum-based chemotherapy.

Lung cancer (both small cell and non-small cell) is the second most common cancer in both men and women (not counting skin cancer). The American Cancer Society's estimates about 235,760 new cases and about 131,880 deaths from lung cancer in the US in 2021. Approximately 85% of lung cancer cases are NSCLC. Patients with EGFR exon 20 insertion mutation metastatic NSCLC make up approximately 1% to 2% of patients with NSCLC. Historically, exon 20 mutation has been associated with a worse prognosis compared to other EGFR mutations.

- Treatment of adult patients with EGFR exon 20 insertion mutation-positive metastatic NSCLC, who have received prior platinum-based chemotherapy

Clinical profile

Mobocertinib is a tyrosine kinase inhibitor specifically designed to selectively target EGFR exon 20 insertion mutations. EGFR is one receptor responsible for uncontrolled cellular division and metastasis when overexpressed.

Pivotal trial data:
The efficacy of mobocertinib was evaluated in a Phase 1/2 study in 114 platinum-pretreated patients with NSCLC and EGFR exon 20 insertion mutations. Updated results were presented at the American Society of Clinical Oncology Annual Meeting in June 2021. Median overall survival (OS) was 24 months. The confirmed objective response rate (ORR) was 28% with a median duration of response (DOR) of 17.5 months.

Safety:
The most common adverse events with mobocertinib use were diarrhea, rash, paronychia, decreased appetite, nausea, dry skin, and vomiting.

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

- Tyrosine kinase inhibitor targeting EGFR
- Oral formulation
- ORR: 28%
- Median OS: 24 months
- Common AEs: Diarrhea, rash, paronychia, decreased appetite, nausea, dry skin, vomiting
- Dosing: Once daily

Mobocertinib (continued...)

Competitive environment

If approved, mobocertinib would be the second targeted therapy for patients with NSCLC and exon 20 insertion mutations. Janssen's Rybrevant™ (amivantamab-vmjw) was approved in May 2021 for this indication. Historically, treatment for these patients was limited to chemotherapy, with few options after treatment failure.

Mobocertinib is administered orally once daily whereas Rybrevant requires weekly IV administration for 4 weeks followed by dosing every 2 weeks thereafter. However, compared indirectly, mobocertinib does appear to be associated with higher rates of gastrointestinal adverse events, particularly diarrhea.

Like Rybrevant, there is a lack of late-stage trial data for mobocertinib and the initial indication will be narrow. An ongoing Phase 3 study is evaluating mobocertinib in the first line setting vs. platinum-based chemotherapy but topline results are not expected until fiscal year 2022.

For reference, the WAC for Rybrevant is approximately $18,000 to $24,000 every 4 weeks.

- Advantages: Limited treatment options for this specific NSCLC mutation, oral and once daily administration
- Disadvantages: Competing with Janssen's recently approved Rybrevant, high rates of gastrointestinal side effects (eg, diarrhea), lack of late-stage trial data, narrow initial target population
- Reference WAC (Rybrevant): ~$18,000 to $24,000 every 4 weeks

Ropeginterferon alfa-2b (Brand Name: To be determined)

Manufacturer: PharmaEssentia
Regulatory designations: Orphan Drug
Expected FDA decision: November 12, 2021

Therapeutic use

Ropeginterferon alfa-2b is in development for treatment of polycythemia vera (PV) in the absence of symptomatic splenomegaly.

PV is a type of myeloproliferative neoplasm characterized by overproduction of blood cells in the bone marrow (myeloproliferation). This results primarily in elevated levels of red blood cells, but the production of white blood cells and platelets are also elevated in most cases. The elevated levels of blood cells can lead to blood thickening and an increased risk of thromboembolic events.

The median age of diagnosis is approximately 60 years and PV affects approximately 44 to 57 per 100,000 people in the U.S.

- Treatment of PV in the absence of symptomatic splenomegaly

Clinical profile

Ropeginterferon alfa-2b is a pegylated formulation of interferon-alfa-2b which is designed to decrease the rate of product removal from the body. Interferons are naturally occurring substances produced by the body that have anti-angiogenic, anti-proliferative, immunomodulatory, and differentiating properties.

- Interferon-alfa 2b
- SC formulation

Pivotal trial data:
The efficacy of ropeginterferon alfa-2b was evaluated in PROUD-PV, a Phase 3, randomized, open-label, active-controlled study in 257 patients with PV. Patients were randomized to ropeginterferon alfa-2 or hydroxyurea, a standard of care treatment option for patients with PV. The primary endpoint was non-inferiority at 12 months of therapy for complete hematologic response (CHR). CHR was achieved in 43.1% and 45.6% of patients treated with ropeginterferon alfa-2b and hydroxyurea, respectfully (non-inferiority met).

- Complete hematological response at 12 months: 43.1% vs. 45.6% with hydroxyurea (non-inferiority met)

In the extension study (CONTINUATION-PV), patients in the hydroxyurea arm PROUD-PV were permitted to switch to best available treatment. An interim analysis was conducted once all patients reached 5 years of treatment. Ropeginterferon alfa-2b achieved higher rates of hematological response (81.8%) vs. the control group (63.2%) ($p = 0.01$).

Safety:
The most common adverse events with ropeginterferon alfa-2b use were arthralgia, influenza-like illness, fatigue, and increased liver enzymes.

- Common AEs: Arthralgia, influenza-like illness, fatigue, increased liver enzymes

Dosing:
In the pivotal trial, ropeginterferon alfa-2b was administered SC once every 2 weeks.

- Dosing: Once every 2 weeks

Ropeginterferon alfa-2b (continued...)

Competitive environment

Ropeginterferon alfa-2b would potentially be the first interferon treatment FDA approved for PV. Hydroxyurea is the current standard of care in PV patients that require cytoreductive medications. The oral JAK inhibitor, Jakafi® (ruxolitinib), is FDA approved in patients who have had an inadequate response to or are intolerant of hydroxyurea. Other off-label alternatives that are used to treat the condition include existing interferon products (eg, Pegasys®), Rituxan® (rituximab), and busulfan.

In addition to potentially being the first approved interferon product for the condition, a differentiator for ropeginterferon alfa-2b is less frequent injections vs. other interferon products (every 2 weeks vs. every week for Pegasys) due to improved pharmacokinetics and the first with robust long-term data vs. hydroxyurea.

For reference, the WAC for Jakafi is approximately $180,000 per year.

- Advantages: Potentially first interferon product approved for PV, more convenient dosing vs. existing interferon products
- Disadvantages: Alternatives available, likely reserved as a second-line option for PV, SC administration
- Reference WAC (Jakafi): ~$180,000 per year

Vosoritide (Brand Name: To be determined)

Manufacturer: BioMarin
Regulatory designations: Orphan Drug
Expected FDA decision: November 20, 2021

Therapeutic use

Vosoritide is in development for the treatment of pediatric patients with achondroplasia.

Achondroplasia is caused by an autosomal dominant mutation in the fibroblast growth factor receptor 3 gene (FGFR3). FGFR3 normally has a negative regulatory effect on bone growth but in achondroplasia, a mutation in the gene causes the pathway to be overly active, leading to severely shortened bones.

Achondroplasia is characterized by disproportionate short stature, dwarfism, distinctive craniofacial features, long-bone shortening that predominantly affects the upper and lower extremities, brachydactyly, kyphoscoliosis, and macrocephaly. These often lead to serious health complications such as foramen magnum compression, sleep apnea, bowed legs, mid-face hypoplasia, permanent sway of the lower back, spinal stenosis and recurrent ear infections. These complications can result in invasive surgeries such as spinal cord decompression and straightening of bowed legs.

Achondroplasia has a prevalence of approximately 1 in 20,000 live births.

- Treatment of pediatric patients with achondroplasia

Clinical profile

Vosoritide is a stabilized analog of C-type natriuretic peptide (CNP). CNP is a positive regulator of bone growth, vasodilator and inhibitor of vascular smooth muscle cell growth. Vosoritide binds to natriuretic peptide receptor B, which inhibits the overactive FGFR3 pathway.

<u>Pivotal trial data:</u>
The efficacy of vosoritide was evaluated in a Phase 3, randomized, double-blind, placebo-controlled study in 121 patients 5 to 14 years old with achondroplasia. Patients were randomized to vosoritide or placebo. The primary endpoint was change from baseline in mean Annualized Growth Velocity (AGV) at one year. Baseline AGV for patients in both the vosoritide and placebo treatment arms was ~4 cm/year. Of note, normal AGV for healthy children ages 4 to 10 years old is 5 to 6 cm/year.

The adjusted mean difference in AGV was 1.57 cm/year ($p < 0.0001$). The change from baseline in mean annualized growth velocity was 1.71 cm/year with vosoritide vs. 0.13 cm/year with placebo. An open-label long-term extension of the Phase 3 study showed that clinical benefit was maintained over 2 years as the adjusted mean difference in AGV was 1.79 cm/year ($p < 0.0001$), with no notable new safety signals.

<u>Safety:</u>
The most common adverse events with vosoritide use were injection site reaction, nasopharyngitis, vomiting, headache, pyrexia, and arthralgia.

<u>Dosing:</u>
In the pivotal trial, vosoritide was administered SC once daily.

- FGFR3 pathway inhibitor
- SC formulation
- Change from baseline in mean annualized growth velocity: 1.71 cm/year with vosoritide vs. 0.13 cm/year with placebo
- Common AEs: Injection site reaction, nasopharyngitis, vomiting, headache, pyrexia, arthralgia
- Dosing: Once daily

Vosoritide (continued...)

Competitive environment

If approved, vosoritide would be the first-to-market pharmacologic treatment for achondroplasia. There is a high unmet need, as current treatments mostly include supportive care of comorbidities or surgical interventions. Vosoritide would represent a potential significant shift in how achondroplasia is treated.

However, whether treatment with vosoritide will improve quality of life or decrease the need for surgical interventions is unknown, as this was not assessed in the clinical trials. In addition, trials demonstrated that the difference in upper to lower body segment proportionality, an important consideration in achondroplasia, was not statistically different between vosoritide and placebo groups.

Moreover, there are other products in the pipeline for achondroplasia, such as Ascendis' TransCon CNP, Pfizer's recifercept, and QED Therapeutics' infigratinib, which all target the FGFR3 pathway. However, none of these manufacturers have yet filed with the FDA for achondroplasia.

- Advantages: Potentially the first pharmacologic treatment for achondroplasia, unmet need
- Disadvantages: Clinical trials did not demonstrate the effect of vosoritide treatment on functionality or body proportionality, alternatives are in development in the pipeline, narrow target population

Ciltacabtagene autoleucel (Brand Name: To be determined)

Manufacturer: Janssen/ Legend Biotech
Regulatory designations: Orphan Drug, Breakthrough Therapy
Expected FDA decision: November 29, 2021

Therapeutic use

- Treatment of relapsed and/or refractory multiple myeloma

Ciltacabtagene autoleucel is in development for the treatment of patients with relapsed and/or refractory multiple myeloma.

Multiple myeloma is a cancer of the plasma cells (white blood cells that produce antibodies). Multiple myeloma is a relatively uncommon cancer with a lifetime risk of 1 in 132 (0.76%). In the U.S., about 34,920 new cases are estimated in 2021 and about 12,410 deaths are expected to occur.

While many treatment options are available for multiple myeloma, many patients who survive initial treatment will eventually relapse and require further therapy. The 5-year survival rate is approximately 50%.

Clinical profile

- BCMA-targeted CAR T cell therapy
- IV formulation
- ORR: 98%
- 18-month OS rate: 81%
- Common AEs: Cytokine release syndrome, neutropenia, anemia, thrombocytopenia, leukopenia, lymphopenia
- Dosing: One-time dose

Ciltacabtagene autoleucel is a B cell maturation antigen (BCMA)-directed chimeric antigen receptor (CAR) T cell therapy.

BCMA promotes plasma cell survival and BCMA is expressed at varying levels in myeloma patients. Ciltacabtagene autoleucel results in CAR-positive T cell proliferation, cytokine secretion, and subsequent cytolytic killing of BCMA-expressing cells.

Pivotal trial data:
Ciltacabtagene autoleucel was evaluated in CARTITUDE-1, a Phase 1b/2, open-label study in adults with relapsed and/or refractory multiple myeloma who received at least 3 prior lines of therapy or were double refractory to a proteasome inhibitor (PI) and immunomodulatory drug (IMiD), received a PI, an IMiD, and anti-CD38 antibody and documented disease progression within 12 months of starting the most recent therapy. The primary objective of the Phase 1b portion of the study was to characterize the safety and confirm the recommended Phase 2 dose. The Phase 2 portion further evaluated the efficacy of with overall response rate (ORR) as the primary endpoint.

At a median follow-up of 18 months, updated results from the study included 97 patients and the ORR was 98%. The 18-month progression-free survival (PFS) rate was 66% (95% CI: 54.9, 75.0) and overall survival (OS) rate was 81% (95% CI: 71.4, 87.6).

Safety:
The most common adverse events with ciltacabtagene autoleucel use were neutropenia, anemia, thrombocytopenia, leukopenia, lymphopenia, and cytokine release syndrome.

Dosing:
In the pivotal trial, ciltacabtagene autoleucel was administered as a one-time IV infusion.

Ciltacabtagene autoleucel (continued...)

Competitive environment

If approved, ciltacabtagene autoleucel would be the second of CAR T cell therapy treatment option for patients with multiple myeloma. Bristol Myers Squibb and bluebird bio's Abecma™ (idecabtagene vicleucel), another BCMA-targeted CAR T cell therapy, was approved in March 2021 for relapsed/refractory multiple myeloma. Compared indirectly, ciltacabtagene autoleucel does appear to have better efficacy with higher response rates demonstrated in the pivotal trial. However, ciltacabtagene autoleucel was associated with higher rates of neurotoxicity adverse events.

Similar to all other CAR T cell therapies, ciltacabtagene autoleucel is expected to have a boxed warning and REMS program for cytokine release syndrome, which would require close monitoring post-administration. Furthermore, treatment delays may also occur due to the long preparation process needed to produce the cells for administration to the patient. These delays can often result in progression while waiting for the therapy.

CAR T cell therapies come with a high one-time cost and ciltacabtagene autoleucel would not only be competing with Abecma, but also other drugs used for relapsed/refractory multiple myeloma, an increasingly crowded market.

For reference, the WAC for Abecma is $419,500 for a one-time dose.

- Advantages: Promising and potentially best-in-class efficacy results, one-time administration
- Disadvantages: Safety concerns (including a likely boxed warning for CRS and REMS program), treatment delays due to preparation needed, crowded marketplace
- Reference WAC (Abecma): $419,500 for a one-time dose

Plinabulin (Brand Name: To be determined)

Manufacturer: BeyondSpring
Regulatory designations: Breakthrough Therapy
Expected FDA decision: November 30, 2021

Therapeutic use

- In combination with G-CSFs, for the prevention of CIN

Plinabulin is an investigational drug intended to be used in combination with granulocyte colony-stimulating factors (G-CSFs), for the prevention of chemotherapy-induced neutropenia (CIN).

Neutropenia is defined as having a lower than normal neutrophil count. Neutrophils are a vital part of the body's immune system and ability to fight against most types of infection. Patients receiving some types of chemotherapy are at risk for developing immunosuppression and in turn, becoming neutropenic. Neutropenia can lead to infection and it is a major dose-limiting toxicity for many chemotherapy regimens.

G-CSFs such as Neulasta® (pegfilgrastim) are the current standard of care for CIN prophylaxis in patients being treated with certain types of chemotherapy.

Clinical profile

- Selective immunomodulating microtubule-binding agent
- IV formulation
- Prevention of grade 4 neutropenia: 31.5% with plinabulin plus Neulasta vs. 13.6% with Neulasta alone
- Common AEs: Gastrointestinal disorders (eg, diarrhea, nausea, constipation, vomiting), headache, fatigue, transient hypertension
- Dosing: Administered on day of chemotherapy

Plinabulin is a novel selective immunomodulating microtubule-binding agent. Plinabulin triggers the release of the immune defense protein, GEF-H1, which leads to an increase in the number of hematopoietic stem/progenitor cells that can ultimately mature into neutrophils.

Pivotal trial data:
The efficacy of plinabulin was evaluated in PROTECTIVE-2, a Phase 3, randomized, double-blind study which compared plinabulin in combination with Neulasta vs. Neulasta alone in 221 patients with breast cancer undergoing myelosuppressive chemotherapy. Plinabulin was administered on the same day as chemotherapy and Neulasta was administered in both arms the day after chemotherapy. The primary endpoint was the proportion of patients with prevention of grade 4 neutropenia in cycle 1 of chemotherapy.

The rate of prevention of grade 4 neutropenia in cycle 1 was 31.5% with plinabulin plus Neulasta vs. 13.6% with Neulasta alone ($p = 0.0015$). The combination regimen also reduced the incidence and severity of febrile neutropenia – the incidence was 3.6% with the combination vs. 6.3% with Neulasta alone. The duration of febrile neutropenia was 1.25 day vs. 2.28 days, respectively. Duration of hospitalization was approximately 50% less in the combination arm (3.75 days) vs. Neulasta alone (7.14 days).

Safety:
The most common adverse events with plinabulin use were gastrointestinal disorders (eg, diarrhea, nausea, constipation, vomiting), headache, fatigue, and transient hypertension.

Dosing:
In the pivotal trial, plinabulin was administered via IV infusion on the day of chemotherapy.

Plinabulin (continued...)

Competitive environment

If approved, plinabulin would offer a novel MOA for prevention of CIN. While G-CSFs have been the standard of care for CIN prophylaxis, there is still an unmet need as patients may still be at risk for developing neutropenia and the downstream consequences, such as hospitalization, particularly in the first week of a chemotherapy cycle. In the pivotal study, plinabulin plus Neulasta combination therapy improved all key primary and secondary endpoints vs. Neulasta alone. A separate supportive study (PROTECTIVE-1) evaluating plinabulin monotherapy vs. Neulasta found that plinabulin was non-inferior to Neulasta for days of severe neutropenia in cycle 1 of chemotherapy. Of note, plinabulin monotherapy was associated with less bone pain and less thrombocytopenia adverse events vs. Neulasta.

The initial indication for plinabulin is expected to be limited to use in combination with G-CSFs, which may reduce its uptake as it could be reserved for patients who are at especially high risk for developing CIN. G-CSFs like Neulasta are administered via SC injection, whereas plinabulin requires IV infusion, although plinabulin is administered on the same day as chemotherapy.

Finally, because of plinabulin's novel MOA, it has demonstrated anti-cancer effects in early stage trials. Recently, BeyondSpring announced positive topline results from a Phase 3 study (DUBLIN-3) in the second- and third-line treatment setting for non-small cell lung cancer (NSCLC). BeyondSpring expects to file for treatment of NSCLC in the first half of 2022.

For reference, the WAC for brand Neulasta is approximately $6,500 per dose.

- Advantages: Novel MOA, demonstrated statistical superiority vs. current standard of care (Neulasta), may reduce some serious adverse events associated with G-CSFs, potential future use for cancer treatment (eg, NSCLC)
- Disadvantages: G-CSFs have been available for decades with biosimilars on the market, initial indication is expected to be limited to combination use with G-CSFs, IV administration
- Reference WAC (Neulasta): ~$6,500 per dose

Pacritinib (Brand Name: To be determined)

Manufacturer: CTI BioPharma
Regulatory designations: Orphan Drug, Fast Track
Expected FDA decision: November 30, 2021

Therapeutic use

Pacritinib is in development for treatment of myelofibrosis in patients with severe thrombocytopenia (platelet counts less than 50 x 10^9/L).

Myelofibrosis is a type of myeloproliferative neoplasm characterized by abnormalities in blood cell production and scarring within the bone marrow. Patients with myelofibrosis are at increased risk for thrombocytopenia and patients that develop thrombocytopenia have greater disease burden and lower overall survival.

The incidence of myelofibrosis is estimated to be 1.5 cases per 100,000 people in the U.S. Patients with severe thrombocytopenia are estimated to make up one-third of patients treated for myelofibrosis.

- Treatment of myelofibrosis in patients with severe thrombocytopenia (platelet counts less than 50 x 10^9/L)

Clinical profile

Pacritinib is a kinase inhibitor with specificity for Janus kinase 2 (JAK2) and interleukin 1 receptor associated kinase 1 (IRAK1). Myelofibrosis is characterized by dysregulated Janus kinase/signal transducers and activators of transcription signaling and excessive production of inflammatory cytokines.

- JAK2/IRAK1 kinase inhibitor
- Oral formulation

<u>Pivotal trial data:</u>
The efficacy of pacritinib was evaluated in two Phase 3 studies: PERSIST-1 and PERSIST-2 in patients with myelofibrosis. PERSIST-1 included 327 patients who were randomized to receive pacritinib 400 mg once daily or best available therapy (BAT) excluding JAK2 inhibitors, until disease progression or unacceptable toxicity. The primary endpoint was spleen volume reduction (SVR) of 35% or more from baseline to week 24 in the intention-to-treat population. At week 24, SVR of 35% or more was achieved by 19% patients in the pacritinib group vs. 5% patients in the BAT group (p = 0.0003).

- SVR ≥ 35% (PERSIST-1): 19% with pacritinib 400 mg QD vs. 5% with best available therapy
- SVR ≥ 35% (PERSIST-2): 22% with pacritinib 200 mg BID vs. 3% with best available therapy
- Common AEs: Anemia, thrombocytopenia, and gastrointestinal events (eg, diarrhea, nausea)
- Dosing: Twice daily

PERSIST-2 included 311 patients with myelofibrosis and platelet count ≤ 100 x 10^9/L. Patients were randomized to receive pacritinib 400 mg once daily, pacritinib 200 mg twice daily, or BAT. The efficacy analysis was conducted in the intention-to-treat population (N = 221), comprising all patients with a randomization date allowing for week 24 data. Co-primary endpoints were rates of patients achieving 35% or more SVR and 50% or more reduction in total symptom score (TSS) at week 24. Pacritinib (arms combined) was more effective than BAT for 35% or more SVR (18% vs. 3%; p = 0.001) and had a numerically (but not statistically significant) greater rate of 50% or more reduction in TSS (25% vs. 14%; p = 0.08). Pacritinib twice daily led to significant improvements in both endpoints over BAT (≥ 35% SVR: 22% vs. 3%; p = 0.001; ≥ 50% reduction in TSS: 32% vs. 14%; p = 0.01).

Pacritinib (continued...)

In addition, CTI BioPharma conducted a Phase 2, dose-finding study following concerns over high-grade cardiac and bleeding events in the PERSIST studies. The study included 161 patients with advanced myelofibrosis who were intolerant of or resistant to Jakafi® (ruxolitinib) and was designed to identify the recommended pacritinib dosage and to establish risk minimization measures. Patients were randomized to pacritinib 100 mg once daily, 100 mg twice daily, or 200 mg twice daily. The study demonstrated that pacritinib 200 mg twice daily had a favorable benefit risk profile. SVR rates were highest among patients treated with pacritinib 200 mg twice daily who had a baseline platelet count of less than 50 x 10^9/L.

Safety:
The most common adverse events with pacritinib use were anemia, thrombocytopenia, and gastrointestinal events (eg, diarrhea, nausea).

Dosing:
In the pivotal trials, pacritinib was administered orally once or twice daily but the approved dosing will likely be twice daily due to more robust efficacy and safety data.

Competitive environment

If approved, pacritinib would provide a treatment option for patients with myelofibrosis with severe thrombocytopenia. There is a high unmet need for this patient population as current treatment options such as Jakafi® (ruxolitinib) and Inrebic® (fedratinib) are not indicated in patients with platelet counts < less than 50 x 10^9/L. Severe thrombocytopenia has historically been associated with poor prognosis due to the lack of available treatments.

The efficacy data for pacritinib does appear more modest when compared indirectly to existing treatment options in the general myelofibrosis population, but it is difficult to compare across trials given differences in study populations. Back in February 2016, the FDA also placed a clinical hold on pacritinib due to excess mortality caused by intracranial hemorrhages. This hold was eventually lifted and CTI BioPharma agreed to conducting an additional dose-finding study that appears to have resolved the safety concerns; however, given the well-established history with Jakafi, and to a lesser extent Inrebic, use of pacritinib could be limited to patients with severe thrombocytopenia which will narrow the target population for the drug.

For reference, the WAC for Inrebic is approximately $22,000 per 30 days.

- Advantages: Potential treatment option in patients with existing thrombocytopenia (high unmet need), oral administration
- Disadvantages: Alternatives available (eg, Jakafi, Inrebic), modest efficacy when compared indirectly to Jakafi and Inrebic, narrow initial indication
- Reference WAC (Inrebic): ~$22,000 per 30 days

Efgartigimod (Brand Name: To be determined)

Manufacturer: Argenx
Regulatory designations: Orphan Drug, Fast Track
Expected FDA decision: December 17, 2021

Therapeutic use

- Treatment of generalized myasthenia gravis

Efgartigimod is in development for treatment of generalized myasthenia gravis.

Myasthenia gravis is an autoimmune, neuromuscular disorder primarily characterized by muscle weakness and muscle fatigue. The condition may be restricted to certain muscle groups, particularly those of the eyes, or may become more generalized, involving multiple muscle groups. Approximately 10% of affected patients develop potentially life-threatening complications due to severe involvement of muscles used during breathing (myasthenic crisis).

Approximately 65,000 people in the U.S. are affected by myasthenia gravis. Symptoms may become apparent at any age, but symptom onset most commonly peaks in women during their 20s or 30s and in men in their 50s or 60s. Most patients with myasthenia gravis have autoantibodies that bind to the acetylcholine receptor (AChR).

Clinical profile

- Neonatal Fc receptor antibody
- IV formulation
- MG-ADL response: 68% vs. 30% with placebo
- Common AEs: Headache, nasopharyngitis (rates were similar to placebo)
- Dosing: Administered as four infusions per cycle (one infusion per week) and repeated as needed depending on clinical response no sooner than 8 weeks

Efgartigimod is an antibody fragment designed to reduce disease-causing immunoglobulin G (IgG) antibodies and block the IgG recycling process. Efgartigimod binds to the neonatal Fc receptor (FcRn), which is widely expressed throughout the body and plays a central role in rescuing IgG antibodies from degradation. Blocking FcRn reduces IgG antibody levels which are involved in the pathogenesis of myasthenia gravis.

<u>Pivotal trial data:</u>
The efficacy of efgartigimod was evaluated in ADAPT, a Phase 3, randomized, double-blind, placebo-controlled study in 167 patients with generalized myasthenia gravis. Patients received efgartigimod or placebo for a total of 26 weeks. ADAPT was designed to enable an individualized treatment approach with an initial treatment cycle followed by a variable number of subsequent treatment cycles. The primary endpoint was the number of acetylcholine receptor antibody-positive (AChR-Ab+) patients who achieved a response on the Myasthenia Gravis Activities of Daily Living (MG-ADL) score defined by at least a two-point improvement for four or more consecutive weeks.

Of the 129 AChR-Ab+ patients, more patients in the efgartigimod group were MG-ADL responders (68%) in cycle 1 than in the placebo group (30%), with an odds ratio of 4.95 (95% CI: 2.21, 11.53, $p < 0.0001$). Additionally, 40% of patients treated with efgartigimod achieved minimal symptom expression defined as MG-ADL scores of zero (symptom free) or one, compared to 11.1% of patients who received placebo.

<u>Safety:</u>
The most common adverse events with efgartigimod use were headache and nasopharyngitis (rates were similar to placebo).

<u>Dosing:</u>
In the pivotal trial, efgartigimod was administered IV as four infusions per cycle (one infusion per week) and repeated as needed depending on clinical response no sooner than 8 weeks.

Efgartigimod (continued...)

Competitive environment

Efgartigimod would offer an additional treatment option for myasthenia gravis with a novel MOA. The current standard of care includes acetylcholinesterase inhibitors (eg, pyridostigmine) as well as other immunosuppressants like corticosteroids. In patients who fail those types of conventional therapies, biologics such as Alexion's Soliris® (eculizumab) are used.

A potential benefit for efgartigimod vs. Soliris is less frequent injections. Soliris is IV administered every 2 weeks whereas efgartigimod is administered weekly for 4 weeks but in the study, patients were not re-dosed until clinical benefit was lost (and no earlier than 8 weeks). Additionally, efgartigimod is in development for other autoimmune conditions such as immune thrombocytopenic purpura and pemphigus vulgaris which could expand its potential market potential.

However, as mentioned above, alternatives are available and generally more conventional therapies are used earlier in the treatment algorithm with biologics reserved for use later in treatment algorithm; efgartigimod would likely be similar to Soliris in terms of being reserved for more severe or refractory cases.

While there is the potential for less frequent injections, its unknown what the final FDA approved dosing recommendation will be for efgartigimod given the variable dosing in the pivotal study. Furthermore, any potential convenience advantage may be diminished in the future as Alexion's Ultomiris® (ravulizumab-cwvz) is also under development for generalized myasthenia gravis and it is dosed once every 8 weeks. Alexion plans to file for the new indication in late 2021 or early 2022.

For reference, the WAC for Ultomiris is approximately $458,000 per year.

- Advantages: Novel MOA, potentially less frequent injections vs. Soliris (administered every 2 weeks), also in development for other autoimmune conditions (eg, immune thrombocytopenic purpura)
- Disadvantages: Alternatives available (eg, pyridostigmine, conventional immunosuppressants), biologics generally used later in treatment algorithm, potential future competition with Alexion's Ultomiris (administered every 8 weeks)
- Reference WAC (Ultomiris): ~$458,000 per year

3rd Quarter 2021

Extended generic pipeline forecast

OptumRx generic pipeline forecast

Brand name	Generic name	Brand manufacturer	Dosage form	Strengths available as generic	Possible launch date
2021 Possible launch date					
THALOMID	thalidomide	Celgene	Capsule	All	2021
DALIRESP	roflumilast	AstraZeneca	Tablet	All	2021
RESTASIS	cyclosporine	Allergan	Ophthalmic	All	2021
BYETTA	exenatide	AstraZeneca	Subcutaneous	All	2021
DUREZOL	difluprednate	Alcon	Ophthalmic	All	2021
TOVIAZ	fesoterodine	Pfizer	Tablet, extended-release	All	2021
CUVPOSA	glycopyrrolate	Merz	Oral solution	All	2021
FORTEO	teriparatide	Eli Lilly	Injection	All	2021
EPIDUO FORTE	adapalene/benzoyl peroxide	Galderma	Gel	All	2021
RESCULA	unoprostone isopropyl	R-Tech Ueno	Ophthalmic	All	2021
NARCAN	naloxone	Emergent BioSolutions	Intranasal	All	2H-2021
LEVEMIR	insulin detemir recombinant	Novo Nordisk	Subcutaneous	All	2H-2021
CHANTIX	varenicline	Pfizer	Tablet	All	2H-2021
TRESIBA FLEXTOUCH	insulin degludec	Novo Nordisk	Subcutaneous	All	2H-2021
SUTENT	sunitinib	Pfizer	Capsule	All	08-2021
JEVTANA KIT	cabazitaxel	Sanofi	Intravenous	All	09-2021
BYSTOLIC	nebivolol	Allergan	Tablet	All	09-2021
LUCENTIS	ranibizumab	Roche	Intravitreal	All	09-2021
INNOPRAN XL	propranolol	Ani Pharmaceuticals	Capsule, extended-release	All	10-2021
CAYSTON	aztreonam lysine	Gilead	Inhalation	All	12-2021
EXPAREL	bupivacaine	Pacira	Injection	All	12-2021
JUBLIA	efinaconazole	Bausch Health	Topical solution	All	12-2021
2022 Possible launch date					
DULERA	formoterol fumarate/mometasone furoate	Merck	Inhalation	All	2022
FLOVENT HFA	fluticasone propionate	GlaxoSmithKline	Inhalation	All	2022

Brand name	Generic name	Brand manufacturer	Dosage form	Strengths available as generic	Possible launch date
DEXILANT	dexlansoprazole	Takeda	Capsule, delayed-release	All	2022
POMALYST	pomalidomide	Celgene	Capsule	All	2022
DUEXIS	ibuprofen/famotidine	Horizon Pharma	Tablet	All	1H-2022
IXEMPRA Kit	ixabepilone	R-Pharm	Intravenous	All	1H-2022
OXAYDO	oxycodone	Egalet	Tablet	All	01-2022
EPANED KIT	enalapril	Silvergate	Oral solution	All	01-2022
ONEXTON	clindamycin/benzoyl peroxide	Bausch Health	Gel	All	01-2022
NEUPRO	rotigotine	UCB	Transdermal patch	All	01-2022
AFINITOR DISPERZ	everolimus	Novartis	Oral suspension	All	01-2022
BALCOLTRA	levonorgestrel/ethinyl estradiol/ferrous bisglycinate	Avion	Tablet	All	01-2022
SELZENTRY	maraviroc	ViiV Healthcare	Tablet	All	02-2022
VIMPAT	lacosamide	UCB	Tablet; oral solution; intravenous	All	03-2022
ZIPSOR	diclofenac potassium	Depomed	Capsule	All	03-2022
CHOLBAM	cholic acid	Retrophin	Capsule	All	03-2022
ABRAXANE	paclitaxel	Celgene/Abraxis	Injection	All	03-2022
REVLIMID	lenalidomide	Bristol-Myers Squibb/Celgene	Capsule	All	03-2022
ARESTIN	minocycline hydrochloride	Bausch Health	Subgingival	All	03-2022
PRADAXA	dabigatran etexilate mesylate	Boehringer Ingelheim	Capsule	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	Tablet, extended-release	All	05-2022
CAPRELSA	vandetanib	Genzyme/Sanofi	Tablet	All	06-2022
VIIBRYD	vilazodone	Forest/Allergan	Tablet	All	06-2022
ELESTRIN	estradiol	Mylan	Gel	All	06-2022
ACTEMRA	tocilizumab	Roche/Chugai	Intravenous; subcutaneous	All	2H-2022
IRESSA	gefitinib	AstraZeneca	Tablet	All	07-2022
EVAMIST	estradiol	Perrigo/Elan	Transdermal solution	All	07-2022

Brand name	Generic name	Brand manufacturer	Dosage form	Strengths available as generic	Possible launch date
KEVEYIS	dichlorphenamide	Strongbridge Biopharma	Tablet	All	08-2022
ORAVIG	miconazole	Galt Pharmaceuticals	Tablet, buccal	All	09-2022
AMZEEQ	minocycline	Foamix	Foam	All	10-2022
XERESE	acyclovir/hydrocortisone	Bausch Health	Cream	All	11-2022
FOLOTYN	pralatrexate	Acrotech/Aurobindo	Intravenous	All	11-2022
RAYOS	prednisone	Horizon	Tablet, delayed-release	All	12-2022
TREANDA	bendamustine	Cephalon/Teva	Intravenous	All	12-2022
ZIOPTAN	tafluprost	Akorn	Ophthalmic	All	12-2022
2023 Possible launch date					
ALPHAGAN P	brimonidine	Allergan	Ophthalmic	All	2023
PREZISTA	darunavir	Janssen	Tablet	75 mg, 150 mg, 300 mg	2023
PROLENSA	bromfenac	Bausch Health	Ophthalmic	All	2023
MYRBETRIQ	mirabegron	Astellas	Tablet, extended-release	All	2023
KOMBIGLYZE XR	saxagliptin/metform	Astra Zeneca	Tablet, extended-release	All	1H-2023
ONGLYZA	saxagliptin	AstraZeneca	Tablet	All	1H-2023
NOXAFIL	posaconazole	Merck	Intravenous	All	01-2023
HUMIRA	adalimumab	AbbVie	Subcutaneous	All	01-2023
XYREM	sodium oxybate	Jazz	Oral solution	All	01-2023
CAMBIA	diclofenac potassium	Assertio	Oral solution	All	01-2023
TROKENDI XR	topiramate	Supernus	Capsule, extended-release	All	01-2023
DUOBRII	halobetasol propionate/tazarotene	Bausch Health	Lotion	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
SUPREP BOWEL PREP KIT	magnesium sulfate anhydrous/potassium sulfate/sodium sulfate	Braintree	Oral solution	All	01-2023
GLOPERBA	colchicine	Avion Pharmaceuticals	Oral solution	All	01-2023
FIRVANQ KIT	vancomycin	Azurity	Oral solution	All	01-2023
LATUDA	lurasidone	Sunovion	Tablet	All	02-2023
GATTEX	teduglutide recombinant	Takeda	Subcutaneous	All	03-2023

Brand name	Generic name	Brand manufacturer	Dosage form	Strengths available as generic	Possible launch date
AGGRASTAT	tirofiban	Medicure	Intravenous	All	03-2023
AUBAGIO	teriflunomide	Sanofi/Genzyme	Tablet	All	03-2023
DEFITELIO	defibrotide	Jazz	Intravenous	All	03-2023
PROVAYBLUE	methylene blue	Provepharm/American Regent	Intravenous	All	04-2023
CLINDESSE	clindamycin phosphate	Perrigo	Vaginal cream	All	04-2023
CORLANOR	ivabradine	Amgen	Tablet	All	04-2023
DALVANCE	dalbavancin	Amgen	Intravenous	All	05-2023
LIVALO	pitavastatin	Eli Lilly/Kowa Pharmaceuticals	Tablet	All	05-2023
KYNMOBI	apomorphine	Sunovion	Sublingual	All	05-2023
BIJUVA	estradiol/progesterone	TherapeuticsMD	Capsule	All	06-2023
XURIDEN	uridine	Wellstat Therapeutics	Oral granules	All	07-2023
TOLAK	fluorouracil	Pierre Fabre	Cream	All	07-2023
MOZOBIL	plerixafor	Sanofi/Genzyme	Subcutaneous	All	07-2023
CYSTADROPS	cysteamine	Recordati	Ophthalmic	All	08-2023
VYVANSE	lisdexamfetamine	Shire/Takeda	Capsule, extended-release	All	08-2023
KATERZIA	amlodipine	Azurity	Oral suspension	All	08-2023
STELARA	ustekinumab	Janssen	Subcutaneous	All	09-2023
VIBATIV	telavancin	Theravance	Intravenous	All	09-2023
LEXETTE	halobetasol	Mayne	Foam	All	09-2023
VOTRIENT	pazopanib	Novartis	Tablet	All	10-2023
OZURDEX	dexamethasone	Allergan	Ophthalmic	All	11-2023
AMTURNIDE	aliskiren/amlodipine/ hydrochlorothiazide	Novartis	Tablet	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									
TAK-721 (SHP-621)	budesonide	Takeda	corticosteroid	Eosinophilic esophagitis	PO	Filed NDA	08/31/2021	Yes	Yes
paliperidone palmitate (6-month)	paliperidone palmitate	Johnson & Johnson	atypical antipsychotic	Schizophrenia	IM	Filed NDA	09/02/2021	Yes	No
INP-104	POD-dihydroergotamine mesylate	Impel NeuroPharma	ergot derivative	Acute migraines	Intranasal	Filed NDA	09/06/2021	No	No
PL-56	budesonide	Calliditas	corticosteroid	Nephropathy	PO	Filed NDA	09/15/2021	No	Yes
INC-424	ruxolitinib	Incyte	janus kinase inhibitor	Atopic dermatitis	TOP	Filed NDA	09/21/2021	Yes	No
VP-102	cantharidin	Verrica	antiviral	Molluscum	TOP	Filed NDA	09/23/2021	No	No
Doria	risperidone	Laboratorios Farmacéuticos Rovi	atypical antipsychotic	Schizophrenia	IM	Filed NDA	09/24/2021	Yes	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
ACP-001 (TransCon Growth Hormone)	lonapegsomatropin	Ascendis Pharma	growth hormone prodrug	Short stature/ growth hormone deficiency	SC	Filed BLA	09/25/2021	Yes	Yes
SHP-625 (LUM-001)	maralixibat	Mirum Pharmaceuticals	apical sodium-dependent bile acid transporter inhibitor	Alagille syndrome	PO	Filed NDA	09/29/2021	Yes	Yes
AB-103	reltecimod	Atox Bio	CD-28 co-stimulatory receptor modulator	Necrotizing soft tissue infections	IV	Filed NDA	9/30/2021	Yes	Yes
S5G4T-1	benzoyl peroxide	Sol-Gel Technologies	benzoyl peroxide	Rosacea	TOP	Filed NDA	3Q2021	No	No
MK-8031	atogepant	AbbVie	calcitonin gene-related peptide receptor antagonist	Migraine prophylaxis	PO	Filed NDA	3Q2021	No	No
RT-002 (Daxi)	daxibotulinumtoxinA	Revance Therapeutics	botulinum toxins	Glabellar lines (frown lines)	IM	Filed BLA	3Q2021	Yes	No
tanezumab	tanezumab	Pfizer/ Eli Lilly	nerve growth factor inhibitor	Osteoarthritis	SC	Filed BLA	3Q2021	Yes	No
CCX-168	avacopan	ChemoCentryx	C5a receptor antagonist	Antineutrophil cytoplasmic antibody-associated vasculitis	PO	Filed NDA	10/07/2021	Yes	Yes
RVT-802	RVT-802	Enzyvant/Roivant	Tissue-based therapy	Congenital athymia	Implant	Filed BLA	10/08/2021	Yes	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
HuMax-TF ADC	tisotumab vedotin	Seagen/ Genmab	tissue factor antibody	Cervical cancer	IV	Filed BLA	10/10/2021	Yes	No
UCB-4940	bimekizumab	UCB	interleukin-17 receptor inhibitor	Plaque psoriasis	SC	Filed BLA	10/15/2021	Yes	No
FT-218	sodium oxybate extended-release	Avadel	dopamine receptor agonist	Narcolepsy	PO	Filed NDA	10/15/2021	Yes	Yes
OMS-721	narsoplimab	Omeros	anti-MASP-2 monoclonal antibody	Hematopoietic stem cell transplant-associated thrombotic microangiopathy	IV	Filed BLA	10/17/2021	Yes	Yes
OS-01 nasal spray	varenicline	Oyster Point Pharma	nicotinic acetylcholine receptor agonist	Dry eye disease	Intranasal	Filed NDA	10/17/2021	No	No
Tyvaso DPI	treprostinil	United Therapeutics	prostacyclin mimetic	Pulmonary arterial hypertension/ pulmonary hypertension	INH	Filed NDA	10/19/2021	Yes	No
PDS-1.0	ranibizumab	Roche/ Genentech	Anti-vascular endothelial growth factor	Wet age-related macular degeneration	Intravitreal implant	Filed BLA	10/23/2021	Yes	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
TAK-788	mobocertinib	Takeda	tyrosine kinase inhibitor	Non-small cell lung cancer	PO	Filed NDA	10/26/2021	Yes	Yes
CLS-1001	triamcinolone acetonide	Clearside	corticosteroid	Macular edema	intraocular/ subretinal	Filed NDA	10/30/2021	Yes	No
MOD-401	somatrogon	Pfizer/ Opko	human growth hormone	Growth hormone deficiency	SC	Filed BLA	10/2021	Yes	Yes
Kyzatrex	testosterone undecanoate	Marius Pharmaceuticals	testosterone replacement therapy	Hypogonadism	PO	Filed NDA	10/31/2021	No	No
SH-111	SH-111	Shorla Pharma	unknown	T-cell leukemia	undisclosed	Filed NDA	10/2021 - 11/2021	Yes	No
ET-101	topiramate	Eton	undisclosed	Seizure disorders	PO	Filed NDA	11/06/2021	No	No
LIQ-861	treprostinil	Liquidia Technologies	prostacyclin analog	Pulmonary arterial hypertension	INH	Filed NDA	11/07/2021	Yes	No
Zimhi	naloxone	Adamis	opioid antagonist	Opioid overdose	IM	Filed NDA	11/12/2021	No	No
ropeginterferon alfa-2b	ropeginterferon alfa-2b	PharmaEssentia	interferon	Polycythemia vera	SC	Filed BLA	11/13/2021	Yes	Yes
DE-117	omidenepag isopropyl	Santen Pharmaceutical	Prostaglandin E Receptor 2 agonist	Glaucoma	OPH	Filed NDA	11/19/2021	No	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
BMN-111	vosoritide	BioMarin	C-type natriuretic peptide analog	Achondroplasia	SC	Filed NDA	11/20/2021	Yes	Yes
Pedmark (STS)	sodium thiosulfate	Fennec	reducing agent	Ototoxicity	IV	Filed NDA	11/27/2021	Yes	Yes
JNJ-4528 (LCAR-B38M)	ciltacabtagene autoleucel	Legend Biotech/ Janssen	chimeric antigen receptor T cell therapy	Multiple myeloma	IV	Filed BLA	11/29/2021	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	tumor vascular disrupting agent	Chemotherapy-induced neutropenia	IV	Filed BLA	11/30/2021	Yes	No
Filsuvez (AP-101)	episalvan	Amryt Pharma	triterpene	Epidermolysis bullosa	TOP	Filed NDA	11/30/2021	No	Yes
DARE-BV1	clindamycin	Daré Bioscience	lincosamide	Bacterial vaginosis	Intravaginal	Filed NDA	12/07/2021	No	No
CAM-2038	buprenorphine	Braeburn	opioid receptor agonist	Opioid use disorder	SC	Filed NDA	12/15/2021	Yes	No
AGEN-2034	balstilimab	Agenus	PD-1 antagonist	Cervical cancer	IV	Filed BLA	12/16/2021	Yes	No
ARGX-113	efgartigimod	Argenx	neonatal Fc receptor antibody	Myasthenia gravis	IV	Filed BLA	12/17/2021	Yes	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
Dextro-amphetamine 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
AGN-190584	pilocarpine	Allergan	cholinergic muscarinic receptor agonist	Presbyopia	OPH	Filed NDA	12/25/2021	No	No
AXS-05	dextromethorphan/ bupropion	Axsome	N-methyl-D-aspartate antagonist/ antidepressant	Treatment-resistant depression	PO	Filed NDA	4Q2021	No	No
PF-04965842	abrocitinib	Pfizer	janus kinase 1 inhibitor	Atopic dermatitis	PO	Filed NDA	4Q2021	Yes	No
E-58425 (MR-308)	celecoxib/tramadol	Esteve	non-steroid anti-inflammatory drug/opioid	Acute pain	PO	Filed NDA	2021	No	No
ET-104	zonisamide	Eton	anticonvulsant	Seizures	PO	CRL	Late 2021	No	No
dapivirine ring	dapivirine	International Partnership for	non-nucleoside reverse transcriptase inhibitor	HIV-1 infection	Intravaginally	Filed NDA	Late 2021	No	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
		Microbicides/ Johnson & Johnson							
mRNA-1273	coronavirus vaccine	Moderna	vaccine	Novel coronavirus disease 2019 (COVID-19)	IM	InTrial	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
ALN-PCSsc (PCSK9si)	inclisiran	Novartis	RNA interfering therapeutic targetting proprotein convertase subtilisin–kexin type 9	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	Asthma	SC	Filed BLA	01/10/2022	Yes	No
SHP-620	maribavir	Shire	benzimidazole	Cytomegalovirus	PO	Filed NDA	01/21/2022	No	Yes
VT-1161	oteseconazole	Mycovia Pharmaceuticals	lanosterol demethylase inhibitor	Vulvovaginal candidiasis	PO	Filed NDA	01/27/2022	No	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
MYK-461 (SAR-439152)	mavacamten	MyoKardia	cardiac myosin allosteric modulator	Obstructive hypertrophic cardiomyopathy	PO	Filed NDA	01/28/2022	Yes	Yes
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
AG-348	mitapivat	Agios	pyruvate kinase-R activator	Pyruvate kinase deficiency	PO	Filed NDA	02/21/2022	Yes	Yes
RTA-402	bardoxolone methyl	Reata Pharmaceuticals/ AbbVie	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
GS-CA1 (GS-6207)	lenacapavir	Gilead	HIV capsid inhibitor	HIV-1	SC	Filed NDA	02/28/2022	No	No
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	CD-20 monoclonal antibody/ phosphoinositide-3 kinase delta inhibitor	Chronic lymphocytic leukemia	IV	Filed NDA	03/25/2022	Yes	Yes
Zydena	udenafil	Mezzion Pharma	phosphodiesterase type 5 inhibitor	Congenital single ventricle heart disease	PO	Filed NDA	03/26/2022	No	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
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
AT-GAA	cipaglucosidase alfa	Amicus	enzyme therapy	Pompe disease	IV	Filed BLA	03/2022	Yes	Yes
IBI-308	sintilimab	Eli Lilly	programmed death-1 receptor inhibitor	Non-small cell lung cancer	IV	Filed BLA	3/2022	Yes	No
F-627	benegrastim	Evive Biotech	granulocyte colony-stimulating factor	Chemotherapy-induced neutropenia	SC	Filed BLA	03/31/2022	Yes	No
ABL-001	asciminib	Novartis	allosteric Bcr-Abl inhibitor	Chronic myeloid leukemia	PO	Filed NDA	1Q2022	Yes	Yes
PRO-140	leronlimab	CytoDyn	C-C chemokine receptor 5 antagonist	HIV	SC	InTrial	1Q2022	Yes	No
Botulax	letibotulinumtoxinA	Hugel Pharma	botulinum toxins	Wrinkles	IM	Filed BLA	03/31/2022	Yes	No
CCD-1042	ganaxolone	Marinus Pharmaceuticals	allosteric modulator of GABA(a) receptors	Seizures	PO	Filed NDA	04/03/2022	No	Yes
ALN-TTRsc02	vutrisiran	Alnylam	siRNA/RNAi	Transthyretin-mediated amyloidosis	SC	Filed BLA	04/14/2022	Yes	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
Purified Cortrophin Gel	corticotropin	ANI Pharmaceuticals	adrenocorticotropic hormone	Multiple sclerosis/ rheumatoid arthritis/ systemic lupus erythematosus/ ulcerative colitis	IV	Filed sNDA	04/29/2022	Yes	No
HMPL-012	surufatinib	Hutchison China MediTech	angio-immunokinase inhibitor	Neuroendocrine tumors	PO	Filed NDA	04/30/2022	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
Furoscix	furosemide	scPharmaceuticals	diuretic	Heart failure	SC	CRL	2Q2022	Yes	No
Rizaport (VersaFilm)	rizatriptan	IntelGenx	triptans	Acute migraines	PO	CRL	1H2022	No	No
BIVV-009 (TNT-009)	sutimlimab	Sanofi	complement C1s subcomponent inhibitor	Cold agglutinin disease	IV	CRL	1H2022	Yes	Yes
ET-105	lamotrigine	Eton	anticonvulsant	Epilepsy	PO	CRL	1H2022	No	No
NVX-CoV2373	coronavirus vaccine	Novavax	vaccine	Novel coronavirus disease 2019 (COVID-19)	IM	InTrial	Mid-2022	No	No
S-265744 LAP (S/GSK-	cabotegravir	ViiV Healthcare	HIV integrase inhibitor	HIV pre-exposure prophylaxis	IM	InTrial	1H2022	No	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
1265744 LAP; GSK-744 LA)									
Ultomiris SC	ravulizumab-cwvz	Alexion	C5 complement inhibitor	paroxysmal nocturnal hemoglobinuria; Hemolytic uremic syndrome	SC	InTrial	Mid-2022	Yes	Yes
AT-007	AT-007	Applied Therapeutics	aldose reductase inhibitor	Galactosemia	undisclosed	InTrial	Mid-2022	Yes	Yes
KB-103	beremagene geperpavec	Krystal Biotech	gene therapy	Epidermolysis bullosa	Topical	InTrial	Mid-2022	Yes	Yes
SPR-994	tebipenem	Spero Therapeutics	carbapenem	Urinary tract infections	PO	InTrial	Mid-2022	No	No
MRTX-849	adagrasib	Mirati Therapeutics	KRAS inhibitor	Non-small cell lung cancer	PO	InTrial	Mid-2022	Yes	No
RG-7828	mosunetuzumab	Roche	anti-CD20/CD3 monoclonal antibody	Follicular lymphoma	IV/SC	InTrial	Mid-2022	Yes	Yes
GZ-402665	olipudase alfa	Sanofi	enzyme replacement therapy	Acid sphingomyelinase deficiency	IV	InTrial	Mid-2022	Yes	Yes
CAT-354	tralokinumab	Leo Pharma	interleukin-13 inhibitor	Atopic dermatitis	SC	CRL	Mid-2022	Yes	No
Neutrolin (CRMD-003, CRMD-004)	citrate/ taurolidine/ heparin	CorMedix	antimicrobial agent/ anticoagulant	Catheter-related infections	IV	CRL	Mid-2022	No	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
Lenti-D	elivaldogene tavalentivec	Bluebird Bio	gene therapy	Adrenomyeloneuropathy	IV	InTrial	Mid-2022	Yes	Yes
MTP-131 (SS-31)	elamipretide	Stealth Biotherapeutics	mitochondrial permeability transition pore inhibitor	Barth syndrome	IV/PO/SC	InTrial	Mid-2022	Yes	Yes
WTX-101	bis-choline tetrathiomolybdate (TTM)	Alexion	chelating agent	Wilson's disease	PO	InTrial	Mid-2022	Yes	Yes
EBV-CTL (ATA-129)	tabelecleucel	Atara Biotherapeutics	cell therapy	Lymphoproliferative disorder	IV	InTrial	Mid-2022	Yes	Yes
ERY-ASP (ERY-001)	L-asparaginase (eryaspase)	Erytech/ Recordati	L-asparaginase	Pancreatic cancer	IV	InTrial	Mid-2022	Yes	Yes
Zynteglo (LentiGlobin)	betibeglogene autotemcel	Bluebird Bio	gene therapy	Beta-thalassemia	IV	InTrial	Mid-2022	Yes	Yes
131I-8H9	omburtamab	Y-mAbs Therapeutics	B7-H3 antagonist	Brain cancer	Intrathecal	InTrial	Mid-2022	Yes	Yes
TAK-003	Dengue fever vaccine	Takeda	vaccine	Dengue fever	SC	InTrial	Mid-2022	Yes	No
SYD-985	[vic-] trastuzumab duocarmazine	Synthon	HER2-targeting antibody-drug conjugate	Breast cancer	IV	InTrial	Mid-2022	Yes	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
LN-145	LN-145	Iovance Biotherapeutics	tumor infiltrating lymphocyte	Cervical Cancer	IV	InTrial	Mid-2022	Yes	No
HM781-36B	poziotinib	Spectrum Pharmaceuticals	pan-HER inhibitor	Non-small cell lung cancer	PO	InTrial	Mid-2022	Yes	No
IMC-gp100	tebentafusp	Immunocore	anti-CD3 antibody	Uveal melanoma	IV	InTrial	Mid-2022	Yes	Yes
JS-001	toripalimab	Junshi Biosciences	anti-PD-1 monoclonal antibody	Nasopharyngeal carcinoma	IV	InTrial	Mid-2022	Yes	Yes
MOR-103 (GSK-165)	otilimab	MorphoSys/ GlaxoSmithKline	granulocyte macrophage colony-stimulating factor antibody	COVID-19	IV	InTrial	Mid-2022	Yes	No
ABI-009	sirolimus and albumin	Aadi Bioscience	mTOR kinase inhibitor	Epithelioid cell caricnoma	IV	InTrial	Mid-2022	Yes	Yes
Adstiladrin	nadofaragene firadenovec	FerGene	gene therapy	Bladder cancer	Intravesical	CRL	Mid-2022	Yes	No
INCB-050465	parsaclisib	Incyte	PI3K-delta inhibitor	Follicular lymphoma/ mantle cell lymphoma/ marginal zone lymphoma	PO	InTrial	Mid-2022	Yes	Yes
REGEN-COV	casirivimab/ imdevimab	Regeneron/Roche	Monoclonal antibody	Coronavirus infection	IV/IM/SC	InTrial	Mid-2022	No	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
Priorix	measles/mumps/ rubella	GlaxoSmithKline	Vaccine	measles/mumps/rubella vaccine	IM/SQ	Filed BLA	8/2/2022	No	No
ACER-001	sodium phenylbutyrate	Acer Therapeutics	BCKDC kinase inhibitor	Urea cycle disorders	PO	Filed NDA	8/9/2022	No	No
NiCord	omidubicel	Gamida	cellular therapy	Hematological cancers	IV	InTrial	3Q2022	Yes	Yes
NX-1207 (NYM-4805, REC 0482)	fexapotide triflutate	Nymox	pro-apoptotic	Benign prostatic hyperplasia	Intratumoral	InTrial	3Q2022	Yes	No
AGIL-AADC	eladocagene exuparvovec	PTC Therapeutics	gene therapy	Aromatic L-amino acid decarboxylase deficiency	Intracerebral	InTrial	3Q2022	Yes	Yes
OBE-2109 (KLH-2109)	linzagolix	ObsEva	gonadotropin-releasing hormone antagonist	Uterine fibroids	PO	InTrial	3Q2022	No	No
AXS-07	meloxicam/rizatriptan	Axsome Therapeutics	non-steroidal anti-inflammatory drug/triptan	Migraine	PO	InTrial	3Q2022	No	No
CUTX-101	copper histidinate	Fortress Biotech	copper replacement	Menkes Disease	SC	InTrial	3Q2022	Yes	Yes
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

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
BHV-3500	vazegepant	Biohaven	calcitonin gene-related peptide receptor antagonist	Migraine	Intranasal	InTrial	4Q2022	No	No
omecamtiv mecarbil	omecamtiv mecarbil	Amgen	myosin 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
Roctavian	valoctocogene roxaparvovec	BioMarin	gene therapy	Hemophilia A	IV	CRL	4Q2022	Yes	Yes
GLPG-0634	filgotinib	Gilead/ Galapagos	janus associated kinase 1 inhibitor	Ulcerative colitis	PO	CRL	4Q2022	Yes	No
LY-686017	tradipitant	Vanda Pharmaceuticals	neurokinin 1 receptor antagonist	Motion sickness/ gastroparesis	PO	InTrial	4Q2022	No	No
CDZ-173	leniolisib	Pharming/ Novartis	phosphatidylinositol-3-4-5-trisphosphate inhibitor	Primary immunodeficiencies	PO	InTrial	4Q2022	Yes	Yes
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

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
PAX-101	suramin	PaxMedica	Unknown	trypanosomiasis	IV	InTrial	4Q2022	No	No
Takecab	vonoprazan fumarate	Phathom Pharmaceuticals	potassium-competitive acid blocker	H. pylori infection	PO	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
REGN-475 (SAR-164877)	fasinumab	Regeneron/ Sanofi-Aventis/ Teva	selective anti-nerve growth factor monoclonal antibody	Osteoarthritis	IV/SC	InTrial	4Q2022	Yes	No
Oxabact (IxOC-3)	oxalobacter	OxThera	probiotic	Hyperoxaluria	PO	InTrial	2H2022	No	Yes
ALT-803	nogapendekin alfa inbakicept	ImmunityBio	interleukin-15 super agonist/ IL-15R alpha-Fc fusion complex	Bladder cancer	Intravesical	InTrial	2H2022	Yes	No
AAI-101	cefepime/enmetazobactam	Allecra	beta-lactam/b-lactamase inhibitor	Urinary tract infection	IV	InTrial	2H2022	No	No
OPNT-003	nalmefene	Opiant	opioid receptor antagonist	Opioid overdose	Intranasal	InTrial	2H2022	No	No
PRV-031	teplizumab	Provention Bio/ MacroGenics	CD3 antigen inhibitor	Diabetes mellitus	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
Sativex	nabiximols	GW Pharmaceuticals/ Otsuka	cannabinoid product	Spasticity	PO	InTrial	2H2022	No	No
dovitinib	dovitinib	Oncology Venture	fibroblast growth factor receptor 3 inhibitor	Renal cell carcinoma	PO	InTrial	2H2022	Yes	No
Iomab-B	iodine I 131 monoclonal antibody BC8	Actinium	anti-CD45 monoclonal antibody	Acute myeloid leukemia/ Myelodysplastic syndrome	IV	InTrial	2H2022	Yes	Yes
SPI-2012	eflapegrastim	Spectrum	granulocyte colony-stimulating factor	Chemotherapy-induced neutropenia	SC	CRL	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
NexoBrid	bromelain	Vericel	peptide hydrolase replacement agent	Burns/ Skin injury	TOP	CRL	2H2022	No	Yes
PRX-102	pegunigalsidase alfa	Protalix	enzyme replacement	Fabry disease	IV	CRL	2H2022	Yes	No
Qtrypta	zolmitriptan	Zosano	triptans	Acute migraines	TOP	CRL	2H2022	No	No
Entyvio (SC formulation)	vedolizumab	Takeda	integrin receptor antagonist	Ulcerative colitis	SC	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
pIL-12 (DNA IL-12)	tavokinogene telsaplasmid	OncoSec Medical	gene therapy	Melanoma	Intratumoral	InTrial	2H2022	Yes	Yes
MLN-4924 (TAK-92)	pevonedistat	Ligand	Nedd 8 Activating Enzyme antagonist	Myelodysplastic syndrome	IV	InTrial	2H2022	Yes	No
177Lu-PSMA-617	Lutetium	Novartis	Radiopharmaceutical	Prostate cancer	IV	InTrial	2H2022	Yes	No
Hepcludex	bulevirtide	Gilead	HBV receptor binder	Hepatitis delta virus	SC	InTrial	2H2022	No	Yes
obeticholic acid	obeticholic acid	Intercept Pharmaceuticals	farnesoid X receptor agonist	Nonalcoholic steatohepatitis	PO	CRL	2H2022	Yes	No
IDP-120	tretinoin/ benzoyl peroxide	Bausch	retinoid	Acne	TOP	InTrial	2H2022	No	No
SPN-830	apomorphine	Supernus Pharmaceuticals	non-ergoline dopamine agonist	Parkinson’s disease	SC infusion	InTrial	2H2022	Yes	No
MGA-012	retifanlimab	Incyte	programmed cell death protein 1 inhibitor	Anal cancer	IV	CRL	2H2022	Yes	Yes
FMXIN-001	naloxone	Nasus Pharma	opioid antagonist	Opioid overdose	Intranasal	InTrial	2H2022	No	No
magrolimab	magrolimab	Gilead	CD47 monoclonal antibody	Myelodysplastic syndrome	IV	InTrial	2H2022	Yes	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
BGB-A317 (BGB-A-317)	tislelizumab	Celgene/ BeiGene	programmed death-1 inhibitor	Hepatocellular cancer	IV	InTrial	2H2022	Yes	No
Nanoflu	influenza vaccine	Novavax	vaccine	Influenza	IM	InTrial	2022	No	No
DS-100	dehydrated alcohol	Eton	undisclosed	Methanol poisoning	SC	CRL	2022	No	Yes
AGEN-1884	zalifrelimab	Agenus	immune checkpoint modulator antibody	Cervical cancer	IV	InTrial	2022	Yes	No
Ovastat	treosulfan	Medexus Pharmaceuticals	alkylating agent	Hematopoietic stem cell transplantation	IV	CRL	2022	Yes	Yes
NuThrax	anthrax vaccine adsorbed/ CPG-7909	Emergent Biosolutions	vaccine/ oligodeoxynucleotide	Anthrax	IM	InTrial	Late 2022	Yes	No
NS-2 (ALDX-1E1, ALDX-1E2, ADX-102)	reproxalap	Aldeyra Therapeutics	aldehyde antagonist	Dry eyes	OP	InTrial	Late 2022	No	No
RP-L102 (RPL-102)	RP-L102	Rocket Pharmaceuticals	gene therapy	Fanconi anemia	IV	InTrial	Late 2022	Yes	Yes
MT-7117	MT-7117	Mitsubishi Tanabe Pharma	Undisclosed	Erythropoietic protoporphyria	PO	InTrial	Late 2022	Yes	No
RGN-259 (GBT-201; RGN-352)	timbetasin	RegeneRx	actin regulating peptide	Dry eyes	OP	InTrial	Late 2022	No	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
PS-433540 (RE-021; DARA)	sparsentan	Travere Therapeutics	dual-acting angiotensin/endothelin receptor antagonist	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
DBV-712 (Viaskin Peanut)	DBV-712	DBV Technologies	Immunotherapy	Peanut allergy	TOP	CRL	Late 2022	No	No
R-667 (RG-667)	palovarotene	Ipsen	selective retinoic acid receptor agonist	Fibrodysplasia ossificans progressiva	PO	InTrial	Late 2022	Yes	Yes
IMGN-853	mirvetuximab soravtansine	ImmunoGen	folate receptor-1 antagonist	Ovarian cancer	IV	InTrial	Late 2022	Yes	Yes
PF-06838435 (SPK-9001)	fidanacogene elaparvovec	Pfizer/ Spark Therapeutics	gene therapy	Hemophilia B	IV	InTrial	Late 2022	Yes	Yes
sulopenem	sulopenem	Iterum Therapeutics	carbapenem	Urinary tract infections	PO	CRL	Late 2022	No	No
AMT-061	etranacogene dezaparvovec	CSL Behring/ uniQure	gene therapy	Hemophilia B	IV	InTrial	Late 2022	Yes	Yes
LY-3298176	tirzepatide	Eli Lilly	glucose-dependent insulinotropic polypeptide/glucagon-like peptide-1 receptor agonist	Diabetes mellitus	SC	InTrial	Late 2022	No	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
PTX-022	rapamycin	Palvella Therapeutics	mTOR kinase inhibitor	Pachyonychia congenita	TOP	InTrial	Late 2022	No	Yes
GSK-2140944	gepotidacin	GlaxoSmithKline	bacterial Type II topoisomerase inhibitor	Bacterial infections	PO/IV	InTrial	Late 2022	No	No
ARQ-151	roflumilast	Arcutis Biotherapeutics	phosphodiesterase-4 inhibitor	Plaque psoriasis	TOP	InTrial	Late 2022	Yes	No
KN-046	KN-046	Alphamab Oncology	PD-L1/CTLA-4 bispecific monoclonal antibody	Thymic cancer	IV	InTrial	Late 2022	Yes	Yes
CERC-802	CERC-802	Cerecor	D-mannose	Mannose-phosphate isomerase deficiency	PO	InTrial	Late 2022	Yes	Yes
scCeftriaxone	ceftriaxone	scPharmaceuticals	Penicillin binding protein inhibitor	Bacterial infections	SC	InTrial	Late 2022	No	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	Proposed new indication	Route of administration	Estimated approval date
Tibsovo	ivosidenib	Agios	IDH1 inhibitor	Cholangiocarcinoma	Treatment for patients with previously treated isocitrate dehydrogenase 1 mutated cholangiocarcinoma	PO	09/01/2021
Brukinsa	zanubrutinib	BeiGene	kinase inhibitor	Marginal zone lymphoma	Treatment of adult patients with marginal zone lymphoma who have received at least one prior anti-CD20-based therapy	PO	09/19/2021
Jakafi	ruxolitinib	Incyte	janus kinase inhibitor	Graft-versus-host disease	Treatment of steroid-refractory chronic graft-versus-host disease in adult and pediatric patients 12 years and older	PO	09/22/2021
Rinvoq	upadacitinib	AbbVie	janus kinase inhibitor	Atopic dermatitis	Treatment of adults and adolescents with moderate to severe atopic dermatitis	PO	3Q 2021
Rinvoq	upadacitinib	AbbVie	janus kinase inhibitor	Psoriatic arthritis	Treatment of adult patients with active psoriatic arthritis	PO	3Q 2021
Rinvoq	upadacitinib	AbbVie	janus kinase inhibitor	Ankylosing spondylitis	Treatment of adult patients with active ankylosing spondylitis	PO	3Q 2021
Olumiant	baricitinib	Eli Lilly	janus kinase 1/2 inhibitor	Atopic dermatitis	Treatment of adults with moderate-to-severe atopic dermatitis	PO	3Q 2021

Brand name	Generic name	Company	Drug class	Therapeutic use	Proposed new indication	Route of administration	Estimated approval date
Tecartus	brexucabtagene autoleucel	Gilead	CD19-directed genetically modified autologous T cell immunotherapy	Acute lymphoblastic leukemia	Treatment of adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia	IV	10/01/2021
Dextenza	dexamethasone	Ocular Therapeutix	corticosteroid	Allergic conjunctivitis	Treatment of ocular itching associated with allergic conjunctivitis	OPH	10/18/2021
Brukinsa	zanubrutinib	BeiGene	kinase inhibitor	Waldenström's Macroglobulinemia	Treatment of adult patients with Waldenström's Macroglobulinemia	PO	10/18/2021
Dupixent	dupilumab	Sanofi/ Regeneron	interleukin 4/13 inhibitor	Asthma	Add-on maintenance treatment in patients with moderate-to-severe asthma aged 6 years and older with an eosinophilic phenotype or with oral corticosteroid dependent asthma	SC	10/21/2021
Verzenio	abemaciclib	Eli Lilly	cyclin-dependent kinase 4 and 6 inhibitor	Early breast cancer	Treatment of hormone receptor positive, HER2 negative, early breast cancer	PO	10/29/2021
Andexxa	coagulation factor Xa (recombinant), inactivated-zhzo	Alexion	recombinant Factor Xa inhibitor antidote	Drug toxicity	In patients presenting with acute intracranial hemorrhage while taking an oral Factor Xa inhibitor	IV	10/31/2021
Tecentriq	atezolizumab	Roche	PD-L1 monoclonal antibody	Non-small cell lung cancer	Adjuvant treatment following surgery and platinum-based chemotherapy for people with non-small cell lung cancer (NSCLC) whose tumors express PD-L1≥1%, as determined by an FDA-approved test	IV	12/02/2021
Cabometyx	cabozantinib	Exelixis/ Ipsen	kinase inhibitor	Thyroid cancer	Treatment of radioactive iodine-refractory differentiated thyroid cancer in patients 12 years and older who have progressed following prior therapy	PO	12/03/2021

Brand name	Generic name	Company	Drug class	Therapeutic use	Proposed new indication	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	phosphodiesterase 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	IV	12/21/2021
Xarelto	rivaroxaban	Janssen	factor Xa inhibitor	Venous thromboembolism	Treatment of venous thromboembolism (VTE) and reduction in the risk of recurrent VTE in patients aged birth to less than 18 years of age after at least five days of initial parenteral anticoagulant treatment; and thromboprophylaxis in patients aged 2 years and older with congenital heart disease who have undergone the Fontan procedure	PO	12/23/2021

Brand name	Generic name	Company	Drug class	Therapeutic use	Proposed new indication	Route of administration	Estimated approval date
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
Xeljanz	tofacitinib	Pfizer	Janus associated kinase (JAK) inhibitor	Axial spondyloarthritis	Treatment of axial spondyloarthritis	PO	12/28/2021
Oxbryta	voxelotor	Global Blood Therapeutics	hemoglobin S polymerization	Sickle cell disease	Treatment of sickle cell disease in children ages 4 to 11 years	PO	01/22/2022
Vonvendi	von Willebrand factor (recombinant)	Takeda	von Willebrand factor	von Willebrand disease	Prophylaxis therapy in von Willebrand disease	IV	01/28/2022
Skyrizi	risankizumab-rzaa	AbbVie	interleukin-23 antagonist	Psoriatic arthritis	Treatment of psoriatic arthritis	SC	02/06/2022
Ukoniq	umbralisib	TG Therapeutics	phosphoinositide-3 kinase delta inhibitor	Chronic lymphocytic leukemia and small lymphocytic lymphoma	Treatment for patients with chronic lymphocytic leukemia and small lymphocytic lymphoma	IV	03/26/2022
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
Cosentyx	secukinumab	Novartis	interleukin 17 receptor antagonist	Juvenile idiopathic arthritis	Treatment of juvenile idiopathic arthritis	SC	04/29/2022

Brand name	Generic name	Company	Drug class	Therapeutic use	Proposed new indication	Route of administration	Estimated approval date
Myfembree	relugolix/ estradiol/ norethindrone acetate	Myovant	gonadotropin-releasing hormone (GnRH) receptor antagonist/ estrogen/ progestin	Endometriosis	Management of moderate to severe pain associated with endometriosis	PO	05/07/2022
Fasenra	benralizumab	AstraZeneca	interleukin 5 receptor alpha inhibitor	Nasal polyposis	Treatment of nasal polyposis	SC	06/05/2022
Qelbree	viloxazine	Supernus	selective norepinephrine reuptake inhibitor	Attention deficit hyperactivity disorder (adults)	Treatment of adults with attention deficit hyperactivity disorder (ADHD)	PO	06/30/2022

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

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