OPTUMRx®

RxOutlook®

3rd Quarter 2020

In this edition of RxOutlook, we highlight 13 key pipeline drugs with potential to launch by the end of the fourth quarter of 2020. In this list of drugs, we continue to see an emphasis on rare diseases. Indeed, almost half of the drugs we review here have FDA Orphan Drug Designation for a rare, or ultra-rare condition. However, this emphasis on rare diseases is also balanced by several drugs for more "mainstream" conditions such as attention deficit hyperactivity disorder, hypercholesterolemia, and osteoarthritis. Seven are delivered via the oral route of administration and three of these are particularly notable because they are the first oral option in their respective categories. Berotralstat is the first oral treatment for hereditary angioedema, relugolix is the first oral gonadotropin releasing hormone receptor antagonist for prostate cancer, and roxadustat is the first oral treatment for anemia of chronic kidney disease. Two drugs this list use RNA-based mechanisms to dampen or "silence" genetic signaling in order to correct an underlying genetic condition: Lumasiran for primary hyperoxaluria type 1, and inclisiran for atherosclerosis and familial hypercholesterolemia. These agents can be given every 3 or 6 months and fill a space between more traditional chronic maintenance drugs the require daily administration and gene therapies that require one time dosing for long term (and possible life-long) benefits.

Key pipeline drugs with FDA approval decisions expected by the end of the 4th quarter 2020

Drug Name	Manufacturer	Indication/Use	Expected FDA Decision Date
Eflapegrastim	Spectrum Pharmaceuticals	Chemotherapy-induced neutropenia	10/24/2020
Viloxazine	Supernus Pharmaceuticals	Attention deficit hyperactivity disorder	11/8/2020
Sutimlimab	Sanofi	Cold agglutinin disease*	11/13/2020
Olanzapine/ samidorphan	Alkermes	Schizophrenia/ bipolar I disorder	11/15/2020
Lonafarnib	Eiger BioPharmaceuticals	Progeria*	11/20/2020
Pralsetinib	Blueprint Medicines	Non-small cell lung cancer*	11/23/2020
Setmelanotide	Rhythm Pharmaceuticals	Genetic disorders of obesity*	11/27/2020
Berotralstat	BioCryst Pharmaceuticals	Hereditary angioedema*	12/3/2020
Lumasiran	Alnylam Pharmaceuticals	Primary hyperoxaluria type 1*	12/3/2020
Relugolix	Myovant Sciences	Prostate cancer	12/20/2020
Roxadustat	FibroGen/AstraZeneca	Chronic kidney disease – anemia	12/23/2020
Inclisiran	Novartis	Hypercholesterolemia	12/2020
Tanezumab	Pfizer/ Eli Lilly	Osteoarthritis	12/2020

* 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 2020.

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 2020 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

Eflapegrastim (Brand Name: Rolontis®)

Manufacturer: Spectrum Pharmaceuticals
FDA approval date: 10/24/2020

Therapeutic use

Eflapegrastim is in development for the treatment of chemotherapy-induced neutropenia (CIN).

CIN is a common adverse event associated with cytotoxic chemotherapy. CIN can lead to infection-related morbidity and mortality. The current standard of care for managing CIN is administration of granulocyte-colony stimulating factor (G-CSF) drugs alongside chemotherapy cycles.

- Treatment of CIN

Clinical profile

Eflapegrastim is a G-CSF with a novel molecular structure – it consists of a recombinant human G-CSF component and a recombinant IgG Fc fragment. This configuration is expected to decrease clearance due to its size, and also have increased uptake to the bone marrow.

- G-CSF
- SC formulation

Pivotal trial data:
The efficacy of eflapegrastim was evaluated in two identical, randomized, active-controlled, open label, Phase 3 studies (ADVANCE and RECOVER) in breast cancer patients following docetaxel and cyclophosphamide chemotherapy. In both studies, patients received eflapegrastim or another G-CSF, pegfilgrastim (eg, Neulasta®). The primary endpoint was the mean duration of severe neutropenia (DSN; defined as absolute neutrophil counts [ANC] < 0.5 x 109/L) in cycle 1.

In ADVANCE (N = 406), the incidence of cycle 1 severe neutropenia was 16% for eflapegrastim vs. 24% for pegfilgrastim, reducing the relative risk by 35% (p = 0.034). The difference in mean cycle 1 DSN (-0.148 day) met the primary endpoint of noninferiority (p < 0.0001) and also showed statistical superiority for eflapegrastim (p = 0.013).

- ADVANCE: 35% reduction in incidence of cycle 1 severe neutropenia vs. pegfilgrastim

In RECOVER (N = 237), the mean cycle 1 DSN was 0.31 days for eflapegrastim and 0.39 days for pegfilgrastim (non-inferiority met; p < 0.0001). Incidence of severe neutropenia was 20% vs. 24% in the eflapegrastim and pegfilgrastim arms respectively, with a relative risk reduction of 14% in favor of eflapegrastim.

- RECOVER: 14% reduction in incidence of cycle 1 severe neutropenia vs. pegfilgrastim

Safety:
The most common adverse events with eflapegrastim use were bone pain, arthralgia, back pain, and myalgia.

- Common AEs: Bone pain, arthralgia, back pain, myalgia

Dosing:
In the pivotal trials, eflapegrastim was administered as a single, fixed-dose subcutaneous (SC) injection on day 2 of each cycle (~24 hours post-chemotherapy).

- Dosing: Single dose on day 2 of each chemotherapy cycle

Eflapegrastim (Brand Name: Rolontis®) (continued...)

Competitive environment

Eflapegrastim would offer an additional long-acting G-CSF treatment option for CIN with a unique molecular structure that is believed to increase bone marrow uptake. Compared to Neulasta, eflapegrastim did demonstrate a modest improvement in efficacy as demonstrated by numerically lower rates of severe neutropenia. In one of the two pivotal trials, eflapegrastim demonstrated statistically superior improvements vs. Neulasta.

However, eflapegrastim would be a late market entry in the G-CSF therapeutic class. Alternatives such as Neupogen® (filgrastim) and Neulasta® (pegfilgrastim) have been established standards of care and biosimilars are also available for both. Eflapegrastim may have difficulty differentiating itself from pegfilgrastim, which is also dosed once per chemotherapy cycle. Additionally, eflapegrastim was similar to pegfilgrastim in rates of febrile neutropenia and was associated with a slightly higher rate of Grade 3 bone pain events (5% vs. < 1% in the ADVANCE trial).

For reference, the Wholesale Acquisition Cost (WAC) price for Neulasta is approximately $6,200 per cycle.

- Advantages: Favorable efficacy results vs. standard of care option (Neulasta)
- Disadvantages: Late market entry with alternatives available (including biosimilars), higher rate of bone pain adverse event vs. Neulasta
- Reference WAC (Brand Neulasta): ~$6,200 per cycle

Viloxazine (Brand Name: To be determined)

Manufacturer: Supernus Pharmaceuticals
Expected FDA decision: 11/8/2020

Therapeutic use

Viloxazine is in development for the treatment of children and adolescents with attention deficit hyperactivity disorder (ADHD).

ADHD is one of the most common neurodevelopmental disorders of childhood. It is usually diagnosed in childhood and often lasts into adulthood. Children and adolescents with ADHD may have trouble paying attention, controlling impulsive behaviors, or be overly active. The approach to management varies by age and is often treated with a combination of behavior therapy and medication.

The estimated number of children ever diagnosed with ADHD, according to a national 2016 parent survey, is 6.1 million and about 3 in 4 children with current ADHD receive treatment.

- Treatment of children and adolescents with ADHD

Viloxazine (continued...)

Clinical profile

Viloxazine is a serotonin norepinephrine modulating agent and would represent a non-stimulant treatment for ADHD.

Pivotal trial data:
The efficacy of viloxazine was evaluated in four Phase 3 studies: two in children ages 6 – 11 years, and two in adolescents age 12 to 17 years. The primary endpoints in these studies was the change from baseline to the end of the study in the ADHD-Rating Scale-5 (ADHD-RS-5) total score. The ADHD-RS-5 is a rating scale based on the diagnostic criteria for ADHD as described in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) and consists of two symptom subscales, inattention (9 items) and hyperactivity-impulsivity (9 items). Each item is scored on a four point scale: No, minor, moderate, or severe problem.

Studies P301 and P303 were randomized, double-blind, placebo controlled studies in children 6 to 11 years of age and a baseline ADHD-RS-5 score of 28 or higher.

- Study 301 randomized a total of 477 patients to viloxazine 100 mg, viloxazine 200 mg, or placebo orally once daily. After 6 weeks of treatment the change from baseline in ADHD-RS-5 for viloxazine 100 mg was -16.6 points ($p = 0.0004$), for viloxazine 200 mg -17.7 points ($p < 0.0001$) vs. -10.9 points for placebo.
- Study P303 randomized a total of 313 patients to receive viloxazine 200 mg, viloxazine 400 mg, or placebo once daily orally. After 8 weeks of treatment, the change from baseline in ADHD-RS-5 score for viloxazine 200 mg was -17.6 points ($p = 0.0038$), viloxazine 400 mg -17.5 points ($p = 0.0063$) vs. -11.7 points for placebo.

Studies P302 and P304 were randomized, double-blind, placebo controlled studies in adolescents 12 to 17 years of age with a baseline ADHD-RS-5 score of 28 or higher.

- Study P302 randomized a total of 310 adolescents to receive viloxazine 200 mg, viloxazine 400 mg, or placebo once daily. After 6 weeks of treatment, the change from baseline in ADHD-RS-5 score for viloxazine 200 mg was -16.0 points ($p = 0.0232$), viloxazine 400 mg -16.5 points ($p = 0.0091$) vs. -11.4 points for placebo.
- Study P304 randomized a total of 297 patients to receive viloxazine 400 mg, viloxazine 600 mg, or placebo once daily. After 7 weeks of treatment the change from baseline in ADHD-RS-5 score for viloxazine 400 mg was -18.3 points ($p = 0.0082$), viloxazine 600 mg -16.7 (not statistically significant), vs. -13.2 points for placebo.

Safety:
The most common adverse events with viloxazine use were somnolence, headache, decreased appetite, fatigue, nausea, and upper abdominal pain.

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

- Serotonin norepinephrine modulating agent
- Oral formulation
- ADHD-RS-5 total score (children 6 to 11 years): Reduction of 16.6 to 17.7 vs. reduction of 10.9 to 11.7 with placebo
- ADHD-RS-5 total score (adolescents 12 to 17 years): Reduction of 16.0 to 18.3 vs. reduction of 11.4 to 13.2 with placebo
- Common AEs: Somnolence, headache, decreased appetite, fatigue, nausea, upper abdominal pain
- Dosing: Once daily

Viloxazine (continued...)

Competitive environment

If approved, viloxazine would offer a novel, non-stimulant treatment option for ADHD. The first-line pharmacological treatment for ADHD is stimulants (eg, amphetamine, methylphenidate) which are highly effective; however, they are controlled substances with a boxed warning for abuse or dependence. Alternative non-stimulant treatment options include the selective norepinephrine reuptake inhibitor, Strattera® (atomoxetine), and alpha-2-adrenergic agonists (eg, clonidine, guanfacine). While these non-stimulant options have lower potential for abuse, they are generally less effective than stimulants and are also associated with a variety of side effects (eg, serious cardiovascular events or hypotension).

Viloxazine was generally well-tolerated in the pivotal trials in ADHD and is supported by robust safety data from Europe where it has been available as an antidepressant. Similar to other non-stimulant therapies, it will likely not be a controlled substance. While the pivotal trials were placebo-controlled, viloxazine demonstrated efficacy as early as 1 week in some of the treatment arms and it appears to have a faster onset of action vs. other non-stimulant options.

However, viloxazine would be entering a very crowded marketplace with many alternatives available, including generic products (stimulant and non-stimulant). While the efficacy results appear promising vs. non-stimulant products (compared indirectly), viloxazine will probably be reserved as a second-line option since there is a lack of comparative data vs. stimulants and the efficacy appears to be modest. Data is also lacking in an adult patient population, although two studies were initiated in adults in the third quarter of 2019.

For reference, the WAC price for brand Strattera is approximately $5,200 per year.

- Advantages: Novel non-stimulant treatment for ADHD, well tolerated, potentially faster onset of action vs. other non-stimulant ADHD treatments
- Disadvantages: Alternatives available (including generics), efficacy appears worse than stimulants, lack of data in adult patient population
- Reference WAC (brand Strattera): $5,200 per year

Sutimlimab (Brand Name: To be determined)

Manufacturer: Sanofi
Regulatory designations: Orphan Drug, Breakthrough Therapy
Expected FDA decision: 11/13/2020

Therapeutic use

- Treatment of hemolysis in adult patients with cold agglutinin disease

Sutimlimab is in development for the treatment of hemolysis in adult patients with cold agglutinin disease.

Cold agglutinin disease is a rare type of autoimmune hemolytic anemia. In affected patients who are exposed to cold temperatures (32° to 50° F), Immunoglobulin M antibodies attach themselves to red blood cells and bind them together into clumps (agglutination). This eventually causes red blood cell hemolysis, anemia, and other associated signs and symptoms. Cold agglutinin disease is classified as primary (unknown cause) or secondary, due to an underlying condition such as an infection, another autoimmune disease, or certain cancers. Patients with cold agglutinin disease are at a higher risk for thromboembolic events and early death.

It is estimated that about 5,000 people in the U.S. are affected by cold agglutinin disease.

Clinical profile

- Monoclonal antibody targeting C1
- IV formulation
- Responder rate: 54%
- Limited safety data
- Maintenance dosing: Once every other week

Sutimlimab is a monoclonal antibody selectively targeting C1 in the classical complement pathway. By blocking C1, it is believed that sutimlimab halts C1-activated hemolysis in patients affected by cold agglutinin disease.

Pivotal trial data:
The efficacy of sutimlimab was evaluated in CARDINAL, a Phase 3, open-label, single-arm study in 24 patients with cold agglutinin disease. The primary endpoint was a responder rate based on a composite of an increase in hemoglobin ≥ 2 g/dL from baseline or reaching a hemoglobin level ≥ 12 g/dL at the 26-week treatment assessment timepoint and the absence of blood transfusions from weeks 5 to 26.

Overall, 54% of patients met the composite endpoint criteria, with 62.5% of patients achieving a hemoglobin ≥ 12 g/dL or an increase of at least 2 g/dL and 71% of patients remaining transfusion-free after week 5. The overall mean increase in hemoglobin was 2.6 g/dL at the treatment assessment timepoint; 83% of the 24 patients enrolled achieved a mean hemoglobin improvement of ≥ 1 g/dL.

Safety:
The safety data for sutimlimab from the Phase 3 trial is limited. It was reported that 7 patients experienced at least 1 treatment-emergent serious adverse event of which none were assessed by investigators as related to sutimlimab.

Dosing:
In the pivotal trial, sutimlimab was administered intravenously (IV) on days 0 and 7, followed by dosing every other week.

Sutimlimab (continued...)

Competitive environment

Sutimlimab would potentially be the first FDA approved therapy for the treatment of cold agglutinin disease. The current treatment approach for the condition depends on the severity of the disease and the underlying cause. Symptomatic anemia may be treated with blood transfusions or with plasmapheresis to remove the IgM antibodies. In severe cases of hemolysis, the standard of care is off-label use of Rituxan® (rituximab), which is effective in about 60% of cases. The response to Rituxan is seen on average within 1 to 2 months of treatment and the effect of the treatment lasts for about 1 to 2 years. Rituxan can also be used in combination with fludarabine to increase response rates, but this regimen is also associated with poor tolerability.

In the pivotal trial, sutimlimab demonstrated a rapid onset of action with patients showing improvements in hemoglobin within weeks of treatment. In addition, based on the information currently available, sutimlimab was well tolerated.

However, the target population for sutimlimab is expected to be small as the efficacy appears to be similar to off-label use of Rituxan in patients with severe disease and patients with milder disease may not require any pharmacotherapy. These milder cases can be managed by lifestyle modifications (eg, avoiding exposure to cold temperatures).

- Advantages: Potentially first FDA approved product for the disease, rapid onset of action, well tolerated
- Disadvantages: Small target population, limited trial data, IV administration

Olanzapine/samidorphan (Brand Name: To be determined)

Manufacturer: Alkermes
Expected FDA decision: 11/15/2020

Therapeutic use

Olanzapine/samidorphan is in development for the treatment of schizophrenia and for the treatment of bipolar I disorder.

Schizophrenia is a mental disorder characterized by disruptions in thought processes, perceptions, emotional responsiveness, and social interactions. Patients can experience positive symptoms (eg, hallucinations and delusions, disorganized speech and thoughts, and agitated or repeated movements) and negative symptoms (eg, depression, blunted emotions and social withdrawal). The exact prevalence of schizophrenia is difficult to determine due overlap with related psychiatric conditions, however, the estimated prevalence of schizophrenia and related psychotic disorders in the U.S. ranges between 0.25% and 0.64%.

Bipolar disorder (manic-depressive disorder) is characterized by dramatic shifts in mood, energy, and activity levels that affect a person's ability to carry out day-to-day tasks. Bipolar I disorder is defined by manic episodes that last at least 7 days, or by manic symptoms that are so severe that the person needs immediate hospital care. Usually, depressive episodes occur as well, typically lasting at least 2 weeks. Bipolar I disorder affects approximately 1% of the adult population in the U.S.

- Treatment of schizophrenia and treatment of bipolar I disorder

Olanzapine/samidorphan (continued...)

Clinical profile

Olanzapine/samidorphan is a fixed-dose combination containing an atypical antipsychotic (olanzapine) and an opioid receptor antagonist (samidorphan). Single-ingredient olanzapine is already available commercially but samidorphan is a novel molecular entity. The combination of olanzapine and samidorphan is intended to provide the antipsychotic efficacy of olanzapine while mitigating weight gain associated with olanzapine; samidorphan is not expected to have antipsychotic properties.

Pivotal trial data:
The efficacy of olanzapine/samidorphan for the treatment of schizophrenia was evaluated in the ENLIGHTEN-1 and ENLIGHTEN-2 studies. ENLIGHTEN-1 was 4-week, Phase 3, randomized, double-blind, active- and placebo-controlled study in 401 patients experiencing an acute exacerbation of schizophrenia. Patients received olanzapine/samidorphan, olanzapine monotherapy, or placebo. The primary endpoint was change from baseline in Positive and Negative Syndrome Scale (PANSS) total score at week 4. The key secondary endpoint was change from baseline in Clinical Global Impressions-Severity of Illness Scale (CGI-S) score at week 4. Treatment with olanzapine/samidorphan resulted in significant improvements vs. placebo in the PANSS total and CGI-S scores from baseline to week 4 (least squares [LS] mean change: -6.4, $p < 0.001$; and -0.38, $p = 0.002$, respectively). Olanzapine monotherapy treatment resulted in similar improvements vs. placebo.

The ENLIGHTEN-2 study was a Phase 3, double-blind, randomized, active-controlled study that evaluated the weight gain profile of olanzapine/samidorphan vs. olanzapine over 24 weeks in 561 patients with stable schizophrenia. The co-primary endpoints were the percent change from baseline in body weight at 24 weeks and the proportion of patients with 10% or more weight gain from baseline. At week 24, the LS mean percent change from baseline in weight was 4.21% vs. 6.59% in the olanzapine/samidorphan vs. olanzapine groups, respectively ($p = 0.003$). The proportion of patients in the olanzapine/samidorphan and olanzapine groups with ≥ 10% weight gain was 17.8% vs 29.8% ($p = 0.003$), respectively. No significant differences in metabolic laboratory parameter changes from baseline to week 24 were noted between olanzapine/samidorphan and olanzapine alone.

Safety:
The most common adverse events with olanzapine/samidorphan use were weight gain, somnolence, dry mouth, and headache.

Dosing:
In the pivotal trials, olanzapine/samidorphan was administered orally once daily.

- Atypical antipsychotic / opioid receptor antagonist
- Oral formulation
- Change in PANSS total score vs. placebo: -6.4
- Mean weight gain: 4.21% vs. 6.59% with olanzapine; 10% weight gain was observed in 17.8% vs. 29.8% with olanzapine
- Common AEs: Weight gain, somnolence, dry mouth, headache
- Dosing: Once daily

Olanzapine/samidorphan (continued...)

Competitive environment

Olanzapine/samidorphan would offer a novel combination for the treatment of schizophrenia and bipolar I disorder with a potential to mitigate weight gain compared to some atypical antipsychotics.

However, there are many alternatives already on the market for the treatment of both conditions (including generics) and the potential mitigation of weight gain appears to be modest vs. olanzapine. Based on the available data, it does not appear that the addition of samidorphan decreases the other metabolic disturbances associated with atypical antipsychotics (eg, glucose and lipid levels). There are also other atypical antipsychotics that have a more favorable side effect profile in terms of weight gain compared to olanzapine (eg, risperidone).

In addition, the FDA filing is expected to only include late stage trial data in a schizophrenia population. If approved, support for the bipolar I disorder indication would likely be based on supportive studies evaluating the pharmacokinetic profile of olanzapine/samidorphan vs. olanzapine.

For reference, the WAC price of Caplyta (lumateperone), another recently approved novel oral therapy for schizophrenia, is approximately $16,000 per year.

- Advantages: Novel combination for the treatment of schizophrenia/ bipolar I disorder, potential to mitigate weight vs. some atypical antipsychotics (eg, single-ingredient olanzapine)
- Disadvantages: Alternatives available (including generics), lack of data demonstrating improvement in metabolic disturbances besides weight gain vs. atypical antipsychotics, lack of late stage trial data in bipolar I disorder
- Reference WAC (Caplyta): ~$16,000 per year

Lonafarnib (Brand Name: Zokinvy™)

Manufacturer: Eiger BioPharmaceuticals
Regulatory designations: Orphan Drug, Breakthrough Therapy
Expected FDA decision: 11/20/2020

Therapeutic use

Lonafarnib is in development for the treatment of progeria and progeroid laminopathies.

Progeria, also known as Hutchinson-Gilford progeria syndrome (HGPS), is an ultra-rare genetic condition that presents in childhood. It is estimated to affect about 400 children worldwide. Affected children experience features resembling premature aging and at approximately 9 to 24 months of age, begin to experience growth delays, resulting in short stature and low weight. Additional disease characteristics include atherosclerosis, cardiovascular disease and stroke, hip dislocations, joint stiffness, and skeletal defects. Without treatment, children with progeria develop progressive cardiovascular disease leading to early death due to myocardial infarction by the age of 13 years. Progeria is caused by a mutation of the *LMNA* gene or lamin A, which encodes the lamin A protein. The result of the mutation is the farnesylated aberrant protein, progerin. Researchers believe that the defective lamin A protein makes the cell nucleus unstable and that cellular instability leads to the process of premature aging in progeria.

Progeroid laminopathies are genetic conditions of accelerated aging caused by different mutations and yielding farnesylated proteins that are distinct from progerin. While non-progerin producing, these genetic mutations result in disease manifestations with phenotypes that overlap with progeria. Worldwide prevalence of progeroid laminopathies is similar to progeria.

- Treatment of progeria and progeroid laminopathies

Lonafarnib (Brand Name: Zokinvy™) (continued...)

Clinical profile

Lonafarnib is an active inhibitor of farnesyltransferase. Persistent farnesylation of progerin causes it to intercalate into the inner nuclear membrane, where it accumulates and exerts damage to cells.

Pivotal trial data:
The efficacy of lonafarnib was evaluated in an observational cohort study that compared lonafarnib-treated patients from two clinical trials (Trial 1 and Trial 2) with an untreated, age-matched, historical control group. Patients were identified through the Progeria Research Foundation International Registry. Patients in Trial 1 received lonafarnib 115 mg/m^2 divided twice daily for 4 months and then increased to 150mg/m^2 divided twice daily. In Trial 2 patients received lonafarnib 150mg/m^2 divided twice daily for the whole trial. The primary outcome was all-cause mortality. The primary analysis compared treated patients from the Trial 1 with matched untreated patients. A secondary analysis compared the combined cohorts from Trial 1 and Trial 2 with matched untreated patients. The median treatment duration was 2.2 years.

Treatment with lonafarnib was associated with lower mortality rate vs matched untreated patients. There was 1 death (3.7%) among 27 patients in the first trial's lonafarnib group and there were 9 deaths (33.3%) among 27 patients in the matched untreated group (hazard ratio [HR] 0.12; 95% CI: 0.01, 0.93; p=0.04). In the combined cohort, there were 4 deaths (6.3%) among 63 patients in the treated group and 17 deaths (27.0%) among 63 patients in the matched untreated group (HR 0.23; 95% CI: 0.06, 0.90; p=0.04).

Safety:
The safety data for lonafarnib for the treatment of progeria is limited.

Dosing:
In clinical trials, lonafarnib was administered orally twice a day.

- Farnesyltransferase inhibitor
- Oral formulation
- Morality rate: 6.3% with lonafarnib vs. 27.0% in a matched untreated group
- Limited safety data
- Dosing: Twice a day

Lonafarnib (Brand Name: Zokinvy™) (continued...)

Competitive environment

Lonafarnib would potentially be the first FDA approved therapy for the treatment of progeria and progeroid laminopathies. There is a high unmet need for treatments for the condition as it is associated with a high mortality rate in children and existing therapies provide symptomatic relieve and supportive care only. The evidence for lonafarnib comes from non-randomized trials; however, the limited data does indicate an improvement in mortality with lonafarnib vs. no treatment.

The initial target population for lonafarnib is expected to be extremely small in the U.S., as progeria and progeroid laminopathies are ultra-rare genetic conditions that affect less than 1,000 people worldwide. Lonafarnib is currently also under development for the treatment of hepatitis delta virus (HDV) infection. HDV occurs only as a co-infection in individuals harboring hepatitis B virus (HBV). HDV leads to more severe liver disease than HBV alone and is associated with accelerated liver fibrosis, liver cancer, and liver failure. Globally, HDV infection is reported to be 4.3% to 5.7% of chronic hepatitis B carriers and no treatments are currently FDA approved for HDV. Topline Phase 3 data for lonafarnib for HDV infection are expected in 2021.

- Advantages: Potentially first FDA approved product for the disease, high unmet need, also being developed for HDV infection, oral administration
- Disadvantages: Small initial target population, trial data was non-randomized

Pralsetinib (Brand Name: To be determined)

Manufacturer: Blueprint Medicines
Regulatory designations: Orphan Drug, Breakthrough Therapy
Expected FDA decision: 11/23/2020

Therapeutic use

Pralsetinib is in development for the (1) treatment of locally advanced or metastatic *RET (REarranged during Transfection)* fusion-positive non-small cell lung cancer (NSCLC); and (2) treatment of patients with advanced or metastatic *RET* mutant medullary thyroid cancer (MTC) and *RET* fusion-positive thyroid cancers.

In the U.S., an estimated 228,820 new cases of lung cancer will be diagnosed in 2020 and about 135,720 deaths are expected to occur. NSCLC accounts for about 84% of all lung cancer cases. An estimated 52,890 new cases of thyroid cancer are expected in 2020 and about 2,180 deaths.

Genomic alterations in *RET* kinase, which include fusions and activating point mutations, lead to overactive *RET* signaling and uncontrolled cell growth. *RET* fusions have been identified in approximately 2% of NSCLC and 10% to 20% of papillary and other thyroid cancers. *RET* mutations are implicated in approximately 90% of patients with advanced MTC.

- Treatment of locally advanced or metastatic *RET* fusion-positive NSCLC; treatment of patients with advanced or metastatic *RET* mutant medullary thyroid cancer (MTC) and *RET* fusion-positive thyroid cancers

Pralsetinib (continued...)

Clinical profile

Pralsetinib is a potent and selective inhibitor of oncogenic *RET* alterations.

Pivotal trial data:
The efficacy of pralsetinib was evaluated in an ongoing single-arm, multi-cohort study (ARROW) in patients with *RET*-driven cancer. The study included 116 patients with NSCLC, including 80 patients with NSCLC previously treated with platinum-based chemotherapy and 26 patients with treatment-naïve NSCLC.

As of a data cutoff of November 18, 2019, the objective response rate (ORR) was 61% (95% CI: 50, 72) in patients previously treated with platinum-based chemotherapy. In patients with no prior systemic therapy, the ORR was 73% (95% CI: 52, 88). Across all patients, regardless of prior therapy, the median duration of response (DOR) was not reached (95% CI: 11 months, not reached). Overall, 74% of confirmed responders were on treatment as of the data cutoff.

The *RET*-altered thyroid cancer portion of the ARROW study included *RET*-mutant MTC and *RET* fusion-positive thyroid cancer patients. The *RET*-mutant MTC cohort consisted of 53 patients with prior Cometriq® (cabozantinib) and/or Caprelsa® (vandetanib) therapy. As of a data cutoff of February 13, 2020, treatment with pralsetinib resulted in an ORR of 60% (95% CI: 46, 74). In the 19 *RET*-mutant MTC patients who received neither Cometriq nor Caprelsa, pralsetinib treatment resulted in an ORR of 74% (95% CI: 49, 91). In addition, the ORR was 91% (95% CI: 59, 100) in 11 patients with *RET* fusion-positive thyroid cancer.

Safety:
The most common adverse events with pralsetinib use were increased aspartate aminotransferase (AST), anemia, increased alanine aminotransferase (ALT), constipation, hypertension, and neutropenia.

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

- RET inhibitor
- Oral formulation
- ORR (NSCLC): 61% to 73%
- ORR (MTC): 60% to 74%
- ORR (thyroid cancer): 91%
- Common AEs: Increased AST, anemia, increased ALT, constipation, hypertension, neutropenia
- Dosing: Once daily

Competitive environment

Pralsetinib would offer an oral targeted therapy for the treatment of NSCLC and thyroid cancer. The initial indication for pralsetinib is narrow as *RET* fusions only represent a small subset of patients with NSCLC and thyroid cancer. Based on the available evidence from the early stage trial, pralsetinib was well tolerated and provided promising response rates.

However, pralsetinib would be the second product approved for *RET*-altered cancers and would be competing with Eli Lilly's Retevmo™ (selpercatinib) which was approved in May 2020 for similar indications. While it is challenging to compare drugs across different clinical trials, response rates with pralsetinib appear to be similar to Retevmo.

For reference, the WAC price for Retevmo is approximately $20,600 per 30 days.

- Advantages: Additional targeted therapy for NSCLC and thyroid cancer, well tolerated, oral administration
- Disadvantages: Narrow initial indication, competing with Retevmo, lack of late stage data
- Reference WAC (Retevmo): ~$20,600 per 30 days

Setmelanotide (Brand Name: To be determined)

Manufacturer: Rhythm Pharmaceuticals
Regulatory designations: Orphan Drug, Breakthrough Therapy
Expected FDA decision: 11/27/2020

Therapeutic use

Setmelanotide is in development for the treatment of pro-opiomelanocortin (POMC) deficiency obesity and leptin receptor (LEPR) deficiency obesity.

Both POMC and LEPR deficiency obesity are caused by genetic variations in the melanocortin signaling pathway that is responsible for satiety and energy expenditure. These conditions cause severe obesity beginning in the first few months of life.

POMC deficiency obesity is caused by a variant in the *POMC* gene that results in decreased production of two key hunger-regulating hormones: alpha-melanocyte stimulating hormone (α-MSH) and beta-MSH (β-MSH). These hormones normally bind to the melanocortin-4 receptor (MC4R) leading to reduced hunger, decreased food intake and increased energy expenditure. However, in POMC deficiency obesity, dysregulation of α-MSH and β-MSH leads to reduced binding to MC4R and results in increased hunger, reduced energy expenditure, overeating and severe obesity. Rhythm estimates there are approximately 100 to 500 patients in the U.S. with POMC deficiency obesity.

LEPR deficiency obesity is caused by mutations in the *LEPR* gene, which encodes the leptin receptor protein. *LEPR* gene mutations that cause leptin receptor deficiency prevent the receptor from responding to leptin, a satiety hormone, leading to reduced downstream stimulation of MC4R. Dysregulation of leptin receptors promotes the excessive hunger and weight gain associated with this disorder. Rhythm estimates there are approximately 500 to 2,000 U.S. patients with LEPR deficiency obesity.

- Treatment of POMC deficiency obesity and leptin receptor LEPR deficiency obesity

Setmelanotide (continued...)

Clinical profile

Setmelanotide is a MC4R agonist. As mentioned above, the MC4R is part of a key biological pathway that regulates energy expenditure and appetite.

Pivotal trial data:
The efficacy of setmelanotide was evaluated in two Phase 3, open-label, single-arm studies in patients with either POMC (N = 10) or LEPR (N = 11) deficiency obesity who were 6 years of age and older. Following screening and dose titration, patients received 10 weeks of daily SC injections of setmelanotide, followed by an 8 week drug withdrawal period, then 32 weeks of open-label treatment with the therapeutic dose of setmelanotide. The primary endpoint in both studies assessed the percentage of participants who reached at least 10% weight loss as compared to historical controls in this population.

Eight of 10 patients with POMC deficiency obesity achieved the primary endpoint of greater than 10% weight loss over approximately one year ($p < 0.0001$). The mean reduction from baseline in body weight was -25.4% ($p < 0.0001$) and the mean weight loss for these patients was 70.2 pounds, over one year on therapy.

Five of 11 patients with LEPR deficiency obesity achieved the primary endpoint of greater than 10% weight loss over one year ($p = 0.0001$). The mean reduction from baseline in body weight for LEPR deficiency obesity patients was -12.5% ($p < 0.0001$), and mean weight loss for these patients was 36.8 pounds, over one year on therapy.

During the withdrawal sequence portion of the trials, participants almost immediately gained weight and experienced an increase in hunger, reversing their downward trends in weight loss and hunger scores observed during the first 12 weeks of the treatment period. In both trials, the mean weight increase during the 4-week placebo period was approximately 11 pounds.

Safety:
The most common adverse events with setmelanotide use were injection site reactions, nausea and vomiting, and increased hyperpigmentation.

Dosing:
In the pivotal trials, setmelanotide was administered SC once daily.

- MC4R agonist
- SC formulation
- Greater than 10% weight loss over one year (POMC deficiency obesity): 8 of 10 patients; mean weight loss of 70.2 pounds over one year on therapy
- Greater than 10% weight loss over one year (LEPR deficiency obesity): 5 of 11 patients; mean weight loss of 36.8 pounds over one year on therapy
- Common AEs: Injection site reactions, nausea and vomiting, increased hyperpigmentation
- Dosing: Once daily

Setmelanotide (continued...)

Competitive environment

Setmelanotide would potentially be the first FDA approved therapy for POMC and LEPR deficiency obesity. There is a high unmet need for treatments as the early-onset obesity with these deficiencies is very difficult to treat with traditional methods for weight loss. While the pivotal trials had study design limitations (eg, single-arm, small sample sizes), the topline weight loss results were promising.

The initial indication for setmelanotide is expected to be very narrow and POMC and LEPR deficiency obesity only accounts for up to 2,500 patients in the U.S. Rhythm is also studying setmelanotide in other rare genetic disorders of obesity, which are cumulatively estimated to affect upwards of 85,000 patients in the U.S. In addition, setmelanotide requires daily administration via SC injection, although a weekly formulation is also currently in development.

- Advantages: Potentially first FDA approved therapy for POMC/LEPR deficiency obesity, high unmet need, impressive weight loss results, also in development for other forms of rare obesity disorders
- Disadvantages: Narrow initial indication, SC administration

Berotralstat (Brand Name: To be determined)

Manufacturer: BioCryst Pharmaceuticals
Regulatory designations: Orphan Drug, Fast Track
Expected FDA decision: 12/3/2020

Therapeutic use

- Prevention of HAE attacks

Berotralstat is in development for the prevention of hereditary angioedema (HAE) attacks.

HAE is a rare inherited disorder characterized by recurrent episodes of the accumulation of fluids outside of the blood vessels and causing rapid swelling of tissues in the hands, feet, limbs, face, intestinal tract, or airway. Swelling of the airway may lead to obstruction, a potentially very serious complication. These symptoms or "attacks" develop as the result of deficiency or improper functioning of certain proteins that help to maintain the normal flow of fluids through the capillaries. The attacks are difficult to predict and vary from person to person. The most common forms of HAE (types I and II) are caused by deficiency or dysfunction in C1 inhibitor, a protein that prevents over production of bradykinin.

HAE affects an estimated 1 in 10,000 to 50,000 individuals worldwide. BioCryst estimates approximately 7,500 people are diagnosed and treated for HAE in the U.S.

Clinical profile

- Plasma kallikrein inhibitor
- Oral formulation
- Reduction of HAE attack rate: 30% to 44% vs. placebo
- Common AEs: Nausea, dyspepsia, diarrhea
- Dosing: Once daily

Berotralstat is an inhibitor of plasma kallikrein. During HAE attacks, unregulated activity of plasma kallikrein (because of the lack of C1 inhibitor) results in excessive bradykinin generation. Bradykinin is a vasodilator which is thought to be responsible for the characteristic HAE symptoms of localized swelling, inflammation, and pain.

Pivotal trial data:
The efficacy of berotralstat was evaluated in APeX-2, a randomized, double-blind, placebo-controlled, three-arm study in 121 patients with type I and II HAE. Patients received placebo or one of the two doses of berotralstat (110 mg and 150 mg). The primary endpoint was the rate of angioedema attacks over 24 weeks.

The mean baseline attack rate prior to randomization was 3 attacks per month. After 24 weeks treatment the attack rate per month was 1.31 with berotralstat 150 mg, 1.65 with berotralstat 110 mg, and 2.35 with placebo. Berotralstat met the primary endpoint for both dose levels, with the 150 mg dose reducing the attack rate in HAE patients by 44% ($p < 0.001$) vs. placebo and the 110 mg dose reducing HAE attack rate by 30% ($p = 0.024$) vs. placebo. In addition, 50% of patients receiving berotralstat 150 mg had a ≥ 70% reduction in their HAE attack rate compared to baseline, compared to 15% of placebo patients ($p = 0.002$).

Safety:
The most common adverse events with berotralstat use were nausea, dyspepsia, and diarrhea.

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

Berotralstat (continued...)

Competitive environment

If approved, berotralstat would be the first oral plasma kallikrein inhibitor for prevention of HAE attacks. For HAE prophylaxis, berotralstat would be primarily competing with C1 inhibitor concentrate products – Cinryze® and Haegarda®, and Takhzyro® (lanadelumab-flyo), a monoclonal antibody targeting plasma kallikrein. Cinryze requires IV administration and Haegarda is SC administered every 3 to 4 days. Takhzyro is also SC administered but it is dosed every 2 to 4 weeks.

Berotralstat would provide an advantage from a route of administration perspective; however, it would be a relatively late market entry and would compete in a crowded market with well-established therapies for a very rare condition. When compared indirectly, berotralstat seems to be less effective than the approved injectable alternatives. For instance, Takhzyro reached a much higher numerical reduction relative to placebo in the HAE attack rate (73% to 87% reduction).

For reference, the WAC price for Takhzyro is approximately $635,000 per year. While specific pricing for berotralstat has not yet been announced, it could be less expensive than the biologic alternatives currently used for HAE prophylaxis.

- Advantages: Potentially the first oral plasma kallikrein inhibitor for HAE prophylaxis, well tolerated, potentially less expensive vs. biologic therapies
- Disadvantages: Well established alternatives available, lower rates of HAE prevention vs. injectable alternatives (compared indirectly)
- Reference WAC (Takhzyro): ~$635,000 per year

Lumasiran (Brand Name: To be determined)

Manufacturer: Alnylam Pharmaceuticals
Regulatory designations: Orphan Drug, Breakthrough Therapy
Expected FDA decision: 12/3/2020

Therapeutic use

- Treatment of PH1

Lumasiran is in development for the treatment of primary hyperoxaluria type 1 (PH1).

PH1 is an ultra-rare disorder that mainly affects the kidneys. It results from excessive buildup of oxalate, which normally is filtered through the kidneys and excreted in the urine. In individuals with PH1, the accumulated oxalate combines with calcium, forming calcium oxalate crystals in the kidney and urinary tract. Renal damage is caused by a combination of tubular toxicity from oxalate, calcium oxalate deposition in the kidneys, and urinary obstruction by calcium oxalate stones. If untreated, PH1 can result in end-stage renal disease. When oxalate can no longer be eliminated in the urine, it accumulates in other organs such as the heart, blood vessels, joints, bones, and eyes.

The prevalence of PH1 is approximately 1 to 3 cases per 1 million people and it is estimated that over 40% of patients present with end-stage kidney disease at the time of diagnosis.

Clinical profile

- RNAi targeting HAO1
- SC formulation
- 24-hour urinary oxalate excretion: 65.4% mean reduction vs. 11.8% with placebo
- Common AEs: Injection site reactions, headache, rhinitis, and upper respiratory tract infection
- Dosing: Once monthly for 3 months followed by quarterly maintenance doses

Lumasiran is an RNA interference (RNAi) therapeutic targeting messenger RNA (mRNA) for hydroxyacid oxidase 1 *(HAO1)*. *HAO1* encodes glycolate oxidase (GO) and by silencing *HAO1* and depleting the GO enzyme, lumasiran inhibits production of oxalate - the metabolite that directly contributes to the pathophysiology of PH1.

<u>Pivotal trial data:</u>
The efficacy of lumasiran was evaluated in ILLUMINATE-A, a randomized, double-blind, placebo-controlled Phase 3 study in 39 children and adults with PH1. Patients received lumasiran or placebo. The primary endpoint was the percent change in 24-hour urinary oxalate excretion from baseline to the end of the trial (average of months 3 to 6).

Lumasiran treatment resulted in a 65.4% mean reduction in urinary oxalate relative to baseline vs. 11.8% with placebo (p = 1.7 x 1014). Approximately half (13/25) of the lumasiran-treated patients achieved urinary oxalate levels within the normal range vs. zero patients in the placebo arm (p = 0.001). At 6 months, the estimated glomerular filtration rate (eGFR) levels and renal stone events were comparable between the two treatment arms.

<u>Safety:</u>
The most common adverse events with lumasiran use were injection site reactions, headache, rhinitis, and upper respiratory tract infection. All injection site reactions were mild in severity and did not result in treatment interruption or discontinuation.

<u>Dosing:</u>
In the pivotal trial, lumasiran was administered SC once monthly for 3 months followed by quarterly maintenance doses.

Lumasiran (continued...)

Competitive environment

Lumasiran would potentially be the first FDA approved treatment for PH1. The current treatment approach emphasizes preventing kidney stones and includes staying hydrated, oral potassium citrate to inhibit calcium oxalate crystallization, and thiazide diuretics to decrease calcium in the urine. Vitamin B_6 is commonly used but is only effective in about 10% to 30% of patients. Patients with disease progression are also candidates for liver or kidney transplantation. Lumasiran demonstrated promising reductions in urinary oxalate and based on the currently available evidence, has a relatively positive safety profile.

Despite improvements in surrogate endpoints, lumasiran did not demonstrate an improvement in renal function or renal stone events. This may be due to the short-term nature of the pivotal trial, however further long-term data is needed to assess the true clinical benefit of lumasiran. In addition, the target population for lumasiran will be very small since PH1 is extremely rare and a subset of patients may respond to non-pharmacological treatment options.

For reference, the WAC price for Givlaari® (givosiran), another Alnylam RNAi therapeutic for an ultra-rare disease (acute hepatic porphyria), is approximately $575,000 per year.

- Advantages: Potentially first approved therapy for PH1, promising improvements in urinary oxalate and positive safety profile
- Disadvantages: Lack of long-term data, small target population
- Reference WAC (Givlaari): ~$575,000 per year

Relugolix (Brand Name: To be determined)

Manufacturer: Myovant Sciences
Expected FDA decision: 12/20/2020

Therapeutic use

- Treatment of advanced prostate cancer

Relugolix is in development for the treatment of men with advanced prostate cancer.

Prostate cancer is the second most common cancer in American men (skin cancer is number 1). The American Cancer Society estimates that in 2020, there will be 191,930 new cases of prostate cancer and about 33,330 deaths from prostate cancer.

Advanced prostate cancer is prostate cancer that has spread or come back after treatment and includes men with biochemical recurrence (in the absence of metastatic disease on imaging), locally advanced disease, or metastatic disease.

Clinical profile

- GnRH receptor antagonist
- Oral formulation
- Sustained testosterone suppression: 96.7% vs. 88.8% with leuprolide
- Common AEs: Hot flashes, fatigue, constipation, diarrhea, arthralgia
- Dosing: Once daily

Relugolix is a gonadotropin-releasing hormone (GnRH) receptor antagonist that reduces production of testicular testosterone. Hormone therapy or androgen deprivation therapy (ADT) is used in prostate cancer to reduce levels of androgens in the body, to stop them from fueling prostate cancer cells. Lowering androgen levels or stopping them from getting into prostate cancer cells often makes prostate cancers shrink or grow more slowly for a time.

Pivotal trial data:
The efficacy of relugolix was evaluated in HERO, a Phase 3, randomized, open-label, active-controlled study in 930 patients with advanced prostate cancer. Patients received oral relugolix or injectable leuprolide, a GnRH agonist, for 48 weeks. The primary endpoint was sustained testosterone suppression to castrate levels (< 50 ng/dL) through 48 weeks. In patients receiving relugolix, 96.7% maintained castration vs. 88.8% with patients receiving leuprolide (difference of 7.9; 95% CI: 4.1 to 11.8). Relugolix showed non-inferiority and superiority vs. leuprolide ($p < 0.001$ for superiority). All other key secondary endpoints showed superiority of relugolix over leuprolide ($p < 0.001$).

Safety:
The most common adverse events with relugolix use were hot flashes, fatigue, constipation, diarrhea, and arthralgia.

In addition, the incidence of major adverse cardiovascular events was 2.9% in the relugolix group and 6.2% in the leuprolide group (HR 0.46; 95% CI: 0.24 to 0.88).

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

Relugolix (continued...)

Competitive environment

If approved, relugolix would be the first oral GnRH receptor antagonist treatment for men with advanced prostate cancer. In the pivotal trial, relugolix demonstrated superiority for testosterone suppression vs. a commonly used GnRH agonist, leuprolide. GnRH agonists cause an initial testosterone surge that may result in a clinical flare of symptoms such as bone pain and obstructive urinary symptoms. Patients often require an antiandrogen agent for the first few weeks after initiation of GnRH agonists. This can be avoided with GnRH antagonists like relugolix but the only other one currently available is injectable Firmagon® (degarelix), which has had limited uptake in part because of injection site reactions. Relugolix demonstrated a better cardiovascular safety profile vs. leuprolide, which is notable because death from cardiovascular causes is the leading cause of death in patients with prostate cancer and accounts for up to 34% of deaths.

While relugolix does offer advantages vs. the current standard of care, it is entering a crowded marketplace with generic alternatives available. An analysis of the key secondary endpoint of castration resistance–free survival vs. leuprolide is ongoing.

Finally, a relugolix fixed-dose combination tablet (relugolix/estradiol/norethindrone acetate) is also in development for women with heavy menstrual bleeding associated with uterine fibroids. Myovant has submitted an application for this indication and an FDA decision is expected in the first half of 2021. It would be competing with AbbVie's GnRH antagonist combination product, Oriahnn (elagolix/estradiol/norethindrone acetate), which is also approved for uterine fibroids.

- Advantages: Potentially first oral GnRH receptor antagonist for prostate cancer, demonstrated superiority vs. leuprolide, also in development for uterine fibroids (as a fixed-dose combination tablet with estradiol and norethindrone acetate)
- Disadvantages: Generic alternatives available, lack of castration resistance-free survival data, competing with elagolix for potential uterine fibroid indication in the future

Roxadustat (Brand Name: To be determined)

Manufacturer: FibroGen/AstraZeneca
Expected FDA decision: 12/23/2020

Therapeutic use

Roxadustat is in development for the treatment of anemia of chronic kidney disease (CKD), in both non-dialysis-dependent (NDD) and dialysis-dependent (DD) patients.

Anemia is a common disease manifestation in patients with CKD, due primarily to reduced production of erythropoietin by the kidney. In the U.S., it is estimated that about 4.8 million individuals are affected with anemia associated with CKD. The prevalence of anemia is higher among patients with more severe forms of renal disease (eg, patients with stage 5 CKD and dialysis dependent patients). Anemia is associated with increased morbidity and mortality related to cardiovascular disease and an increased risk of hospitalization.

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

- Treatment of anemia of CKD, in both NDD and DD patients

Roxadustat (continued...)

Clinical profile

Roxadustat is a first-in-class hypoxia-inducible factor prolyl hydroxylase (HIF-PH) inhibitor. When oxygen levels decrease, HIF-PH enzyme activity decreases, resulting in the accumulation of HIF-α subunits and an increase in HIF transcriptional activity, which induces the expression of erythropoietin, erythropoietin receptors, and proteins that promote intestinal absorption of iron.

Roxadustat increases hemoglobin (Hb) levels by mimicking the body's natural response to low oxygen.

Pivotal trial data:
The efficacy of roxadustat was evaluated in six Phase 3 studies in CKD patients with anemia. The primary efficacy endpoint was the mean Hb change from baseline compared to placebo in patients not on dialysis and to an ESA (ie, epoetin alfa) in patients on dialysis.

In the pooled analysis of NDD patients (OLYMPUS, ANDES, ALPS trials; N = 4,277), roxadustat was statistically superior to placebo, demonstrating an improvement of 1.85 g/dL in patients' Hb levels from baseline to the average over 28 to 52 weeks vs. 0.13 g/dL among patients in the placebo arm, for an overall treatment difference of 1.72 g/dL ($p < 0.001$). The rate of rescue therapy (RBC transfusion, ESA, or IV iron) required in the first year of treatment among patients treated with roxadustat was 8.9% vs. 31.1% with placebo (HR 0.19; 95% CI: 0.16, 0.23; $p < 0.0001$).

In the pooled analysis of DD patients (HIMALAYAS, SIERRAS, and ROCKIES trials; N = 3,880), roxadustat was statistically superior to epoetin alfa, demonstrating an improvement of 1.22 g/dL in patients' Hb levels from baseline to the average over 28 to 52 weeks vs. 0.99 g/dL among patients in the epoetin alfa arm, for an overall treatment difference of 0.23 g/dL ($p < 0.0001$). The rate of RBC transfusions required in the first year of treatment was also lower with roxadustat (9.5%) than with epoetin alfa (12.8%) (HR 0.82; 95% CI: 0.679, 0.997; $p = 0.046$).

Safety:
The most common adverse events with roxadustat use were hyperkalemia and metabolic acidosis.

A pooled analysis of cardiovascular safety endpoints was conducted in both the NDD and DD patient populations. Endpoints included time to first major adverse cardiovascular event (MACE; defined as all-cause mortality, myocardial infarction, and stroke), MACE+ (includes MACE, unstable angina requiring hospitalization, and congestive heart failure requiring hospitalization), and all-cause mortality.

In the NDD patient population, risks of MACE, MACE+, and all-cause mortality in roxadustat patients were comparable to placebo based on a reference non-inferiority margin of 1.3. In the DD patient population, risks of MACE and all-cause mortality in roxadustat patients were not increased compared to those for patients receiving epoetin alfa based on a reference non-inferiority margin of 1.3. The risk of MACE+ was 14% lower in roxadustat-treated patients vs. epoetin alfa ($p = 0.028$).

Dosing:
In the pivotal trials, roxadustat was administered orally three times weekly.

- HIF-PH inhibitor
- Oral formulation
- Pooled analysis of NDD population: Hb improvement of 1.85 g/dL vs. 0.13 g/dL with placebo
- Pooled analysis of DD population: Hb improvement of 1.22 g/dL vs. 0.99 g/dL with epoetin alfa
- Common AEs: Hyperkalemia, metabolic acidosis
- Dosing: Three times weekly

Roxadustat (continued...)

Competitive environment

If approved, roxadustat would be the first novel therapy for the treatment of CKD-related anemia since the introduction of ESAs and would offer an oral alternative to injectable products. In the head-to-head trials vs. epoetin alfa in DD patients, roxadustat demonstrated slightly better improvements in Hb and roxadustat-treated patients required fewer RBC transfusions and less monthly IV iron use vs. epoetin alfa. A reduction in the need for iron supplementation would be advantageous as IV iron is associated with its own safety concerns and adverse events, including hypersensitivity reactions.

Roxadustat may be associated with an improved CV safety profile compared to ESAs, which have a boxed warning for increased risk of death, myocardial infarction, stroke, and venous thromboembolism. However, additional data is needed to assess the potential long-term risks of roxadustat for CV outcomes.

Roxadustat will be entering the market at a time when multiple biosimilars are now available for ESAs. Published studies in a Chinese population found that roxadustat was associated with higher rates of hyperkalemia and metabolic acidosis vs. placebo and ESAs, which is particularly concerning since CKD patients are predisposed to these adverse events. Finally, roxadustat may face future competition as other HIF-PH inhibitors are currently in development.

For reference, the WAC price for Procrit is approximately $1,500 per 30 days.

- Advantages: Novel MOA, oral administration, potential to reduce need for IV iron and may have a better cardiovascular adverse event profile vs. ESAs
- Disadvantages: Competing with ESAs – with biosimilars available, higher rates of hyperkalemia and metabolic acidosis vs. ESAs, unknown long-term safety, potential future competition
- Reference WAC (Procrit): ~$1,500 per 30 days

Inclisiran (Brand Name: To be determined)

Manufacturer: Novartis
Expected FDA decision: 12/2020

Therapeutic use

Inclisiran is in development for treatment of elevated low-density lipoprotein cholesterol (LDL-C) in patients with atherosclerotic cardiovascular disease (ASCVD) and familial hypercholesterolemia (FH). FH is caused by genetic mutations that impact breakdown of LDL-C and patients can have one copy (heterozygous) or two copies (homozygous) of the genetic defect.

An estimated 29.1 million people are affected with ASCVD and FH in the U.S. Of these patients, about 22.0 million are treated with oral lipid lowering therapies.

- Treatment of elevated LDL-C in patients with ASCVD and FH

Clinical profile

Inclisiran is an RNA interfering (RNAi) therapeutic agent that interferes with the production of proprotein convertase subtilisin–kexin type 9 (PCSK9). Reduction in PCSK9 leads to higher LDL receptor levels in the liver, and subsequently lower LDL-C levels.

- RNAi targeting PCSK9
- SC formulation
- Placebo-corrected percentage change in LDL-C (at day 510): 47.9% to 52.3%
- Time-adjusted percentage change in LDL-C (after day 90 and up to day 540): 44.3% to 53.8%
- Common AE: Injection-site adverse events
- Maintenance dose: Once every 6 months

<u>Pivotal trial data:</u>
The efficacy of inclisiran was evaluated in three pivotal trials: ORION-9, ORION-10, and ORION-11.

ORION-9 was a Phase 3, randomized, double-blind, placebo-controlled study in 482 adults who had heterozygous familial hypercholesterolemia (HeFH). At day 510, the percent change in the LDL-C level was a reduction of 39.7% in the inclisiran group vs. an increase of 8.2% in the placebo group (difference 47.9; 95% CI: -53.5, -42.3; $p < 0.001$). The time-averaged percent change in the LDL-C level between day 90 and day 540 was a reduction of 38.1% in the inclisiran group and an increase of 6.2% in the placebo group (difference -44.3; 95% CI: -48.5, -40.1; $p < 0.001$).

ORION-10 and ORION-11 were Phase 3, randomized, double-blind, placebo-controlled studies in patients with ASCVD (ORION-10; N = 1,561) and patients with ASCVD or an ASCVD risk equivalent (ORION-11; N = 1,617) who had elevated LDL-C levels despite receiving statin therapy at the maximum tolerated dose. In the ORION-10 study at day 510, the percent change in the LDL-C level was a reduction of 51.3% vs. an increase of 1.0% in the placebo group (difference -52.3; 95% CI: -55.7, -48.8; $p < 0.001$). The time-averaged percent change in the LDL-C level between day 90 and day 540 was a reduction of 51.3% with inclisiran vs. an increase of 2.5% with placebo (difference -53.8; 95% CI: -56.2, -51.3; $p < 0.001$).

In the ORION-11 study at day 510, the percent change in the LDL-C level was a reduction of 45.8% vs. an increase of 4.0% in the placebo group (difference -49.9; 95% CI: -53.1, -46.6; $p < 0.001$). The time-averaged percent change in the LDL-C level between day 90 and day 540 was a reduction of 45.8% with inclisiran vs. an increase of 3.4% with placebo (difference -49.2; 95% CI: -51.6, -46.8; $p < 0.001$).

<u>Safety:</u>
The most common adverse event with inclisiran use was injection-site adverse events.

<u>Dosing:</u>
In the pivotal trials, inclisiran was administered SC on day 1, day 90, and every 6 months thereafter.

Inclisiran (continued...)

Competitive environment

If approved, inclisiran would provide an additional PCSK9 targeted therapy for the reduction of LDL-C. Inclisiran has a unique mechanism action compared to Repatha® (evolocumab) and Praluent® (alirocumab), which are monoclonal antibodies that inhibit PCSK9. The primary advantage for inclisiran is that it can be administered every 6 months whereas Repatha and Praluent have to be SC administered every 2 to 4 weeks.

Inclisiran would be a relatively late market entry as both Repatha and Praluent have been available since 2015. While inclisiran does have a favorable dosing schedule, it will likely require administration by a healthcare provider whereas Repatha and Praluent can be self-administered. In addition, inclisiran' s long-term cardiovascular outcomes trial (ORION-4) is ongoing and topline results are not expected until 2024. In the absence of cardiovascular outcomes data, healthcare providers may be reluctant to switch to inclisiran from other cholesterol lowering therapies, including the PCSK9 monoclonal antibodies.

For reference, the WAC price for Repatha and Praluent is approximately $5,850 per year.

- Advantages: Administration every 6 months (fewer annual injections)
- Disadvantages: Late market entry, likely requires healthcare provider administration, lack of cardiovascular outcomes data
- Reference WAC (Repatha/ Praluent): ~$5,850 per year

Tanezumab (Brand Name: To be determined)

Manufacturer: Pfizer/Eli Lilly
Regulatory designations: Fast Track
Expected FDA decision: 12/2020

Therapeutic use

Tanezumab is in development for the treatment of patients with chronic pain due to moderate-to-severe osteoarthritis (OA) who have experienced inadequate pain relief with other analgesics.

OA is a degenerative joint disease that is caused by damage or breakdown of joint cartilage between bones. OA can cause pain, stiffness, and swelling. In some cases, it also causes reduced function and disability and patients may no longer be able to do daily tasks or work.

OA occurs most frequently in the hands, hips, and knee and it is estimated to affect over 32.5 million U.S. adults. About 11 million people are estimated to have moderate-to-severe OA.

- Treatment of patients with chronic pain due to moderate-to-severe OA who have experienced inadequate pain relief with other analgesics

Tanezumab (continued...)

Clinical profile

Tanezumab is a monoclonal antibody that works by selectively targeting, binding to and inhibiting nerve growth factor (NGF). NGF levels increase in the body as a result of injury, inflammation or in chronic pain states. By inhibiting NGF, tanezumab may help to keep pain signals produced by muscles, skin and organs from reaching the spinal cord and brain.

Pivotal trial data:

The efficacy of a SC administered formulation of tanezumab for moderate-to-severe OA was evaluated in three Phase 3 studies. The first study was a 16-week, randomized, double-blind, placebo-controlled trial in 698 patients with OA of the knee or hip. Patients were randomized to placebo, tanezumab 2.5 mg every eight weeks, or tanezumab 2.5 mg followed by one dose of tanezumab 5 mg eight weeks later. Three co-primary endpoints were used: The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain subscale, the WOMAC Physical Function subscale, and the Patient Global Assessment (PGA) of their OA. The WOMAC Pain and Physical Function subscales utilizes an 11-point numerical rating scale and the PGA-OA utilizes a 5-point numerical rating of the patient's condition, where 1 equals 'very good' and 5 equals 'very poor'.

The difference between tanezumab 2.5 mg vs. placebo in LS mean change in WOMAC pain score was -0.60 points ($p = 0.0129$) and the difference between tanezumab 2.5 mg/5 mg vs. placebo was -0.73 points ($p = 0.0023$). The difference between tanezumab 2.5 mg and tanezumab 2.5 mg/5 mg vs. placebo in mean change in WOMAC physical function score was -0.66 points ($p = 0.0065$) and -0.89 points ($p = 0.0002$), respectively. The difference between tanezumab 2.5 mg and tanezumab 2.5 mg/5 mg vs. placebo in mean change in PGA-OA score was -0.22 points ($p = 0.0109$) and -0.25 points ($p = 0.0038$), respectively.

The second study was a 24-week, randomized, double-blind, placebo-controlled trial in 849 patients. Patients were randomized to tanezumab 2.5 mg or 5 mg or placebo every 8 weeks (three doses). The co-primary endpoints were the same as study 1. At week 24, there was a statistically significant improvement from baseline for tanezumab 5 mg vs. placebo for WOMAC pain (LS mean difference -0.62; $p = 0.0006$), WOMAC physical function (LS mean difference -0.71; $p < 0.0001$), and PGA-OA (LS mean difference -0.19; $p = 0.0051$). For the tanezumab 2.5 mg arm, there was a statistically significant improvement in WOMAC pain (-0.46; $p = 0.0088$) and WOMAC physical function (-0.59; $p = 0.0008$), but not PGA-OA (-0.11; $p = 0.1092$).

The third study was a 56-week, randomized, double-blind, active-controlled trial in 3,021 patients. Patients were randomized to tanezumab 2.5 mg or 5 mg every eight weeks or oral NSAIDs (ie, naproxen, celecoxib, or diclofenac). The tanezumab 5 mg treatment arm met two of the three co-primary efficacy endpoints, demonstrating a statistically significant improvement in WOMAC pain and physical function compared to NSAIDs at the 16-week analysis, while patients' PGA-OA was not statistically different than NSAIDs. Patients who received tanezumab 2.5 mg did not experience a statistically significant improvement in any of the endpoints at 16 weeks vs. NSAIDs.

- NGF inhibitor
- SC formulation
- Statistically significant improvement in WOMAC pain and function vs. placebo
- Common AEs: Nasopharyngitis, pain in extremity, paresthesia
- Dosing: Every 8 weeks

Tanezumab (continued...)

Safety:
The most common adverse events with tanezumab use were nasopharyngitis, pain in extremity, and paresthesia.

Across the clinical trials, tanezumab was associated with joint safety events and rapidly progressive osteoarthritis (RPOA). For example, in the safety analysis of the third study, there was a higher rate of joint safety events in the tanezumab arms vs. NSAIDs at 80 weeks (7.1% in the tanezumab 5 mg arm, 3.8% in the tanezumab 2.5 mg arm and 1.5% in the NSAIDs arm; $p < 0.05$ for both tanezumab arms vs. NSAIDs). RPOA accounted for the majority of events observed in the composite joint safety endpoint. The incidence of RPOA was 6.3% in the tanezumab 5 mg arm, 3.2% in the tanezumab 2.5 mg arm and 1.2% in the NSAIDs arm. The incidence of total joint replacement was 8.0% in the tanezumab 5 mg arm, 5.3% in the tanezumab 2.5 mg arm and 2.6% in the NSAIDs arm.

Dosing:
In the pivotal trials, tanezumab was administered SC every 8 weeks.

Competitive environment

If approved, tanezumab would offer a novel MOA for the treatment of OA. OA is one of the most common chronic conditions in the U.S. and there are a lack of effective treatment options in patients who fail conventional pharmacological such as acetaminophen and NSAIDs. Tanezumab could be an alternative in patients who are difficult to treat and also reduce the need for opioids which are often used for OA despite safety concerns and risks of abuse and addiction.

However, the use of tanezumab has several limitations and concerns. Most notably, NGF inhibitors have been in development for many years but have none have come to market because of lingering safety concerns. The clinical program for an IV formulation of tanezumab was put on hold back in 2010 due to joint safety events. This eventually led to the development of a SC formulation at lower dosages but the most recent pivotal trials still indicate an increased risk of joint safety events and a higher rate of total joint replacement surgery. Due to these concerns, Pfizer and Eli Lilly are only pursuing the 2.5 mg strength of SC tanezumab. While this lower strength has been shown to be more effective than placebo, the numerical improvements are modest and it was not shown to be superior to NSAIDs.

The safety concerns and modest efficacy will likely result in tanezumab being reserved as a backline treatment option for OA and it is expected to require administration by a healthcare provider. Its use will also be further limited by the fact that it cannot be used as an add-on to NSAIDs because of increased adverse events that were reported in earlier studies with combination use of tanezumab plus NSAIDs.

- Advantages: Novel MOA for OA, large target population, potential alternative to opioids
- Disadvantages: Safety concerns (joint safety events, higher rate of joint replacement surgery), modest efficacy, SC administration, cannot be administered with NSAIDs

3rd Quarter 2020

Extended generic pipeline forecast

OptumRx generic pipeline forecast

Brand name	Generic name	Brand manufacturer	Dosage form	Strengths available as generic	Possible launch date
2020 Possible launch date					
CUVPOSA	glycopyrrolate	Merz	Oral solution	All	2020
PREPOPIK	citric acid/magnesium oxide/sodium picosulfate	Ferring Pharmaceuticals	Oral solution	All	2020
DESONATE	desonide	LEO Pharma	Gel	All	2020
SUPRENZA	phentermine	Citius/Akrimax	Tablet, orally disintegrating	All	2020
VIVLODEX	meloxicam	Iroko/iCeutica	Capsule	All	2020
PRESTALIA	perindopril/amlodipine	Symplmed	Tablet	All	2020
SAMSCA	tolvaptan	Otsuka	Tablet	All	2020
FERRIPROX	deferiprone	ApoPharma/Apotex	Tablet	All	2020
RESTASIS	cyclosporine	Allergan	Ophthalmic	All	2020
OMNARIS	ciclesonide	Covis	Intranasal	All	2020
THALOMID	thalidomide	Celgene	Capsule	All	2020
CIPRODEX	ciprofloxacin/dexamethasone	Alcon	Otic	All	2020
DORYX MPC	doxycycline hyclate	Mayne	Tablet, delayed-release	All	2020
SYNDROS	dronabinol	Insys Therapeutics	Oral solution	All	2020
DUREZOL	difluprednate	Alcon	Ophthalmic	All	2020
BYETTA	exenatide	AstraZeneca	Subcutaneous	All	2020
MOVIPREP	PEG-3350/sodium sulfate/sodium chloride/potassium chloride/sodium ascorbate/ascorbic acid	Salix/Bausch Health	Oral solution	All	2020
ULTRAVATE	halobetasol	Sun	Lotion	All	2020
ADRENALIN	epinephrine	Par/Endo	Intramuscular	All	2020
APTENSIO XR	methylphenidate	Rhodes	Capsule, extended-release	All	1H-2020
DEPO-SUBQ PROVERA	medroxyprogesterone	Pfizer	Subcutaneous	All	05-2020
NYMALIZE	nimodipine	Arbor	Oral solution	All	05-2020
LANTUS	insulin glargine	Sanofi	Subcutaneous	All	06-2020
ENTEREG	alvimopan	Merck	Capsule	All	2H-2020

Brand name	Generic name	Brand manufacturer	Dosage form	Strengths available as generic	Possible launch date
TIROSINT	levothyroxine	IBSA Institut Biochemique	Capsule	All	2H-2020
ENBREL	etanercept	Amgen	Subcutaneous	All	2H-2020
KORLYM	mifepristone	Corcept	Tablet	All	2H-2020
SYNERA	lidocaine/tetracaine	Galen	Transdermal patch	All	07-2020
PEGASYS	peginterferon alfa-2A	Roche	Subcutaneous	All	08-2020
PEG-INTRON	peginterferon alfa-2B	Merck	Subcutaneous	All	08-2020
POMALYST	pomalidomide	Celgene	Capsule	All	08-2020
MARQIBO KIT	vincristine	Talon Therapeutics/Spectrum	Intravenous	All	09-2020
TYKERB	lapatinib	Novartis	Tablet	All	09-2020
BIDIL	isosorbide dinitrate/hydrazaline	Arbor	Tablet	All	09-2020
TRUVADA	emtricitabine/tenofovir	Gilead	Tablet	200 mg/300 mg	09-2020
ATRIPLA	efavirenz/emtricitabine/ tenofovir	Gilead	Tablet	All	09-2020
KUVAN	sapropterin	BioMarin	Tablet; oral solution	All	10-2020
RISPERDAL CONSTA	risperidone	Janssen	Injection, extended-release	All	11-2020
XOLEGEL	ketoconazole	Almirall	Gel	All	11-2020
EPIDUO FORTE	adapalene/benzoyl peroxide	Galderma	Gel	All	12-2020
OFIRMEV	acetaminophen	Mallinckrodt	Intravenous	All	12-2020
ABSORICA	isotretinoin	Sun	Capsule	All	12-2020
TOVIAZ	fesoterodine	Pfizer	Tablet, extended-release	All	12-2020
DALIRESP	roflumilast	AstraZeneca	Tablet	All	12-2020
DEXILANT	dexlansoprazole	Takeda	Capsule, delayed-release	All	12-2020
VELPHORO	sucroferric oxyhydroxide	Fresenius	Tablet, chewable	All	12-2020
SAPHRIS	asenapine	Allergan	Tablet, sublingual	All	12-2020
FORTEO	teriparatide	Eli Lilly	Injection	All	12-2020
2021 Possible launch date					
BEPREVE	bepotastine	Bausch Health	Ophthalmic	All	2021
KERYDIN	tavaborole	Pfizer	Topical solution	All	2021
EMTRIVA	emtricitabine	Gilead	Capsule	All	1H-2021
AMITIZA	lubiprostone	Sucampo/Takeda	Capsule	All	01-2021
CRIXIVAN	indinavir	Merck	Capsule	All	02-2021
NORTHERA	droxidopa	H. Lundbeck	Capsule	All	02-2021

Brand name	Generic name	Brand manufacturer	Dosage form	Strengths available as generic	Possible launch date
MYALEPT	metreleptin	Aegerion	Subcutaneous	All	02-2021
FORTICAL	calcitonin salmon recombinant	Upsher-Smith	Intranasal	All	02-2021
YONSA	abiraterone	Sun	Tablet	All	03-2021
IMPAVIDO	miltefosine	Knight Therapeutics	Capsule	All	03-2021
ACTOPLUS MET XR	pioglitazone/metformin	Takeda	Tablet, extended-release	All	03-2021
OVIDREL	choriogonadotropin	EMD Serono/Merck	Intramuscular; subcutaneous	All	03-2021
NEUPRO	rotigotine	UCB	Transdermal patch	All	03-2021
LYRICA CR	pregabalin	Pfizer	Tablet, extended-release	All	04-2021
ERAXIS	anidulafungin	Pfizer	Intravenous	All	04-2021
ZOMIG	zolmitriptan	Impax/Grunenthal	Intranasal	All	05-2021
PERFOROMIST	formoterol fumarate	Mylan	Inhalation	All	06-2021
APTIOM	eslicarbazepine	Sunovion/Bial	Tablet	All	06-2021
INTELENCE	etravirine	Janssen	Tablet	All	06-2021
FLOVENT HFA	fluticasone propionate	GlaxoSmithKline	Inhalation	All	2H-2021
TECFIDERA	dimethyl fumarate	Biogen	Tablet	All	2H-2021
FERAHEME	ferumoxytol	AMAG Pharmaceuticals	Intravenous	All	07-2021
RESCULA	unoprostone isopropyl	R-Tech Ueno	Ophthalmic	All	07-2021
ALTRENO	tretinoin	Bausch Health	Lotion	All	08-2021
BALCOLTRA	levonorgestrel/ethinyl estradiol/ferrous bisglycinate	Avion	Tablet	All	08-2021
SUTENT	sunitinib	Pfizer	Capsule	All	08-2021
SELZENTRY	maraviroc	ViiV Healthcare	Tablet	All	08-2021
JEVTANA KIT	cabazitaxel	Sanofi	Intravenous	All	09-2021
BYSTOLIC	nebivolol	Allergan	Tablet	All	09-2021
PRADAXA	dabigatran etexilate mesylate	Boehringer Ingelheim	Capsule	All	4Q-2021
INNOPRAN XL	propranolol	Ani Pharmaceuticals	Capsule, extended-release	All	10-2021
MIRCERA	methoxy polyethylene glycol-epoetin beta	Roche/Royalty Pharma	Subcutaneous	All	11-2021
BROVANA	arformoterol	Sunovion	Inhalation	All	11-2021
ONEXTON	clindamycin/benzoyl peroxide	Bausch Health	Gel	All	12-2021
EPANED KIT	enalapril	Silvergate	Oral solution	All	12-2021
CHANTIX	varenicline	Pfizer	Tablet	All	12-2021

Brand name	Generic name	Brand manufacturer	Dosage form	Strengths available as generic	Possible launch date
CAYSTON	aztreonam lysine	Gilead	Inhalation	All	12-2021
BETHKIS	tobramycin	Chiesi	Inhalation	All	12-2021
MYTESI	crofelemer	Napo	Tablet, delayed-release	All	12-2021
EXPAREL	bupivacaine	Pacira	Injection	All	12-2021
SUPREP BOWEL PREP KIT	magnesium sulfate anhydrous/potassium sulfate / sodium sulfate	Braintree	Oral solution	All	12-2021
AFINITOR DISPERZ	everolimus	Novartis	Oral suspension	All	12-2021
2022 Possible launch date					
PREZISTA	darunavir	Janssen	Tablet	75 mg, 150 mg, 300 mg	2022
SOLIRIS	eculizumab	Alexion	Intravenous	All	1H-2022
NATPARA	parathyroid hormone 1-84	NPS/Nycomed	Subcutaneous	All	01-2022
NPLATE	romiplostim	Amgen	Subcutaneous	All	01-2022
OXAYDO	oxycodone	Egalet	Tablet	All	01-2022
VIMPAT	lacosamide	UCB	Intravenous; tablet; oral solution	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	Celgene	Capsule	All	03-2022
ARESTIN	minocycline hydrochloride	Bausch Health	Subgingival, sustained-release	All	03-2022
MAVENCLAD	cladribine	Serono	Tablet	All	03-2022
LEXISCAN	regadenoson	Astellas	Intravenous	All	04-2022
COMBIGAN	brimonidine/timolol	Allergan	Ophthalmic	All	04-2022
TEFLARO	ceftaroline fosamil	Allergan	Intravenous	All	04-2022
ZOLADEX	goserelin	TerSera Therapeutics	Subcutaneous	All	04-2022
DUOBRII	halobetasol propionate/tazarotene	Bausch Health	Lotion	All	04-2022
BANZEL	rufinamide	Eisai	Tablet; oral suspension	All	05-2022
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

Brand name	Generic name	Brand manufacturer	Dosage form	Strengths available as generic	Possible launch date
VIIBRYD	vilazodone	Forest/Allergan	Tablet	All	06-2022
ELESTRIN	estradiol	Mylan	Gel	All	06-2022
QBRELIS	lisinopril	Silvergate	Oral solution	All	06-2022
BIJUVA	estradiol/progesterone	TherapeuticsMD	Capsule	All	2H-2022
IRESSA	gefitinib	AstraZeneca	Tablet	All	07-2022
EYLEA	aflibercept	Regeneron	Intraocular	All	07-2022
ACTEMRA	tocilizumab	Roche/Chugai	Intravenous; subcutaneous	All	07-2022
EVAMIST	estradiol	Perrigo/Elan	Transdermal solution	All	07-2022
IXEMPRA Kit	ixabepilone	R-Pharm	Intravenous	All	07-2022
VOSEVI	sofosbuvir/velpatasvir/ voxilaprevir	Gilead	Tablet	All	07-2022
VIBATIV	telavancin	Theravance	Intravenous	All	08-2022
SOLOSEC	secnidazole	Symbiomix Therapeutics	Oral granules	All	09-2022
ORAVIG	miconazole	Midatech/R-Pharm	Tablet, buccal	All	09-2022
HALFLYTELY with BISACODYL	bisacodyl / polyethylene glycol 3350, potassium chloride, sodium bicarbonate, sodium chloride	Braintree	Tablet/oral solution	All	10-2022
ORENCIA	abatacept	Bristol-Myers Squibb	Intravenous; subcutaneous	All	11-2022
XERESE	acyclovir/hydrocortisone	Bausch Health	Cream	All	11-2022
NAGLAZYME	galsulfase	BioMarin	Intravenous	All	11-2022
FOLOTYN	pralatrexate	Acrotech/Aurobindo	Intravenous	All	11-2022
NASCOBAL	cyanocobalamin	Par/Endo	Intranasal	All	12-2022
MYRBETRIQ	mirabegron	Astellas	Tablet, extended-release	All	12-2022
DYLOJECT	diclofenac	Hospira/Pfizer/Javelin	Intravenous	All	12-2022
RAYOS	prednisone	Horizon	Tablet, delayed-release	All	12-2022
TREANDA	bendamustine	Cephalon/Teva	Intravenous	All	12-2022
ZIOPTAN	tafluprost	Akorn	Ophthalmic	All	12-2022
SEGLUROMET	ertugliflozin/metformin	Merck	Tablet	All	12-2022

+ = may launch during the stated date or later

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
2020 Possible launch date									
DBV-712 (Viaskin Peanut)	DBV-712	DBV Technologies	Immunotherapy	Peanut allergy	TOP	Filed BLA	8/5/2020	No	No
TRV-130	oliceridine	Trevena	opioid receptor agonist	Pain	IV	Filed NDA	8/7/2020	Yes	No
KTE-X19	brexucabtagene autoleucel	Gilead	chimeric antigen receptor (CAR) T cell therapy	Mantle cell lymphoma	IV	Filed BLA	8/10/2020	Yes	Yes
EM-100	ketotifen	Eton/ Bausch Health	antihistamine	Allergic conjunctivitis	OP	Filed NDA	8/10/2020	No	No
Pedmark (STS)	sodium thiosulfate	Fennec	reducing agent	Ototoxicity	IV	Filed NDA	8/10/2020	Yes	Yes
SA-237 (RG-6168)	satralizumab	Roche	interleukin-6 (IL-6) monoclonal antibody	Neuromyelitis optica spectrum disorder	SC	Filed BLA	8/15/2020	Yes	Yes
GSK-2857916	belantamab mafodotin	GlaxoSmithKline/ Seattle Genetics	anti-BCMA antibody-drug conjugate	Multiple myeloma	SC	Filed BLA	8/16/2020	Yes	Yes
GLPG-0634	filgotinib	Gilead/ Galapagos	janus associated kinase-1 (JAK) inhibitor	Rheumatoid arthritis	PO	Filed NDA	8/18/2020	Yes	No
BMN-270	valoctocogene roxaparvovec	BioMarin	gene therapy	Hemophilia A	IV	Filed BLA	8/21/2020	Yes	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
TRC-101	veverimer	Tricida	carrier protein modulator	Chronic kidney disease	PO	Filed NDA	8/22/2020	Yes	No
RG-7916 (RO-7034067)	risdiplam	Roche/ PTC Therapeutics	SMN2 splicing modifier	Spinal muscular atrophy	PO	Filed NDA	8/24/2020	Yes	Yes
XaraColl	bupivacaine implant	Innocoll	sodium channel blocker	Pain	implant	Filed NDA	8/26/2020	Yes	No
Winlevi	clascoterone	Cassiopea	androgen antagonist	Acne vulgaris	TOP	Filed NDA	8/27/2020	No	No
Tlando	testosterone	Lipocine	androgen	Hypogonadism	PO	Filed NDA	8/28/2020	No	No
MOR-208	tafasitamab	MorphoSys	CD-19 antagonist	Diffuse large B-cell lymphoma	IV	Filed BLA	8/30/2020	Yes	Yes
CC-486	azacitidine	Bristol Myers Squibb/ Celgene	DNA methylation inhibitor	Acute myeloid leukemia	PO	Filed NDA	9/3/2020	Yes	Yes
Lucassin	terlipressin	Mallinckrodt	V-1 (vasopressin) agonist	Hepato-renal syndrome	IV	Filed BLA	9/12/2020	Yes	Yes
NNC-0195-0092 (NN-8640)	somapacitan	Novo Nordisk	recombinant human growth hormone (rhGH)	Growth hormone deficiency	SC	Filed BLA	9/21/2020	Yes	No
LJPC-0118	artesunate	La Jolla Pharmaceutical	protozoacide	Malaria	Undisclosed	Filed NDA	9/25/2020	No	Yes
Libervant	diazepam	Aquestive Therapeutics	benzodiazepine	Seizures	SL/ Transmucosal	Filed NDA	9/27/2020	No	Yes
Prochymal	remestemcel-L	Mesoblast	mesenchymal stem cells	Graft vs. Host disease	IV	Filed BLA	9/30/2020	Yes	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
Infacort	hydrocortisone	Diurnal Group	corticosteroid	Adrenal insufficiency	PO	Filed NDA	9/29/2020	No	Yes
NS-065 (NCNP-01)	viltolarsen	Nippon Shinyaku	morpholino antisense oligonucleotide	Duchenne muscular dystrophy	IV	Filed BLA	3Q2020	Yes	Yes
OMB-157	ofatumumab	Novartis/ Genmab	CD20 monoclonal antibody	Multiple sclerosis	SC	Filed BLA	9/2020	Yes	No
tramadol	tramadol	Avenue Therapeutics	opioid receptor agonist	Pain	IV	Filed NDA	10/9/2020	No	No
Qtrypta	zolmitriptan	Zosano	triptans	Acute migraines	TOP	Filed NDA	10/20/2020	No	No
SPI-2012	eflapegrastim	Spectrum	granulocyte colony-stimulating factor (GCSF)	Neutropenia	SC	Filed BLA	10/24/2020	Yes	No
REGN-EB3	REGN-EB3	Regeneron	anti-Ebola virus	Ebola	IV	Filed BLA	10/25/2020	Yes	Yes
KPI-121 0.25%	loteprednol etabonate	Kala Pharmaceuticals	corticosteroid	Dry eyes	OP	Filed NDA	10/30/2020	No	No
Bronchitol	mannitol	Pharmaxis	osmotic gradient enhancer; mucus clearance enhancer	Cystic fibrosis	INH	Filed NDA	11/1/2020	No	Yes
SPN-812	viloxazine	Supernus Pharmaceuticals	selective norepinephrine reuptake inhibitor	Attention deficit hyperactivity disorder	PO	Filed NDA	11/8/2020	No	No
BIVV-009 (TNT-009)	sutimlimab	Sanofi	complement C1s subcomponent inhibitor	Cold agglutinin disease	IV	Filed BLA	11/13/2020	Yes	Yes
AR-19	amphetamine	Arbor Pharmaceuticals	CNS stimulant	Attention-deficit/hyperactivity disorder	PO	Filed NDA	11/15/2020	No	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
ALKS-3831	olanzapine/ samidorphan	Alkermes	dopamine receptor antagonist/ opioid receptor antagonist	Schizophrenia/ Bipolar disorder	PO	Filed NDA	11/15/2020	No	No
Zimhi	naloxone	Adamis	opioid antagonist	Opioid overdose	IM	Filed NDA	11/15/2020	No	No
JCAR-017	lisocabtagene maraleucel	Bristol-Myers Squibb/ Celgene	chimeric antigen receptor (CAR) T cell therapy	Diffuse large B-cell lymphoma	IV	Filed BLA	11/16/2020	Yes	Yes
EBP-994 (rEBP-994; Sarasar)	lonafarnib	Eiger Biopharmaceuticals	prenylation inhibitor	Progeria and progeroid laminopathies	PO	Filed NDA	11/20/2020	Yes	Yes
BLU-667	pralsetinib	Blueprint Medicines	RET inhibitor	Non-small cell lung cancer	PO	Filed NDA	11/23/2020	Yes	Yes
LIQ-861	treprostinil	Liquidia Technologies	prostacyclin analog	Pulmonary arterial hypertension	INH	Filed NDA	11/24/2020	Yes	No
RT-002 (Daxi)	daxibotulinumtoxinA	Revance Therapeutics	botulinum toxins	Glabellar lines (frown lines)	IM	Filed BLA	11/25/2020	Yes	No
BIM-22493 (RM-493)	setmelanotide	Rhythm Pharmaceuticals	melanocortin 4 receptor (MC4R) agonist	Rare genetic disorders of obesity	SC	Filed NDA	11/27/2020	Yes	Yes
3-F8 (Hu-3F8)	naxitamab	Y-mAbs Therapeutics	GD2 antagonist	Neuroblastoma	IV	Filed BLA	11/30/2020	Yes	Yes
nifurtimox	nifurtimox	Bayer	anti-parasitic, anti-protozoal	Chagas disease	PO	Filed NDA	11/30/2020	No	Yes
CAM-2038	buprenorphine	Braeburn	opioid receptor agonist (partial)	Opioid use disorder/ Pain	SC	Tentative Approval	12/1/2020	Yes	No
ALNG-01 (ALN-G-01)	lumasiran	Alnylam	glycolate oxidase antagonist	Hyperoxaluria	SC	Filed NDA	12/3/2020	Yes	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
BCX-7353	berotralstat	BioCryst	kallikrein inhibitor	Hereditary angioedema	PO	Filed NDA	12/3/2020	Yes	Yes
MAGH-22	margetuximab	MacroGenics	HER2 oncoprotein antagonist	Breast cancer	IV	Filed BLA	12/18/2020	Yes	No
TAK-385	relugolix	Myovant Sciences	gonadotropin-releasing hormone (GnRH) receptor antagonist	Prostate cancer/ uterine fibroids	PO	Filed NDA	12/20/2020	Yes	No
FG-4592 (ASP-1517)	roxadustat	FibroGen/ AstraZeneca	hypoxia-inducible factor prolyl hydroxylase (HIF-PH) inhibitor	Anemia	PO	Filed NDA	12/23/2020	Yes	No
LY-03005	ansofaxine	Luye Pharma	serotonin-norepinephrine-dopamine triple reuptake inhibitor	Major depressive disorder	PO	Filed NDA	12/26/2020	No	No
MK-4618 (KRP-114V, RVT-901)	vibegron	Urovant Sciences	selective beta 3 adrenergic receptor agonist	Overactive bladder	PO	Filed NDA	12/26/2020	No	No
tanezumab	tanezumab	Pfizer/ Eli Lilly	nerve growth factor (NGF) inhibitor	Osteoarthritis	SC	Filed BLA	12/2020	Yes	No
ALN-PCSsc (PCSK9si)	inclisiran	Novartis	RNA interfering therapeutic targetting proprotein convertase subtilisin–kexin type 9 (PCSK9)	Hyperlipidemia	SC	Filed NDA	12/2020	Yes	Yes
Leukotac	inolimomab	ElsaLys Biotech	IL-2 monoclonal antibody	Graft vs. host disease	IM	Filed BLA	4Q2020	Yes	Yes
Ontinua ER	arbaclofen extended-release	Osmotica	muscle relaxant	Multiple sclerosis	PO	Filed NDA	12/29/2020	Yes	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
Furoscix	furosemide	scPharmaceuticals	diuretic	Heart failure	SC	Filed NDA	12/30/2020	Yes	No
Ygalo (Melflufen)	melphalan-flufenamide	Oncopeptides AB	alkylating agent/ DNA synthesis inhibitor	Multiple myeloma	IV	Filed NDA	12/30/2020	No	Yes
ET-105	lamotrigine	Eton	anticonvulsant	Epilepsy	PO	CRL	Late 2020	No	No
2021 Possible launch date									
TSR-042	dostarlimab	GlaxoSmithKline	PD-1 checkpoint inhibitor	Endometrial cancer	IV	Filed BLA	1/14/2021	Yes	No
BAY-1021189 (MK-1242)	vericiguat	Merck/ Bayer	guanylate cyclase stimulator	Heart failure	PO	Filed NDA	1/20/2021	Yes	No
Luveniq	voclosporin	Aurinia Pharmaceuticals	calcineurin inhibitor	Lupus nephritis	PO	Filed NDA	1/22/2021	Yes	No
PRX-102	pegunigalsidase alfa	Protalix	enzyme replacement	Fabry disease	IV	Filed BLA	1/27/2021	Yes	No
ropeginterferon alfa-2b	ropeginterferon alfa-2b	PharmaEssentia	interferon	Polycythemia vera	SC	Filed BLA	Early 2021	Yes	Yes
TGR-1202	umbralisib	TG Therapeutics	phosphoinositide-3 kinase (PI3K) delta inhibitor	Marginal zone lymphoma/ follicular lymphoma	PO	Filed NDA	2/21/2021	Yes	Yes
CPP-1X/ sulindac (DFMO)	eflornithine/ sulindac	Cancer Prevention Pharma	ornithine decarboxylase inhibitor/ non-steroidal anti-inflammatory drug (NSAID)	Familial adenomatous polyposis	PO	Filed NDA	2/28/2021	Yes	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
KP-415	D-threo-methylphenidate controlled-release	KemPharm	CNS stimulant	Attention deficit hyperactivity disorder	PO	Filed NDA	3/2/2021	No	No
Neutrolin (CRMD-003, CRMD-004)	citrate/ taurolidine/ heparin	CorMedix	antimicrobial agent/ anticoagulant	Catheter-related infections	IV	Filed NDA	3/8/2021	No	No
BIIB-037	aducanumab	Biogen	amyloid beta-protein inhibitor	Alzheimer's disease	IV	Filed BLA	3/8/2021	Yes	No
RG-3477 (ACT-128800)	ponesimod	Johnson & Johnson	sphingosine 1 phosphate receptor agonist	Multiple sclerosis	PO	Filed NDA	3/18/2021	Yes	No
arimoclomol	arimoclomol	Orphazyme	cytoprotectives	Niemann-Pick Disease	PO	Filed NDA	3/20/2021	Yes	Yes
ZP-4207 (ZP-GA-1)	dasiglucagon	Zealand Pharma	glucagon analog	Diabetes mellitus	SC	Filed NDA	3/27/2021	No	Yes
S-265744 (S/GSK-1265744)	cabotegravir	ViiV Healthcare	HIV integrase inhibitor	HIV	PO	CRL	1Q2021	Yes	No
TMC-278-LA	cabotegravir (long-acting)/ rilpivirine (long-acting)	ViiV Healthcare	HIV integrase inhibitor/ non-nucleoside reverse transcriptase inhibitor (NNRTI)	HIV	IM	CRL	1Q2021	Yes	No
bb-2121	idecabtagene vicluecel	Bristol-Myers Squibb/ bluebird Bio	chimeric antigen receptor (CAR) T cell therapy	Multiple myeloma	IV	InTrial	1Q2021	Yes	Yes
Tivopath (AV-951, KRN-951, ASP-4130)	tivozanib	AVEO Oncology	VEGF inhibitor	Renal cell cancer	PO	Filed NDA	3/31/2021	Yes	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
mAb114	ansuvimab	Ridgeback Therapeutics	Monoclonal antibody	Ebola	IM	Filed BLA	1Q2021	No	Yes
KX-01 (KX2-391)	tirbanibulin	Athenex	Src kinase and tubulin inhibitor	Actinic keratosis	TOP	Filed NDA	1Q/2021	No	No
Estelle	estetrol/ drospirenone	Mayne Pharma/ Mithra Pharmaceuticals	estrogen receptor agonist	Pregnancy prevention	PO	Filed NDA	4/16/2021	No	No
DS-100	dehydrated alcohol	Eton	undisclosed	Methanol poisoning	SC	Filed NDA	5/27/2021	No	Yes
FP-001 (LMIS)	leuprolide mesylate	Foresee	gonadotropin-releasing hormone (GnRH) analog	Prostate cancer	SC	Filed NDA	5/27/2021	Yes	No
StrataGraft Skin Tissue	StrataGraft Skin Tissue	Mallinckrodt	autologous skin tissue	Burn injury	TOP	Filed BLA	6/8/2021	Yes	Yes
ACP-001 (TransCon Growth Hormone)	lonapegsomatropin	Ascendis Pharma	growth hormone prodrug	Short stature/ growth hormone deficiency	SC	Filed BLA	6/26/2021	Yes	No
Ryplazim	human plasminogen	ProMetic/ Hematech	plasminogen	Plasminogen deficiency	IV	CRL	2Q2021	Yes	Yes
Translarna	ataluren	PTC Therapeutics	gene transcription modulator	Duchenne muscular dystrophy	PO	CRL	2Q2021	Yes	Yes
131I-8H9	omburtamab	Y-mAbs Therapeutics	B7-H3 antagonist	Brain cancer	Undisclosed	InTrial	2Q2021	Yes	Yes
AB-103	reltecimod	Atox Bio	CD-28 co-stimulatory receptor modulator	Bacterial infections	IV	InTrial	2Q2021	Yes	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
CAT-354	tralokinumab	Leo Pharma	interleukin-13 (IL-13) inhibitor	Atopic dermatitis	SC	Filed BLA	2Q2021	Yes	No
SRP-4045	casimersen	Sarepta	morpholino antisense oligonucleotide	Duchenne muscular dystrophy	IV	Filed BLA	1H2021	Yes	Yes
AGIL-AADC	AGIL-AADC	PTC Therapeutics	gene therapy	Aromatic L-amino acid decarboxylase deficiency	Intracerebral	InTrial	1H2021	Yes	Yes
OMS-721	narsoplimab	Omeros	anti-MASP-2 monoclonal antibody	Hematopoietic stem cell transplant-associated thrombotic microangiopathy	IV/SC	InTrial	1H2021	Yes	Yes
Entyvio (SC formulation)	vedolizumab	Takeda	integrin receptor antagonist	Ulcerative colitis/ Crohn's disease	SC	CRL	1H2021	Yes	No
NexoBrid	bromelain	Vericel	peptide hydrolase replacement agent	Burns/ Skin injury	TOP	Filed BLA	6/30/2021	No	Yes
nadofaragene firadenovec	nadofaragene firadenovec	Ferring Pharmaceuticals/ Blackstone Life Sciences	gene therapy	Bladder cancer	Intravesical	CRL	1H2021	Yes	No
cyclic pyranopterin monophosphate (ALXN-1101)	fosdenopterin	BridgeBio Pharma/ Origin Biosciences	molybdenum cofactor stimulant	Molybdenum cofactor deficiency	IV	InTrial	Mid-2021	Yes	Yes
sulopenem	sulopenem	Iterum Therapeutics	carbapenem	Bacterial infection	IV/PO	InTrial	Mid-2021	No	No
CMX-001	brincidofovir	Chimerix	DNA-directed DNA polymerase inhibitor	Smallpox	PO	InTrial	Mid-2021	No	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
EBV-CTL (ATA-129)	tabelecleucel	Atara Biotherapeutics	cell therapy	Lymphoproliferative disorder	IV	InTrial	Mid-2021	Yes	Yes
S5G4T-1 (DER-45-EV)	benzoyl peroxide	Sol-Gel Technologies	benzoyl peroxide	Rosacea	TOP	InTrial	Mid-2021	No	No
BGJ-398	infigratinib	BridgeBio	FGFR inhibitor	Biliary tract cancer	PO	InTrial	Mid-2021	Yes	Yes
Vicinium (VB-4-845)	oportuzumab monatox	Sesen Bio	anti-ECAM exotoxin A fusion protein	Bladder cancer	Intravesical	InTrial	Mid-2021	Yes	No
JNJ-4528 (LCAR-B38M)	JNJ-4528 (LCAR-B38M)	Janssen	chimeric antigen receptor (CAR) T cell therapy	Multiple myeloma	IV	InTrial	Mid-2021	Yes	Yes
EMD-1214063	tepotinib	Merck	c-Met receptor tyrosine kinase inhibitor	Non-small cell lung cancer	PO	InTrial	Mid-2021	Yes	No
APL-2	pegcetacoplan	Apellis	complement C3 inhibitor	Paroxysmal nocturnal hemoglobinuria	IV	InTrial	Mid-2021	Yes	Yes
GZ-402666 (NeoGAA)	avalglucosidase alfa	Sanofi	enzyme therapy	Pompe disease	IV	InTrial	Mid-2021	Yes	No
SCY-078 (MK-3118)	ibrexafungerp	Scynexis	glucan synthase inhibitors	Fungal infections	IV/PO	InTrial	Mid-2021	No	Yes
CLS-1001	triamcinolone acetonide	Clearside	corticosteroid	Macular edema	intraocular/ subretinal	CRL	Mid-2021	Yes	No
AGEN-2034	balstilimab	Agenus	PD-1 antagonist	Cervical cancer	IV	InTrial	Mid-2021	Yes	No
ISIS 304801 (ISIS-APOCIIIRx)	volanesorsen	Ionis	antisense drug	Familial chylomicronemia syndrome	SC	CRL	Mid-2021	Yes	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
ABI-009	sirolimus and albumin	Aadi Bioscience	mTOR kinase inhibitor	Epithelioid cell caricnoma	IV	InTrial	Mid-2021	Yes	Yes
REGN-1500	evinacumab	Regeneron	angiopoietin-like 3 (ANGPTL3) antagonist	Hyperlipidemia	IV/SC	InTrial	Mid-2021	Yes	No
TadFin	tadalafil and finasteride	Veru	phosphodiesterase type 5 inhibitor /5-alpha-reductase inhibitor	Benign prostatic hyperplasia	PO	InTrial	Mid-2021	No	No
CCX-168	avacopan	ChemoCentryx	C5a receptor (C5aR) antagonist	Vasculitis	PO	Filed NDA	7/9/2021	Yes	Yes
UCB-4940 (CDP-4940)	bimekizumab	UCB	interleukin-17 (IL-17) receptor inhibitor	Plaque psoriasis	IV	InTrial	7/2021	Yes	No
BMN-111	vosoritide (vasoritide)	BioMarin/ Chugai	C-type natriuretic peptide (CNP) analog	Achondroplasia	SC	InTrial	3Q2021	Yes	Yes
ET-101	ET-101	Eton	undisclosed	Seizure disorders	PO	InTrial	3Q2021	No	No
LN-144	lifileucel	Iovance Biotherapeutics	tumor infiltrating lymphocyte	Melanoma	IV	InTrial	3Q2021	Yes	Yes
TAK-721 (SHP-621)	budesonide	Shire	corticosteroid	Eosinophilic esophagitis	PO	InTrial	3Q2021	Yes	Yes
NiCord	omidubicel	Gamida	cellular therapy	Hematological cancers	IV	InTrial	3Q2021	Yes	Yes
PF-04965842	abrocitinib	Pfizer	janus kinase 1 (JAK-1) inhibitor	Atopic dermatitis	PO	InTrial	4Q2021	Yes	No
PF-06482077	multivalent group B streptococcus vaccine	Pfizer	vaccine	Bacterial infection	IM	InTrial	4Q2021	Yes	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
APR-246	eprenetapopt	Aprea Therapeutics	p53 tumor suppressor protein stimulator	Myelodysplastic syndrome	IV	InTrial	4Q2021	Yes	Yes
AXS-05	dextromethorphan/ bupropion	Axsome	N-methyl-D-aspartate (NMDA) antagonist/ antidepressant	Treatment-resistant depression	PO	InTrial	4Q2021	No	No
VBP-15	vamorolone	Santhera	corticosteroid	Duchenne muscular dystrophy	PO	InTrial	4Q2021	Yes	Yes
MOD-401	somatrogon	OPKO Health/ Pfizer	enzyme replacement	Growth hormone deficiency	SC	InTrial	2H2021	Yes	Yes
INC-424	ruxolitinib	Incyte	janus kinase (JAK) inhibitor	Atopic dermatitis	TOP	InTrial	4Q2021	Yes	No
AXS-07	meloxicam/rizatriptan	Axsome Therapeutics	non-steroidal anti-inflammatory drug/triptan	Migraine	PO	InTrial	4Q2021	No	No
OS-01 nasal spray	OC-01	Oyster Point Pharma	nicotinic acetylcholine receptor (nAChR) agonist	Dry eye disease	Intranasal	InTrial	4Q2021	No	No
OPNT-003	nalmefene	Opiant	opioid receptor antagonist	Opioid overdose	Intranasal	InTrial	4Q2021	No	No
KD-025	KD-025	Kadmon	ROCK2 (Rho-associated coiled-coiled kinase 2) inhibitor	Graft vs. Host disease	PO	InTrial	4Q2021	No	Yes
ublituximab (LFB-R603, TG20, TGTX-1101, TG-1101, Utuxin)	ublituximab	TG Therapeutics	CD-20 monoclonal antibody	Chronic lymphocytic leukemia/ multiple sclerosis	IV	InTrial	2H2021	Yes	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
JZP-458 (PF-743)	recombinant crisantaspase	Jazz Pharmaceutics/ Pfenex	asparaginase	Acute lymphoblastic leukemia	IM/IV	InTrial	2H2021	Yes	No
REGN-2477	garetosmab	Regeneron	Activin A antibody	Fibrodysplasia ossificans progressiva	IV/SC	InTrial	2H2021	Yes	Yes
AT-007	AT-007	Applied Therapeutics	aldose reductase inhibitor	Galactosemia	undisclosed	InTrial	2H2021	Yes	Yes
AKB-6548	vadadustat	Akebia Therapeutics/ Vifor Pharma	hypoxia-inducible factor-prolyl hydroxylase (HIF-PH) inhibitor	Anemia	PO	InTrial	2H2021	Yes	No
BBI-608	napabucasin	Sumitomo Dainippon	stem cell inhibitor	Colorectal cancer	PO	InTrial	2H2021	Yes	No
ABT-888	veliparib	AbbVie	poly (ADP-ribose) polymerase (PARP) inhibitor	Ovarian cancer; breast cancer	PO	InTrial	2H2021	Yes	Yes
MLN-4924 (TAK-92)	pevonedistat	Ligand	Nedd 8 Activating Enzyme (NAE) antagonist	Myelodysplastic syndrome	IV	InTrial	2H2021	Yes	No
Estybon	rigosertib (ON 01910.Na)	Onconova	non-ATP competitive kinase inhibitor	Myelodysplastic syndrome	IV	InTrial	2H2021	Yes	Yes
Iomab-B	iodine I 131 monoclonal antibody BC8	Actinium	anti-CD45 monoclonal antibody	Acute myeloid leukemia/ Myelodysplastic syndrome	IV	InTrial	2H2021	Yes	Yes
ARGX-113	efgartigimod	Argen NV	Fc antagonist	Myasthenia gravis	IV/SC	InTrial	2H2021	Yes	Yes
IDP-120	tretinoin/ benzoyl peroxide	Bausch	retinoid	Acne	TOP	InTrial	2H2021	No	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
PL-56	budesonide	Calliditas	corticosteroid	Nephropathy	PO	InTrial	2H2021	No	Yes
AGEN-1884	zalifrelimab	Agenus	immune checkpoint modulator (CPM) antibody	Cervical cancer	IV	InTrial	2H2021	Yes	No
paliperidone palmitate	paliperidone palmitate	Johnson & Johnson	atypical antipsychotic	Schizophrenia	IM	InTrial	2H2021	Yes	No
MEDI-546	anifrolumab	AstraZeneca/ BMS	interferon receptor antagonist	Systemic lupus erythematosus	IV	InTrial	2H2021	Yes	No
PRV-031	teplizumab	Provention Bio/ MacroGenics	CD3 antigen inhibitor	Diabetes mellitus	IV	InTrial	2H2021	Yes	Yes
SHP-620	maribavir	Shire	benzimidazole	Cytomegalovirus	PO	InTrial	2H2021	No	Yes
dovitinib	dovitinib	Oncology Venture	fibroblast growth factor receptor 3 (FGFR3) inhibitor	Renal cell carcinoma	PO	InTrial	2H2021	Yes	No
INP-104	POD-dihydroergotamine mesylate (POD-DHE)	Impel/ 3M	ergot derivative	Acute migraines	Intranasal	InTrial	2H2021	No	No
HMPL-012	surufatinib	Hutchison China MediTech	angio-immunokinase inhibitor	Neuroendocrine tumors	PO	InTrial	2H2021	Yes	Yes
CUTX-101	copper histidinate	Fortress Biotech	copper replacement	Menkes Disease	SC	InTrial	2H2021	Yes	Yes
PRO-145223	etrolizumab	Genentech	IgG1 monoclonal antibody	Ulcerative colitis	SC	InTrial	2H2021	Yes	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
PDR-001	spartalizumab	Novartis	PD-1 checkpoint inhibitor	Melanoma	IV	InTrial	2H2021	Yes	No
MTP-131 (SS-31)	elamipretide	Stealth Biotherapeutics	mitochondrial permeability transition pore inhibitor	Barth syndrome	IV/PO/SC	InTrial	2H2021	Yes	Yes
LY-686017	tradipitant	Vanda Pharmaceuticals	neurokinin 1 receptor (NK-1R) antagonist	Motion sickness	PO	InTrial	2H2021	No	No
S-110 (SGI-110)	guadecitabine	Otsuka	DNA methyltransferase inhibitor	Myelodysplastic syndrome	SC	InTrial	2H2021	Yes	No
SGX-301	synthetic hypericin	Access Pharmaceuticals	synthetic hypericin	Cutaneous T-cell lymphoma	TOP	InTrial	2H 2021	Yes	Yes
R-667 (RG-667)	palovarotene	Ipsen	selective retinoic acid receptor agonist (RAR-gamma)	Fibrodysplasia ossificans progressiva (FOP)	PO	InTrial	2H2021	Yes	Yes
NPI-2358	plinabulin	BeyondSpring	tumor vascular disrupting agent (tVDA)	Neutropenia/ non-small cell lung cancer	IV	InTrial	2H2021	Yes	No
TWIN (S6G5T-1; S6G5T-3)	benzoyl peroxide/ tretinoin	Sol-Gel Technologies	retinoid	Acne vulgaris	TOP	InTrial	2H2021	No	No
SYD-985	[vic-] trastuzumab duocarmazine	Synthon	HER2-targeting antibody-drug conjugate	Breast cancer	IV	InTrial	2H2021	Yes	No
Oraxol	HM-30181A/ paclitaxel	Athenex	P-glycoprotein pump inhibitor/ taxane	Breast cancer	PO	InTrial	2H2021	Yes	No
NX-1207 (NYM-4805, REC 0482)	fexapotide triflutate	Nymox	pro-apoptotic	Benign prostatic hyperplasia	Intratumoral	InTrial	2H2021	Yes	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
RTA-408	omaveloxolone	Reata Pharmaceuticals	Nrf2 activator	Friedreich's ataxia	PO	InTrial	2H2021	Yes	Yes
LN-145	LN-145	Iovance Biotherapeutics	tumor infiltrating lymphocyte	Cervical Cancer	IV	InTrial	2H2021	Yes	No
RG-7440 (GDC-0068)	ipatasertib	Roche	pan-Akt inhibitor	Prostate cancer; breast cancer	PO	InTrial	2H2021	Yes	No
TG-1303	ublituximab/ TGR-1202	TG Therapeutics	CD-20 monoclonal antibody/ phosphoinositide-3 kinase (PI3K) delta inhibitor	Chronic lymphocytic leukemia/ Non-Hodgkin lymphoma	IV/PO	InTrial	2H2021	Yes	Yes
CR-845	difelikefalin	Cara Therapeutics	opioid receptor agonist	Pruritus	IV/PO	InTrial	2H2021	No	No
ADCT-402	loncastuximab tesirine	ADC Therapeutics	antibody drug conjugate	Diffuse large B-cell lymphoma	IV	InTrial	2H2021	Yes	Yes
AmnioFix	dehydrated human amnion/chorion membrane (dHACM)	MiMedx	amniotic tissue membrane	Plantar fasciitis/ achilles tendonitis	INJ	InTrial	2H2021	Yes	No
IDP-124	pimecrolimus	Bausch Health	calcineurin Inhibitor	Atopic dermatitis	TOP	InTrial	2H2021	No	No
Taclantis	paclitaxel injection concentrate for suspension	Sun Pharma Advanced Research Company (SPARC)	taxane	Breast cancer; lung cancer; pancreatic cancer	IV	CRL	2H2021	No	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
Sci-B-Vac	hepatitis B vaccine	VBI Vaccines	vaccine	Hepatitis B	IM	InTrial	2H2021	No	No
RTA-402	bardoxolone methyl	Reata Pharmaceuticals/ AbbVie	Nrf2 activator	Alport syndrome/ diabetes mellitus/ chronic kidney disease/ pulmonary arterial hypertension/ interstitial lung diseases	PO	InTrial	2021	Yes	Yes
GSP-301	mometasone furoate/ olopatadine HCl	Glenmark/ Hikma Pharmaceuticals	corticosteroid/ antihistamine	Allergic rhinitis	Intranasal	CRL	2021	No	No
Apealea (Paclical)	paclitaxel	Oasmia	taxane	Ovarian cancer	IV	InTrial	2021	Yes	Yes
RVT-802	RVT-802	Enzyvant/Roivant	Tissue-based therapy	Congenital athymia	Implant	CRL	2021	Yes	Yes
Remune	AG-1661	Immune Response BioPharma	vaccine	HIV	IM	CRL	2021	Yes	Yes
Trevyent	treprostinil	United Therapeutics	prostacyclin analog	Pulmonary arterial hypertension	SC	CRL	2021	Yes	Yes
Contepo	fosfomycin	Nabriva Therapeutics	cell wall inhibitor	Bacterial infections	IV	CRL	2021	Yes	No
ZYN-002	ZYN-002	Zynerba	cannabinoid product	Fragile X syndrome	TOP	InTrial	2021	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 (ACTH)	Multiple sclerosis/ rheumatoid arthritis/ systemic lupus erythematosus/ ulcerative colitis	IV	InTrial	2021	Yes	No
RSV-F (ResVax)	respiratory syncytial virus vaccine	Novavax	vaccine	Respiratory syncytial virus infection	IM	InTrial	2021	Yes	No
glatiramer acetate depot	glatiramer acetate long-acting	Mylan	immunosuppressant	Multiple sclerosis	IM	InTrial	Late 2021	Yes	No
PRO-140	leronlimab	CytoDyn	C-C chemokine receptor 5 (CCR5) antagonist	HIV	SC	InTrial	Late 2021	Yes	Yes
CT-100	corticotrophin	Eton	adrenocorticotropic hormone (ACTH)	Rheumatoid arthritis	INJ	InTrial	Late 2021	No	No
OTL-200 (GSK-2696274)	OTL-200 (GSK-2696274)	Orchard Therapeutics	gene therapy	Leukodystrophy	IV	InTrial	Late 2021	Yes	Yes
AMAG-423	digoxin immune fab (DIF)	AMAG/ Velo	digitalis-like factor antagonist	Preeclampsia	IV	InTrial	Late 2021	Yes	Yes
pIL-12 (DNA IL-12)	tavokinogene telsaplasmid	OncoSec Medical	gene therapy	Melanoma	Intratumoral	InTrial	Late 2021	Yes	Yes
RGN-259 (GBT-201; RGN-352)	timbetasin	RegeneRx	actin regulating peptide	Dry eyes	OP	InTrial	Late 2021	No	Yes
MT-7117	MT-7117	Mitsubishi Tanabe Pharma	Undisclosed	Erythropoietic protoporphyria	PO	InTrial	Late 2021	Yes	No
CAT-1004	edasalonexent	Catabasis	NF-kB inhibitor	Duchenne muscular dystrophy	PO	InTrial	Late 2021	Yes	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
JNJ-6372	amivantamab	Johnson & Johnson	EGFR and cMET antibody	Non-small cell lung cancer	IV	InTrial	Late 2021	Yes	No
Ultomiris SC	ravulizumab-cwvz	Alexion	C5 complement inhibitor	paroxysmal nocturnal hemoglobinuria; Hemolytic uremic syndrome	SC	InTrial	Late 2021	Yes	Yes
HTX-011	bupivacaine/ meloxicam	Heron Therapeutics	anesthetic/ Nonsteroidal Anti-inflammatory Drug (NSAID)	Pain	Instillation	CRL	Late 2021	No	No
AT-GAA	recombinant human acid alpha-glucosidase + AT2220	Amicus	enzyme therapy	Pompe disease	IV	InTrial	Late 2021	Yes	Yes
ATI-1501	metronidazole	Appili Therapeutics	nitroimidazole	Fungal infections, anaerobic bacterial infections	PO	InTrial	Late 2021	No	No
ADV-7103	tripotassium citrate monohydrate/ potassium hydrogen carbonate	Advicenne	undisclosed	Distal rental tubular acidosis	PO	InTrial	Late 2021	Yes	No
FT-2102	olutasidenib	Forma Therapeutics	dehydrogenase 1 (IDH1) inhibitor	Acute myeloid leukemia	PO	InTrial	Late 2021	Yes	Yes
ACT-541468	daridorexant	Idorsia Pharmaceuticals	orexin receptor antagonist	Insomnia	PO	InTrial	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
SHP-625 (LUM-001)	maralixibat	Mirum Pharmaceuticals	apical sodium-dependent bile acid transporter (ABST) inhibitor	Alagille syndrome	PO	InTrial	Late 2021	Yes	Yes
NNZ-2566	trofinetide	Neuren	insulin-like growth factor 1 (IGF-1) derivative	Rett syndrome	IV/PO	InTrial	Late 2021	Yes	Yes
PDS-1.0	ranibizumab	Roche/ Genentech	Anti-VEGF (vascular endothelial growth factor)	Wet age-related macular degeneration	Intravitreal implant	InTrial	Late 2021	Yes	No
obeticholic acid	obeticholic acid	Intercept Pharmaceuticals	farnesoid X receptor (FXR) agonist	Nonalcoholic steatohepatitis	PO	CRL	Late 2021	Yes	No
ABL-001	asciminib	Novartis	allosteric Bcr-Abl inhibitor	Chronic myelogenous leukemia	PO	InTrial	Late 2021	Yes	Yes
2022 Possible launch date									
MYK-461 (SAR-439152)	mavacamten	MyoKardia	mysoin inhibitor	Cardiomyopathy	PO	InTrial	1Q2022	Yes	Yes
Zynteglo (LentiGlobin)	lentiviral beta-globin gene transfer	Bluebird Bio	gene therapy	Beta-thalassemia	IV	InTrial	1Q2022	Yes	Yes
TBR-652 (TAK-652, CVC)	cenicriviroc	Allergan	C-C chemokine receptor 5 (CCR5) and receptor 2 antagonist	Nonalcoholic steatohepatitis	PO	InTrial	1Q2022	Yes	No
OBE-2109 (KLH-2109)	linzagolix	ObsEva/ Kissei	gonadotropin-releasing hormone (GnRH) antagonist	Uterine fibroids/ Endometriosis	PO	InTrial	1Q2022	No	No
COR-003	levoketoconazole	Strongbridge Biopharma	azole antifungal	Cushing's syndrome	PO	InTrial	1Q2022	No	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
BXCL-501	dexmedetomidine	BioXcel Therapeutics	selective alpha 2a receptor agonist	Schizophrenia and bipolar disorder	PO	InTrial	1Q2022	No	No
SB-206	SB-206	Novan Therapeutics	nitric oxide-releasing compound	Molluscum contagiosum	TOP	InTrial	2Q2022	No	No
ONS-5010	bevacizumab-vikg	Outlook Therapeutics	anti-VEGF antibody	wet age-related macular degeneration	Intravitreal	InTrial	1H2022	Yes	No
Lenti-D	elivaldogene tavalentivec	Bluebird Bio	gene therapy	Adrenomyeloneuropathy	IV	InTrial	1H2022	Yes	Yes
177Lu-PSMA-617	Lutetium	Novartis	Radiopharmaceutical	Prostate cancer	IV	InTrial	1H2022	Yes	No
CERC-801	CERC-801	Cerecor	D-galactose	Phosphoglucomutase 1 (PGM1) deficiency	PO	InTrial	1H2022	Yes	Yes
S-265744 LAP (S/GSK-1265744 LAP; GSK-744 LA)	cabotegravir	ViiV Healthcare	HIV integrase inhibitor	HIV	IM	InTrial	1H2022	No	No
ACER-001	sodium phenylbutyrate	Acer Therapeutics	BCKDC kinase inhibitor	Urea cycle disorders	PO	InTrial	1H2022	No	No
DARE-BV1	clindamycin	Daré Bioscience	lincosamide	Bacterial vaginosis	Intravaginal	InTrial	1H2022	No	No
CaPre	omega-3 fatty acids	Acasti Pharma	fatty acids	Hypertriglyceridemia	PO	InTrial	1H2022	No	No
AMT-061	etranacogene dezaparvovec	CSL Behring/ uniQure	gene therapy	Hemophilia B	IV	InTrial	1H2022	Yes	Yes
GS-010	GS-010	GenSight Biologics	gene therapy	Optic neuropathy	Intraocular	InTrial	Mid-2022	Yes	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
MIN-102	hydroxypioglitazone	Minoryx Therapeutics	PPAR gamma agonist	Adrenomyeloneuropathy	Undisclosed	InTrial	Mid-2022	Yes	Yes
GZ-402665	olipudase alfa	Sanofi	sphingomyelinase	Acid sphingomyelinase deficiency	IV	InTrial	Mid-2022	Yes	Yes
IMGN-853 (M-9346A-sulfo-SPDB-DM4)	mirvetuximab soravtansine	ImmunoGen	folate receptor-1 antagonist	Ovarian cancer	IV	InTrial	Mid-2022	Yes	Yes
OTL-103 (GSK-2696275)	OTL-103 (GSK-2696275)	Orchard Therapeutics	gene therapy	Wiskott-Aldrich syndrome	IV	InTrial	Mid-2022	Yes	Yes
idebenone	idebenone	Santhera	co-enzyme Q-10 analog	Duchenne muscular dystrophy	PO	InTrial	Mid-2022	Yes	Yes
AG-348	mitapivat	Agios	pyruvate kinase-R (PKR) activator	Pyruvate kinase deficiency	PO	InTrial	Mid-2022	Yes	Yes
M-7824	bintrafusp alfa	GlaxoSmithKline	PD-L1 / TGF-beta immunoinhibition	Biliary tract cancer	IV	InTrial	Mid-2022	Yes	Yes
PF-06838435 (SPK-9001)	PF-06838435 (SPK-9001)	Pfizer/ Spark Therapeutics	gene therapy	Hemophilia B	IV	InTrial	Mid-2022	Yes	Yes
RG-7433 (ABT-263)	navitoclax	AbbVie	Bcl-2 inhibitor	Myelofibrosis	PO	InTrial	Mid-2022	Yes	Yes
ALN-APC (ALN-AT3)	fitusiran	Sanofi/ Alnylam	RNAi therapeutic	Hemophilia	SC	InTrial	Mid-2022	Yes	Yes
CORT-125134	relacorilant	Corcept Therapeutics	Glucocorticoid receptor II (GR-II) antagonist	Cushing's syndrome	PO	InTrial	4Q2022	Yes	Yes
STS-101	dihydroergotamine	Satsuma Pharmaceuticals	ergotamine	Migraine	Intranasal	InTrial	2H2022	No	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
RG-7716 (RO-6867461)	faricimab	Roche/ Chugai	bispecific VEGF-A/ angiopoietin-2 antagonist	Diabetic macular edema; age-related macular degeneration	Intravitreal	InTrial	2H2022	Yes	No
Oxabact (IxOC-3)	oxalobacter	OxThera	probiotic	Hyperoxaluria	PO	InTrial	2H2022	No	Yes
QGE-031	ligelizumab	Novartis	Anti-IgE antibody	Urticaria	SC	InTrial	2H2022	Yes	No
PDP-716	brimonidine	Sun Pharma Advanced Research Company (SPARC)	alpha-2 agonist	Glaucoma	OP	InTrial	2H2022	No	No
AMG-157 (MEDI-9929)	tezepelumab	AstraZeneca/ Amgen	thymic stromal lymphopoietin antagonist	Asthma/ Atopic dermatitis	IV/SC	InTrial	2022	Yes	No
MBG-453	MBG-453	Novartis	anti-TIM-3	Myelodysplastic syndrome	IV	InTrial	2022	Yes	No
HY-01	minocycline	Hovione	tetracycline	Rosacea	TOP	InTrial	2022	No	No
REGN-475 (SAR-164877)	fasinumab	Regeneron/ Sanofi-Aventis/ Teva	selective anti-nerve growth factor (NGF) monoclonal antibody	Osteoarthritis	IV/SC	InTrial	2022	Yes	No
BHV-3500	vazegepant	Biohaven	calcitonin gene-related peptide (CGRP) receptor antagonist	Migraine	Intranasal	InTrial	2022	No	No
pentoxifylline	pentoxifylline	Eton	phosphodiesterase inhibitor	Peyronie's disease	PO	InTrial	2022	No	No

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
GSK-2894512 (WBI-1001)	tapinarof	Dermavant Sciences	therapeutic aryl hydrocarbon receptor modulating agent (TAMA)	Plaque psoriasis	TOP	InTrial	2022	Yes	No
ND-0612H	levodopa/ carbidopa	NeuroDerm	dopamine precursor/ dopa-decarboxylase inhibitor	Parkinson's disease	SC	InTrial	2022	Yes	No
HuMax-TF ADC	tisotumab vedotin	Genmab/ Seattle Genetics	tissue factor antibody	Cervical cancer	IV	InTrial	2022	Yes	No
ND-0612L	levodopa/ carbidopa	NeuroDerm	dopamine precursor/ dopa-decarboxylase inhibitor	Parkinson's disease	SC	InTrial	2022	Yes	No
PW-4142 (T-111)	nalbuphine ER	Trevi Therapeutics/ Endo	opioid agonist/ antagonist	Prurigo nodularis	PO	InTrial	2022	No	No
IPX-203	carbidopa/ levodopa	Amneal	dopamine precursor/ dopa-decarboxylase inhibitor	Parkinson's disease	PO	InTrial	2022	No	No
CNTX-4975	CNTX-4975	Centrexion Therapeutics	TRPV1 agonist	Osteoarthritis	Intra-articular	InTrial	2022	Yes	No
Doria	risperidone	Laboratorios Farmacéuticos Rovi	atypical antipsychotic	Schizophrenia	IM	InTrial	2022	Yes	No
OTL-101	ADA-transduced autologous stem cell therapy	Orchard Therapeutics	gene therapy	Adenosine deaminase-deficient severe combined immunodeficiency	Undisclosed	InTrial	2022	Yes	Yes
FCX-007 (GM-HDF-COL7, INXN-3002)	FCX-007 (GM-HDF-COL7, INXN-3002)	Fibrocell Science/ Intrexon	gene-modified autologous fibroblast	Epidermolysis Bullosa	Undisclosed	InTrial	2022	Yes	Yes

Drug name	Generic name	Company	Drug class	Therapeutic use	Route of administration	Regulatory status	Estimated release date	Specialty drug	Orphan drug
CM-AT	CM-AT	Curemark	protein absorption enhancer	Autism	PO	InTrial	2022	Yes	No
CERC-802	CERC-802	Cerecor	D-mannose	Mannose-phosphate isomerase deficiency	PO	InTrial	2022	Yes	Yes
VGX-3100	VGX-3100	Inovio	vaccine	Cervical cancer/dysplasia	IM	InTrial	2022	Yes	No
R-1658 (RG-1658, JTT-705, RO-4607381)	dalcetrapib	DalCor/ Japan Tobacco/ Roche	cholesteryl ester transfer protein inhibitor	Acute coronary syndrome	PO	InTrial	Late 2022	Yes	No
RP-L102 (RPL-102)	RP-L102	Rocket Pharmaceuticals	gene therapy	Fanconi anemia	IV	InTrial	Late 2022	Yes	Yes
pacritinib	pacritinib	CTI BioPharma/ Baxalta	janus associated kinase-2 (JAK2) inhibitor	Myelofibrosis	PO	InTrial	Late 2022	Yes	Yes
MK-8031	atogepant	Allergan/ Merck	calcitonin gene-related peptide (CGRP) receptor antagonist	Migraine	PO	InTrial	Late 2022	No	No
GSK-2140944	gepotidacin	GlaxoSmithKline	bacterial Type II topoisomerase inhibitor	Bacterial infections	PO/IV	InTrial	Late 2022	No	No
CSL-112 (reconstituted HDL, rHDL)	CSL-112 (reconstituted HDL, rHDL)	CSL Limited	plasma-derived apolipoprotein A-I (apoA-I).	Myocardial infarction	IV	InTrial	Late 2022	Yes	No
NuThrax	anthrax vaccine adsorbed/ CPG-7909	Emergent Biosolutions	vaccine/ oligodeoxynucleotide	Anthrax	IM	InTrial	Late 2022	Yes	No
SDP-037, SDN-037	difluprednate	Sun Pharma Advanced Research Company (SPARC)	Corticosteroid	Ocular inflammation/pain	OP	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
NS-2 (ALDX-1E1, ALDX-1E2, ADX-102)	reproxalap	Aldeyra Therapeutics	aldehyde antagonist	Allergic conjunctivitis/ dry eyes	OP	InTrial	Late 2022	No	No

IM = intramuscular, INH = inhalation, INJ = injection, IUD = intrauterine device, IV = intravenous, OP = ophthalmic, PO = oral, SC = subcutaneous, SL = sublingual, TOP = topical, VG = vaginal

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
Trelegy Ellipta	fluticasone furoate/ umeclidinium/ vilanterol	GlaxoSmithKline	inhaled corticosteroid (ICS)/ long-acting muscarinic agent (LAMA)/ long-acting beta agonist (LABA)	Asthma	Treatment of asthma	INH	7/24/2020
Epidiolex	cannabidiol	Greenwich Biosciences	cannabinoid	Tuberous Sclerosis Complex (TSC)	Treatment of tuberous sclerosis complex (TSC)	PO	7/31/2020
Spravato	esketamine	J&J/ Janssen	NMDA receptor antagonist	Major depressive disorder	For the rapid reduction of depressive symptoms in adult patients with major depressive disorder (MDD) who have active suicidal ideation with intent	Intranasal	8/2/2020
Stelara	ustekinumab	Janssen	human interleukin-12 and -23 antagonist	Plaque psoriasis	Treatment of pediatric (ages 6 to 11) patients with moderate to severe plaque psoriasis (PsO).	SC	8/7/2020
Ryanodex	dantrolene sodium	Eagle Pharmaceuticals	ryanodine receptor inhibitor	Exertional heat stroke (EHS)	Treatment of exertional heat stroke (EHS), in conjunction with external cooling methods	IV	8/8/2020
Dovato	dolutegravir and lamivudine	GlaxoSmithKline (ViiV)	integrase inhibitor/nucleoside analogue reverse transcriptase inhibitor (NRTI)	HIV-1	As a switch treatment for HIV-1 infection in virologically suppressed adults on a stable antiretroviral regimen with no treatment failure	PO	8/14/2020

Brand name	Generic name	Company	Drug class	Therapeutic use	Proposed new indication	Route of administration	Estimated approval date
Xolair	omalizumab	Novartis	IgE antagonist	Nasal polyps	Treatment of adults with chronic rhinosinusitis with nasal polyps (CRSwNP) who have not adequately responded to intranasal corticosteroids	SC	8/15/2020
Imbruvica	ibrutinib	AbbVie		Chronic lymphocytic leukemia/small lymphocytic lymphoma	In combination with rituximab for the first-line treatment of younger patients (70 years old or younger) with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)	PO	9/8/2020
Fetroja	cefiderocol	Shionogi	cephalosporin	Pneumonia	Treatment of adult patients with hospital-acquired bacterial pneumonia (HABP) and ventilator-associated bacterial pneumonia (VABP) caused by susceptible Gram-negative pathogens	IV	9/27/2020
Keytruda	pembrolizumab	Merck	anti-PD-1 inhibitor	Classical Hodgkin lymphoma	Treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL)	IV	10/30/2020
Imbruvica	ibrutinib	AbbVie		Waldenström's macroglobulinemia	In combination with rituximab ,for the treatment of Waldenström's macroglobulinemia (WM)	PO	10/31/2020
Linzess	linaclotide	Allergan/ Ironwood Pharmaceuticals	guanylate cyclase C receptor agonist	Abdominal symptoms	Treatment of abdominal symptoms	PO	10/31/2020

Brand name	Generic name	Company	Drug class	Therapeutic use	Proposed new indication	Route of administration	Estimated approval date
Brilinta	ticagrelor	AstraZeneca	thienopyridine	Stroke prevention	For the reduction of subsequent stroke in patients who experienced an acute ischemic stroke or transient ischemic attack (TIA)	PO	11/9/2020
Darzalex	daratumumab	Janssen		Multiple myeloma (with Kyprolis and dexamethasone)	In combination with Kyprolis (carfilzomib) and dexamethasone (DKd) for relapsed/refractory multiple myeloma	IV	11/15/2020
Xofluza	baloxavir	Genentech/ Shionogi	polymerase acidic (PA) endonuclease inhibitor	Influenza	Post-exposure prophylaxis of influenza in people one year of age and older	PO	11/23/2020
Xofluza	baloxavir	Genentech/ Shionogi	polymerase acidic (PA) endonuclease inhibitor	Influenza	Treatment of acute uncomplicated influenza in otherwise healthy children aged one to less than 12 years of age who have been symptomatic for no more than 48 hours	PO	11/23/2020
Nucala	mepolizumab	GlaxoSmithKline	IL-5 antagonist monoclonal antibody	Hypereosinophilic syndrome (HES)	Treatment of hypereosinophilic syndrome (HES)	SC	11/27/2020
Gocovri	amantadine extended-release	Adamas	NMDA receptor antagonist	Parkinson’s disease	Treatment for OFF episodes in Parkinson’s disease (PD) patients receiving levodopa-based therapy	PO	2/1/2021
Entresto	valsartan/ sacubitril	Novartis	Angiotensin-receptor/ neprilysin inhibitor (ARNI)	Heart failure with preserved ejection fraction	To reduce the risk of cardiovascular death and hospitalization for heart failure in patients with chronic heart failure (New York Heart Association [NYHA] Class II-IV) and preserved ejection fraction	PO	2/28/2021

Brand name	Generic name	Company	Drug class	Therapeutic use	Proposed new indication	Route of administration	Estimated approval date
Xpovio	selinexor	Karyopharm Therapeutics	selective inhibitor of nuclear export	Multiple myeloma	Treatment for patients with multiple myeloma after at least one prior line of therapy	PO	3/20/2021
Botox	Onabotulinumtoxin A	Allergan	botulinum toxin analog	Detrusor overactivity	Treatment of signs and symptoms of detrusor overactivity associated with an underlying neurologic condition (eg, spina bifida, spinal cord injuries) in pediatric patients (5 -17 years of age)	IM	3/30/2021
Rinvoq	upadacitinib	AbbVie	janus associated kinase (JAK) inhibitor	Psoriatic arthritis	Treatment of adult patients with active psoriatic arthritis	PO	4/1/2021
Nuplazid	pimavanserin	Acadia	5-HT-2A receptor agonist	Dementia-related psychosis	Treatment of hallucinations and delusions associated with dementia-related psychosis (DRP)	PO	4/3/2021
Ibsrela	tenapanor	Ardelyx	sodium-hydrogen exchanger-3 (NHE-3) inhibitor	Hyperphosphatemia	To control serum phosphorus in adult patients with chronic kidney disease (CKD) on dialysis	PO	4/30/2021

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

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