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Pharmacy Solutions

- **Recent COVID-19 updates**
- **FDA approvals for rare disease therapies**
- **Upcoming gene therapy developments**

Pipeline Report

November 2021

This quarterly publication is developed by our Clinical Pharmacy Drug Information team to increase your understanding of the drug pipeline, ensuring that you are equipped with insights to prepare for shifts in prescription drug management.

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During the past quarter, progress continued on the COVID-19 vaccine front. All three currently available vaccines have received Emergency Use Authorization (EUA) from the FDA for use as heterologous booster doses in adults after completion of a primary vaccination series. The **Pfizer vaccine** was granted an EUA expansion for use in children as young as five years of age, from a previous authorization of at least 12 years of age. In contrast, however, the FDA has decided to delay its decision on the use of the **Moderna vaccine** in adolescents 12 years of age and older in order to review its myocarditis risk in this population. The decision will likely be delayed until at least January 2022. Distribution of **bamlanivimab + etesevimab** resumed following data which showed that the combination is active against the Delta variant, and shortly thereafter it received an EUA for use as post-exposure prophylaxis. An FDA authorization of **molnupiravir** would be a significant addition to the COVID therapeutics armamentarium, as it would be the first *oral* antiviral therapy aimed at treatment of adults with mild to moderate COVID-19 who are at high risk for progression to severe disease. The EUA request has been submitted to the FDA with a decision expected as early as December. Even more cause for optimism is that **Paxlovid** is following close behind, another oral antiviral therapy that appears highly effective at reducing severe COVID 19-related disease and death.

In non-COVID-19 news, one notable FDA approval this past quarter is **Rethymic** (allogeneic processed thymus tissue–agdc), the first regenerative tissue-based therapy for immune reconstitution in pediatric patients with congenital athymia. This disease state had previously only been treatable with supportive care and typically resulted in death by age two or three. Another notable approval is a new indication for existing CAR T-cell therapy **Tecartus** (brexucabtagene autoleucel) in the treatment of adults with relapsed or refractory acute lymphoblastic leukemia (ALL). This new indication extends the treatable ALL population beyond that which is covered by **Kymriah**, which is approved for use in patients who are up to 25 years of age with the same diagnosis.

We continue to monitor developments of pipeline gene therapies, and 2022 promises to be a boon for some of these. Signs point to a BLA submission for **AMT-061** (etranacogene dezaparvovec) for the treatment of hemophilia B in or around the first quarter of 2022. In addition, a BLA resubmission for **Roctavian** (valoctocogene roxaparvovec) for hemophilia A is expected in the second quarter, with potential FDA approval of both before the end of 2022. As for **ciltacabtagene autoleucel** for relapsed or refractory multiple myeloma, an FDA decision date has been pushed out until February 2022 to allow for review of additional data submitted by the manufacturer. An eventual FDA approval will add an anti-BCMA CAR-T therapy option other than **Abecma** in this therapeutic space.

Our pipeline report is just one of many ways we are committed to providing helpful tools and resources to our clients and partners. We look forward to sharing more updates with you in the months ahead.

Ross Hoffman, MD

To provide comments, feedback or requests for report enhancements, please email us at Communications@EnvolveHealth.com.

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FDA-APPROVED AGENTS					
Drug Name	**Manufacturer(s)**	**FDA Approval Date**	**Therapeutic Class**	**Comments**	**Cost (WAC)**
Veklury *remdesivir* intravenous infusion	Gilead	EUA: 5/1/2020 FDA Approval: 10/22/2020	Treatment - antiviral	• 10/22/2020 - FDA-approved for the treatment of adults and pediatric patients ≥ 12 years of age and weighing ≥ 40 kg requiring hospitalization for COVID-19 • 5/1/2020 - Veklury is available through an FDA Emergency Use Authorization (EUA) for the treatment of COVID-19 in hospitalized pediatric patients weighing 3.5 kg to < 40 kg or < 12 years of age and weighing ≥ 3.5 kg • Veklury should only be administered in a hospital or healthcare setting capable of providing acute care comparable to inpatient hospital care	$520 for a 100 mg single dose vial $3,120 for a 5-day course $5,720 for a 10-day course

***Initially, the federal government will supply the vaccine at no cost.**

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AGENTS GRANTED FDA EMERGENCY USE AUTHORIZATION (EUA)					
Drug Name	**Manufacturer(s)**	**EUA Approval Date**	**Therapeutic Class**	**Comments**	**Cost (WAC)**
Comirnaty *Pfizer COVID-19 vaccine* intramuscular injection	Pfizer	Original EUA: 12/11/2020 Expanded EUA: 5/10/2021, 8/12/2021, 9/22/2021, 10/20/2021, 10/29/2021, 11/19/2021 Full FDA approval: 8/23/2021	Vaccine	• 11/19/2021: FDA amended the EUA to authorize use of a single booster dose for all individuals 18 years of age and older after completion of primary vaccination with any FDA-authorized or approved COVID-19 vaccine • 10/29/21: FDA expanded the EUA to include use for prevention of COVID-19 in individuals 5-11 years of age • 10/20/2021: A single booster dose may be administered as a heterologous booster dose following completion of primary vaccination with another authorized COVID-19 vaccine • The eligible population(s) and dosing interval for the heterologous booster dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination • 9/22/21: FDA expanded the EUA to include booster shots in individuals — 65 years of age and older, 18–64 years of age at high risk of severe COVID-19, and 18–64 years of age with frequent institutional or occupational exposure to SARS-CoV-2 • 8/23/2021: FDA granted full FDA approval for the 2-dose regimen for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older (use in people 12-15 years of age, and use of a third dose for immunocompromised people, are still authorized under the previous EUA) • 8/12/2021: FDA expanded the existing EUA to include a third dose in certain immunocompromised people • 5/10/2021: FDA expanded the existing EUA to include adolescents 12-15 years of age, amending the EUA originally issued on 12/11/2020 for administration in individuals 16 years of age and older • **No cost to patients**	$19.50 per dose*

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Drug Name	Manufacturer(s)	EUA Approval Date	Therapeutic Class	Comments	Cost (WAC)

Moderna COVID-19 Vaccine
mRNA 1273
intramuscular injection
	Moderna	12/18/2020
		
		Expanded EUA: 8/12/2021, 8/30/2021, 10/20/2021, 11/19/2021
			Vaccine	• 11/19/2021: FDA amended the EUA to authorize use of a single booster dose for all individuals 18 years of age and older after completion of primary vaccination with any FDA-authorized or approved COVID-19 vaccine
				• 10/20/2021: EUA expansion for booster dose as follows:
				  • A single Moderna COVID-19 Vaccine booster dose (0.25 mL) may be administered IM at least six months after completing a primary series of the Moderna COVID-19 Vaccine to individuals — 65 years of age and older, 18-64 years of age at high risk of severe COVID-19, and 18-64 years of age with frequent institutional or occupational exposure to SARS-CoV-2
				  • A single booster dose of the Moderna COVID-19 Vaccine (0.25 mL) may be administered as a heterologous booster dose following completion of primary vaccination with another authorized or approved COVID-19 vaccine
				• The eligible population(s) and dosing interval for the heterologous booster dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination
				• 10/15/2021: FDA is delaying its decision on the use of the Moderna COVID-19 vaccine in adolesents 12-17 years of age, in order to assess the potential risk of myocarditis in this population
				• 8/30/2021: Warning added re: postmarketing data demonstrating increased risks of myocarditis and pericarditis (observed risk is higher among males under 40 years of age), particularly within seven days following the second dose
				• 8/12/2021: FDA expanded the existing EUA to include a third dose in certain immunocompromised people
				• 6/1/2021: Moderna initiated rolling submission of BLA for full FDA licensure in individuals 18 years of age and older
				• 6/10/2021: Moderna filed for EUA expansion in adolescents ages 12-17; mRNA vaccine that expresses SARS-CoV2 spike protein
				• **No cost to patients**
					$15-37 per dose*

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Drug Name	Manufacturer(s)	EUA Approval Date	Therapeutic Class	Comments	Cost (WAC)

Ad26.COV2-S intramuscular injection	J&J; Janssen	Original: 2/27/2021 Updated: 4/23/2021, 7/12/2021, 10/20/2021	Vaccine	• 10/20/2021: Janssen vaccine received expanded EUA for use as a booster dose:
				  • A single Janssen COVID-19 Vaccine booster dose (0.5 mL) may be administered at least 2 months after primary vaccination with the Janssen COVID-19 Vaccine, to individuals 18 years of age and older
				  • A single booster dose of the Janssen COVID-19 Vaccine (0.5 mL) may be administered as a heterologous booster dose following completion of primary vaccination with another authorized or approved COVID-19 vaccine; the eligible population(s) and dosing interval for the heterologous booster dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination
				• 7/12/2021: Warning added to the EUA that adverse event reporting suggests an increased risk of Guillain-Barré syndrome during the 42 days following vaccination
				• 4/23/2021: EUA Fact Sheet for Recipients and Caregivers has been updated to include information about the remote risk of blood clots
				  • Most people who developed these blood clots and low levels of platelets were females ages 18 - 49 years of age; symptoms began approximately one-twoweeks following vaccination
				• Non-replicating adenovirus 26-vector dsDNA expressing SARS-CoV-2 spike protein
				• **No cost to patients**
					$10 per dose*

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Drug Name	Manufacturer(s)	EUA Approval Date	Therapeutic Class	Comments	Cost (WAC)
REGEN-COV *casirivimab + imdevimab* intravenous infusion	Regeneron	Original: 11/21/2020 Updated: 6/3/2021, 7/30/2021	Treatment - monoclonal antibody	• 11/8/2021: Data from an ongoing Phase 3 trial of REGEN-COV reported a reduction in the risk of contracting COVID-19 by 81.6% when given within 2–8 months after exposure • 9/23/2021: The NIH updated its COVID-19 Treatment Guidelines to recommend use of any one of the three authorized anti-SARS-CoV-2 mAbs to treat nonhospitalized patients with mild to moderate COVID-19 who are at high risk of clinical progression (REGEN-COV, sotrovimab, or bamlanivimab/etesevimab) • 7/30/2021: EUA was revised to authorize emergency use as post-exposure prophylaxis for COVID-19 in adults and pediatric individuals (≥ 12 years of age and weighing ≥ 40 kg) who are at high risk for progression to severe COVID-19, including hospitalization or death • REGEN-COV is not authorized for pre-exposure prophylaxis to prevent COVID-19 before being exposed to the SARS-CoV-2 virus —only after exposure to the virus • 6/3/2021: Updates made to the EUA label include a change in the authorized dosage (from 1200 mg of casirivimab and 1200 mg of imdevimab to 600 mg of casirivimab and 600 mg of imdevimab), the addition of a subcutaneous route of administration as an alternative to the intravenous route, and the addition of a new REGEN-COV co-formulated product in a single vial • EUA is for casirivimab and imdevimab to be administered together for the treatment of mild to moderate COVID-19 in adults and pediatric patients (≥ 12 years of age and weighing ≥ 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization • **No cost to patients, although healthcare facilities may charge fees related to administration**	$1,500 single dose infusion $450 administration cost

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Drug Name	Manufacturer(s)	EUA Approval Date	Therapeutic Class	Comments	Cost (WAC)
LY-CoV555 + LY-CoV016 *bamlanivimab + etesevimab* intravenous infusion	Eli Lilly	Original: 2/9/2021 Revised: 6/25/2021, 9/16/2021	Treatment - monoclonal antibody	• 9/16/2021 - The FDA revised the EUA to include emergency use as post-exposure prophylaxis for COVID-19 in adults and pediatric patients (≥ 12 years of age and weighing ≥ 40 kg) who are at high risk for progression to severe COVID-19, including hospitalization or death; in this revision of the EUA, bamlanivimab and etesevimab, administered together, are authorized for use after exposure to the virus and are not authorized for pre-exposure prophylaxis to prevent COVID-19 before being exposed to the SARS-CoV-2 virus • 9/23/2021: The NIH updated its COVID-19 Treatment Guidelines to recommend use of any one of the three authorized anti-SARS-CoV-2 mAbs to treat nonhospitalized patients with mild to moderate COVID-19 who are at high risk of clinical progression (REGEN-COV, sotrovimab, or bamlanivimab/etesevimab) • 9/2/2021: Distribution of Eli Lilly's bamlanivimab/etesevimab combination resumed in the United States following a pause due to prevalence of the Beta and Gamma variants; data show that the combination may be ineffective against these 2 variants but retains activity against the Delta variant, which is the dominant sustained variant in the United States • EUA issued for the emergency use of bamlanivimab and etesevimab administered together for the treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients (≥ 12 years of age and weighing ≥ 40 kg) with positive results of direct SARS-CoV2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization • **Outpatient only - no cost to patients, although healthcare facilities may charge fees related to administration**	N/A

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Drug Name	Manufacturer(s)	EUA Approval Date	Therapeutic Class	Comments	Cost (WAC)
sotrovimab intravenous infusion	GlaxoSmithKline; Vir	EUA: 5/26/2021	Treatment - monoclonal antibody	• 9/23/2021: The NIH updated its COVID-19 Treatment Guidelines to recommend use of any one of the three authorized anti-SARS-CoV-2 mAbs to treat nonhospitalized patients with mild to moderate COVID-19 who are at high risk of clinical progression (REGEN-COV, sotrovimab, or bamlanivimab/etesevimab) • FDA granted an EUA for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (≥ 12 years of age and weighing ≥ 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death • Sotrovimab is not authorized for use in patients who are hospitalized due to COVID-19	$2,100 single dose infusion
LY-CoV555 *bamlanivimab* intravenous infusion	Eli Lilly	Original: 11/9/2020 Revoked: 4/16/2021	Treatment - monoclonal antibody	• 4/16/2021 - FDA revoked the EUA for bamlanivimab when administered alone • EUA was for the treatment of mild to moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are ≥ 12 years of age and weighing ≥ 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization	$1,250 single dose infusion $450 administration cost
Convalescent plasma intravenous infusion	U.S. Dept of Health and Human Services	Original: 8/23/2020 Revised: 2/4/2021	Treatment - blood product	• 10/5/2021: JAMA study found that convalescent plasma treatment is futile to treat critically ill COVID-19 patients • The study found that the treatment resulted in a low likelihood of providing improvement for severe COVID-19 patients who participated in the trial, but the research did not conclude why it was ineffective • Current EUA is for the use of high titer convalescent plasma for the treatment of hospitalized patients early in the disease course and to those hospitalized patients who have impaired humoral immunity and cannot produce an adequate antibody response	Unknown at this time

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Drug Name	Manufacturer(s)	Anticipated Date of EUA or FDA Approval	Therapeutic Class	Comments	Cost (WAC)
Olumiant *baricitinib* oral tablet	Eli Lilly	Original: 11/19/2020 Revised: 7/28/2021	Treatment - ARDS	· 7/28/2021: EUA authorizes baricitinib as monotherapy for the treatment of COVID-19 in hospitalized patients two years of age or older requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO) · Under the revised EUA, baricitinib is no longer required to be administered with remdesivir (Veklury) · 11/19/2020: EUA for use in combination with Gilead's Veklury (remdesivir) for treating hospitalized patients with COVID-19 infection in patients aged two years of age or older, with suspected or laboratory confirmed COVID-19 requiring supplemental oxygen, invasive mechanical ventilation, or extracorporeal membrane oxygenation • **4 mg once daily for 14 days or until hospital discharge**	$2,553 for 14-day course $91.17 per 2 mg tablet
Actemra *tocilizumab* intravenous infusion	Roche; Genentech	6/24/2021	Treatment - IL-6 receptor antagonist	· EUA for the treatment of COVID-19 in hospitalized patients two years of age and older who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO) • **8-12 mg/kg single IV infusion; one additional infusion may be administered**	$3,228 for a single infusion for a 70 kg patient
PIPELINE AGENTS					
Drug Name	**Manufacturer(s)**	**Anticipated Date of EUA or FDA Approval**	**Therapeutic Class**	**Comments**	**Cost (WAC)**
Vaxzevria *AZD 1222* intramuscular injection	AstraZeneca	Currently unknown	Vaccine	· 9/30/2021: Vaxzevria found to have 74% efficacy in preventing symptomatic disease in the US, according to a report published in the New England Journal of Medicine · Non-replicating chimpanzee adenovirus-vector dsDNA expressing SARS-CoV-2 spike protein • **No cost to patients**	Projected $3-$4 per dose*

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Drug Name	Manufacturer(s)	Anticipated Date of EUA or FDA Approval	Therapeutic Class	Comments	Cost (WAC)
NVX-CoV2373 intramuscular injection	Novavax	2H 2021	Vaccine	· 6/2021: NVX-CoV2373 was found to be 100% effective at protecting against moderate and severe disease, according to findings from the Phase 3 PREVENT-19 trial · SARS-CoV-2 spike glycoprotein nanoparticle + adjuvant vaccine • **No cost to patients**	Projected $10-$16 per dose*
Covaxin *BBV152* intramuscular injection	Ocugen	2H 2022	Vaccine	· 11/5/2021: EUA request was submitted to the FDA for prevention of COVID-19 in children 2-18 years of age based on results of an immuno-bridging trial in pediatric patients which showed comparable neutralizing antibody response as in a large adult Phase 3 trial, the latter of which reported 93.4% efficacy against severe COVID-19 disease, 77.8% overall efficacy, 63.6% efficacy against asymptomatic disease, and 65.2% efficacy against the Delta variant in nearly 25,800 adults · Whole-virion, inactivated vaccine • **No cost to patients**	No projected pricing yet
lenzilumab intravenous infusion	Humanigen, Inc.	2022	Monoclonal antibody	· 9/9/2021: The FDA declined to approve the EUA for lenzilumab stating it was unable to conclude that the known and potential benefits of lenzilumab outweigh the known and potential risks of its use as a treatment for COVID-19 · Humanigen expects an ongoing study to provide additional safety and efficacy data to support its new EUA request · 5/28/2021: EUA request submitted to the FDA, Lenzilumab achieved its primary endpoint with a 54% relative improvement in the likelihood of survival without ventilation compared to placebo · Lenzilumab is a proprietary first-in-class monoclonal antibody that neutralizes GM-CSF, a cytokine of importance in the hyperinflammatory cascade associated with COVID-19 and other indications	No projected pricing yet

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Drug Name	Manufacturer(s)	Anticipated Date of EUA or FDA Approval	Therapeutic Class	Comments	Cost (WAC)
AZD7442 *tixagevimab and cilgavimab* intravenous infusion	AstraZeneca	2H 2021	Monoclonal antibody	• 10/14/2021: AstraZeneca submitted an EUA request to the FDA for prophylaxis of symptomatic COVID-19. Top-line data from the Phase III PROVENT trial showed that the treatment cut the risk of developing symptomatic COVID-19 by a significant 77% compared to placebo • The FDA submission also included results from the Phase III STORM CHASER study involving participants recently exposed to the SARS-CoV-2 virus, although that trial had failed to meet its primary endpoint of preventing COVID-19 in these patients • The monoclonal antibodies tixagevimab and cilgavimab bind to distinct sites on the SARS-CoV-2 spike protein; they have been optimised with half-life extension and reduced Fc receptor and complement C1q binding	No projected pricing yet
Lagevrio *molnupiravir* oral therapy	Merck; Ridgeback Therapeutics	4Q 2021	Antiviral	• 10/14/2021: Merck filed for EUA. FDA advisory committee to meet 11/30/2021 to discuss safety & effectiveness of molnupiravir for the treatment of mild-to-moderate COVID-19 in adults who have tested positive and are at high risk for progression to severe illness. • The FDA is not expected to issue a decision until December 2021 at the earliest. Recent results from the Phase III MOVe-OUT trial showed that molnupiravir halved the risk of hospitalisation or death versus placebo in at risk, non-hospitalised adults with mild-to-moderate COVID-19. Molnupiravir would become the first oral antiviral medication for COVID-19, if cleared by the FDA • Phase 2 - results showed that the percentage of outpatients who received treatment were hospitalized and/or died less frequently vs. the placebo-treated group • **Dose: oral twice daily for five days**	No projected pricing yet

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Drug Name	Manufacturer(s)	Anticipated Date of EUA or FDA Approval	Therapeutic Class	Comments	Cost (WAC)
favipiravir oral tablet	Fujifilm; Others	2022	Antiviral	· 11/12/2021: In the Phase 3 PRESECO trial, favipiravir as a potential therapy for patients with mild-to-moderate COVID-19 did not achieve statistical significance on the primary endpoint of time to sustained clinical recovery. Additional analyses of the trial data are ongoing • **Dose: Loading dose twice daily on Day 1, then twice daily on Days 2-7**	Overseas priced at $1 per tablet
Paxlovid *PF-07321332* oral tablet	Pfizer	2022	Protease inhibitor	· Interim results from the Phase 2/3 EPIC-HR trial demonstrated significantly reduced hospitalization and death in non-hospitalized adult patients with COVID-19 who are at high risk of progressing to severe illness. The interim analysis showed an 89% reduction in risk of COVID-19-related hospitalization or death from any cause compared to placebo in patients treated within three days of symptom onset; 0.8% of patients who received Paxlovid were hospitalized through Day 28 following randomization (no deaths), compared to 7.0% of patients who received placebo and were hospitalized or died ($p<0.0001$). Similar reductions in COVID-19-related hospitalization or death were observed in patients treated within five days of symptom onset; 1.0% of patients who received Paxlovid were hospitalized through Day 28 following randomization (no deaths), compared to 6.7% of patients who received a placebo ($p<0.0001$). In the overall study population through Day 28, no deaths were reported in patients who received Paxlovid as compared to 10 (1.6%) deaths in patients who received placebo. · Pfizer has initiated the phase 2/3 EPIC-PEP trial of this novel oral protease inhibitor to prevent illness in people who have been exposed to COVID-19 infection • **Co-administered with a low dose of ritonavir twice daily for five or 10 days**	No projected pricing yet

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Drug Name	Manufacturer(s)	Anticipated Date of EUA or FDA Approval	Therapeutic Class	Comments	Cost (WAC)
Zyesami *aviptadil* intravenous infusion	NRx Pharmaceuticals	2H 2021	Synthetic vasoactive intestinal peptide	• 11/5/2021: FDA declined to issue an EUA, citing insufficient data to establish a positive benefit-risk profile. NRx plans to supply the FDA with data regarding at least 150 additional patients already treated in the ACTIV-3b trial. • 10/14/2021: NRx Pharma reported a 60-day survival rate of 81% of critical COVID-19 patients suffering from respiratory failure who were treated with the drug Zyesami, compared to a survival rate of 21% among those who received standard care • 7/2021: NRx presented data from a randomized phase 2b/3 trial shows patients treated with Zyesami are less likely to experience IL-6 cytokine rise, and have improved survival and recovery from respiratory failure, compared to patients receiving placebo. Data have been submitted to FDA for EUA support • 6/2021: EUA request resubmitted to the FDA after inital denial	No projected pricing yet; available overseas

Available at: A AcariaHealth P PANTHERx Rare # Other

Drug Name	Manufacturer(s)	Indication(s)	FDA Approval Date	Comments	Cost (WAC)
ENDOCRINOLOGY					
1 8 **Nexviazyme** *avalglucosidase alfa-ngpt* intravenous infusion	Genzyme; Sanofi	Pompe disease	8/6/2021	· FDA-approved for the treatment of late-onset Pompe disease — it is the second enzyme replacement therapy to be FDA-approved for Pompe disease, after Lumizyme · Prescribing Information includes black box warnings regarding severe hypersensitivity reactions, infusion-associated reactions, and risk of acute cardiorespiratory failure in susceptible patients · Projected impact: cost replacement of existing therapies	$600,000/year
2 **Livmarli** *maralixibat* oral solution	Mirum Pharmaceuticals	Cholestatic pruritus in patients with Alagille syndrome (ALGS)	9/29/2021	· Approved for the treatment of patients one year of age and older · There are currently ~2,000-2,500 children with ALGS in the U.S. who would be eligible for treatment with maralixibat · Projected impact: cost increase	$391,000/year
5 **Voxzogo** *vosoritide* subcutaneous injection	BioMarin	Achondroplasia	11/19/21	· Once-daily injection approved for use in children 5 years of age and older whose growth plates are still open · There are no FDA-approved agents for achondroplasia · Injectable growth hormone products have been used off-label in a limited number of cases · Projected impact: cost increase	$328,000/year
HEMATOLOGY					
P 3 **Tavneos** *avacopan* oral capsule	ChemoCentryx	Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV)	10/7/2021	· Existing therapies for ANCA-associated vasculitis typically include broad immunosuppression with daily doses of glucocorticoids such as prednisone or methylprednisone, followed by maintenance therapy with a cyclophosphamide- or rituximab-based regimen · Intended for use as an adjunct to existing therapies · Estimated U.S. prevalence: 55,000 people; ~15% have relapsed disease · Projected impact: cost increase	$176,000/year

[1] Accredo, [2]Mirum Access Plus, [3]Amber, [4]Hospital Administration, [5]Pending Launch, [8]Orsini

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Available at: A AcariaHealth P PANTHERx Rare # Other

Drug Name	Manufacturer(s)	Indication(s)	FDA Approval Date	Comments	Cost (WAC)
IMMUNOLOGY					
[4] **Rethymic** *allogeneic processed thymus tissue–agdc* surgical implant	Enzyvant	Congenital athymia	10/8/2021	· Tissue-based regenerative therapy, intended for use once per lifetime · In the absence of treatment, children born with congenital athymia have no ability to fight infections and typically die within the first 24 months of life · Currently only available at Duke University Hospital · Estimated prevalence: ~1 in 300,000 infants	$2,729,500/one-time treatment
NEPHROLOGY					
[5] **Korsuva** *difelikefalin* intravenous infusion	Cara Therapeutics	Uremic pruritus in chronic kidney disease (CKD)	8/23/2021	· Approved for the treatment of moderate-to-severe uremic pruritus in CKD patients undergoing hemodialysis · Administered at the end of each dialysis session · Projected impact: cost replacement of existing therapies	Pending launch
ONCOLOGY					
[6] [7] **Welireg** *belzutifan* oral tablet	Merck	Von Hippel Lindau (VHL)-associated tumors	8/13/2021	· Approved for the treatment of VHL- associated renal cell carcinoma (RCC), central nervous system hemangioblastomas, or pancreatic neuroendocrine tumors, not requiring immediate surgery · The Welireg Prescribing Information includes a black box warning regarding embryo-fetal toxicity · Patients with VHL disease are at risk for benign blood vessel tumors as well as several cancers · Estimated prevalence: 1 in 36,000 people (~10,000 cases in the U.S.); as many as 70% of people with VHL disease develop RCC · Projected impact: cost replacement of existing therapies	$320,000/year

[5]Pending launch, [6]Biologics, [7]Onco360

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Available at: A AcariaHealth P PANTHERx Rare # Other

Drug Name	Manufacturer(s)	Indication(s)	FDA Approval Date	Comments	Cost (WAC)
6 **Exkivity** *mobocertinib* oral capsule	Takeda	Non-small cell lung cancer (NSCLC)	9/15/2021	· Approved for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, whose disease has progressed on or after platinum-based chemotherapy · Rybrevant is now FDA-approved for the same indication, with a higher overall response rate and overall tolerability, albeit with an intravenous route of administration · Projected impact: cost replacement of existing therapies	$304,000/year
A **Tivdak** *tisotumab vedotin-tftv* intravenous infusion	Genmab/Seagen	Cervical cancer	9/20/2021	· Approved for the treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy · Will compete with Keytruda in this indication · FDA-approved with a black box warning regarding ocular toxicity · Projected impact: cost replacement of existing therapies	$400,000/year
4 **Tecartus** *brexucabtagene autoleucel* intravenous infusion	Gilead	Acute lymphoblastic leukemia (ALL)	10/1/2021	· New indication for an existing CAR-T cell therapy · Tecartus was previously FDA-approved only for the treatment of mantle cell lymphoma. · The new indication is for the treatment of adults with relapsed or refractory B-cell precursor ALL · Kymriah is similarly FDA-approved for ALL, but only for patients up to 25 years of age · Projected impact: cost increase	$399,000/one-time treatment
A **Scemblix** *asciminib* oral tablets	Novartis	Chronic myeloid leukemia (CML)	10/29/2021	· Approved for use in adult patients with Philadelphia chromosome-positive CML (Ph+ CML) in chronic phase (CP), previously treated with two or more tyrosine kinase inhibitors, and for Ph+ CML in CP with the T315I mutation · Scemblix will compete with Iclusig (ponatinib), which is FDA-approved for the same two indications · Projected impact: cost replacement of existing therapies	Pending launch

● [4]Hospital Administration

 | Data is current as of 11/19/2021

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Available at: A AcariaHealth P PANTHERx Rare # Other

Drug Name	Manufacturer(s)	Indication(s)	FDA Approval Date	Comments	Cost (WAC)
6 7 9 **Besremi** *ropeginterferon alfa-2b-njft* subcutaneous injection	PharmaEssentia Corporation	Polycythemia vera (PV)	11/12/2021	• FDA-approved for the treatment of adults with PV • Prescribing Information includes a black box warning re: fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders • Designed for administration once every two weeks, followed by once every four weeks during long-term maintenance • PV is a cancer originating from a disease-initiating stem cell in the bone marrow, estimated to affect more than 160,000 people in the U.S., who have progressively burdensome symptoms; without proper management, the disease progresses into malignancies including myelofibrosis and acute myeloid leukemia • Projected impact: cost replacement of existing therapies	Pending launch

[6]Biologics, [7]Onco 360, [9]US Bioservices

 | Data is current as of 11/19/2021

Drug Name	Manufacturer(s)	Indication(s)	FDA Approval Date	Comments	Cost (WAC)
DERMATOLOGY					
Opzelura *ruxolitinib* topical cream	Incyte	Atopic dermatitis (AD)	9/21/2021	· Approved for the topical short-term and non-continuous chronic treatment of mild to moderate AD in non-immunocompromised patients ≥ 12 years of age whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable · Approved with a black box warning re: serious infections, mortality, malignancy, MACE, and thrombosis (same warnings that occur on the labels of oral JAK inhibitors, even though Opzelura is a topical JAK inhibitor product)	$1,950/60 gm tube
NEUROLOGY					
Qulipta *atogepant* oral tablet	AbbVie	Episodic migraines	9/28/2021	· FDA approved for the preventive treatment of episodic migraine in adults · Will compete with Nurtec ODT as the second oral calcitonin gene-related peptide (CGRP) receptor antagonist, as well as with the injectable CGRP antagonists (Aimovig, Ajovy, Emgality, Vyepti) in the migraine prophylaxis space	$12,000/year
OPHTHALMOLOGY					
Tyrvaya *varenicline* nasal spray	Oyster Point Pharma, Inc.	Dry eye disease	10/15/2021	· Administered as a preservative-free, aqueous nasal spray, while all other available agents for this indication are ophthalmic drops · Will comepte with Cequa, Restasis, and Xiidra in this indication	$296/4.2 mL bottle
Vuity *pilocarpine* ophthalmic solution	AbbVie	Presbyopia	10/28/2021	· Once-daily eye drop · Presbyopia is a progressive condition that reduces the eye's ability to focus on near objects and usually impacts people after age 40 · U.S. prevalence is > 115 million people · Currently eyeglasses and contact lenses are used for treatment	$74/2.5 mL bottle

 | Data is current as of 11/19/2021

Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Cost	Anticipated Approval Date
CARDIOVASCULAR DISEASE						
Leqvio *inclisiran* intravenous infusion	Alnylam; Novartis	Atherosclerotic cardiovascular disease (ASCVD) and familial hypercholesterolemia (FH)	PCSK9 synthesis inhibitor	· Proposed for use in secondary prevention patients with ASCVD · Dosed by subcutaneous injection administered in the doctor's office as a single dose every six months after an initial two doses given three months apart · Would compete with Repatha and Praluent for patients who are already on maximized statin therapy	$6,000/year	1/1/2022
COAGULATION DISORDERS						
Roctavian* *valoctocogene roxaparvovec* intravenous infusion	BioMarin	Hemophilia A	Gene therapy	· On August 19, 2020, BioMarin received a Complete Response Letter for its BLA for valoctocogene roxaparvovec · The FDA recommended two years of data from the Company's ongoing Phase 3 trial in order to provide substantial evidence of a durable effect · BLA resubmission is anticipated in 2Q 2022	$2 million/ one-time treatment	4Q 2022

***Expected to cost > $500,000 per member.**

 | Data is current as of 11/19/2021

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Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Cost	Anticipated Approval Date

AMT-061* *etranacogene dezaparvovec* intravenous infusion	Uniqure; CSL Behring	Hemophilia B	Gene therapy	· For the treatment of adults with severe disease (~40% of the total hemophilia B population)
				· Current standard of care is factor IX replacement therapy
				· Recent data from the Phase 3 HOPE-B study showed continued durable, sustained increases in FIX activity at 52 weeks post-infusion with a mean FIX activity of 41.5% of normal
				  · During the 52-week period, a single dose significantly reduced the annualized rate of bleeding requiring treatment by 80%
				  · The annualized rate of spontaneous bleeding requiring treatment was also significantly reduced by 85% during the 52-week period
				  · Usage of FIX replacement therapy in all patients declined 96%, with 52 of 54 patients successfully discontinuing their prophylactic infusions
				· Estimated U.S. prevalence of hemophilia B: ~6,300 people; ~40% have severe disease
				· Anticipated BLA filing: 1Q 2022
					$1-2 million/ one-time treatment	2H 2022

***Expected to cost > $500,000 per member.**

 | Data is current as of 11/19/2021

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Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Cost	Anticipated Approval Date

SPK-8011* intravenous infusion	Spark; Roche	Hemophilia A	Gene therapy	· Proposed for the treatment of adults with severe disease (~60% of the total hemophilia A population)
				· Current standard of care is factor VIII replacement therapy or Hemlibra
				· In the ongoing Ph I/II trial, factor VIII expression was sustained in 16 of 18 participants with up to four years of follow-up
				  · Across all dose cohorts, there was a 91.2% reduction in annualized bleed rate
				  · There were no deaths and no FVIII inhibitor development in the four years
					$1-2 million/ one-time treatment	2023

SB-525* *giroctocogene fitelparvovec* intravenous infusion	Sangamo BioSciences, Inc; Pfizer	Hemophilia A	Gene therapy	· For the treatment of adults with severe disease (~60% of the total hemophilia A population) · This product is being studied in the Phase 3 AFFINE trial, which has been voluntarily paused by the manufacturers to address the observation that some patients had factor VIII activity of 150% or more, potentially raising their risk of blood clots. A study protocol amendment is pending. · Current standard of care is factor VIII replacement therapy or Hemlibra	$1-2 million/ one-time treatment	2023
DERMATOLOGY						
Filsuvez *oleogel-S10* topical ointment	Amryt	Epidermolysis bullosa (EB)	Keratinocyte migration promoter	· Proposed for the treatment of the cutaneous manifestations of junctional and dystrophic EB, which is a rare genetic skin disorder that can cause skin to blister and tear from the slightest friction or trauma	$100,000/ year	11/30/2021

***Expected to cost > $500,000 per member.**

 | Data is current as of 11/19/2021

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Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Cost	Anticipated Approval Date
PF-04965842 *abrocitinib* oral tablet	Pfizer	Atopic dermatitis	Janus kinase 1 (JAK1) inhibitor	· Proposed for the treatment of moderate to severe disease in patients 12 years of age and older · FDA has indicated that its decision on abrocitinib is delayed due to an ongoing safety review	$45,000/year	4Q 2021
ENDOCRINOLOGY						
LV-101 *carbetocin* intranasal spray	Levo Therapeutics	Prader-Willi syndrome (PWS)	Oxytocin analog	· Proposed for the treatment of hyperphagia and behavioral distress associated with PWS · Would be the first FDA-approved therapy for these PWS-related symptoms	$250,000/ year	12/1/2021
Recorlev *levoketoconazole* oral tablet	Strongbridge Biopharma	Cushing's syndrome	Cortisol synthesis inhibitor	· Racemic ketoconazole is already used off-label for the treatment of Cushing's syndrome, but levoketoconazole is claimed to have improved efficacy, as it may inhibit hydroxylases more potently and reaches 3-fold higher plasma levels in humans	$250,000/ year	1/1/2022
ALN-TTRsc02 *vutrisiran* subcutaneous infusion	Alnylam	Transthyretin-mediated (hATTR) amyloidosis	TTR-targeting RNA interference agent	· Proposed for the treatment of polyneuropathy of hATTR amyloidosis in adults · Would compete with Onpattro (IV infusions every three weeks) and Tegsedi (weekly subcutaneous injections) for the same indication, with quarterly subcutaneous infusions	$400,000/ year	4/14/2022

 | Data is current as of 11/19/2021

CONTINUED

Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Cost	Anticipated Approval Date
AT-GAA* *cipaglucosidase alfa/miglustat* intravenous infusion plus oral therapy	Amicus Therapeutics	Pompe disease	Cipaglucosidase alfa: recombinant human acid alpha-glucosidase enzyme replacement therapy (ERT) Miglustat: pharmacological chaperone	· Proposed for the treatment of late-onset Pompe disease · Estimated U.S prevalence of Pompe disease: ~1 in 40,000 people · Lumizyme and Nexviazyme are available FDA approved ERT alternatives (Nexviazyme for late-onset disease).	$500,000/ year	5/29/2022
HEMATOLOGY						
pacritinib oral therapy	CTI BioPharma Corp	Myelofibrosis	Kinase inhibitor	· Proposed for the treatment of patients with intermediate and high-risk myelofibrosis with low platelet counts of < 50,000/microliter	$175,000/year	11/30/2021

***Expected to cost > $500,000 per member.**

Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Cost	Anticipated Approval Date
AG-348 *mitapivat* oral therapy	Agios Pharmaceuticals	Pyruvate kinase deficiency (PKD)	Pyruvate kinase stimulator	• Proposed for the treatment of adults with PKD • The estimated prevalence of PK deficiency with hemolytic anemia is ~3.3-12.2 per million in Western populations; transfusion-dependent patients account for 15-20% of those with PKD • The Phase 3 ACTIVATE-T trial (n=27) in regularly transfused adults demonstrated a statistically significant and clinically meaningful reduction in transfusion burden; in the 24-week fixed dose period, 37% achieved a ≥ 33% reduction in transfusion burden compared to individual historical transfusion burden, and 22% were transfusion-free • In the Phase 3 ACTIVATE trial in adults who do not receive regular transfusions, 40% of patients randomized to mitapivat achieved a hemoglobin response compared to zero patients who received placebo	$250,000/ year	2/17/2022
Vafseo *vadadustat* oral tablet	Akebia/Vifor	Anemia of CKD	Hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI)	• Proposed for use in both dialysis- and non-dialysis-dependent CKD • Would compete with erythropoietin stimulating agents (ESAs, e.g., Procrit, Aranesp)	$13,000/year	3/9/2022

 | Data is current as of 11/19/2021

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Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Cost	Anticipated Approval Date
Beti-cel* *betibeglogene autotemcel* intravenous infusion	bluebird bio	Transfusion-dependent beta-thalassemia (TDT)	Gene therapy	· Proposed for the treatment of patients with beta-thalassemia who require regular blood transfusions · Demonstrated ability to dramatically decrease or terminate the need for chronic blood transfusions · Twenty-five of 29 patients (86%) in a Phase 3 trial demonstrated transfusion independence (TI) after treatment, with a median ongoing TI duration of 26.3 months (min-max: 13.1 – 39.4) · The BLA was submitted to the FDA in September 2021	$1-2 million/ one-time treatment	1H 2022
INFECTIOUS DISEASE						
SHP620 *maribavir* oral tablet	Takeda	Post-transplant cytomegalovirus (CMV) infection	Viral DNA synthesis inhibitor	· Proposed for the treatment of both solid organ transplant and hematopoietic stem cell transplant recipients	$150,000/ year	11/19/2021
GS-6207 *lenacapavir* subcutaneous injection	Gilead	Human immunodeficiency virus (HIV)-1	HIV-1 capsid inhibitor	· Proposed for the treatment of multi-drug resistant HIV-1 infection in heavily treatment-experienced (HTE) patients in combination with other antiretroviral agents · Would be the only HIV-1 treatment option administered every six months · Trogarzo has the same indication	$120,000/ year	2/28/2022

***Expected to cost > $500,000 per member.**

 | Data is current as of 11/19/2021

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Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Cost	Anticipated Approval Date
MUSCULOSKELETAL CONDITIONS						
PF-06939926* *fordadistrogene movaparvovec* intravenous infusion	Pfizer	Duchenne muscular dystrophy (DMD)	Gene therapy	· One-time treatment · Three serious adverse effects were identified in the Phase 3 CIFFREO trial, muscle weakness including two cases of myocarditis, attributed to the gene therapy · The study protocol is being amended to exclude patients with any mutation (exon deletion, exon duplication, insertion, or point mutation) affecting exons 9-13, inclusive, or a deletion that affects both exon 29 and exon 30; these mutations are estimated to represent ~15% of patients with DMD	$1-2 million/ one-time treatment	2023
GALGT2* *AAVrh74.MHCK.GALGT2* intra-arterial injection	Sarepta Therapeutics	DMD	Gene therapy	· Would compete with SRP-9001 gene therapy for those with mutations between exons 18 and 58 · SRP-9001 is further along in the pipeline process, but comparative safety and efficacy are undetermined	$1-2 million/ one-time treatment	2023

***Expected to cost > $500,000 per member.**

 | Data is current as of 11/19/2021

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Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Cost	Anticipated Approval Date
SRP-9001* *delandistrogene moxeparvovec* intravenous infusion	Sarepta Therapeutics	DMD	Gene therapy	· Targets exons 18-58 (~60-75% of DMD patients have mutations in these exons) · In October 2021 the global pivotal Phase 3 EMBARK trial was initiated · Results from Study SRP-9001-101 (n=4, ages 4-7) found that participants improved 8.6 points on the North Star Ambulatory Assessment (NSAA) compared to a matched natural history cohort three years following a single administration of SRP-9001 (p<0.0001) · In Study SRP-9001-102, SRP-9001-treated participants 6-7 years of age (n=12) had a positive 2.9-point difference on NSAA change from baseline compared to a matched natural history control (p=0.0129) · The first functional results were presented from Study SRP-9001-103 (ENDEAVOR), which uses commercially representative SRP-9001 material · Results from the first 11 participants in Cohort 1, 4-7 years of age, demonstrated a 3.0-point improvement from baseline on NSAA six months after treatment	$1-2 million/ one-time treatment	2023
SGT-001* intravenous infusion	Solid Biosciences	DMD	Gene therapy	· The FDA's previous clinical holds on the IGNITE-DMD trial have been lifted · Interim data recently released suggest a benefit on functional outcomes such as ambulation and lung function 12-24 months after administration of SGT-001	$1-2 million/ one-time treatment	2023

***Expected to cost > $500,000 per member.**

 | Data is current as of 11/19/2021

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Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Cost	Anticipated Approval Date
NEPHROLOGY						
RTA 402 *bardoxolone methyl* oral capsule	Reata Pharmaceuticals	CKD in Alport syndrome	Nrf2 activator	· Proposed for the treatment of CKD caused by Alport syndrome · Estimated prevalence of Alport syndrome: ~10,000-60,000 people · Alport syndrome is estimated to account for 3% of children with CKD and 0.2% of adults with end-stage renal disease in the U.S.	$150,000/ year	2/25/2022
NEUROLOGY						
ARGX-113 *efgartigimod* intravenous infusion	argenx	Generalized myasthenia gravis (gMG)	Anti-IgG antibody	· Would compete with several other available therapies currently in use for gMG, such as cholineserase inhibitors, steroids, immunosuppressants, plasmapheresis, IVIG, Rituxan and Soliris	$400,000/ year	12/17/2021
ganaxolone oral therapy	Marinus Pharmaceuticals	Seizures associated with CDKL5 deficiency disorder (CDD)	Positive allosteric modulator of GABA-A	· CDD is a serious and rare genetic disorder that predominantly affects girls and is characterized by early-onset, difficult-to-control seizures and severe neuro-developmental impairment · Most children affected by CDKL5 cannot walk, talk, or care for themselves · Many also suffer from scoliosis, visual impairment, gastrointestinal difficulties, and sleeping disorders · Currently, there are no approved therapies for CDD	$150,000/ year	3/20/2022

 | Data is current as of 11/19/2021

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Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Cost	Anticipated Approval Date

PTC-AADC* *eladocagene exuparvovec* intraputamenal injection	PTC Therapeutics	Aromatic L-amino acid decarboxylase (AADC) deficiency	Gene therapy	• There are no approved therapies for the treatment of AADC deficiency, which is an ultra-rare enzyme deficiency disorder
				• Estimated prevalence: ~5,000 patients worldwide, with a live-birth incidence of approximately 1 in 40,000 worldwide
				• Five-year follow-up results from a clinical trial show that motor function improvements after PTC-AADC therapy were sustained, demonstrating that the treatment effect is durable
				  • Across three clinical trials, improvements in motor development were recorded in all children from as early as three months
				  • Cognitive and language skills were also reported to improve significantly from baseline, as measured by Bayley-III scores, with children able to understand their caregivers and express themselves
				  • The rate of respiratory infection declined from an average of 2.4 episodes per year at 12 months to 0.6 episodes per year at two years and 0.3 episodes per year at five years
				  • Almost all treated children went from a baseline weight below the third percentile to making age-appropriate weight gains by 12 months following treatment
				• Planned BLA submission in 1Q 2022
					$1-2 million/ one-time treatment	2022

***Expected to cost > $500,000 per member.**

 | Data is current as of 11/19/2021

CONTINUED

Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Cost	Anticipated Approval Date
Lenti-D* *elivaldogene autotemcel* intravenous infusion	bluebird bio	Cerebral drenoleukodystrophy (cALD)	Gene therapy	· Currently, the only therapeutic option for patients with cALD is allogeneic hematopoietic stem cell transplant (HSCT); beneficial effect has been reported if performed early in the course of cALD progression · On 8/9/2021, bluebird bio announced that one patient in the ALD-104 clinical trial had developed myelodysplastic syndrome, and that it was likely related to Lenti-D therapy; the ALD-104 trial has been placed on clinical hold pending further investigation into this case · In the U.S., newborn screening for ALD has been added to the Recommended Universal Screening Panel and is currently active in 20 states, accounting for ~60% of U.S. newborns · The worldwide incidence of ALD is ~1 in 5,000 to 1 in 17,000 newborns (both male and female), and ~1 in 20,000 to 1 in 30,000 newborn males; cALD develops in approximately 40% of affected boys and in a smaller number of adult men	$1-2 million/ one-time treatment	2H 2022
ONCOLOGY						
JNJ-68284528 *ciltacabtagene autoleucel* intravenous infusion	Janssen	Multiple myeloma	Anti-BCMA CAR-T therapy	· Proposed for the treatment of relapsed/ refractory disease after at least three prior lines of therapy · Demonstrated a 97% overall response rate and 67% achieved a stringent complete response at a median follow-up of 12.4 months in the Phase I/ II CARTITUDE-1 trial	$450,000/ one-time treatment	2/28/2022

***Expected to cost > $500,000 per member.**

 | Data is current as of 11/19/2021

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envolve Pharmacy Solutions

Pipeline Report

November 2021

Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Cost	Anticipated Approval Date
Kymriah *tisagenlecleucel* intravenous infusion	Novartis	Follicular lymphoma (FL)	CAR-T therapy	· New indication for an existing CAR-T cell therapy · Proposed for the treatment of adults with relapsed or refractory FL after two prior lines of treatment · In the pivotal Phase II ELARA trial, 66% achieved a complete response and the overall response rate was 86% in heavily pretreated patients; no patients experienced grade 3 or higher cytokine release syndrome related to Kymriah within the first eight weeks following infusion · Yescarta is another CAR T-cell therapy that is FDA-approved as 3rd-line treatment for relapsed or refractory FL	$475,000/ one-time treatment	2/27/2022
Tyvyt *sintilimab* intravenous infusion	Eli Lilly	Non-small cell lung cancer (NSCLC)	Immunoglobulin G4 (IgG4) monoclonal antibody	· Proposed for use in combination with pemetrexed and platinum chemotherapy for first-line treatment of nonsquamous NSCLC	$175,000/year	3/18/2022
TG-1101 *ublituximab* intravenous infusion	TG Therapeutics	Chronic lymphocytic leukemia (CLL) and small lymphocytic leukemia (SLL)	Anti-CD20 monoclonal antibody	· Proposed for use in combination with umbralisib (Ukoniq) · It is estimated that there are approximately 20,000 new cases of CLL diagnosed each year in the United States	$125,000/ year	3/25/2022
HMPL-012 *surufatinib* oral therapy	Hutchison China MediTech Limited	Neuroendocrine tumors (NETs)	Tyrosine kinase inhibitor	· Proposed for the treatment of advanced and progressive pancreatic and extra-pancreatic NETs in patients who are not amenable for surgery	$200,000/ year	4/30/2022
BMS-986016 *relatlimab* intravenous infusion	Bristol Myers Squibb	Melanoma	LAG-3-blocking antibody	· Proposed for use in combination with nivolumab (Opdivo) for the treatment of adult and pediatric patients (≥ 12 years of age and weighing ≥ 40 kg) with unresectable or metastatic melanoma	$175,000/year	3/19/2022

 | Data is current as of 11/19/2021

CONTINUED

Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Cost	Anticipated Approval Date
^{177}Lu-PSMA-617 intravenous infusion	Novartis	Metastatic castration-resistant prostate cancer (mCRPC)	Targeted radioligand therapy	• Proposed for use in the post androgen receptor pathway inhibition, post taxane-based chemotherapy setting • In the pivotal, Phase III VISION study ^{177}Lu-PSMA-617 plus standard of care significantly improved overall survival and radiographic progression-free survival for men with progressive PSMA-positive mCRPC compared to standard of care alone	$150,000/year	1H 2022
BGB-A317 *tislelizumab* intravenous infusion	BeiGene/Novartis	Esophageal carcinoma	Humanized IgG4 anti-PD-1 monoclonal antibody	• Proposed for the treatment of patients with unresectable recurrent locally advanced or metastatic esophageal squamous cell carcinoma after prior systemic therapy	$175,000/year	7/12/2022
RESPIRATORY						

AMG157
tezepelumab
subcutaneous injection
	AstraZeneca; Amgen	Asthma	Anti-thymic stromal lymphopoietin (TSLP) monoclonal antibody	• Proposed for the treatment of severe uncontrolled asthma in adults and adolescents
				• Would compete with Dupixent, Cinqair, Nucala, Fasenra;
				  • All of these, however, except Dupixent, are only approved for the eosinophilic subtype
				  • Dupixent is also approved for those who are oral corticosteroid-dependent
				• Non-eosinophilic disease accounts for around half of severe asthma cases
					$42,000/year	1/7/2022

 | Data is current as of 11/19/2021

Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Approval Date
CARDIOVASCULAR					
MYK461 *mavacamten* oral capsule	MyoKardia	Obstructive hypertrophic cardiomyopathy (oHCM)	Allosteric modulator of cardiac myosin	• Proposed for the treatment of symptomatic oHCM • Mavacamten is the first agent to target the cardiac muscle proteins that drive the excessive contractility and impaired relaxation that are hallmarks of HCM with the intent of correcting the abnormal function of the heart	1/28/2022
DERMATOLOGY					
DMVT-505 *tapinarof* topical cream	Dermavant	Plaque psoriasis	Aryl hydrocarbon receptor modulating agent	• Proposed for use in the adult population • Would compete with multiple existing topical therapy alternatives	2Q 2022
INFECTIOUS DISEASE					
TMC120 *dapivirine* vaginal ring	Janssen/ International Partnership for Microbicides	HIV-1	Non-nucleoside reverse transcriptase inhibitor (NNRTI)	• Proposed for the prevention of HIV-1 infection through vaginal sex • Once monthly self-administered vaginal ring	12/1/2021
VT-1161 *oteseconazole* oral therapy	Mycovia Pharmaceuticals	Vulvovaginal candidiasis (VVC)	Fungal CYP51 inhibitor	• Proposed for the treatment of recurrent VVC, which is generally defined as three or more yeast infections per year	1/27/2022

 | Data is current as of 11/19/2021

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Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Approval Date
NEPHROLOGY					
Nefecon *budesonide, modified release* oral therapy	Pharmalink AB	Primary IgA nephropathy	Modified-release corticosteroid	· The modified-release formulation is designed to deliver the drug to the Peyer's patch region of the lower small intestine, where the disease originates	12/15/2021
NEUROLOGY					
ACT 541468 *daridorexant* oral tablet	Idorsia	Insomnia	Dual orexin receptor antagonist	· Has the same mechanism of action as Belsomra	1/8/2022
PSYCHIATRY					
AXS-05 *bupropion/ dextromethorphan* oral tablet	Axsome	Major depressive disorder	N-methyl-D-aspartate receptor antagonist and sigma-1 receptor agonist + norepinephrine and dopamine reuptake inhibitor	· Would enter a crowded antidepressant market · Bupropion serves to increase the bioavailability of dextromethorphan	11/15/2021
BXCL501 *dexmedetomidine* sublingual film	BioXcel Therapeutics	Schizophrenia and bipolar disorder	alpha-2a receptor agonist	· Proposed for the acute treatment of agitation associated with schizophrenia and bipolar disorders I and II · Dexmedetomidine as a solution for intravenous infusion is widely used for clinical anesthesia and sedation in an intensive care setting	1/5/2022
RESPIRATORY					
MK-7264 *gefapixant* oral therapy	Merck	Chronic cough	P2X3 receptor antagonist	· Proposed for the treatment of refractory or unexplained chronic cough	12/21/2021

 | Data is current as of 11/19/2021

Drug Name	Manufacturer(s)	Biosimilar Reference Drug	Indication(s)	Status/Estimated Approval	Biosimilar Currently Launched?	Comments
ENDOCRINOLOGY						
Semglee *insulin glargine-yfgn* subcutaneous injection	Mylan; Viatris	Lantus	Diabetes mellitus	FDA-approved: 7/28/2021	Yes - original Semglee formulation without interchangeable status	• Semglee is the first insulin biosimilar product to be granted interchangeable status by the FDA • The interchangeable Semglee product is differentiated from the previously available Semglee with new NDCs and a new interchangeable label; the previously available Semglee product is technically not interchangeable
MYL-1601D *insulin aspart* subcutaneous injection	Mylan; Biocon	Novolog	Diabetes mellitus	BLA is under FDA review (BsUFA date: 4Q 2021)	No	• First insulin aspart biosimilar application after reclassification of insulin products as biologic agents
HEMATOLOGY						
MSB11455 *pegfilgrastim* subcutaneous injection	Fresenius Kabi	Neulasta	Neutropenia	BLA is under FDA review (BsUFA date: 1/1/2022)	Yes - Fulphila, Udenyca, Ziextenzo	• Another biosimilar to Neulasta, after Fulphila, Udenyca, and Ziextenzo
Lupifil-P *pegfilgrastim* subcutaneous injection	Lupin Pharmaceuticals	Neulasta	Neutropenia	BLA is under FDA review (BsUFA date: 2/2/2022)	Yes - Fulphila, Udenyca, Ziextenzo	• Another biosimilar to Neulasta, after Fulphila, Udenyca, and Ziextenzo

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Drug Name	Manufacturer(s)	Biosimilar Reference Drug	Indication(s)	Status/Estimated Approval	Biosimilar Currently Launched?	Comments
IMMUNOLOGY						
Cyltezo *adalimumab-adbm* subcutaneous injection	Boehringer Ingelheim	Humira	Interchangeable status for all of the following indications: Rheumatoid arthritis, juvenile idiopathic arthritis (JIA), psoriatic arthritis, ankylosing spondylitis, Crohn's disease (CD), ulcerative colitis, plaque psoriasis	New indications FDA-approved: 10/20/2021	No	• Cyltezo is the first Humira biosimilar to be granted interchangeable status by the FDA • The FDA has also expanded the JIA and CD indications to include pediatric patients at least 2 years of age and at least 6 years of age, respectively • Anticipated launch: July 2023
AVT02 *adalimumab* subcutaneous injection	Alvotech	Humira	Rheumatoid arthritis	BLA is under FDA review (BsUFA date: 4Q 2021)	No	• Another biosimilar to Humira, after Abrilada, Amjevita, Cyltezo, Hadlima, Hulio, Hyrimoz
CHS-1420 *adalimumab* subcutaneous injection	Coherus BioSciences	Humira	Rheumatoid arthritis	BLA is under FDA review (BsUFA date: 12/1/2021)	No	• Another biosimilar to Humira, after Abrilada, Amjevita, Cyltezo, Hadlima, Hulio, Hyrimoz • If approved, Coherus plans to launch this product in the U.S. on or after July 1, 2023, per the terms of an agreement with Humira manufacturer AbbVie
ONCOLOGY						
BAT1706 *bevacizumab* intravenous infusion	Bio-Thera Solutions, Inc.	Avastin	Colorectal; Non-small cell lung; Cervical cancers; Glioblastoma; Renal cell carcinoma	BLA is under FDA review (BsUFA date: 11/27/2021)	Yes - Mvasi, Zirabev	• Another biosimilar to Avastin, after Mvasi and Zirabev

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Drug Name	Manufacturer(s)	Biosimilar Reference Drug	Indication(s)	Status/Estimated Approval	Biosimilar Currently Launched?	Comments
MYL-1402O *bevacizumab* intravenous infusion	Mylan; Biocon	Avastin	Breast cancer	BLA is under FDA review (BsUFA date: 4Q 2021)	Yes - Mvasi, Zirabev	· Another biosimilar to Avastin, after Mvasi and Zirabev
Alymsys *bevacizumab* intravenous infusion	Amneal Pharmaceuticals	Avastin	Colorectal; Non-small cell lung; Cervical cancers; Glioblastoma; Renal cell carcinoma	BLA is under FDA review (BsUFA date: 4/15/2022)	Yes - Mvasi, Zirabev	· Another biosimilar to Avastin, after Mvasi and Zirabev
OPHTHALMOLOGY						
Byooviz *ranibizumab-nuna* intraocular injection	Samsung Bioepis; Biogen	Lucentis	Neovascular (wet) age-related macular degeneration; macular edema; myopic choroidal neovascularization	FDA-approved: 9/17/2021	No	· Is the first FDA-approved Lucentis biosimilar agent · Anticipated launch: June 2022
FYB201 (aka CHS-201) *ranibizumab* intraocular injection	Formycon AG; Bioeq; Coherus	Lucentis	Neovascular (wet) age-related macular degeneration	BLA is under FDA review (BsUFA date: 8/2/2022)	No	· Another biosimilar after Byooviz

Recent Approvals			
GENERIC NAME	**BRAND NAME**	**MANUFACTURER(S)**	**MARKET LAUNCH DATE**
sunitinib malate	Sutent	Sun	8/16/2021
everolimus	Afinitor (10 mg), Afinitor Disperz	Biocon Breckenridge; Mylan	10/1/2021
Pipeline Agents			
GENERIC NAME	**BRAND NAME**	**MANUFACTURER(S)**	**ANTICIPATED LAUNCH DATE**
fingolimod hydrochloride	Gilenya (0.25 mg)	Teva	11/11/2021
carglumic acid	Carbaglu	Novitium/Eton Pharmaceuticals	4Q 2021
ritonavir	Norvir (capsules)	Hikma; Mylan/Viatris	2021
posaconazole	Noxafil (oral suspension)	Par/Endo (AG); Roxane/Hikma; Sandoz	2021
maraviroc	Selzentry (tablet)	Hetero; Sandoz	2/7/2022
lenalidomide	Revlimid (5, 10, 15, 25 mg)	Arrow International Ltd/Natco Pharma	3/1/2022
paclitaxel	Abraxane	Actavis/Teva	3/31/2022
regadenoson	Lexiscan	Accord; Dr. Reddy's; Gland Pharma; Glenmark; Sandoz; Sun; USV; Wockhardt	4/11/2022
bortezomib	Velcade	Amneal; Apotex; Eugia Pharma/Aurobindo; Fresenius; Hetero; Pharmascience; Qilu Pharmaceutical Co.; Teva; Zydus	5/1/2022
pemetrexed disodium	Alimta (100 mg, 500 mg, 750 mg, 1000 mg)	Accord; Amneal; Apotex; Fresenius; Biocon; Dr. Reddy's; Glenmark; Hospira; Sandoz; Sun; Teva; Wockhardt; Zydus	5/25/2022
gefitinib	Iressa	Apotex; Cipla; Natco Pharma; Qilu Pharmaceutical Co.; Synthon	7/13/2022

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Recent Approvals			
GENERIC NAME	**BRAND NAME**	**MANUFACTURER(S)**	**MARKET LAUNCH DATE**
famotidine/ibuprofen	Duexis	Alkem Labs	8/4/2021
enalapril maleate	Epaned oral solution	Bionpharma	8/12/2021
difluprednate	Durezol	Cipla	9/13/2021
nebivolol hydrochloride	Bystolic	ANI Pharmaceuticals; Hetero; Indchemie Health Specialties; Torrent	9/17/2021
varenicline	Chantix	Par	9/22/2021
ezetimibe/rosuvastatin calcium	Roszet	Althera Pharmaceuticals	9/30/2021
fenofibrate	Antara (30 mg, 90 mg)	Lupin Pharmaceuticals	10/26/2021
Pipeline Agents			
GENERIC NAME	**BRAND NAME**	**MANUFACTURER(S)**	**ANTICIPATED LAUNCH DATE**
vasopressin	Vasostrict	Eagle Pharmaceuticals	2H 2021
oxycodone hydrochloride	Oxaydo (7.5 mg)	Par	1/1/2022
lacosamide	Vimpat (oral tablets, oral solution, injection)	Apotex; Aurobindo; Glenmark; Teva; Zydus	3/17/2022
diclofenac potassium	Zipsor	Aurobindo; Bionpharma/Teva; Strides Pharma	3/24/2022
vilazodone	Viibryd	Accord; Alembic; InvaGen/Cipla	6/4/2022
clobetasol propionate	Impoyz	Glenmark	7/27/2022
brimonidine tartrate/timolol maleate	Combigan	Sandoz	2022

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Term	Definition
AADC	aromatic L-amino acid decarboxylase
ALGS	Alagille syndrome
ALL	acute lymphoblastic leukemia
ANCA-AAV	anti-neutrophil cytoplasmic antibody-associated vasculitis
ASCVD	atherosclerotic cardiovascular disease
BCMA	B-cell maturation antigen
BLA	biologics license application
BsUFA	Biosimilar User Fee Act
cALD	cerebral adrenoleukodystrophy
CAR T-cell	chimeric antigen receptor T-cell
CDD	CDKL5 deficiency disorder

Term	Definition
CGRP	calcitonin gene-related peptide
cGvHD	chronic graft-vs-host disease
CKD	chronic kidney disease
CLL	chronic lymphocytic leukemia
CMV	cytomegalovirus
COVID-19	coronavirus disease 2019
CP	chronic phase
DMD	Duchenne muscular dystrophy
EB	epidermolysis bullosa
ERT	enzyme replacement therapy
EUA	Emergency Use Authorization

Term	Definition
FDA	Food and Drug Administration
FH	familial hypercholesterolemia
FL	follicular lymphoma
gMG	generalized myasthenia gravis
hATTR	hereditary transthyretin-mediated
HIF-PHI	hypoxia-inducible factor prolyl hydroxylase inhibitor
HIV	human immunodeficiency virus
IgG4	immunoglobulin G4
JAK1	Janus kinase 1
LBL	lymphoblastic lymphoma
MACE	major adverse cardiovascular event

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Term	Definition
mCRPC	metastatic castration-resistant prostate cancer
NET	neuroendocrine tumor
NNRTI	non-nucleoside reverse transcriptase inhibitor
Nrf2	nuclear factor erythroid 2–related factor 2
NSCLC	non-small cell lung cancer
oHCM	obstructive hypertrophic cardiomyopathy
PCSK9	proprotein convertase subtilisin/kexin type 9
PD-1	Programmed death-1
PKD	pyruvate kinase deficiency
PWS	Prader-Willi syndrome
PV	polycythemia vera

Term	Definition
RCC	renal cell carcinoma
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SLL	small lymphocytic leukemia
T1D	Type 1 diabetes
T2D	Type 2 diabetes
TDT	transfusion-dependent beta-thalassemia
TI	transfusion independence
TSLP	thymic stromal lymphopoietin
VHL	von Hippel-Lindau
VVC	vulvovaginal candidiasis
WAC	Wholesale Acquisition Cost

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To prepare this report, our team accesses a wide range of clinical resources. This information is then analyzed, resulting in updates across multiple disease states including recent and anticipated drug approvals, key changes in the biosimilar agent landscape, and notes on recent and anticipated generic product launches. Learn more about how we simplify pharmacy benefit management, while maximizing benefits for our clients at **EnvolveRx.com**. You can also connect with us on **LinkedIn** to view our latest news and updates.

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