Pipeline Report

JANUARY 2024

HIGHLIGHTS

- Recent FDA approvals including CASGEVY™ and LYFGENIA™ for sickle cell disease and FILSUVEZ® for dystrophic and junctional epidermolysis bullosa
- Upcoming approvals including Pz-cel for recessive dystrophic epidermolysis bullosa
- Developments for gene therapies including OTL-200 for the treatment of metachromatic leukodystrophy and KRESLADI™ for the treatment of leukocyte adhesion deficiency type 1

This quarterly publication is developed by our Clinical Pharmacy Drug Information team to provide additional drug pipeline information and insights to help health care leaders prepare for shifts in prescription drug management.

AcariaHealth™
Specialty Pharmacy

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Two breakthrough therapies for sickle cell disease were FDA-approved during the past quarter. The two agents – **CASGEVY™** (*exagamglogene autotemcel*) and **LYFGENIA™** (*lovotibeglogene autotemcel*) are the first gene therapies to be approved for sickle cell disease, with CASGEVY™ additionally being the first gene therapy using CRISPR/Cas9 gene editing technology to ever be approved for any indication. Both agents are similarly promising for their potential to dramatically change the current treatment paradigm for sickle cell disease. Both are multi-million-dollar therapies, albeit with a significant cost difference between them. Commercial launch success will depend on multiple factors, not the least of which include patient acceptance, treatment tolerability, and provider preference.

Activity has been increasing in the rare disease epidermolysis bullosa space with the recent FDA approval of **FILSUVEZ®** (*birch triterpenes*) for dystrophic and junctional epidermolysis bullosa, and the impending FDA approval of **Pz-cel** (*prademagene zamikeracel*) gene-corrected epidermal sheets for recessive dystrophic epidermolysis bullosa. Both agents add to the existing treatment armamentarium, and to market competition for previously FDA-approved, high-cost gene therapy VYJUVEK® (*beremagene geperpavec-svdt*) for the dystrophic form of the disease.

Other notable pipeline developments include the upcoming potential FDA approvals of yet another two gene therapies, both for rare or ultra-rare genetic conditions that manifest primarily in the pediatric population. **OTL-200** (*atidarsagene autotemcel*) is under FDA review for the treatment of metachromatic leukodystrophy, and **KRESLADI™** (*marnetegragene autotemcel*) is being reviewed for the treatment of leukocyte adhesion deficiency type 1. In both instances, the gene therapies would be the first FDA-approved agents to treat the conditions. The FDA is expected to make its decision on both agents before the end of the quarter.

Alan R. Smith, MD
Vice President, Medical Director

 | Data is current as of 1/25/2024

AcariaHealth Specialty Pharmacy

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Drug Name	Manufacturer(s)	Indication(s)	FDA Approval Date	Comments	Cost (WAC)
DERMATOLOGY					
[1] **FILSUVEZ®** *birch triterpenes* topical gel	Chiesi Global Rare Diseases	Epidermolysis bullosa (EB)	12/18/2023	· Approved for the treatment of wounds associated with dystrophic and junctional epidermolysis bullosa (DEB and JEB) in adult and pediatric patients ≥ 6 months of age · Will compete with VYJUVEK® for DEB; is the first FDA-approved agent for the treatment of JEB · The prevalence of DEB is ~3.3 per one million, and for JEB is ~3 per one million · Projected impact: for DEB, cost replacement of existing therapy; for JEB, new cost for a small population	Pending launch
ENDOCRINOLOGY					
[2] **ADZYNMA™** *ADAMTS13, recombinant-krhn* intravenous (IV) infusion	Takeda Pharmaceuticals	Congenital thrombotic thrombocytopenic purpura (cTTP)	11/9/2023	· Approved for prophylactic or on demand enzyme replacement therapy (ERT) in adult and pediatric patients with cTTP · cTTP is an ultra-rare, chronic subtype of TTP that has an estimated prevalence of fewer than one case/million · The current standard of care for cTTP is plasma therapy · Projected impact: new cost for a very small population	~$255,000 - $510,000/year depending on dosing regimen
HEMATOLOGY					
[1] **RYZNEUTA®** *efbemalenograstim alfa-vuxw* subcutaneous (SC) injection	Evive Biotechnology	Febrile neutropenia	11/16/2023	· Approved to decrease the incidence of infection, as manifested by febrile neutropenia, in adult patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with clinically significant incidence of febrile neutropenia · Will compete with NEUPOGEN®, NEULASTA®, and biosimilars of both agents · Projected impact: cost replacement of existing therapy	Pending launch

Dispensing Specialty Pharmacy: # [1]Pending launch, [2]Orsini

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Drug Name	Manufacturer(s)	Indication(s)	FDA Approval Date	Comments	Cost (WAC)
FABHALTA® (3, 4) *iptacopan* oral capsule	Novartis	Paroxysmal nocturnal hemoglobinuria (PNH)	12/5/2023	• Is the first oral complement inhibitor to be FDA-approved for the treatment of PNH in adults • Will compete with other complement inhibitors that are IV- or SC-administered, including SOLIRIS®, ULTOMIRIS®, and EMPAVELI® • Projected impact: cost replacement of existing therapy	$550,000/year
CASGEVY™ (5) *exagamglogene autotemcel* IV infusion	CRISPR Therapeutics and Vertex	Sickle cell disease (SCD) and transfusion-dependent β-thalassemia (TDT)	12/8/2023 and 1/16/2024	• 12/8/2023: Approved for the treatment of SCD in patients ≥ 12 years of age with recurrent vaso-occlusive crises (VOCs) • SCD affects approximately 100,000 Americans • 1/16/2024: Approved for the treatment of TDT in patients ≥ 12 years of age • Is the first FDA-approved gene therapy that utilizes CRISPR/Cas9 gene editing technology • This gene therapy administration requires a myeloablative pre-conditioning regimen plus an extended post-treatment inpatient hospitalization • Will compete with LYFGENIA™ gene therapy for the SCD indication and with ZYNTEGLO™ gene therapy for the TDT indication • Projected impact: incremental cost increase	$2.2 million/one-time treatment
LYFGENIA™ (5) *lovotibeglogene autotemcel* IV infusion	bluebird bio	SCD	12/8/2023	• Approved for the treatment of patients ≥ 12 years of age with SCD and a history of vaso-occlusive events (VOEs) • SCD affects approximately 100,000 Americans • The LYFGENIA™ Prescribing Information includes a Boxed Warning regarding an increased risk of hematologic malignancies • This gene therapy administration requires a myeloablative pre-conditioning regimen plus an extended post-treatment inpatient hospitalization • Will compete with CASGEVY™ gene therapy for the SCD indication • Projected impact: incremental cost increase	$3.1 million/one-time treatment

Dispensing Specialty Pharmacy: # [3]Biologics, [4]Onco 360, [5] Hospital Administration

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Drug Name	Manufacturer(s)	Indication(s)	FDA Approval Date	Comments	Cost (WAC)
NEUROLOGY					
[2] **WAINUA™** *eplontersen* SC injection	AstraZeneca and Ionis	Polyneuropathy	12/21/2023	• Approved for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults • Self-injected subcutaneously once every four weeks • Will compete with ONPATTRO®, TEGSEDI®, and AMVUTTRA®, which are all FDA-approved for the same indication • Projected impact: cost replacement of existing therapies	$499,000/year

Dispensing Specialty Pharmacy: # [2]Orsini

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Drug Name	Manufacturer(s)	Indication(s)	FDA Approval Date	Comments	Cost (WAC)
ONCOLOGY					
[6] **KEYTRUDA®** *pembrolizumab* IV infusion	Merck & Co	Gastric or gastroesophageal junction (GEJ) adenocarcinoma	11/7/2023, 11/16/2023, 12/15/2023, 1/12/2024	• New indications for an existing agent • 11/7/2023: Approved for use in combination with HERCEPTIN® (trastuzumab), fluoropyrimidine- and platinum-containing chemotherapy, for the first-line treatment of patients with locally advanced unresectable or metastatic HER2-positive gastric or GEJ adenocarcinoma whose tumors express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test • Restricts the use of KEYTRUDA® for this indication to patients whose tumors express PD-L1 • 11/16/2023: Approved for use in combination with fluoropyrimidine- and platinum-containing chemotherapy, for the first-line treatment of adults with locally advanced unresectable or metastatic HER2-negative gastric or GEJ adenocarcinoma • Represents an FDA label expansion to include patients with HER2-negative disease • OPDIVO® is FDA-approved for the same indication • 12/15/2023: Approved for use in combination with PADCEV® (*enfortumab vedotin*), for the treatment of adult patients with locally advanced or metastatic urothelial cancer • Converts the accelerated approval of the combination to regular approval for all first-line locally advanced or metastatic urothelial cancer patients, expanding the indication to cisplatin-eligible patients • 1/12/2024: Approved for use in combination with chemoradiotherapy for the treatment of patients with FIGO 2014 Stage III-IVA cervical cancer • Allows for use in earlier lines of cervical cancer therapy • Projected impact: cost replacement of existing therapies	$200,071/year

Dispensing Specialty Pharmacy: # [6]Hospital, doctor's office, or infusion center administration

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Drug Name	Manufacturer(s)	Indication(s)	FDA Approval Date	Comments	Cost (WAC)
FRUZAQLA™ *fruquintinib* oral capsule (2, 4)	Takeda Pharmaceuticals	Colorectal cancer	11/8/2023	· Approved for the treatment of patients with metastatic colorectal cancer who have been previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-vascular endothelial growth factor (VEGF) biological therapy, and, if RAS wild-type, an anti-epidermal growth factor receptor (EGFR) therapy · Will compete with STIVARGA®, LONSURF® ± AVASTIN® · Projected impact: cost replacement of existing therapies	$302,400/year
AUGTYRO™ *repotrectinib* oral capsule (A, 7)	Bristol Myers Squibb	Non-small cell lung cancer (NSCLC)	11/15/2023	· Approved for the treatment of adult patients with ROS1-positive locally advanced or metastatic NSCLC · Will compete with ROZLYTREK® and XALKORI® · Projected impact: cost replacement of existing therapies	$352,800/year
TRUQAP™ *capivasertib* oral tablet (2, 4)	AstraZeneca	Breast cancer	11/16/2023	· Approved for use in combination with FASLODEX® (*fulvestrant*) for the treatment of adult patients with HR-positive, HER2-negative, locally advanced or metastatic breast cancer with one or more PIK3CA/AKT1/PTEN-alterations as detected by FDA-approved test following progression on at least one endocrine-based regimen in the metastatic setting or recurrence on or within 12 months of completing adjuvant therapy · PIQRAY® is also FDA-approved for PIK3CA-mutated advanced or metastatic breast cancer · Projected impact: for PIK3CA-mutated breast cancer, cost replacement of existing therapy; for other mutations, new cost for small populations	$298,000/year
OGSIVEO™ *nirogacestat* oral tablet (2, 4)	Springworks Therapeutics	Desmoid tumors	11/27/2023	· Approved for the treatment of adult patients with progressing desmoid tumors who require systemic treatment · Current therapies include chemotherapy, hormone therapy, anti-inflammatory agents, tyrosine kinase inhibitors, and surgery · Projected impact: cost replacement of existing therapies	$353,000/year

Dispensing Specialty Pharmacy: A AcariaHealth # [2]Biologics, [4]Onco360, [7]CVS Caremark

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Drug Name	Manufacturer(s)	Indication(s)	FDA Approval Date	Comments	Cost (WAC)
[1] **IWILFIN™** *eflornithine* oral tablet	US WorldMeds	Neuroblastoma	12/13/2023	• Approved to reduce the risk of relapse in adult and pediatric patients with high-risk neuroblastoma who have demonstrated at least a partial response to prior multiagent, multimodality therapy including anti-GD2 immunotherapy • IWILFIN™ is taken until disease progression, unacceptable toxicity, or for a maximum of two years • Projected impact: cost replacement of existing therapies	$65,700 to $262,800/year, depending on body surface area (BSA)

Dispensing Specialty Pharmacy: # [1]Pending launch

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

PF-06838435/SPK-9001* *fidanacogene elaparvovec* intravenous (IV) infusion	Pfizer and Spark Therapeutics	Hemophilia B	Gene therapy	• Current standard of care is factor IX (FIX) replacement therapy
				• The Phase III BENEGENE-2 study in adult males with moderately severe to severe hemophilia B met its primary endpoint of reduction in annualized bleeding rate (ABR) of total bleeds, with a mean ABR reduction of 71% (p<0.0001)
				  • Also reported was a 92% reduction in annualized FIX infusion rate (p<0.0001)
				  • Mean FIX activity was 27% at 15 months and 25% at 24 months
				  • *Fidanacogene elaparvovec* was generally well-tolerated; no deaths, serious adverse events associated with infusion reactions, thrombotic events, or FIX inhibitors were reported
				• Would compete with HEMGENIX® (*etranacogene dezaparvovec-drlb*) gene therapy for the same indication
				• The FDA accepted the BLA for review
					$3-3.5 million/ one-time treatment	4/27/2024

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

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Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Cost	Anticipated Approval Date
PF-06741086 *marstacimab* subcutaneous (SC) injection	Pfizer	Hemophilia A or B	Tissue factor pathway inhibitor (TFPI)-neutralizing antibody	· Proposed for the prevention of bleeding episodes in patients > 12 years of age with hemophilia A or B with or without inhibitors · Once weekly subcutaneous injection · For hemophilia A, would compete directly with HEMLIBRA® and factor VIII (FVIII) replacement therapy, while providing a chronic therapy alternative to ROCTAVIAN™ gene therapy · For hemophilia B, would compete directly with FIX replacement therapy while providing a chronic therapy alternative to HEMGENIX® gene therapy	$450,000/ year	4Q 2024

SPK-8011*
dirloctogene samoparvovec
IV infusion
	Spark Therapeutics and 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 FVIII replacement therapy or Hemlibra
				· In the ongoing Phase I/II trial, FVIII expression was sustained in 21 of 23 (91%) participants with up to five years of follow-up
				  · Of these 21 participants, there was a 92% reduction in ABR
				  · There were no deaths, no thrombotic events, and no FVIII inhibitor development reported in the five years
				· The Phase III Keystone-1 trial has launched
				· Would compete with ROCTAVIAN™ (*valoctocogene roxaparvovec-rvox*) gene therapy for the same indication
					$2-3 million/ one-time treatment	2025

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

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Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Cost	Anticipated Approval Date
SB-525* *giroctocogene fitelparvovec* IV infusion	Pfizer and Sangamo Therapeutics	Hemophilia A	Gene therapy	· For the treatment of adults with severe disease (~60% of the total hemophilia A population) · Current standard of care is FVIII replacement therapy or HEMLIBRA® · SB-525 was being studied in the Phase III AFFINE trial, which had been voluntarily paused by the manufacturers to address the observation that some patients had FVIII activity of 150% or more, potentially raising their risk of blood clots · After a study protocol amendment, the AFFINE trial was re-started and a pivotal readout is expected in the first half of 2024 · Meanwhile, updated results from the Phase I/II Alta trial showed that, among five patients receiving the highest dose of SB-525, mean FVIII levels were 25.4% at two years; during Year 2, one patient had eight bleeds, while another had one · Would compete with ROCTAVIAN™ (*valoctocogene roxaparvovec-rvox*) gene therapy for the same indication	$2-3 million/ one-time treatment	2025
DERMATOLOGY						
Pz-cel* *prademagene zamikeracel* epidermal sheet	Abeona Therapeutics	Recessive dystrophic epidermolysis bullosa (RDEB)	Gene therapy	· Proposed for the treatment of RDEB in patients ≥ 6 years of age · Pz-cel is produced as autologous, COL7A1 gene-corrected epidermal sheets which are laid over RDEB wounds to promote wound healing and pain reduction · VYJUVEK® is another gene therapy that is also FDA-approved for RDEB, but which is applied topically weekly until wound closure	$1-2 million/ one-time treatment	5/25/2024

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

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Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Cost	Anticipated Approval Date
ENDOCRINOLOGY						
OTL-200* *atidarsagene autotemcel* IV infusion	Orchard Therapeutics	Metachromatic leukodystrophy (MLD)	Gene therapy	· MLD is a rare and life-threatening inherited disease occurring in approximately one in every 100,000 live births, caused by a mutation in the ARSA gene · In its late infantile form, mortality at 5 years from onset is estimated at 50% and 44% at 10 years for juvenile patients · Currently, there are no effective treatments for MLD · The Institute for Clinical and Economic Review (ICER) published a Final Evidence Report assessing the comparative clinical effectiveness and value of OTL-200 for MLD · In the Final report, ICER assigned an Evidence Rating of high certainty of A (substantial net health benefit) vs. usual standard of care for OTL-200 treatment in children with presymptomatic late-infantile and early juvenile forms of MLD · An Evidence Rating of moderate certainty of a B+ (moderate certainty of a small or substantial net health benefit with high certainty of at least a small net health benefit) vs. usual standard of care was assigned for early symptomatic early juvenile MLD	$3-4 million/ one-time treatment	3/18/2024
TransCon PTH *palopegteriparatide* SC injection	Ascendis Pharmaceuticals	Hypoparathyroidism	Prodrug of parathyroid hormone	· Proposed for the treatment of adult patients with hypoparathyroidism · Would compete with NATPARA® until NATPARA® manufacturing ceases at the end of 2024	$130,000/ year	5/14/2024

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

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Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Cost	Anticipated Approval Date
Miplyffa *arimoclomol* oral therapy	Zevra Therapeutics	Niemann-Pick type C (NPC) disease	Heat-shock protein modulator	• NPC is an ultra-rare, progressive, neurodegenerative genetic disorder with a prevalence of approximately one person per million in the U.S.	$400,000/ year	6/21/2024
GASTROENTEROLOGY						
MGL-3196 *resmetirom* oral therapy	Madrigal Pharmaceuticals	Metabolic dysfunction-associated steatohepatitis (MASH)	β-selective thyroid hormone receptor agonist	• Proposed for the treatment of MASH with liver fibrosis • Would be the first FDA-approved agent for MASH • MASH affects an estimated 6% of the U.S. population	$50,000/ year	3/14/2024
GFT505 *elafibranor* oral tablet	Genfit	Primary biliary cholangitis (PBC)	Peroxisome proliferator-activator receptor agonist	• Proposed for the treatment of PBC in adults with inadequate response to ursodeoxycholic acid • Would compete with OCALIVA®, potentially with a lower rate of pruritus	$110,000/ year	6/10/2024
HEMATOLOGY						
ACH-4471 *danicopan* oral tablet	AstraZeneca	Paroxysmal nocturnal hemoglobinuria (PNH)	Complement pathway factor D inhibitor	• Proposed for the treatment of PNH in combination with SOLIRIS® (*eculizumab*) or ULTOMIRIS® (*ravulizumab*) for patients with clinically significant extravascular hemolysis (EVH)	$150,000/ year	2/15/2024
KRESLADI™ *marnetegragene autotemcel* IV infusion	Rocket Pharmaceuticals	Leukocyte adhesion deficiency-I (LAD-I)	Lentiviral vector-based gene therapy	• LAD-I is a rare genetic condition that results in recurrent life-threatening bacterial and fungal infections that respond poorly to antibiotics and require frequent hospitalizations • LAD-I is estimated to occur in one in every one million people worldwide • Bone marrow transplant is the only available curative therapy, but mortality in patients with severe LAD-I remains at 60-75% prior to 2 years of age and survival beyond 5 years of age is uncommon	$3-4 million/ one-time treatment	3/31/2024

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

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Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Cost	Anticipated Approval Date
RG6107 *crovalimab* SC injection	Genentech	PNH	C5 complement inhibitor	· Proposed for the treatment of PNH in patients ≥ 12 years of age · Self-administered subcutaneous injection once monthly · Would compete with EMPAVELI® (*SC injection*), SOLIRIS®, and ULTOMIRIS® as other injectable complement-mediated therapies	$450,000/ year	6/15/2024
IMMUNOLOGY						
CTP-543 *deuruxolitinib* oral therapy	Sun Pharmaceuticals	Alopecia areata (AA)	JAK1 and JAK2 inhibitor	· Proposed for the treatment of moderate-to-severe AA · Would compete with OLUMIANT® and LITFULO™, two other JAK inhibitors that are FDA-approved for AA	$45,000/year	4/6/2024
X4P-001-RD *mavorixafor* oral capsule	X4 Pharmaceuticals	Warts, hypogamma-globulinemia, infections, and myelokathexis (WHIM) syndrome	CXCR antagonist	· Proposed for the treatment of patients ≥ 12 years of age with WHIM syndrome · The prevalence of WHIM syndrome in the general population has been estimated at 0.2 per million live births	$200,000/ year	4/30/2024
CSL312* *garadacimab* SC injection	CSL Behring	Hereditary angioedema (HAE)	Factor XIIa-inhibitory monoclonal antibody	· Proposed for the prevention of hereditary angioedema attacks in patients ≥ 12 years of age · Once monthly subcutaneous injection · Would compete with other HAE prophylactic therapies including CINRYZE®, HAEGARDA®, ORLADEYO®, and TAKHZYRO®	$500,000/ year	10/14/2024
MUSCULOSKELETAL CONDITIONS						
ITF2357 *givinostat* oral suspension	Italfarmaco	Duhenne muscular dystrophy (DMD)	Histone deacetylase (HDAC) inhibitor	· Twice daily oral dosing, for use as an adjunct to existing corticosteroid therapy · Acts on the pathogenetic events downstream of DMD-related genetic defects, thus is potentially a treatment for the whole DMD population	$350,000/ year	3/21/2024

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

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Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Cost	Anticipated Approval Date
PF-06939926* *fordadistrogene movaparvovec* IV infusion	Pfizer	DMD	Gene therapy	· One-time treatment · Three serious adverse effects were identified in the Phase III CIFFREO trial, muscle weakness including two cases of myocarditis, attributed to the gene therapy · The study protocol was 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 · There are indications that the muscle-related adverse effects associated with specific exon gene mutations may be a class effect across DMD gene therapies · Phase III data is anticipated during 1H 2024 · Would compete with FDA-approved ELEVIDYS™ (*delandistrogene moxeparvovec*) gene therapy	$2-3 million/ one-time treatment	2025
GALGT2* *AAVrh74.MHCK.GALGT2* intra-arterial injection	Sarepta Therapeutics	DMD	Gene therapy	· Would compete with FDA-approved ELEVIDYS™ (*delandistrogene moxeparvovec*) gene therapy	$2-3 million/ one-time treatment	2025

Expected to cost ≥ $500,000 per member.

 | Data is current as of 1/25/2024

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

LY3002813
donanemab
IV infusion
	Eli Lilly & Co	Early Alzheimer's Disease (AD)	Anti-amyloid monoclonal antibody	• Proposed for the treatment of early symptomatic AD
				• Final results of the Phase III TRAILBLAZER-2 trial for donanemab for early Alzheimer's disease demonstrated a slowing of clinical decline of 35% at 18 months in people who received donanemab compared to placebo
				  • 52% of participants with intermediate tau levels completed their course of treatment by one year and 72% completed by 18 months as a result of achieving plaque clearance
				  • In this study, the incidence of serious ARIA was 1.6%, including two participants whose death was attributed to ARIA and a third participant who died after an incident of serious ARIA
				• If approved, donanemab would compete with LEQEMBI®, and it would likely be subject to the same coverage restrictions imposed by the CMS NCD for this class of agents
					$30,000/ year	1Q 2024

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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 one 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/year at 12 months to 0.6 episodes/year at two years and 0.3 episodes/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 2024
					$3-4 million/ one-time treatment	2024

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

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ONCOLOGY						
BGB-A317 *tislelizumab* IV infusion	BeiGene and Novartis	Esophageal squamous cell carcinoma (ESCC)	Humanized IgG4 anti-PD-1 monoclonal antibody	· Proposed for the treatment of patients with unresectable recurrent locally advanced or metastatic ESCC after prior systemic therapy · Also proposed for use as a first-line treatment for patients with unresectable, recurrent, locally advanced, or metastatic ESCC, with an FDA decision due in July 2024 · The FDA deferred its decision on the BLA for later-line use due to lack of inspections in a foreign manufacturing facility	$175,000/ year	1Q 2024
LN-144 *lifileucel* IV injection	Iovance Biotherapeutics	Melanoma	Autologous tumor infiltrating lymphocyte cell therapy	· Proposed for the treatment of advanced (unresectable or metastatic) melanoma that has progressed after anti-PD-1/L1 therapy, and if BRAF mutation positive, also prior BRAF or BRAF/MEK inhibitor therapy · Administered as a one-time dose · If approved, this would be the first cell therapy to target a solid tumor	$500,000/ one-time treatment	2/24/2024
BREYANZI® *lisocabtagene maraleucel* IV infusion	Bristol Myers Squibb	Chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma (SLL)	CAR T-cell therapy	• **New indication for an existing CAR T-cell therapy** · Proposed for the treatment of patients with relapsed and/or refractory CLL or SLL who received a prior Bruton tyrosine kinase inhibitor and B-cell lymphoma 2 inhibitor · If approved, Breyanzi would be the first and only CAR-T cell therapy available for CLL or SLL	$447,227/ one-time treatment	3/14/2024
REGN1979 *odronextamab* IV infusion	Regeneron Pharmaceuticals	Follicular lymphoma (FL) or diffuse large B-cell lymphoma (DLBCL)	CD20xCD3 bispecific antibody	· Proposed for the treatment of adult patients with relapsed/refractory FL or relapsed/refractory DLBCL, who have progressed after at least two prior systemic therapies	$350,000/ year	3/31/2024

 | Data is current as of 1/25/2024

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Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Cost	Anticipated Approval Date
ABECMA® *idecabtagene vicleucel* IV infusion	Bristol Myers Squibb	Relapsed or refractory multiple myeloma (RRMM)	CAR T-cell therapy	• **New indication for an existing CAR T-cell therapy** · Proposed for the treatment of adult patients with RRMM who have received an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody · Proposes use as third line of therapy or later; ABECMA® is currently FDA-approved for use after four or more prior lines of therapy	$458,000/ one-time treatment	1Q 2024
OPDIVO® *nivolumab* IV infusion	Bristol Myers Squibb	Urothelial carcinoma	PD-1 inhibitor	• **New indication for an existing agent** · Proposed for the first-line treatment of adult patients with unresectable or metastatic urothelial carcinoma in combination with cisplatin-based chemotherapy · Is currently FDA-approved for use with disease progression on or after platinum-containing chemotherapy	$191,000/ year	4/5/2024
ANKTIVA® *nogapendekin alfa inbakicept* intravesical instillation	ImmunityBio	Non-muscle invasive bladder cancer (NMIBC)	Beta gamma T-cell receptor binder	· Proposed for use in combination with bacillus Calmette-Guérin (BCG), for the treatment of BCG-unresponsive non-muscle-invasive bladder cancer (NMIBC) carcinoma in situ with or without Ta or T1 disease	$200,000/ year	4/23/2024
DAY101 *tovorafenib* oral therapy	Day One Biopharmaceuticals	Pediatric low-grade glioma (pLGG)	Pan-RF kinase inhibitor	· Proposed for the treatment of relapsed or progressive pLGG as a monotherapy	$250,000/ year	4/30/2024
rivoceranib + camrelizumab oral therapy + IV infusion	Elevar Therapeutics	Hepatocellular carcinoma	Tyrosine kinase inhibitor + PD-1 inhibitor	· Proposed for combination use as a first-line treatment option for unresectable hepatocellular carcinoma	$400,000/ year	5/16/2024
AMG 757 *tarlatamab* IV infusion	Amgen	Small-cell lung cancer (SCLC)	DLL3-targeting bispecific T-cell engager (BiTE) therapy	· Proposed for the treatment of adults with advanced SCLC who have had disease progression on or after platinum-based chemotherapy	$450,000/ year	6/12/2024

 | Data is current as of 1/25/2024

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Drug Name	Manufacturer(s)	Indication(s)	Mechanism(s) of Action	Comments	Anticipated Cost	Anticipated Approval Date
GRN163L *imetelstat* IV infusion	Geron Corporation	Myelodysplastic syndromes (MDS)	Telomerase inhibitor	• Proposed for the treatment of adult patients with transfusion-dependent anemia due to Low- or Intermediate-1 risk MDS who have failed to respond to, have lost response to, or are ineligible for, erythropoiesis-stimulating agents	$200,000/ year	6/16/2024
HER3-DXd *patritumab deruxtecan* IV infusion	Daiichi Sankyo and Merck & Co.	Non-small cell lung cancer (NSCLC)	HER3-directed antibody drug conjugate	• Proposed for the treatment of patients with metastatic or locally advanced EGFR-mutated NSCLC with disease progression on or after treatment with two or more systemic therapies	$350,000/ year	6/26/2024
RESPIRATORY DISEASE						
MK-7962 *sotatercept* SC injection	Merck & Co.	Pulmonary arterial hypertension (PAH)	TGF-beta selective ligand trap	• Proposed for the treatment of adult patients with PAH • Self-administered subcutaneous injection every 21 days • First potentially disease-modifying therapy in the PAH space, intended to be added on to stable background therapy	$400,000/ year	3/26/2024

 | Data is current as of 1/25/2024

Drug Name	Manufacturer(s)	Biosimilar Reference Drug	Indication(s)	Status/Estimated Approval	Biosimilar Currently Launched?	Comments
DERMATOLOGY						
FYB202 *ustekinumab* subcutaneous (SC) injection	Formycon and Fresenius Kabi	STELARA®	Plaque psoriasis	BLA is under FDA review (BsUFA date: 9/30/2024)	No	· Would be the second STELARA® biosimilar, after WEZLANA™
SB17 *ustekinumab* SC injection	Samsung Bioepsis	STELARA®	Plaque psoriasis	BLA is under FDA review (BsUFA date: 11/1/2024)	No	· Would be a subsequent STELARA® biosimilar, after WEZLANA™
DMB-3115 *ustekinumab* SC injection	Accord BioPharma	STELARA®	Plaque psoriasis	BLA is under FDA review (BsUFA date: 4Q 2024)	No	· Would be a subsequent STELARA® biosimilar, after WEZLANA™
ENDOCRINOLOGY						
denosumab SC injection	Sandoz	PROLIA® and XGEVA®	Osteoporosis, skeletal-related complications of bone metastases, giant cell tumor of the bone, hypercalcemia of malignancy	BLA is under FDA review (BsUFA date: 1/5/2024)	No	· Would be the first approved PROLIA® and XGEVA® biosimilar product
HEMATOLOGY						
ABP-959 *eculizumab* intravenous (IV) infusion	Amgen	SOLIRIS®	Paroxysmal nocturnal hemoglobinuria	BLA is under FDA review (BsUFA date: 2/15/2024)	No	· Would be the first approved SOLIRIS® biosimilar product Anticipated launch: March 2025 due to a SOLIRIS® patent litigation agreement

 | Data is current as of 1/25/2024

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Drug Name	Manufacturer(s)	Biosimilar Reference Drug	Indication(s)	Status/Estimated Approval	Biosimilar Currently Launched?	Comments
IMMUNOLOGY						
AVT02 *adalimumab* SC injection	Alvotech and Teva Pharmaceuticals	HUMIRA®	Rheumatoid arthritis (RA)	BLA is under FDA review (BsUFA date: 2/24/2024)	Yes	· Interchangeable designation has been requested as part of the BLA for this high-concentration formulation
HADLIMA™ interchangeability status adalimumab-bwwd SC injection	Samsung Bioepsis	HUMIRA®	RA, JIA, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis, plaque psoriasis, hidradenitis suppurativa (HS), uveitis	BLA is under FDA review (BsUFA date: 6/15/2024)	Yes	· Could be subsequent HUMIRA® interchangeable biosimilar product (CYLTEZO® and ABRILADA™ have interchangeable status)
ONCOLOGY						
AVZIVI® bevacizumab-tnjn IV infusion	Bio-Thera Solutions	AVASTIN®	Colorectal cancer, non-small cell lung cancer, glioblastoma, renal cell carcinoma, cervical cancer, epithelial ovarian, fallopian tune, or primary peritoneal cancer	FDA approval: 12/6/2023	Yes	· Is the fifth biosimilar to AVASTIN® after ALYMSIS®, MVASI®, VEGZELMA®, and ZIRABEV®
HLX02 *trastuzumab* IV infusion	Henlius Biotech	HERCEPTIN®	Breast cancer, gastric or gastroesophageal junction (GEJ) cancer	BLA is under FDA review (BsUFA date: 1/15/2024)	Yes	· Would be the sixth HERCEPTIN® biosimilar to be FDA-approved after HERZUMA®, KANJINTI®, OGIVRI®, ONTRUZANT®, and TRAZIMERA®
DRL_RI *rituximab* IV infusion	Dr. Reddy's Laboratories	RITUXAN®	Non-Hodgkin's lymphoma, RA	BLA is under FDA review (BsUFA date: 2Q 2024)	Yes	· Would be the fourth RITUXAN® biosimilar to be FDA-approved after RIABNI™, RUXIENCE®, and TRUXIMA®

 | Data is current as of 1/25/2024

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Drug Name	Manufacturer(s)	Biosimilar Reference Drug	Indication(s)	Status/Estimated Approval	Biosimilar Currently Launched?	Comments
OPHTHALMOLOGY						
MYL1701P *aflibercept* intraocular injection	Biocon and Johnson & Johnson	EYLEA®	Wet age-related macular degeneration (AMD)	BLA is under FDA review (BsUFA date: 2/25/2024)	No	Could be the first FDA-approved biosimilar to EYLEA®
Xlucane *ranibizumab* intraocular injection	Xbrane Biopharma and Bausch + Lomb	LUCENTIS®	Wet AMD	BLA is under FDA review (BsUFA date: 4/21/2024)	Yes	Would be the third LUCENTIS® biosimilar to be FDA-approved after BYOOVIZ™ and CIMERLI®
FYB203 *aflibercept* intraocular injection	Formycon	EYLEA®	Wet AMD	BLA is under FDA review (BsUFA date: 6/29/2024)	No	Could be one of the first FDA-approved biosimilars to EYLEA®
CTP42 *aflibercept* intraocular injection	Celltrion	EYLEA®	Wet AMD	BLA is under FDA review (BsUFA date: 6/29/2024)	No	Could be one of the first FDA-approved biosimilars to EYLEA®

Recent Approvals			
GENERIC NAME	**BRAND NAME**	**MANUFACTURER(S)**	**MARKET LAUNCH DATE**
teriparatide	FORTEO®	Teva Pharmaceuticals	11/17/2023
mifeprisone	KORLYM®	Teva Pharmaceuticals	1/19/2024
Pipeline Agents			
GENERIC NAME	**BRAND NAME**	**MANUFACTURER(S)**	**ANTICIPATED LAUNCH DATE**
nilotinib hydrochloride	TASIGNA®	Apotex	1/31/2024
lamivudine/raltegravir	DUTREBIS™	Undetermined	4/4/2024
dasatinib	SPRYCEL® (20, 50, 70, 80, 100, 140 mg)	Apotex	9/1/2024

Includes generic agents with ≥ 50% launch probability

 | Data is current as of 1/25/2024

Term	Definition
AA	alopecia areata
AADC	aromatic L-amino acid decarboxylase
ABR	annualized bleeding rate
AChR	acetylcholine receptor
AD	Alzheimer's disease
AMD	age-related macular degeneration
AML	acute myeloid leukemia
ARIA	amyloid-related imaging abnormalities
ARSA	arylsulfatase A
AS	ankylosing spondylitis
ATTRv-PN	transthyretin-mediated amyloid polyneuropathy
BCG	bacillus Calmette-Guérin
BiTE	bispecific T-cell engager
BLA	biologics license application
BMI	body mass index
BRCA	breast cancer gene
BsUFA	Biosimilar User Fee Act
BTC	biliary tract cancer
CAR T-cell	chimeric antigen receptor T-cell
CD	Crohn's disease

Term	Definition
CDC	Centers for Disease Control and Prevention
CDR-SB	Clinical Dementia Rating-Sum of Boxes
CKD	chronic kidney disease
CLDN18.2	claudin 18.2
CLL	chronic lymphocytic leukemia
CMS	Centers for Medicare & Medicaid Services
COPD	chronic obstructive pulmonary disease
CRBSI	catheter-related bloodstream infection
cSCC	cutaneous squamous cell carcinoma
cTTP	congenital thrombotic thrombocytopenic purpura
CV	cardiovascular
DEB	dystrophic epidermolysis bullosa
DED	dry eye disease
DLBCL	diffuse large B-cell lymphoma
DMD	Duchenne muscular dystrophy
EB	epidermolysis bullos
EGFR	epidermal growth factor receptor
ERT	enzyme replacement therapy
EVH	extravascular hemolysis
ET	essential thrombocythemia

Term	Definition
FIX	factor IX
FVIII	factor VIII
FDA	Food and Drug Administration
FIGO	Federation Internationale de Gynecolgie et d'Obstetrique (in French); International Federation of Gynecology and Obstetrics (in English)
FL	follicular lymphoma
FOP	fibrodysplasia ossificans progressiva
GA	geographic atrophy
GCA	giant cell arteritis
GEJ	gastroesophageal junction
GIP	glucose-dependent insulinotropic polypeptide
GLP-1	glucagon-like peptide-1
gMG	generalized myasthenia gravis
HAE	hereditary angioedema
HDAC	histone deacetylase
HER	human epidermal growth factor receptor
HF	heart failure
HR	hormone receptor
HS	hidradenitis suppurativa
ICER	Institute for Clinical and Economic Review
IV	intravenous

 | Data is current as of 1/25/2024

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Term	Definition
JAK1	Janus Kinase 1
JAK2	Janus Kinase 2
JEB	junctional epidermolysis bullosa
LAD-I	leukocyte adhesion deficiency-I
LBCL	large B-cell lymphoma
LRTD	lower respiratory tract disease
MACE	major adverse cardiovascular events
MASH	metabolic dysfunction-associated steatohepatitis
mCRPC	metastatic castration-resistant prostate cancer
MDD	major depressive disorder
MDS	myelodysplastic syndrome
MI	myocardial infarction
MF	myelofibrosis
MLD	metachromatic leukodystrophy
MS	multiple sclerosis
MuSK	muscle-specific tyrosine kinase
NCD	National Coverage Determination
NMIBC	non-muscle invasive bladder cancer
NPC	nasopharyngeal carcinoma
NSAA	North Star Ambulatory Assessment
NSCLC	non-small cell lung cancer

Term	Definition
NTF	neurotrophic factor
PAH	pulmonary arterial hypertension
PBC	primary biliary cholangitis
PD-L1	programmed death-ligand 1
PH1	primary hyperoxaluria type 1
pJIA	polyarticular juvenile idiopathic arthritis
pLGG	pediatric low-grade glioma
PPD	post-partum depression
PNH	paroxysmal nocturnal hemoglobinuria
PsA	psoriatic arthritis
PV	polycythemia vera
RA	rheumatoid arthritis
RDEB	recessive dystrophic epidermolysis bullosa
RRMM	relapsed or refractory multiple myeloma
RSV	respiratory syncytial virus
SC	subcutaneous
SCD	sickle cell disease
SCLC	small cell lung cancer
sJIA	systemic juvenile idiopathic arthritis
SLL	small lymphocytic lymphoma
T2DM	type 2 diabetes mellitus

Term	Definition
TDT	transfusion-dependent β-thalassemia
TFPI	tissue factor pathway inhibitor
TGF	transforming growth factor
UC	ulcerative colitis
UTI	urinary tract infection
VEGF	vascular endothelial growth factor
VOC	vaso-occlusive crisis
VOE	vaso-occlusive event
WAC	Wholesale Acquisition Cost
WHIM	warts, hypogammaglobulinemia, infections, and myelokathexis

 | Data is current as of 1/25/2024

AcariaHealth is a national comprehensive specialty pharmacy focused on improving care and outcomes for patients living with complex conditions, such as hepatitis C, multiple sclerosis, oncology, rheumatoid arthritis, hemophilia, cystic fibrosis and other conditions. Offering specialized care management services in these disease states, AcariaHealth is dedicated to enhancing the patient care offering, collaborating with providers and capturing relevant data to measure patient outcomes.

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