Drug and Biologic Pipeline Update

Q4 2020

IngenioRx SM

IngenioRx's quarterly *Drug and Biologic Pipeline Update*

The Q4 2020 *IngenioRx Drug and Biologic Pipeline Update* provides more insight into the biopharma pipeline, following our inaugural edition in the third quarter. This update is essential for understanding how the drug and biologic pipeline could unfold in the coming months and its effects on improving health, reducing waste, lowering the total cost of care, and estimating the impact of future costs.

This issue begins with an examination of a proposed treatment awaiting U.S. Food and Drug Administration (FDA) approval that would be the first therapy to possibly slow clinical decline in patients with Alzheimer's disease. It also includes in-depth reviews of proposed treatments for uterine fibroids and a rare metabolic disease in children.

In addition, the *IngenioRx Drug and Biologic Pipeline Update* analyzes how and why specialty drugs are prominent in the pipeline, and dives into market trends likely affecting the pipeline. We also examine the state of gene therapies and the potential of these treatments.

Unless otherwise noted, the information contained in this document was obtained from the Centers for Disease Control and Prevention (cdc.gov), the Food and Drug Administration (fda.gov), clinicaltrials.gov, releases from pharmaceutical manufacturers, and UpToDate.com (registration required). Information in this document is accurate as of November 5, 2020.

Top emerging new therapies

We expect these products to have significant impact on health plans and members.

ADUCANUMAB

Product:
Aducanumab

Indication:
Treatment of Alzheimer's disease

Estimated FDA approval:
March 2021

Therapeutic class:
Anti-beta-amyloid antibody

Route of administration:
Intravenous (IV) infusion

FDA designations:
Fast track; Priority

Manufacturer:
Biogen

Condition:

Alzheimer's disease (AD) is the most common type of dementia.[1] Plaques containing deposits of a protein fragment called beta-amyloid are present in the brain. Scientists believe when those plaques form clumps, it may cause AD. The disease has been shown to profoundly affect memory, thinking, and behavior. An estimated 5.8 million people in the United States age 65 and older have dementia due to AD. There is no cure for AD, and it is the sixth-leading cause of death in the United States.[2]

Role in treatment:

If approved, aducanumab would become the first treatment to possibly slow clinical decline in AD. It would do so by reducing the number of plaques in the brain. Current treatments only reduce symptoms.

Efficacy:

Biogen stopped two early disease clinical trials, called ENGAGE and EMERGE, before completion as it appeared they would miss their primary endpoints to prove efficacy. Following the discontinuations, additional data emerged from these trials. Analysis found patients in EMERGE who received the highest dose of aducanumab may have had slower cognitive and functional decline compared with placebo. However, ENGAGE did not meet this goal. The FDA will be examining the data from ENGAGE and EMERGE to make their regulatory decision.

Safety:

In both trials, the most commonly reported adverse events were amyloid-related imaging abnormalities (ARIA) and headaches. ARIA was reported in 41% of all high-dose aducanumab patients. ARIA may include brain swelling and bleeding or confusion.

Financial impact:

If approved, aducanumab is projected to generate more than $2 billion in peak sales, while **significantly increasing medical spend in the senior population.**[3] Sales may be hindered by factors such as aducanumab's modest efficacy, potential safety risks, invasive IV delivery, required testing prior to administration, and utilization in early stage disease. However, pent-up demand for new treatments that can inhibit disease progression may drive uptake.

IngenioRx view:

On November 6, 2020, an FDA advisory committee recommended against approval of aducanumab. Typically, the FDA follows the recommendations of their committees, however, it is not mandatory. If approved — the likelihood of which is unclear — aducanumab would be the first FDA-approved therapy that may reduce the clinical decline seen in AD. It could also be the first to show that removing beta-amyloid may result in improved clinical outcomes. This is important because there are many agents in development for AD that affect beta-amyloid. Despite the drug's limitations and safety concerns, the large unmet need could fuel interest.

1 Alzheimer's Association: *What is Alzheimer's disease?* (accessed October 2, 2020): alz.org.
2 Alzheimer's Association: *Facts and Figures* (accessed October 2, 2020): alz.org.
3 Decision Resources Group website (accessed September 2020): insights.decisionresourcesgroup.com (registration required).

RELUGOLIX COMBINATION TABLET

Product:
Relugolix combination tablet (relugolix, estradiol, and norethindrone acetate)

Indication:
Heavy menstrual bleeding associated with uterine fibroids

Estimated FDA approval:
June 2021

Therapeutic class:
Gonadotropin-releasing hormone (GnRH) antagonist

Route of administration:
Oral

FDA designations:
None

Manufacturer:
Myovant Sciences Ltd.

Condition:
Uterine fibroids are benign tumors that grow in the uterine muscle tissue, most often occurring in women during their reproductive years. Uterine fibroids can cause heavy menstrual bleeding and pain. Their exact prevalence is uncertain, but at least 20% and as many as 80% of women develop uterine fibroids by age 50.[4]

Role in treatment:
Treatment for heavy menstrual bleeding due to fibroids may start with hormonal birth control with or without a GnRH agent before moving onto more invasive surgical therapies. Relugolix is a new chemical entity combined with currently available hormone agents in a single tablet, taken once daily. It would be the second oral FDA-approved GnRH agent for heavy menstrual bleeding associated with uterine fibroids. It would compete with another oral GnRH antagonist combination tablet, Oriahnn™, which is taken twice daily, and Lupron Depot®, an injectable GnRH agonist.

Efficacy:
In two clinical trials, the relugolix combination tablet performed significantly better than a placebo in reducing the amount of menstrual blood loss.

Safety:
The side effect profile for the relugolix combination tablet was comparable to the placebo, including similar changes in markers of bone loss with up to one year of use. Due to the risk of irreversible bone loss, Lupron and Oriahnn list a three- and 24-month maximum recommended duration of use, respectively. The approved duration for relugolix has yet to be determined.

Financial impact:
As the second-to-market oral GnRH antagonist, **relugolix is likely to have a moderate impact on drug spend**. It is expected to be priced at a slight discount to Oriahnn, at approximately $9,800 per year, with projected peak sales of $170 million.[5] Relugolix will largely compete based on its once-daily formulation to gain market share against Oriahnn.

IngenioRx view:
Relugolix will compete directly with Oriahnn, including newly diagnosed women and existing Oriahnn users. One remaining important question is whether GnRH agents may help to delay or avoid the need for surgery, which may boost uptake.

4 U.S. Department of Health and Human Services, Office of Women's Health: *Uterine fibroids* (accessed October 2, 2020): womenshealth.org.
5 Decision Resources Group website (accessed September 2020): insights.decisionresourcesgroup.com (registration required).

FOSDENOPTERIN

Product:
Fosdenopterin

Indication:
Molybdenum cofactor deficiency (MoCD) type A

Estimated FDA approval:
April 2021

Therapeutic class:
Cyclic pyranopterin monophosphate (cPMP) replacement therapy

Route of administration:
Intravenous (IV) infusion

FDA designations:
Orphan; Breakthrough; Priority

Manufacturer:
BridgeBio

Condition:

MoCD type A is a metabolic disorder resulting in a toxic elevation of sulfite levels, which causes neurological damage, including neonatal seizures and severe encephalopathy. Disease progression is rapid, and death occurs within months of birth. This condition is extremely rare, estimated to occur in 1 in 100,000 to 200,000 newborns worldwide.[6] It is believed that the condition is often misdiagnosed as cerebral palsy or other conditions in which the brain does not receive enough oxygen.[7]

Role in treatment:

Fosdenopterin would be the first FDA-approved treatment for MoCD type A. Current experimental therapies are not FDA-approved with unknown efficacy and safety. MoCD type A is rare, but these patients currently have limited options.

Efficacy:

The manufacturer has two clinical trials underway. Data from an early observational, retrospective trial using an *Escherichia coli* derived cPMP product demonstrated positive results and reported no safety issues. Positive results, including a reduction in seizures and, for a few patients, near-normal development for up to five years, appeared dependent on how early treatment began.[8]

Safety:

No significant safety issues have been reported.

Financial impact:

Although the product is expected to have a high cost, **it is unlikely to have a major impact on overall medical spend due to the rarity of the disease**.

IngenioRx view:

Fosdenopterin would be the first FDA-approved treatment for this condition. Efficacy and safety information are limited at this time. Whether approval of fosdenopterin will lead to increased disease awareness and diagnosis remains unclear.

6 MedlinePlus: *Molybdenum cofactor deficiency* (August 18, 2020): medlineplus.gov.
7 Molecular Case Studies: *Mortality in a neonate with molybdenum cofactor deficiency illustrates the need for a comprehensive rapid precision medicine system* (October 30, 2019): molecularcasestudies.cshlp.org.
8 The Lancet: *Efficacy and safety of cyclic pyranopterin monophosphate substitution in severe molybdenum cofactor deficiency type A: a prospective cohort study* (November 14, 2015): thelancet.com.

In addition to the treatments listed previously, there are additional important drugs and biologics scheduled to receive FDA approval within the next 18 months.

Other significant product approvals

We expect these products to reach the market in 2021.*

Drug or biologic manufacturer	Indication/ route**	Place in therapy**	Estimated approval date	Impact on overall drug spend
Cabenuva® (cabotegravir/ rilpivirine long acting) GlaxoSmithKline	HIV-1 treatment/IM	**Addition to class:** once-monthly, two-drug combination option; uptake may be slow due to resistance concerns	First quarter 2021	—
Vocabria® (cabotegravir long acting) GlaxoSmithKline	HIV-1 treatment/oral	**Addition to class:** would be taken as an oral lead-in with an already-approved, once-daily, oral tablet formulation of rilpivirine	First quarter 2021	—
Dostarlimab GlaxoSmithKline	Endometrial cancer/IV	**Addition to class:** would compete with Keytruda® for microsatellite instability-high disease (MSI-H); dostarlimab has activity against MSI-H and microsatellite stable disease; currently no FDA-approved treatments for microsatellite stable disease	01/14/2021	—
Vericiguat Merck	Chronic heart failure with reduced ejection fraction (HFrEF)/oral	**First in class:** would compete with Entresto® and Farxiga®	01/20/2021	—
Voclosporin Aurinia Pharmaceuticals	Lupus nephritis/oral	**Addition to class:** would be first FDA-approved treatment for this indication	01/22/2021	

* As of November 5, 2020.

**** Key:**

CART: chimeric antigen receptor T-cell

GnRH: gonadotropin-releasing hormone

HIV: human immunodeficiency virus

IM: intramuscular

IV: intravenous

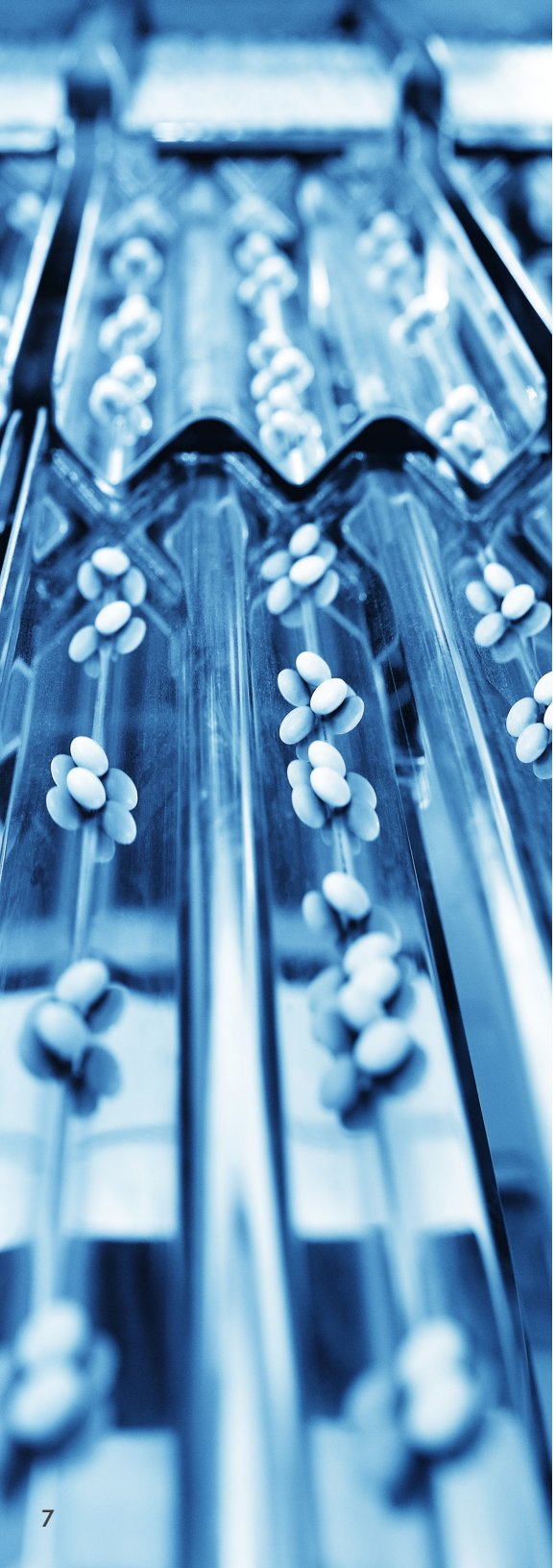
PD-1: programmed cell death-1

SC: subcutaneous

Rolling submission: when a drug company submits completed sections of its application for review instead of waiting until every section of the application is completed; decision date is assigned when the application is complete

Orphan drug/rare disease; potential high cost, but minimal impact on drug spend due to low prevalence of disease or utilization

Significant potential impact to overall incremental or new drug spend due to cost or prevalence of disease



Other significant product approvals (continued)

Drug or biologic manufacturer	Indication/route**	Place in therapy**	Estimated approval date	Impact on overall drug spend
Pegunigalsidase alfa Protalix Biotherapeutics	Fabry disease/IV	**Addition to class:** enzyme replacement therapy (ERT); will compete with Fabrazyme®; potential advantage of decreased dosing frequency	01/27/2021	
Evinacumab Regeneron	Homozygous familial hypercholesterolemia/IV	**Addition to class:** will compete with statins; ezetimibe; Kynamro®; Juxtapid™; and Repatha®	02/11/2021	
Trilaciclib G1 Therapeutics	Myelopreservation in small cell lung cancer/IV	**Addition to class:** potential advantages over current therapies include improvement in neutropenia, fatigue, and anemia; reduction of red blood cell transfusions; decreased use of rescue therapies; and fewer chemotherapy dose reductions	02/15/2021	—
Amondys 45™ (casimersen) Sarepta	Duchenne muscular dystrophy (DMD)/IV	**Addition to class:** would be first agent for individuals with DMD with deletions amenable to exon 45 skipping	02/25/2021	
Aducanumab Biogen	Alzheimer's disease/IV	**First in class:** would be first anti-amyloid antibody for early disease; potential to slow disease progression	03/07/2021	
Arimoclomol Orphazyme	Niemann-Pick disease/oral	**First in class:** would be first FDA-approved agent for this indication; may compete or be used in combination with off-label Zavesca™	03/17/2021	

Other significant product approvals (continued)

Drug or biologic manufacturer	Indication/route**	Place in therapy**	Estimated approval date	Impact on overall drug spend
Ponesimod Johnson & Johnson	Multiple sclerosis/ oral	**Addition to class:** sphingosine-1-phosphate (S1P) receptor; no clear advantage over others in class	03/18/2021	—
Idecabtagene vicleucel Bristol Myers Squibb/ bluebird bio	Multiple myeloma/IV	**Addition to class:** would be first CART therapy for multiple myeloma; will compete with other treatments such as PD-1 inhibitors	03/27/2021	
Tralokinumab AstraZeneca	Atopic dermatitis/SC	**Addition to class:** would compete with Dupixent®	Second quarter 2021	—
Fosdenopterin BridgeBio	Molybdenum cofactor deficiency type A/IV	**First in class:** would be first FDA-approved treatment for this indication	04/11/2021	
Abrocitinib Pfizer	Atopic dermatitis/oral	**Addition to class:** would be first janus kinase (JAK) inhibitor for treatment of atopic dermatitis; would compete with Dupixent®	04/30/2021	—
Relugolix Myovant	Uterine fibroids/oral	**Addition to class:** second GnRH antagonist approved for uterine fibroids; will compete with Oriahnn™; filing as a combination tablet with estradiol and norethindrone acetate	06/01/2021	—
Bimekizumab UCB	Plaque psoriasis/SC	**Addition to class:** IL-17 inhibitor will compete with other biologics	July 2021	—

Other significant product approvals (continued)

Drug or biologic manufacturer	Indication/route**	Place in therapy**	Estimated approval date	Impact on overall drug spend
Avacopan ChemoCentryx	Anti-neutrophil cytoplasmic antibody-associated vasculitis/oral	**Addition to class:** would be first antibody complement 5a receptor inhibitor for this indication; will compete with prednisone	07/07/2021	
Vosoritide BioMarin	Achondroplasia/SC	**Addition to class:** would be first FDA-approved treatment for this indication	08/21/2021	
Narsoplimab Omeros Corporation	Hematopoietic stem cell transplant-associated thrombotic microangiopathy/IV	**Addition to class:** would be first FDA-approved treatment for this indication	2021 (rolling submission)	
Zynteglo®/ LentiGlobin™ (betibeglogene autotemcel) bluebird bio	Beta thalassemia/IV	**First in class:** would be first gene therapy approved for treatment of beta thalassemia	2021 (rolling submission)	

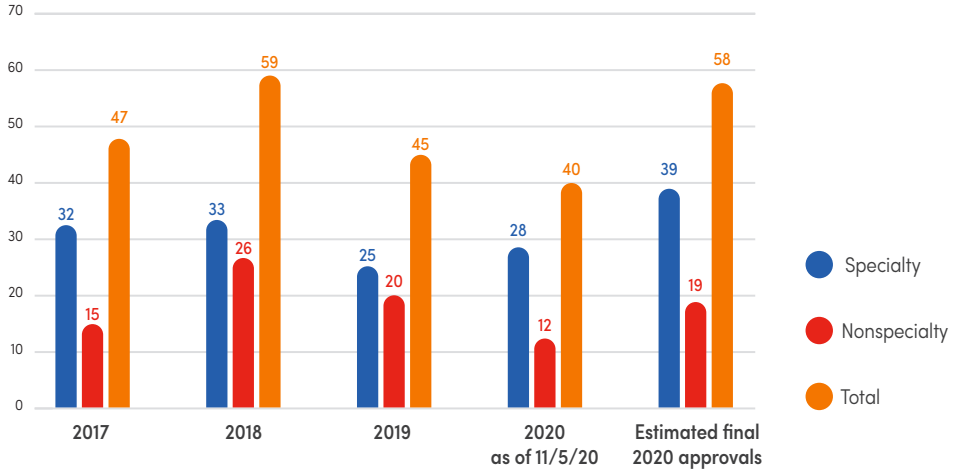
Analysis: the continued abundance of specialty drugs and biologics in the pipeline

Specialty drug and biologic approvals have historically outpaced nonspecialty drug approvals. This trend is expected to continue in 2020. Although specialty accounted for a little more than 2% of total prescription volume in 2018,[9] it accounted for 45% of all drug and biologic spend[10] — a figure expected to rise to 50% in 2020.[11]

What's more, experts estimate about half of all specialty drug and biologic expenses will be covered under the medical rather than the pharmacy benefit.[12] Many of these agents are in oncology, autoimmune disorders, and inflammatory conditions.

Those trends make it important to monitor the specialty pipeline, as members and plan sponsors face higher costs as a result: Specialty products are often priced considerably higher than nonspecialty drugs. Although many specialty drugs and biologics treat rare diseases, dampening their overall financial impact, some are used for more common conditions, often substantially increasing utilization.

FDA approval trends



Total number of final approvals is dependent on FDA reviews and potential denials, delays, or both. As a result, the final 2020 number will likely be lower than shown above. Counts may differ slightly from the FDA, depending on how new molecular entity (NME) is defined.

Sources: U.S. Food and Drug Administration: *Novel Drug Approvals for 2017* (November 11, 2019): fda.gov
U.S. Food and Drug Administration: *Novel Drug Approvals for 2018* (November 11, 2019): fda.gov
U.S. Food and Drug Administration: *Novel Drug Approvals for 2019* (January 14, 2020): fda.gov
U.S. Food and Drug Administration: *Novel Drug Approvals for 2020* (November 5, 2020): fda.gov

9 IQVIA: *Medicine use and spending in the U.S.* (May 9, 2019): iqvia.com.
10 Managed Care: *Specialty drug spend soars. Can formulary management bring it down to Earth?* (September 18, 2019): managedcaremag.com.
11 IQVIA: *Global medicine spending and usage trends:* outlook to 2024 (March 5, 2020): iqvia.com.
12 Midwest Business Group on Health: *Medical vs. Pharmacy Benefit* (accessed October 6, 2020): specialtyrxtoolkit.org.

More specialty drugs expected for approval

Specialty drug and biologic approvals continue to dominate the pipeline, with 28 specialty products receiving FDA approval in 2020 through November 5, compared with 12 nonspecialty products. We expect as many as 39 specialty treatments to receive approval in 2020 as a whole, and 19 nonspecialty treatments. These overall numbers may be considerably lower depending on FDA delays or denials.

Specialty products accounted for $220 billion drug spend in 2018,[13] even though it represented just 2.2% of all prescriptions.[14] In 2020, specialty is expected to account for half of all drug spend, and 52% by 2024.[15]

Since 2013, the FDA has approved more than 140 new specialty drugs and biologics, and approximately 60% of new products awaiting FDA approval through 2021 are specialty.[16]

Oncology agents, considered specialty treatments, remain the most common class for FDA approval (specialty or otherwise), accounting for approximately 27% of all new drug and biologic approvals in the United States since 2010.[17] Through October, oncology has accounted for 36% of all new approvals in 2020.[18]

Orphan diseases are a group of approximately 7,000 rare conditions[19] that affect fewer than 200,000 people nationwide.[20] Less than 10% have an FDA-approved treatment available. Therapies to treat these diseases are often considered specialty drugs due to their high costs, how they are administered, or both.

By 2024, drugs and biologics for orphan diseases are expected to account for more than 18%, or $217 billion, of overall prescription sales, as the pipeline for these agents remains robust.[21]

13 IQVIA: *Medicine use and spending in the U.S.* (May 9, 2019): iqvia.com.
14 Managed Care: *Specialty drug spend soars. Can formulary management bring it down to Earth?* (September 18, 2019): managedcaremag.com.
15 IQVIA: *Global medicine spending and usage trends: outlook to 2024* (March 5, 2020): iqvia.com.
16 Certara: *Key Trends in U.S. Specialty Pharmacy: Payer Perspectives and Developer Strategies, 2020-23* (Spring, 2020): cdn-assets.certara.com.
17 ASCO Post: *New Report Finds Cancer Drugs Account for Over a Quarter of All New Drug Approvals in the United States* (October 1, 2019): ascopost.com.
18 U.S. Food and Drug Administration: *Novel Drug Approvals for 2020* (November 5, 2020): fda.gov.
19 U.S. Food and Drug Administration: *Rare Disease Cures Accelerator* (accessed October 14, 2020): fda.gov.
20 U.S. Food and Drug Administration: *Orphan Products: Hope for People With Rare Diseases* (accessed October 14, 2020): fda.gov.
21 Evaluate: *EvaluatePharma Orphan Drug Report 2020* (accessed October 14, 2020): evaluate.com.

Therapy market trends

1. **We continue to see significant utilization and growth with Dupixent®, the first and only FDA-approved biologic for atopic dermatitis.** Dupixent sales in the United States are expected to exceed $4.9 billion by 2028,[22,23] although competitors could enter the market as early as 2021, including the first janus kinase inhibitor for atopic dermatitis. Dupixent's sales estimates include already FDA-approved indications as well as new label expansions anticipated in the near future.

2. **FDA approval of expanded indications continues to fuel growth for several important therapeutic classes.** Anti-inflammatory biologics, including targeted immune modulators (TIMs), could reach $150 billion in sales by 2027.[24] This drug class primarily includes injectable biologics and some competing oral agents for rheumatoid arthritis, plaque psoriasis, and inflammatory bowel disease. A combination of high prices for existing TIMs, increase in utilization, label expansions for existing TIMs, and additional novel TIMs in the pipeline contribute to their extensive growth. However, competition does increase as more products gain similar indications.

   The treatment landscape for cystic fibrosis (CF) using a cystic fibrosis transmembrane conductance regulator (CFTR) modulator continues to grow. With triple-combination therapy Trikafta's approval in October 2019, the percentage of CF patients eligible for treatment grew from approximately 60% to 80%.[25] By 2021, 90% of patients may be eligible for treatment due to pediatric and additional mutation label expansions,[26] contributing to forecasted domestic sales of $6.4 billion in 2028.[27]

   Sodium glucose co-transporter 2 (SGLT2) inhibitors are approved for the treatment of type 2 diabetes (T2D) but are gaining traction in the treatment of heart failure. Farxiga® recently gained FDA approval in adults with heart failure with reduced ejection fraction (HFrEF) with and without T2D. Jardiance® will soon apply for the same indication. In addition, these agents are planning on submissions in adults with preserved ejection fraction (HFpEF). There are currently no treatment options for patients with HFpEF, creating potential for continued growth for the SGLT2 inhibitors outside of T2D. U.S. sales for branded and generic SGLT2 inhibitors for heart failure are estimated to exceed $3.6 billion by 2029.[28]

22 Regeneron: *Regeneron Reports First Quarter 2020 Financial and Operating results* (May 5, 2020 press release): newsroom.regeneron.com.
23 Regeneron: *Regeneron Reports Second Quarter 2020 Financial and Operating results* (August 5, 2020 press release): newsroom.regeneron.com.
24 GlobeNewswire: Anti-Inflammatory Biologics Market to Reach USD 149.80 Billion by 2027; Ongoing Trials for Anti-Tumor Necrosis Factor (TNF) to Elevate Market Scope, states Fortune Business Insights (May 11, 2020): globenewsire.com.
25 Cystic Fibrosis Foundation: *2019 Cystic Fibrosis Foundation Patient Registry Highlights* (accessed October 2020): cff.org.
26 Vertex: *Second-Quarter 2020 Financial Results* (July 30, 2020 press release): investors.vrtx.com.
27 Decision Resources Group website (accessed October 2020): insights.decisionresourcesgroup.com (registration required).
28 Decision Resources Group website (accessed October 2020): insights.decisionresourcesgroup.com (registration required).

Therapy market trends (continued)

3. **The FDA has issued several significant complete response letters (CRLs) this year.** A CRL indicates that a product is not ready for approval for reasons such as efficacy, safety, proposed labeling, or manufacturing.[29] The following products received CRLs:
   - Viaskin™ for peanut allergies
   - Roctavian, a gene therapy for hemophilia A
   - Instiladrin®, a gene-based therapy for bladder cancer
   - Veverimer for metabolic acidosis associated with chronic kidney disease.

All of these treatments were highly anticipated with the potential for significant utilization.

29 U.S. Food and Drug Administration: *Complete Response Letter Final Rule* (accessed October 2020): fda.gov.

Update on gene therapies

Unlocking the potential in gene therapy

Gene therapy, a technique which introduces genetic material into the body, is a novel approach to treatment that has the potential to cure certain diseases with a single dose. As a result of this potential, drug companies are investigating more than 900 gene therapies.[30]

The current state of gene therapy

The FDA has created additional guidance to expedite gene therapy development and manufacturing. Several gene therapy technologies exist, but the most advanced is viral-based gene therapy, in which the infectious parts of viruses are replaced with a gene that can be used to help treat or modify a disease. To date, the FDA has approved two gene therapies for rare diseases: Luxturna®, which treats inherited retinal diseases, and Zolgensma®, which treats spinal muscular atrophy for children under 2 years of age. The FDA denied approval for two other gene therapies, Instiladrin® and Roctavian, but both manufacturers are planning to re-file their applications.

Limitations of gene therapy

As to be expected with a new approach, gene therapy has drawbacks:

- Gene therapy costs millions of dollars with no guarantee of long-term efficacy, and it is unclear how insurers will be able to pay for these treatments on a wide-scale basis.
- It is unknown if gene therapies provide a permanent cure, and there are questions regarding whether a patient can receive more than one dose of the gene therapy.
- There can be safety issues, such as immune responses to the virus used to deliver gene therapy.
- For some diseases, patients must undergo a toxic chemotherapy regimen prior to receiving gene therapy.
- There are challenges with complex manufacturing processes.

Gene therapy pipeline and future

The vast majority of gene therapies are in the preclinical stage; approximately 350 gene therapies are in early clinical development, while around 35 are in late-stage clinical trials.[31] We see four or more gene therapies with the potential for 2021 approval (see chart on page 14). In the future, we could see several gene therapy approvals each year. Because of limitations, price, and other unresolved questions regarding gene therapy, it remains to be seen if gene therapy will be a long-term solution for members and plan sponsors.

30 U.S. Food and Drug Administration: *FDA Continues Strong Support of Innovation in Development of Gene Therapy Products* (January 28, 2020): fda.gov.
31 Alliance for Regenerative Medicine: *Innovation in the Time of COVID-19: ARM Global Regenerative Medicine & Advanced Therapy Sector Report* (accessed October 14, 2020): alliancerm.org.

**** Key:**
Single-dose injections for each gene therapy, except where noted in the route column

GnRH: gonadotropin-releasing hormone

IV: intravenous

FIX: factor 9

HCT: hematopoietic cell transplantation

Gene-based therapy: Traditional gene therapies introduce genetic material into the body and are intended to cure or lessen the severity of disease. Gene-based therapies use genetic material to fight disease.

Update on gene therapies (continued)

Gene therapies with potential 2021 approval

Gene therapy manufacturer	Indication/route**	Place in therapy**
Etranacogene dezaparvovec (AMT-061) UniQure	Hemophilia B/IV	First gene therapy for this indication; will compete with FIX products
Ofranergene obadenovec (VB-111) VBL Therapeutics	Ovarian cancer/IV (multiple doses)	First gene-based therapy for this indication; used in combination with paclitaxel
PTC-AADC (AGIL-AADC) PTC Therapeutics	Aromatic L-amino acid decarboxylase deficiency/intracerebral	First gene therapy for this indication
TAVO (tavokinogene telseplasmid) OncoSec Medical	Advanced melanoma/ intratumoral (multiple doses)	First gene-based therapy for this indication; used in combination with Keytruda®

Gene therapies with potential late 2021/early 2022 approval

Gene therapy manufacturer	Indication/route**	Place in therapy**
ABO-102 Abeona Therapeutics	Mucopolysaccharidosis IIIA (Sanfilippo Type A)/IV	First gene therapy for this indication
FCX-007 Castle Creek Pharmaceutical	Epidermolysis bullosa/ autologous, gene-modified skin grafts (multiple skin grafts)	Potential to be the first gene-based therapy for this indication; will compete with other gene therapies in development
Bercolagene telserpavec (B-VEC; KB103) Krystal Biotech	Epidermolysis bullosa/ topical gel (multiple doses)	Addition to class; will compete with other gene-based therapy in development

Update on gene therapies (continued)

Gene therapies with potential late 2021/early 2022 approval

Gene therapy manufacturer	Indication/route**	Place in therapy**
EB-101 Abeona Therapeutics	Epidermolysis bullosa/ autologous, gene-modified skin grafts (multiple skin grafts)	Addition to class; will compete with other gene-based therapy in development
Lenti-D™ bluebird bio	Cerebral adrenoleukodystrophy/IV	First gene therapy for this indication; will compete with HCT
OTL-103 Orchard Therapeutics	Wiskott-Aldrich syndrome/IV	First gene therapy for this indication; will compete with HCT
OTL-200 Orchard Therapeutics	Metachromatic leukodystrophy/IV	First gene therapy for this indication; will compete with HCT
Timrepigene emparvovec (BIIB111) Biogen	Choroideremia/subretinal	First gene therapy for this indication
Zynteglo®/LentiGlobin™ bluebird bio	Beta-thalassemia/IV	First gene therapy for treatment of beta thalassemia; potential 2022 submission for sickle cell disease (SCD)

For more insights: **ingenio-rx.com**

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