U.S. FOOD & DRUG ADMINISTRATION

ADVANCING HEALTH THROUGH INNOVATION: NEW DRUG THERAPY APPROVALS 2021

Impact | Innovation | Predictability | Access

CENTER FOR DRUG EVALUATION AND RESEARCH

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Table of Contents


SUN
MON
TUE
WED
FRI

Director's Message

Patrizia Cavazzoni, M.D.,
Director, Center for Drug Evaluation and Research

Welcome to FDA's Center for Drug Evaluation and Research's (CDER) annual report, *Advancing Health Through Innovation: New Drug Therapy Approvals 2021*, representing our 11th consecutive year of reporting CDER's notable human drug approvals. This report illustrates our role in bringing innovative drug therapies that are safe and effective to patients in need.

Throughout the year, the COVID-19 pandemic continued to present significant challenges to our entire staff. In spite of these hardships, we have approved many therapies that will advance health for the American public. As in the past, this year's new drug therapies span many areas of medicine and disease areas.

This is our fifth consecutive year of publishing an expanded version of the report with an overview of non-novel notable approvals — for instance, approvals in which a previously approved drug will be used to treat a different disease or a new patient population, such as children.

Our report showcases the new therapies we evaluated for safety and efficacy, as well as important regulatory tools we used to expedite the review and approval of these applications. We approved the large majority of these therapies by or before their goal dates as defined by congressionally authorized agreements with industry (referred to as user fee programs). Most drugs were also approved in the U.S. before any other country.

This report also highlights the year's biosimilar product approvals. Of particular note, CDER approved the first two interchangeable biosimilar products in 2021, which are biological products that meet additional requirements and may be substituted for the reference product at the pharmacy without the intervention of a prescriber, similar to how generic drugs are substituted for brand name drugs. More biosimilar and interchangeable biosimilar products mean greater competition that may lead to increased access to therapies and potentially lower costs to patients.

Our work in reviewing and approving new therapies includes thorough safety examinations. New drugs must not only meet our rigorous premarket safety standards, but also undergo postmarket safety surveillance. We will discuss our comprehensive safety activities in a different report.

This report summarizes CDER's 2021 approvals and highlights examples of innovative treatments. FDA's Center for Biologics Evaluation and Research (CBER) also approves important therapies to advance and protect public health. Perhaps most significantly in 2021, CBER approved a COVID-19 vaccine, a milestone in our continued fight against this pandemic. For more information about CBER actions, please visit CBER's webpage for 2021 Biological Approvals.

In closing, we hope the following overview of new drug therapy approvals will promote greater understanding of the CDER mission to improve treatment options for patients.

Executive Summary

See page 10 for a complete list of these therapies.

In 2021, CDER approved many different drug therapies, helping patients have a better quality of life, reducing disease symptoms or severity, and in many instances, protecting patients against life-threatening illnesses.

Heart, Blood, Kidney, and Endocrine Diseases

In 2021, CDER took important steps in advancing treatment options for patients with **diabetes**. CDER approved several **diabetes** medications, including one interchangeable biosimilar insulin product and one biosimilar insulin product, which can provide patients with additional safe, high-quality, and potentially more cost-effective options. CDER also approved a treatment for pediatric patients ages 10 and older with **type 2 diabetes** and a therapy for **severe hypoglycemia**, or low blood sugar, in patients aged six years and older with **diabetes**.

We approved a therapy to reduce the risk of serious complications in adults with **chronic kidney disease associated with type 2 diabetes**. In addition, we approved a treatment to reduce the risk of serious outcomes in adults with **chronic kidney disease at risk of chronic kidney disease progression**.

For patients with **obesity** and **overweight**, CDER approved a new add-on therapy for **chronic weight management** in certain adults — the first drug approved for this indication since 2014 and a tool that may help combat our nation's obesity epidemic. A treatment was also approved to reduce the frequency of **chemotherapy-induced bone marrow suppression** in adults with types of small cell lung cancer.

Drug approvals for rare diseases in this area include: 1) several add-on therapies to treat certain patient populations with **homozygous familial hypercholesterolemia**, a life-threatening condition characterized by severely high cholesterol levels; 2) a treatment

for **paroxysmal nocturnal hemoglobinuria**, a rare and serious blood disease; 3) the first treatment to increase height in people with **achondroplasia**, the most common type of dwarfism; 4) a treatment for **polycythemia vera**, a rare chronic disease involving circulatory risks caused from the overproduction of red blood cells; and 5) a treatment for children aged 4-11 years with **sickle cell disease**, an inherited disorder characterized by dysfunctional red blood cells.

Autoimmune, Inflammatory, and Lung Diseases

2021 was an important year for treatments for **inflammatory bowel disease (IBD)**, or disorders that involve digestive tract inflammation. For example, CDER approved a therapy for adults with **moderately to severely active ulcerative colitis**, a type of **IBD** in which the lining of the colon becomes inflamed and develops tiny open sores, or ulcers. CDER also approved a therapy for pediatric patients with **moderately to severely active ulcerative colitis** — the first therapy in this biologics class for this patient population that can be administered at home rather than at an infusion center. On the biosimilars front, CDER approved an interchangeable biosimilar and a biosimilar to treat **ulcerative colitis in adults**, **Crohn's disease** (another type of **IBD** that affects the lining of the digestive tract) and other inflammatory diseases, including **different types of arthritis**.

2021 was an important year for treatments for inflammatory bowel disease.

In 2021, CDER also approved a treatment for **systemic lupus erythematosus (SLE)**. **SLE** is the most common form of lupus, a disease in which the immune system attacks the body's own tissues, causing inflammation and tissue damage. In addition, CDER approved a therapy for adults with **active lupus nephritis**, a serious kidney disease associated with lupus.

CDER approved a drug to treat **pruritus (itchiness)** that can occur in patients with chronic kidney disease. CDER also approved two new therapies to treat **moderate-to-severe atopic dermatitis (eczema)** that has not responded to other therapies.

Approvals of note to treat rare diseases in this area include: 1) a therapy for children aged 6-11 years with the most common mutation for **cystic fibrosis**, a progressive disorder that causes severe lung damage and limits the ability to breathe; 2) a therapy to prevent **organ rejection in patients receiving lung transplants**; 3) a treatment for **systemic sclerosis-associated interstitial lung disease,** a multi-organ autoimmune disorder characterized by inflammation, vascular injury and tissue scarring; 4) a medication to treat **anti-neutrophil cytoplasmic antibody-associated vasculitis**, a group of diseases characterized by destruction and inflammation of small vessels; and 5) drugs to treat **pruritus** associated with rare liver disorders, often occurring in children.

Infectious Diseases

In 2021, CDER continued to help advance the treatment and prevention of **HIV-1 infection**, the most common type of HIV. Early in the year, we approved the first extended-release injectable drug that functions as a complete regimen, administered monthly, to treat **HIV-1 infection** in adults. We also approved a combination drug product, administered as a single tablet and taken once a day, to treat **HIV-1** infection in children aged two years or older. By year's end, CDER approved the first extended-release, injectable, antiviral drug administered every two months, to prevent **HIV-1** infection in adults and adolescents.

Also in the antiviral area, CDER approved a drug to treat **human smallpox disease** in adult and pediatric patients, including newborn babies. Although the World Health Organization has declared **smallpox** eradicated, there have been longstanding concerns that **smallpox** virus could be used as a bioweapon. This approval is therefore an important medical countermeasure.

2021 marked an important year for new HIV-1 treatments and preventive therapies.

CDER also approved the first antiviral drug to treat adults and adolescents with **post-transplant cytomegalovirus (CMV) infection or disease that does not respond to other antiviral drugs**. This approval is an important advancement in treating **CMV infection or disease**, where there has been an unmet medical need for patients receiving transplants.

For patients with rare infectious diseases, CDER approved the first all-oral treatment for **sleeping sickness (Human African trypanosomiasis)**, a disease caused by parasites transmitted by infected tsetse flies and endemic in sub-Saharan Africa. Other sleeping sickness therapies include oral components taken together with non-oral drugs.

Neurological and Psychiatric Disorders

To help address the opioid crisis, we approved two therapies to reverse an **opioid overdose** in an emergency situation. Using the accelerated approval pathway, CDER approved a new drug to treat **Alzheimer's disease**. This drug is the first new treatment approved for **Alzheimer's disease** since 2003 and the first therapy that targets the fundamental disease pathophysiology. CDER also approved two drugs that help reduce the frequency of **migraine attacks** in patients with **episodic migraines**.

Approvals of note for rare neurological disorders include: 1) a treatment for certain patients with **Duchenne muscular dystrophy**, a genetic disorder occurring primarily in young boys that leads to progressive muscle degeneration and weakness; and 2) a treatment for **myasthenia gravis**, a chronic neuromuscular disease.

Cancers

2021 marked the 50th anniversary of the National Cancer Act, landmark legislation committed to fighting cancer. In this anniversary year, CDER approved many therapies for different cancers. Four new drugs were approved for **non-small cell lung cancer**, including one **non-small cell lung cancer** type previously thought to be resistant to treatment. CDER also approved a therapy for some types of **basal cell carcinoma**, the most common form of skin cancer, for certain patient populations.

In 2021, CDER approved four new therapies for non-small cell lung cancer.

The first approved immunotherapy to be used as a first-line treatment for **esophageal (esophagus-related) cancer**, **gastric (stomach) cancer**, and **gastroesophageal junction (GEJ) adenocarcinoma** was an important cancer approval for 2021. CDER approved two other therapies for certain patients with **HER2-positive gastric cancer** and **GEJ adenocarcinoma**; one of these therapies was also approved for **esophageal cancer**, **advanced kidney cancer** and as an **adjuvant treatment for kidney cancer**.

With regard to breast cancer, CDER approved a therapy for **early-stage, triple negative breast cancer**, or cancer that does not respond to hormone therapies or medications that target HER2 protein receptors.

Other CDER approvals for rare cancers include: 1) two treatments for adults with certain kinds of **cholangiocarcinoma**, a group of aggressive cancers that start in the bile duct; 2) a therapy for adults to treat certain tumors that are associated with **von Hippel-Lindau disease**, an inherited disorder characterized by tumors and cysts; 3) a therapy to be used together with other treatments for **light chain amyloidosis**, a condition that interferes with normal organ functions due to abnormal protein build-up; and 4) the first FDA-approved treatment for **locally advanced unresectable or metastatic perivascular epithelioid cell tumor (PEComa)**, a group of rare tumors that form in the soft tissues of the stomach, intestines, lungs and other body parts.

(Note that FDA's Oncology Center of Excellence will produce its 2021 annual report to feature important cancer therapies approved in 2021 by CDER, CBER, and FDA's Center for Devices and Radiological Health [CDRH].)

Other Advances in Drug Therapies

In other advances of 2021, CDER approved 1) a drug for **late-onset Pompe disease**, a rare disease that causes muscle weakness and premature death; and 2) a medication to treat **neurogenic detrusor overactivity**, a bladder dysfunction, in children.

CDER's drug approvals of 2021 will help advance patient care in many new areas.

CDER's Drug Approvals of 2021

See Appendix B for a summary chart of designations for CDER's novel approvals.

In 2021, CDER approved 50 new drugs, either as new molecular entities (NMEs) under New Drug Applications (NDAs), or as new therapeutic biologics under Biologics License Applications (BLAs). The active ingredient or ingredients in a new drug have never before been approved in the U.S. The novel drugs CDER approved in 2021 are collectively notable for their potential positive impact and unique contributions to patient care.

CDER's novel drug approvals for 2021 are listed alphabetically below*

Trade Name	Active Ingredient(s)
Adbry	tralokinumab-ldrm
Aduhelm	aducanumab-avwa
Amondys 45	casimersen
Azstarys	serdexmethylphenidate and dexmethylphenidate
Besremi	ropeginterferon alfa-2b-njft
Brexafemme	ibrexafungerp
Bylvay	odevixibat
Cabenuva	cabotegravir and rilpivirine (co-packaged)
Cosela	trilaciclib
Cytalux	pafolacianine
Empaveli	pegcetacoplan
Evkeeza	evinacumab-dgnb
Exkivity	mobocertinib
	fexinidazole**
Fotivda	tivozanib
Jemperli	dostarlimab-gxly
Kerendia	finerenone
Korsuva	difelikefalin
Leqvio	inclisiran
Livmarli	maralixibat
Livtencity	maribavir
Lumakras	sotorasib
Lupkynis	voclosporin
Lybalvi	olanzapine and samidorphan
Nextstellis	drospirenone and estetrol

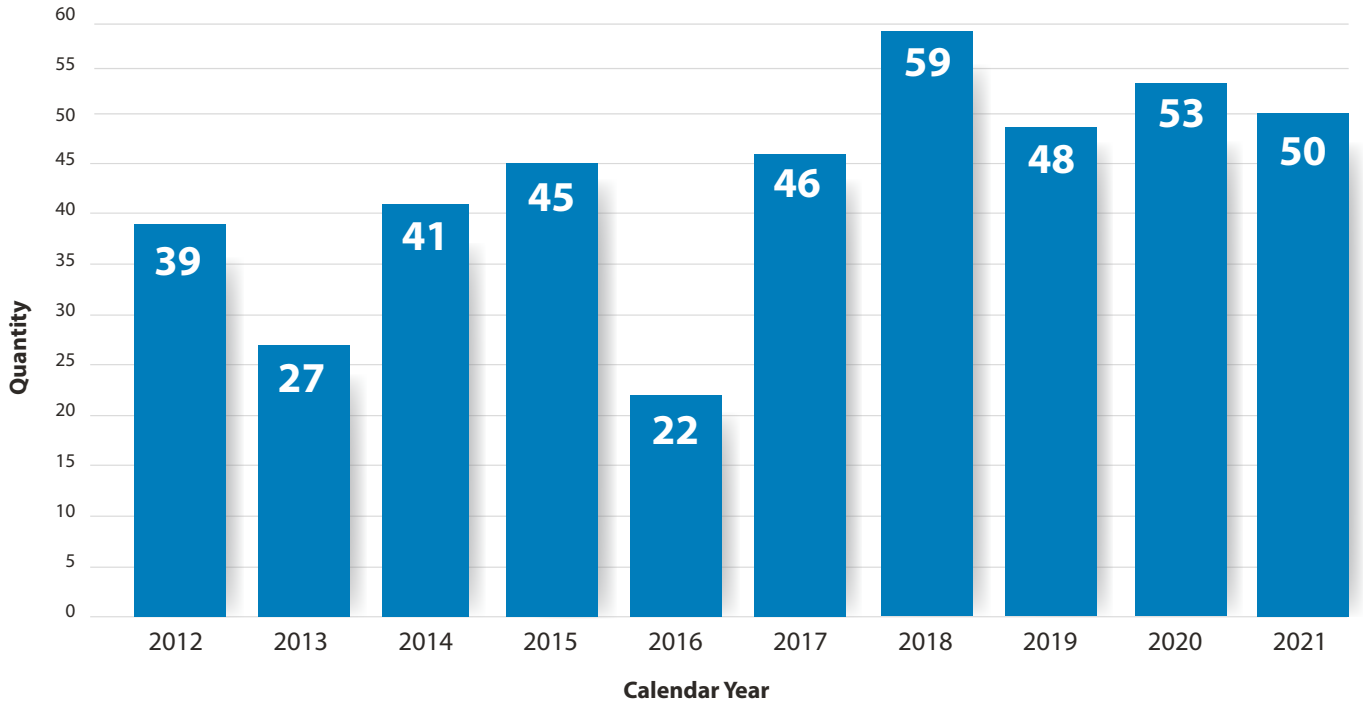
Trade Name	Active Ingredient(s)
Nexviazyme	avalglucosidase alfa-ngpt
Nulibry	fosdenopterin
Pepaxto	melphalan flufenamide
Ponvory	ponesimod
Pylarify	piflufolastat F 18
Qelbree	viloxazine
Qulipta	atogepant
Rezurock	belumosudil
Rybrevant	amivantamab-vmjw
Rylaze	asparaginase erwinia chrysanthemi (recombinant)-rywn
Saphnelo	anifrolumab-fnia
Scemblix	asciminib
Skytrofa	lonapegsomatropin-tcgd
Tavneos	avacopan
Tepmetko	tepotinib
Tezspire	tezepelumab-ekko
Tivdak	tisotumab vedotin-tftv
Truseltiq	infigratinib
Ukoniq	umbralisib
Verquvo	vericiguat
Voxzogo	vosoritide
Vyvgart	efgartigimod alfa-fcab
Welireg	belzutifan
Zegalogue	dasiglucagon
Zynlonta	loncastuximab tesirine-lpyl

* This information is accurate as of December 31, 2021. In rare instances FDA may need to change a drug's NME designation or the status of its application as a novel BLA. For instance, new information may become available that could lead to a reconsideration of the original designation or status. If FDA makes these types of changes, the agency intends to communicate the nature of, and the reason for, any revisions as appropriate.

** Product approved with no trade name

CDER's Annual Novel Drug Approvals: 2012–2021

The 10-year graph below shows that from 2012 through 2021, CDER has averaged 43 novel drug approvals per year.



First-in-Class Drugs

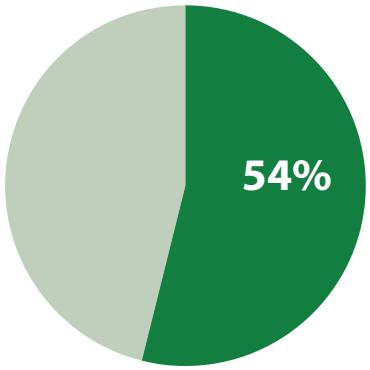
CDER identified 27 of the 50 novel drugs approved in 2021 (54%) as first-in-class. These drugs have mechanisms of action different from those of existing therapies.

Novel drugs approved in 2021 that CDER identified as first-in-class were:
Adbry, Aduhelm, Besremi, Brexafemme, Bylvay, Cosela, Cytalux, Empaveli, Evkeeza, Kerendia, Korsuva, Leqvio, Livtencity, Lumakras, Lupkynis, Nulibry, Rezurock, Rybrevant, Saphnelo, Tavneos, Tezspire, Tivdak, Verquvo, Voxzogo, Vyvgart, Welireg, Zynlonta

Examples of notable First-in-Class novel approvals for 2021 include:

- **Adbry** (tralokinumab-ldrm) injection [see also Opzelura on page 32] to treat moderate-to-severe **atopic dermatitis (eczema)** in adults whose disease cannot be adequately controlled by therapies applied directly on the skin.
- **Aduhelm** (aducanumab-avwa) injection to treat **Alzheimer's disease.** This drug is the first therapy for Alzheimer's that targets the fundamental disease pathophysiology.

First-in-Class Drugs



CDER identified 27 of the 50 (54%) novel drugs approved in 2021 as first-in-class.

- **Brexafemme** (ibrexafungerp) tablets to treat **vulvovaginal candidiasis**, a type of yeast infection. This is the first approved drug in a new antifungal class in more than 20 years.
- **Cosela** (trilaciclib) injection to reduce the frequency of **chemotherapy-induced bone marrow suppression** in certain adults treated for extensive-stage small cell lung cancer.
- **Evkeeza** (evinacumab-dgnb) [see also Praluent on page 24 and Repatha on page 26] injection as an add-on treatment for patients aged 12 years and older with **homozygous familial hypercholesterolemia**, a genetic condition that causes severely high cholesterol.
- **Leqvio** (inclisiran) [see Repatha on page 26] injection to treat **heterozygous familial hypercholesterolemia**, a genetic condition that causes severely high cholesterol, and **clinical atherosclerotic cardiovascular disease**, which involves cholesterol buildup in the arteries.
- **Livtencity** (maribavir) capsules to treat adults with **post-transplant cytomegalovirus (CMV) infection**. **CMV** is a common virus that doesn't normally cause any symptoms. However, people with weakened immune systems, including patients receiving transplants, can develop severe and life-threatening complications from **CMV**.
- **Lupkynis** (voclosporin) capsules to treat adults with **active lupus nephritis**, a serious kidney disease and complication of lupus, a disease in which the immune system attacks the body's own tissues.
- **Kerendia** (finerenone) tablets to reduce the risk of several serious complications in adults with **chronic kidney disease associated with type 2 diabetes**.
- **Korsuva** (difelikefalin) injection to treat **moderate-to-severe pruritus (itching)** associated with **chronic kidney disease** in adults undergoing hemodialysis.
- **Rezurock** (belumosudil) tablets to treat patients with **chronic graft-versus-host disease** after failing at least two previous systemic (throughout the body) therapies.
- **Rybrevant** (amivantamab-vmjw) injection to treat adults with certain forms of **non-small cell lung cancer** whose tumors have specific mutations. Rybrevant is the first FDA-approved treatment for this **subset of non-small cell lung cancer** and was approved through the accelerated approval pathway.

- **Saphnelo** (anifrolumab-fnia) injection to treat **systemic lupus erythematosus (SLE)**. **SLE** is the most common type of **lupus**, a disease in which the immune system attacks the body's own tissues.
- **Tezspire** (tezepelumab) injection as an add-on treatment for patients aged 12 and older with **severe asthma**.
- **Welireg** (belzutifan) tablets for adults who require treatment for certain tumors associated with **von Hippel-Lindau disease**. These tumors include renal cell carcinoma, central nervous system hemangioblastomas, or pancreatic neuroendocrine tumors that do not require immediate surgery.

Drugs in brackets refer to other treatments for the same or similar disease.

Drugs for Orphan Diseases

In 2021, 26 of CDER's 50 novel drug approvals (52%) were approved to treat rare or "orphan" diseases (diseases that affect than 200,000 people in the U.S.). Patients with rare diseases often have fewer or no drugs available to treat their conditions.

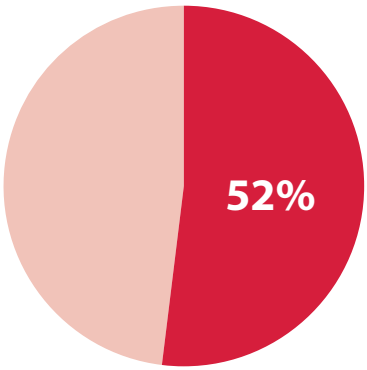
Novel drugs approved in 2021 with the orphan drug designation were:
Amondys 45, Besremi, Bylvay, Cytalux, Empaveli, Evkeeza, Exkivity, fexinidazole*, Livmarli, Livtencity, Lumakras, Nexviazyme, Nulibry, Pepaxto, Rezurock, Rylaze, Scemblix, Skytrofa, Tavneos, Tepmetko, Truseltiq, Ukoniq, Voxzogo, Vyvgart, Welireg, Zynlonta

*approved without a trade name

Notable examples of novel approvals of 2021 for orphan diseases include:

- **Besremi** (ropeginterferon alfa-2b-njft) injection to treat adults with **polycythemia vera**, a blood disease that causes the overproduction of red blood cells. The excess cells thicken the blood, slowing blood flow and increasing the chance of blood clots.
- **Bylvay** (odevixibat) capsules and oral pellets to treat **pruritus (itching) in progressive familial intrahepatic cholestasis (PFIC)**, a disorder that causes progressive liver disease and typically leads to liver failure. This is the first approved treatment for **pruritus** in patients with **PFIC**.

Orphan Drug Approvals



26 (52%) of CDER's 50 novel drug approvals were for rare or orphan diseases.

- **Cytalux** (pafolacianine) injection to help identify **ovarian cancer** lesions during surgery. **Ovarian cancer** is hard to detect early, making it difficult to successfully treat.
- **Empaveli** (pegcetacoplan) injection to treat adults with **paroxysmal nocturnal hemoglobinuria**, a rare, life-threatening blood disease.
- **fexinidazole** (no trade name) tablets to treat **sleeping sickness (Human African trypanosomiasis)**, a life-threatening disease caused by parasites transmitted by infected tsetse flies that is endemic in many sub-Saharan African countries. Fexinidazole is the first all-oral treatment for sleeping sickness. (Other treatments include oral components taken together with non-oral drugs.)
- **Livmarli** (maralixibat) oral solution to treat **cholestatic (liver-related) pruritus in Alagille syndrome**, an inherited condition in which bile builds up in the liver.
- **Lumakras** (sotorasib) tablets to treat adults with a specific type of **non-small cell lung cancer** that is locally advanced or metastatic. Adults must have received a prior systemic (throughout the body) therapy. The mutation (KRAS G12C) involved in this cancer was previously considered resistant to drug therapy.
- **Nexviazyme** (avalglucosidase alfa-ngpt) infusion to treat patients one year and older with **late-onset Pompe disease**, a disease characterized by an enzyme deficiency that causes muscle weakness and premature death from respiratory or heart failure.
- **Nulibry** (fosdenopterin) injection to reduce the risk of death due to **molybdenum cofactor deficiency type A**, an inherited disorder that typically presents in the first few days of life, causing hard-to-control seizures, brain injury, and death. Nulibry is the first approved therapy for this disease.
- **Rylaze** (asparaginase erwinia chrysanthemi (recombinant)-rywn) injection as a component of a chemotherapy regimen to treat **acute lymphoblastic leukemia**, the most common type of childhood cancer, and **lymphoblastic lymphoma** in patients who are allergic to the E. coli-derived asparaginase products used most commonly for treatment. The only other FDA-approved drug for patients with allergic reactions has been in global shortage for years.
- **Skytrofa** (lonapegsomatropin-tcgd) injection to treat pediatric patients with **growth hormone deficiency**. Patients can take Skytrofa weekly; other approved human

growth hormone formulations for this indication must be administered daily.

- **Tavneos** (avacopan) capsules to treat **anti-neutrophil cytoplasmic antibody-associated vasculitis**, a group of diseases characterized by destruction and inflammation of small vessels. The diseases can affect organs and cause skin lesions.

Other Novel Drug Approvals

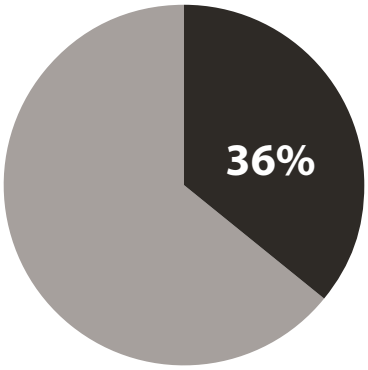
In addition to the first-in-class and orphan-designated drugs, the 2021 novel drug field also includes these notable approvals:

- **Cabenuva** (cabotegravir and rilpivirin) [see also Vocabria on page 32 and Apretude on page 30] injectable formulation as the first monthly complete regimen to treat **HIV**.
- **Jemperli** (dostarlimab) injection to treat a specific genetic form of **recurrent or advanced endometrial cancer**, or cancer that begins in the uterus, that has progressed despite other specific treatments. Jemperli was approved under the accelerated approval pathway.
- **Nextstellis** (drospirenone and estetrol) oral contraceptive tablets to prevent **pregnancy**.
- **Qelbree** (viloxazine) capsules to treat **attention deficit hyperactivity disorder (ADHD)** in patients aged six to 18. Qelbree is one of a few approved nonstimulant medications for **ADHD**.
- **Qulipta** (atogepant) [see also Nurtec ODT on page 24] tablets to help reduce the frequency of **migraine attacks** in patients with **episodic migraines**.
- **Verquvo** (vericiguat) tablets to reduce the risk of **cardiovascular death and heart failure** hospitalization in certain high-risk patients.
- **Zegalogue** (dasiglucagon) injection to treat **severe hypoglycemia**, or low blood sugar, in patients aged six years and older with diabetes.

Drugs in brackets refer to other treatments for the same or similar disease.

In 2021, CDER approved a therapy to treat patients with recurrent or advanced endometrial cancer.

Fast Track



CDER designated 18 of the 50 novel drugs (36%) as Fast Track.

Innovation: Use of Expedited Development and Review Pathways

CDER used diverse regulatory pathways to enhance and expedite drug product review in 2021. These pathways facilitate increased flexibility, efficiency, and interactions between CDER staff and drug developers. These pathways also allow shorter review times to speed the availability of new therapies to patients with serious conditions, especially when there are no satisfactory alternative therapies, while preserving appropriate standards for safety and effectiveness.

Fast Track

CDER designated 18 of the 50 novel drugs (36%) in 2021 as Fast Track status. Fast Track speeds new drug development and review by increasing the level of communication between FDA and drug developers and by enabling CDER to review portions of a drug application on a rolling basis.

Drugs designated with Fast Track status were:
Aduhelm, Amondys 45, Brexafemme, Bylvay, Cabenuva, Cytalux, Empaveli, Exkivity, Kerendia, Lumakras, Lupkynis, Nexviazyme, Rylaze, Saphnelo, Scemblix, Truseltiq, Verquvo, Vyvgart

Breakthrough Therapy

CDER designated 14 of the 50 novel drugs (28%) in 2021 as Breakthrough Therapies. A Breakthrough Therapy designation includes all the Fast Track program features and offers more intensive FDA guidance on efficiencies for drug development.

Drugs designated with Breakthrough therapy status were:
Cosela, Evkeeza, Exkivity, Jemperli, Korsuva, Livmarli, Livtencity, Lumakras, Nexviazyme, Nulibry, Rezurock, Rybrevant, Scemblix, Ukoniq

Priority Review

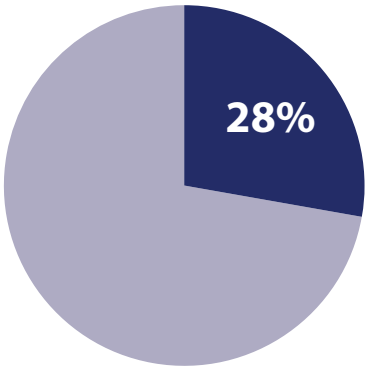
In 2021, 34 of the 50 novel drugs approved (68%) were designated Priority Review. A drug receives a Priority Review if CDER determines that the drug could potentially provide a significant advance in medical care. This means CDER aims to take action on a drug application within six months of filing (compared to 10 months under standard review).

In some instances, sponsors may redeem a priority review voucher under CDER's Priority Review Voucher program. Such drugs are not included in the list below.

Drugs designated Priority Review were:
Aduhelm, Amondys 45, Brexafemme, Bylvay, Cabenuva, Cosela, Cytalux, Empaveli, Evkeeza, Exkivity, fexinidazole*, Jemperli, Kerendia, Korsuva, Livmarli, Livtencity, Lumakras, Lupkynis, Nexviazyme, Nulibry, Pepaxto, Pylarify, Rezurock, Rybrevant, Scemblix, Tepmetko, Tezspire, Tivdak, Truseltiq, Ukoniq, Verquvo, Voxzogo, Welireg, Zynlonta

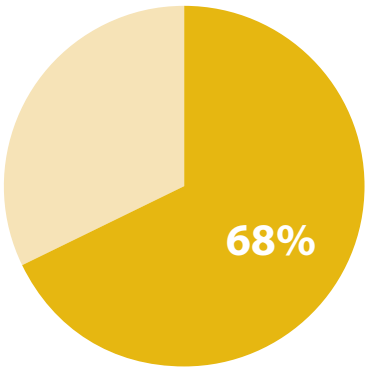
* approved with no trade name

Breakthrough Therapy



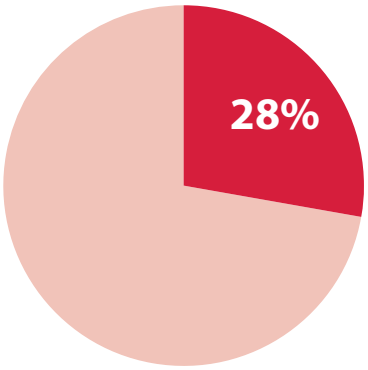
CDER identified 14 of the 50 (28%) novel drugs of 2021 as Breakthrough Therapies.

Priority Review



CDER identified 34 of the 50 (68%) drugs approved in 2021 as priority review.

Accelerated Approvals



CDER identified 14 of the 50 (28%) novel drugs as Accelerated Approvals.

Accelerated Approval

CDER approved 14 of the 50 novel drugs (28%) in 2021 under Accelerated Approval. This program aims to bring drugs that can provide important treatment advances sooner to market than with traditional approvals. It provides FDA more flexibility in what endpoints can be used to approve a drug that offers a benefit over current treatments for a serious or life-threatening illness. These accelerated approval endpoints may include those that are reasonably likely to predict clinical benefit, which may enable the drug to show benefits over a shorter treatment duration (whereas longer-term demonstration of benefit is needed for traditional approval). Subsequent confirmatory trials must be conducted to support traditional approval.

The Novel drugs approved in 2021 via Accelerated Approval were:
Aduhelm, Amondys 45, Exkivity, Jemperli, Lumakras, Pepaxto, Rybrevant, Scemblix, Tepmetko, Tivdak, Truseltiq, Ukoniq, Voxzogo, Zynlonta

Overall Use of Expedited Development and Review Methods

Thirty-seven of the 50 novel drug approvals of 2021 (74%) used one or more expedited programs, specifically Fast Track Designation, Breakthrough Therapy Designation, Priority Review, and/or Accelerated Approval.

Novel drugs approved in 2021 that used at least one expedited program were:
Aduhelm, Amondys 45, Brexafemme, Bylvay, Cabenuva, Cosela, Cytalux, Empaveli, Evkeeza, Exkivity, fexinidazole*, Jemperli, Kerendia, Korsuva, Livmarli, Livtencity, Lumakras, Lupkynis, Nexviazyme, Nulibry, Pepaxto, Pylarify, Rezurock, Rybrevant, Rylaze, Saphnelo, Scemblix, Tepmetko, Tezspire, Tivdak, Truseltiq, Ukoniq, Verquvo,Voxzogo, Vyvgart, Welireg, Zynlonta

* approved with no trade name

CDER used at least one expedited program to speed approval for 74% of all novel drugs approved in 2021.

Predictability: Meeting PDUFA Goals

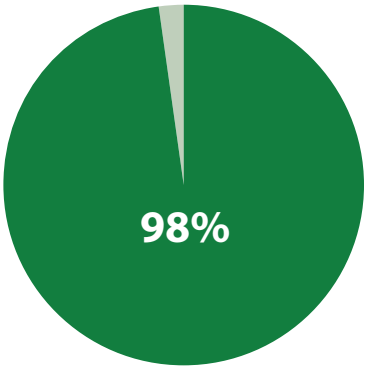
Under the Prescription Drug User Fee Act (PDUFA), industry are assessed user fees. With PDUFA, applications are reviewed targeting specific timeframes. Throughout 2021, CDER met or exceeded the PDUFA goal date for taking action on 98% (49 of 50) of the novel drugs approved.

Novel drugs approved in 2021 on or before their PDUFA goal dates were:
Adbry, Aduhelm, Amondys 45, Azstarys, Besremi, Brexafemme, Bylvay, Cabenuva, Cosela, Cytalux, Empaveli, Evkeeza, Exkivity, fexinidazole*, Fotivda, Kerendia, Korsuva, Leqvio, Livmarli, Livtencity, Lumakras, Lupkynis, Lybalvi, Nextstellis, Nexviazyme, Nulibry, Pepaxto, Ponvory, Pylarify, Qelbree, Qulipta, Rezurock, Rybrevant, Rylaze, Saphnelo, Scemblix, Skytrofa, Tavneos, Tepmetko, Tezspire, Tivdak, Truseltiq, Ukoniq, Verquvo, Voxzogo, Vyvgart, Welireg, Zegalogue, Zynlonta

*approved with no trade name

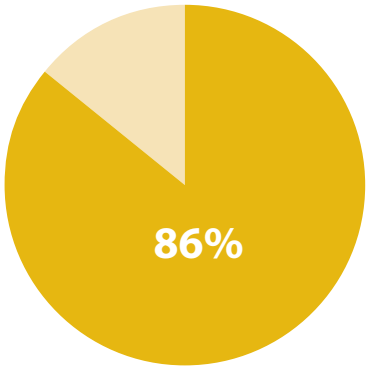
CDER met its PDUFA goal date for 98% of the novel drugs approved in 2021.

Meeting PDUFA Goals



In 2021, 49 (98%) of 50 novel drugs were approved on or before their PDUFA goal date.

First Cycle Approvals



CDER approved 43 of the 50 novel drugs of 2021 (86%) on the first cycle.

The high percentage of first cycle approvals reflects the extent to which CDER staff provide clarity to drug developers.

Access: First Cycle Approval and First in U.S. Approvals

First Cycle Approvals

CDER approved 43 of the 50 novel drugs of 2021 (86%) on the "first cycle" of review. This high percentage reflects the extent to which CDER staff provide clarity to drug developers on the necessary study design elements and other data needed in the drug application to support a full and comprehensive drug assessment.

Novel drugs approved in 2021 on the first cycle were:
Aduhelm, Amondys 45, Azstarys, Brexafemme, Bylvay, Cosela, Cytalux, Empaveli, Evkeeza, Exkivity, Fotivda, Jemperli, Kerendia, Korsuva, Livmarli, Livtencity, Lumakras, Lupkynis, Nextstellis, Nexviazyme, Nulibry, Pepaxto, Ponvory, Pylarify, Qulipta, Rezurock, Rybrevant, Rylaze, Saphnelo, Scemblix, Skytrofa, Tavneos, Tepmetko, Tezspire, Tivdak, Truseltiq, Ukoniq, Verquvo, Voxzogo, Vyvgart, Welireg, Zegalogue, Zynlonta

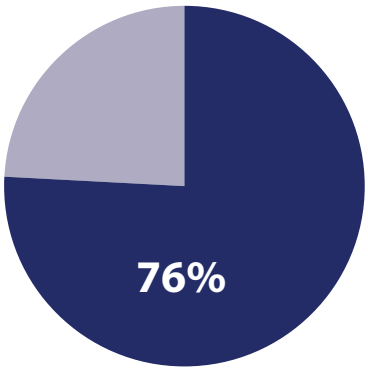
Approval in the U.S. Before Other Countries

Thirty-eight of the 50 novel drugs approved in 2021 (76%) were approved in the U.S. before any other country.

Novel drugs of 2021 approved first in the United States were: Aduhelm, Amondys 45, Azstarys, Brexafemme, Cosela, Cytalux, Empaveli, Evkeeza, Exkivity, Jemperli, Kerendia, Korsuva, Livmarli, Livtencity, Lumakras, Lupkynis, Lybalvi, Nexviazyme, Nulibry, Pepaxto, Ponvory, Pylarify, Qulipta, Rezurock, Rybrevant, Rylaze, Saphnelo, Scemblix, Skytrofa, Tezspire, Tivdak, Truseltiq, Ukoniq, Verquvo, Vyvgart, Welireg, Zegalogue, Zynlonta

76% of the novel drugs approved in 2021 were approved in the U.S. before any other country.

First in the U.S.



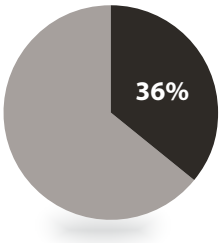
38 of the 50 novel drugs (76%) approved in 2021 were first approved in the U.S.

2021's Novel Drug Approvals

Expedited Review Programs

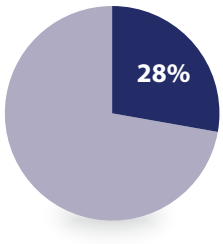
Fast Track (18 of 50)

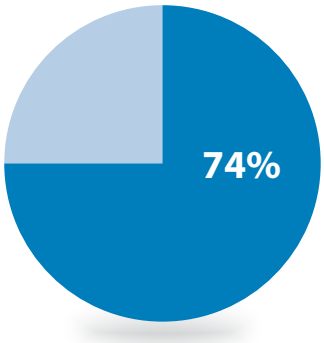
Aduhelm
Amondys 45
Brexafemme
Bylvay
Cabenuva
Cytalux
Empaveli
Exkivity
Kerendia
Lumakras
Lupkynis
Nexviazyme
Rylaze
Saphnelo
Scemblix
Truseltiq
Verquvo
Vyvgart



Breakthrough Therapy (14 of 50)

Cosela
Evkeeza
Exkivity
Jemperli
Korsuva
Livmarli
Livtencity
Lumakras
Nexviazyme
Nulibry
Rezurock
Rybrevant
Scemblix
Ukoniq





Used One or More Expedited Program (37 of 50)

Aduhelm
Amondys 45
Brexafemme
Bylvay
Cabenuva
Cosela
Cytalux
Empaveli
Evkeeza
Exkivity
fexinidazole*
Jemperli
Kerendia
Korsuva
Livmarli
Livtencity
Lumakras
Lupkynis
Nexviazyme
Nulibry
Pepaxto
Pylarify
Rezurock
Rybrevant
Rylaze
Saphnelo
Scemblix
Tepmetko
Tezspire
Tivdak
Truseltiq
Ukoniq
Verquvo
Voxzogo
Vyvgart
Welireg
Zynlonta

Priority Review (34 of 50)

Aduhelm
Amondys 45
Brexafemme
Bylvay
Cabenuva
Cosela
Cytalux
Empaveli
Evkeeza
Exkivity
fexinidazole*
Jemperli
Kerendia
Korsuva
Livmarli
Livtencity
Lumakras
Lupkynis
Nexviazyme
Nulibry
Pepaxto
Pylarify
Rezurock
Rybrevant
Scemblix
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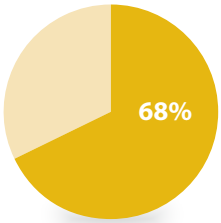
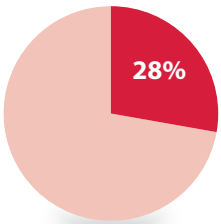
Tezspire
Tivdak
Truseltiq
Ukoniq
Verquvo
Voxzogo
Welireg
Zynlonta

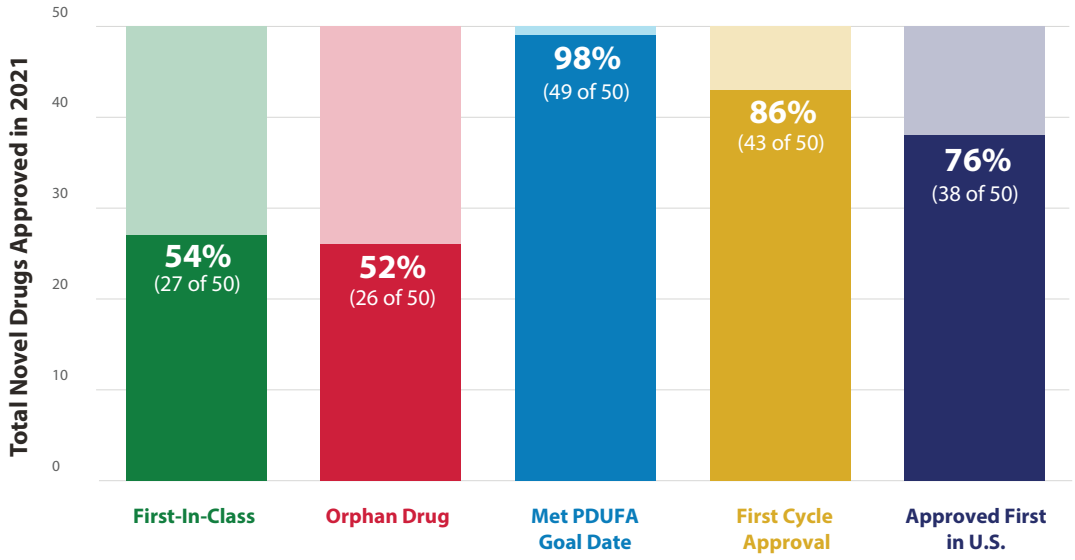


Accelerated Approval (14 of 50)

Aduhelm
Amondys 45
Exkivity
Jemperli
Lumakras
Pepaxto
Rybrevant
Scemblix
Tepmetko
Tivdak
Truseltiq
Ukoniq
Voxzogo
Zynlonta



Other Key Measures



New Uses of Approved Drugs

After CDER approves a new treatment, a drug sponsor may generate new data about the approved product that suggests an additional use. The drug sponsor may then submit an application to modify or expand the use of an approved drug based on this new data.

The products below are some notable approvals of 2021 for new uses or indications of an approved drug:

- **Actemra** (tocilizumab) injection. Originally approved to treat rheumatoid arthritis, Actemra was approved in 2021 to slow the rate of decline in **pulmonary function in adults with systemic sclerosis-associated interstitial lung disease**, an autoimmune disorder characterized by inflammation, vascular injury, and tissue scarring.
- **Ayvakit** (avapritinib) tablets were originally approved to treat advanced or inoperable gastrointestinal stromal tumors in patients with a certain mutation. In 2021, CDER approved Ayvakit to treat adults with **advanced systemic mastocytosis**, a group of rare disorders in which too many white blood cells known as "mast" cells build up in the body.
- **Cabometyx** (cabozantinib) tablets, which were originally approved in 2016, were approved in 2021 for patients undergoing treatment for **advanced renal (kidney) cell carcinoma** and for patients aged 12 years and older with **locally advanced or metastatic differentiated thyroid cancer** that has progressed after prior therapy.
- **Carbaglu** (carglumic acid) tablets were originally approved as an add-on or maintenance therapy to treat patients with high blood levels of ammonia. In 2021, Carbaglu became the first approved treatment for **hyperammonemia due to propionic acidemia (PA) or methylmalonic acidemia (MMA)**. PA and MMA are rare inherited metabolic disorders.
- **Darzalex Faspro** (daratumumab and hyaluronidase-fihj), injection, originally approved in 2020, was approved in 2021 to help treat patients newly diagnosed with **light chain amyloidosis**, a condition that interferes with normal organ functions due to abnormal protein build-up.
- **Enhertu** (fam-trastuzumab deruxtecan-nxki) injection, which was first approved in 2019, was approved in 2021 for adults with **locally advanced or metastatic HER2-positive gastric (stomach) or gastroesophageal junction (lower part of the esophagus that connects to the stomach) adenocarcinoma** who have received a certain prior therapy.

- **Farxiga** (dapagliflozin) oral tablets were originally approved to help improve glycemic control in adults with type 2 diabetes. In 2021, CDER approved Farxiga to reduce the **risk of kidney function decline, kidney failure, cardiovascular death, and hospitalization for heart failure in adults with chronic kidney disease who are at risk of disease progression**.
- **Keytruda** (pembrolizumab) injection, which was first approved in 2014, was approved for new or expanded indications in 2021, either to be used alone or in combination with other therapies. These indications include: certain types of **esophageal or gastroesophageal junction carcinoma**; some kinds of **gastric or gastroesophageal junction adenocarcinoma; locally advanced cutaneous squamous cell carcinoma (a type of skin cancer) that is not curable by surgery or radiation; advanced endometrial (lining of the uterus) cancer; early-stage, triple negative breast cancer; advanced kidney cancer**; some stages of **melanoma**; and certain types of **cervical cancer**.
- **Myrbetriq** (mirabergon) extended-release tablets, approved to treat certain patients with overactive bladder, was approved in 2021 to treat **neurogenic detrusor overactivity** (a neurological impairment of bladder function) in patients aged three years and older.
- **Nurtec ODT** (rimegepant) [see also Qulipta on page 15] orally disintegrating tablets, originally approved to treat acute migraine, received approval in 2021 to help reduce the frequency of **migraine attacks** in patients with episodic migraines.
- **Opdivo** (nivolumab) injection, which was first approved in 2014, was approved in 2021 as a first-line treatment for **gastric cancer**, **esophageal cancer** in certain patients, and as an adjuvant treatment for patients with **high-risk urothelial carcinoma**, a type of bladder cancer.
- **Praluent** (alirocumab) [see also Evkeeza on page 12 and Repatha on page 26] injection, originally approved in 2015, was approved in 2021 to treat **homozygous familial hyperfamilial hypercholesterolemia**, a genetic condition that causes severely high cholesterol.
- **Prograf** (tacrolimus) capsules were previously approved to prevent organ rejection in patients receiving liver, kidney, and heart transplants. In 2021, Prograf was approved as the first immunosuppressant drug to prevent **organ rejection in patients receiving lung transplants**.

- **Solosec** (secnidazole) oral granules were originally approved to treat a bacterial type of vaginal inflammation. In 2021, CDER approved the drug to treat **trichomoniasis**, a common sexually transmitted disease.
- **Tecentriq** (atezolizumab) injection, which was originally approved for certain patients with locally advanced or metastatic urothelial carcinoma, was approved in 2021 as an adjuvant treatment following surgical removal and platinum-based chemotherapy in patients with **stage II to IIIa non-small cell lung cancer with specific tumor characteristics**.
- **Xalkori** (crizotinib) capsules, which were first approved in 2011 for patients with certain types of non-small cell lung cancer, were approved in 2021 to treat **systemic anaplastic large cell lymphoma that is ALK-positive** in pediatric patients aged one year and older, and certain young adults who have had a history of the disease. "ALK-positive" refers to a certain genetic constitution.
- **Zeposia** (ozanimod) [see also Humira on page 26] capsules were approved in 2020 to treat relapsing forms of multiple sclerosis. In 2021, CDER approved Zeposia to treat **moderately to severely active ulcerative colitis** in adults.

Drugs in brackets refer to other treatments for the same or similar disease.

Approved Drugs Expanded for New Pediatric Populations

The Pediatric Research Equity Act (PREA), which gives FDA the authority to require pediatric studies under certain circumstances, has been largely responsible for the inclusion of pediatric information in the labeling for many drugs. Upon drug approval, FDA may require pediatric studies of that drug under PREA. In response to that requirement, sponsors may submit new data to support the safe and effective use of the drug in the pediatric population studied. Sponsors submit this data in an application to expand the patient population.

- **Biktarvy** (bictegravir, emtricitabine, and tenofovir alafenamide) tablets were originally approved in 2018 to treat certain patients with **HIV**. In 2021, CDER extended the patient population down to ages two years and older.
- **Bydureon and Bydureon BCise** (exenatide extended-release) injection was approved in 2012 to help improve blood sugar levels in adults with **type 2 diabetes**. In 2021, CDER extended the indication to include pediatric patients aged 10 years and older.

- **Epclusa** (sofosbuvir/velpatasvir), [see also Mavyret, below] tablets and oral pellets, were originally approved by CDER to treat certain adults with chronic **hepatitis C virus (HCV) genotypes 1, 2, 3, 4, 5, and 6**. In 2021, CDER approved Epclusa to treat children aged three years and older with any of the **six HCV genotypes without cirrhosis (liver disease) or with mild cirrhosis**. **HCV** causes liver inflammation that can lead to diminished liver function or liver failure.

- **Humira** (adalimumab) [see also Zeposia on page 25] injection, first approved in 2002, is now approved for indications including **rheumatoid arthritis, Crohn's disease, ulcerative colitis,** and **psoriasis**. In 2021, Humira was approved to treat **moderately to severely active ulcerative colitis** in pediatric patients aged five years and older. This is the first pediatric treatment for **moderately to severely active ulcerative colitis** that can be administered at home rather than at an infusion center.

- **Mavyret** (glecaprevir and pibrentasvir) [see also Epclusa, above] tablets were first approved in 2017 to treat patients older than age 12 with certain types of **HCV**. In 2021, CDER extended the age group down to three years for the same indications. Mavyret is another hepatitis C treatment regimen available to treat all **six genotypes of HCV**.

- **Rapivab** (peramivir) injection was originally approved in 2014 to treat adults with **acute uncomplicated influenza (flu)**. In 2021, CDER extended the indication to include patients six months and older.

- **Repatha** (evolocumab) [see Evkeeza and Leqvio on page 12 and Praluent on page 24] injection, previously approved for adults, was approved in 2021 to help treat patients aged 10 years and older with **heterozygous familial hypercholesterolemia** or **homozygous familial hypercholesterolemia**, which are life-threatening conditions characterized by severely high cholesterol.

- **Oxbryta** (voxelotor) tablets, originally approved in 2019 under the accelerated approval pathway to treat patients aged 12 years and older with **sickle cell disease**, a blood disorder that disrupts oxygen transport. In 2021, CDER expanded approved use of the drug to afflicted children as young as four years.

- **Pradaxa** (dabigatran etexilate) capsules were originally approved in 2010 to reduce the **risk of stroke and blood vessel blockage** in adults with a certain type of irregular

heartbeat. In 2021, CDER expanded Pradaxa use to **prevent and treat blood clots** in certain specified patients as young as eight years old. Pradaxa is the first FDA-approved oral blood thinning medication for children.

- **Trikafta** (elecaftor/lexacaftor/ivacaftor), co-packaged for oral use, was originally approved in 2019 to treat patients aged 12 and older with the most common genetically defined form of **cystic fibrosis**. In 2021, CDER extended the patient population to include children as young as six years old.
- **Xarelto** (rivaroxaban) tablets were originally approved in 2011 to reduce the risk of stroke and systemic embolism in adults with nonvalvular atrial fibrillation. In 2021, Xarelto was approved to treat pediatric patients from birth onward at risk of **recurrent venous thromboembolism (VTE), or blood clots that form in the veins**. The 2021 expanded approval also extends to certain patients with congenital heart disease as young as two years old at risk of **thrombosis (blood clots)**.

Drugs in brackets refer to other treatments for the same or similar disease.

CDER approved the first oral blood thinning medication for children in 2021.

Biosimilar and Interchangable Biosimilar Approvals

The biosimilar pathway is an abbreviated approval pathway for biological products that are highly similar to and have no clinically meaningfully differences from an FDA-approved biological reference product. This abbreviated approval pathway was established to provide more treatment options, increase patient access, and potentially reduce the cost of important and complex therapies for serious conditions through competition.

In 2021, CDER approved four new biosimilar products. Of particular note, CDER approved the first two interchangeable biosimilar products, which may be substituted for the reference product at the pharmacy without the intervention of a prescriber, subject to state law, similar to how generic drugs are substituted for brand name drugs.

- **Semglee** (insulin glargine-yfgn) injection and **Rezvoglar** (insulin glargine-aglr) injection were approved as an interchangeable biosimilar and biosimlar, respectively, to Lantus (insulin glargine) to **improve glycemic control in adults and pediatric patients with type 1 diabetes and**

in adults with type 2 diabetes. Semglee and Rezvoglar are long-acting insulins that have no peak and start to work in about three to four hours.

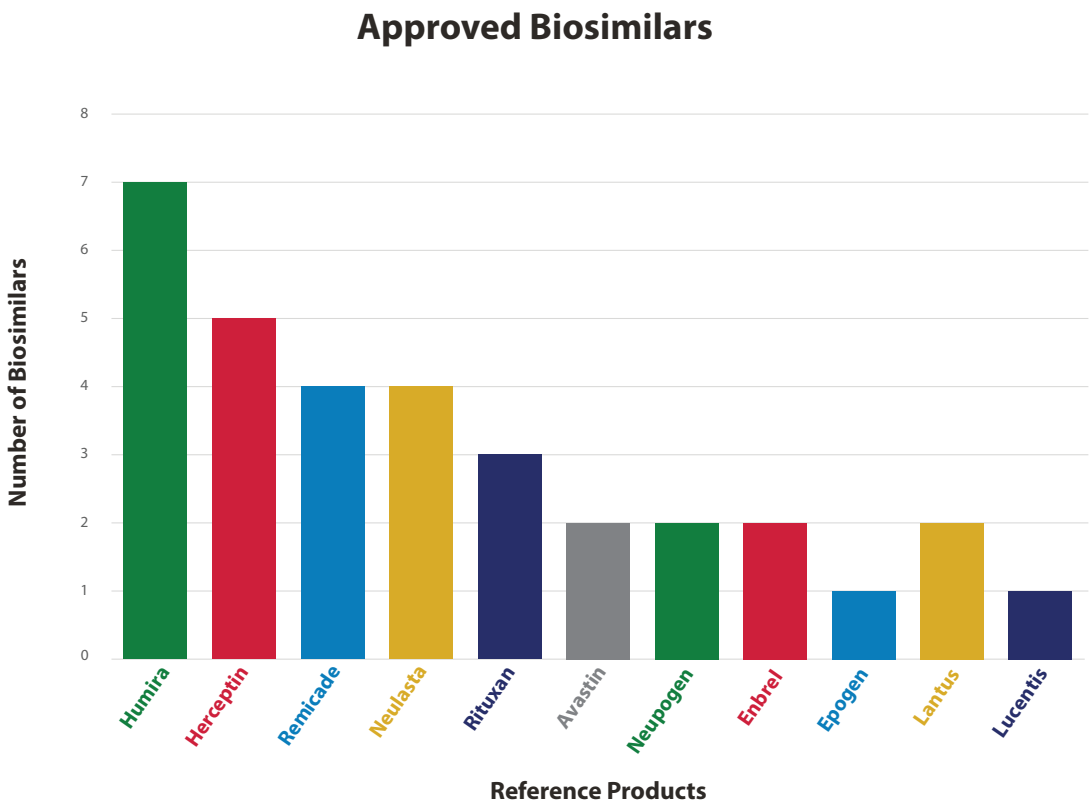
- **Byooviz** (ranibizumab-nuna) injection was approved as the first biosimilar to Lucentis (ranibizumab) to treat several eye diseases and conditions, including **neovascular (wet) age-related macular degeneration**, a leading cause of vision loss and blindness for Americans aged 65 years and older. Byooviz was also approved to treat **macular edema (fluid build-up) following retinal vein occlusion (vein blockage in the retina)** and **myopic choroidal neovascularization**, a vision-threatening complication of myopia (nearsightedness).
- **Yusimry** (adalimumab-aqvh) injection was approved as a biosimilar to Humira (adalimumab) to treat patients with **rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis in adults** and **plaque psoriasis**.

In 2021, CDER also approved a change to one biosimilar product:

- A biosimilar to Humira, **Cyltezo** (adalimumab-adbm) originally approved in 2017, was approved in 2021 as an interchangeable biosimilar to treat a variety of conditions, including **ulcerative colitis in adults, Crohn's disease,** and **different types of arthritis**. Cyltezo is the first FDA-approved interchangeable monoclonal antibody.

CDER has approved a total of 33 biosimilar products for 11 different reference products since 2015. This includes at least one biosimilar for each of these top selling biological products in the U.S. CDER has now approved seven biosimilars to Humira; five biosimilars to Herceptin; four biosimilars to Remicade and Neulasta; three biosimilars to Rituxan; two biosimilars to Avastin, Neupogen, Lantus and Enbrel; and one biosimilar to Epogen and Lucentis. There are now also two approved interchangeable biosimilars. Multiple biosimilar products for an approved reference product can enhance competition, which may lead to reduced costs for both patients and our health care system.

Biosimilars expand treatment options and bring competition to the U.S. marketplace.



Other Non-Novel Approvals

New formulations of approved drugs can offer significant advances in therapy. Similarly, new dosage forms (such as from a capsule to a chewable tablet for those unable to swallow) can improve patient health by helping to increase adherence, making sure patients take the proper dose, and improving quality of life for patients who must use the medication on a prolonged basis. Below are notable new formulations, new dosage forms, as well as other notable non-novel drug approvals of 2021.

- **Apretude** (cabotegravir) [see also Cabenuva on page 15 and Vocabria on page 32] injection. Cabotegravir (the active ingredient) was approved and marketed as Cabenuva in early 2021 to treat HIV as a long-acting therapy that patients receive once a month. In December 2021, Apretude (with the same active ingredient) was approved as the first long-acting antiviral to **prevent HIV** that patients receive once every two months.

- **Astepro** (azelastine hydrochloride) nasal spray was previously approved as a prescription drug to treat **seasonal and perennial allergic rhinitis**, commonly known as allergies. In 2021, CDER approved Astepro for nonprescription use through a process called a partial prescription to nonprescription switch. This is a partial switch because the lower strength, which includes the perennial allergy indication for children six months to 11 years and the seasonal allergy indication for children aged two years and older, will remain prescription-based.

CDER approved the conversion of two prescription drugs to nonprescription drugs in 2021.

- **Kloxxado** (naloxone hydrochloride) [see also Zimhi on page 32] nasal spray to treat **opioid overdose** was approved in 2021.

- **Fabrazyme** (agalsidase beta) injection was approved under accelerated approval in 2003 to treat **Fabry disease**, a rare inherited disorder of glycosphingolipid (fat) metabolism. In 2021, CDER converted Fabrazyme from accelerated approval to traditional approval.

FDA converted a drug for Fabry disease from an accelerated approval to a traditional approval.

- **Fyarro** (sirolimus protein-bound particles for injectable suspension) (albumin-bound), a new formulation of sirolimus, was approved to treat **locally advanced unresectable or metastatic perivascular epithelioid cell tumor (PEComa).**

- **Lastacaft** (alcaftadine) ophthalmic solution was initially approved in 2010 to prevent itching associated with **allergic conjunctivitis**, or eye inflammation due to pollen. In 2021, CDER approved Lastacaft for nonprescription use through a process called a full prescription to nonprescription switch.

- **Midazolam** injection was originally approved in 1985 as a sedation medication. In 2021, CDER approved midazolam in sodium chloride injection as a **sedation therapy as a component of anesthesia or during treatment in a critical care situation**. It is also available as a concentration that can be administered via infusion without additional dilution.

- **Opzelura** (ruxolitinib) [see also Adbry on page 11] tablets were originally approved in 2011 under the brand name Jakafi to treat patients with intermediate or high-risk myelofibrosis. In 2021, CDER approved it as a cream to treat **mild-to-moderate atopic dermatitis (eczema)** in patients aged 12 and older who do not respond to, or who cannot take, certain other topical therapies.
- **Vocabria** (cabotegravir) tablets [see also Cabenuva on page 15 and Apretude on page 30] were approved in 2021 as an oral "lead-in" to assess the tolerability of the HIV treatment Cabenuva and as an oral therapy for patients who will miss a planned injection of Cabenuva. Vocabria was approved to be used in combination with Edurant, another HIV medication.
- **Wegovy** (semaglutide) injection was approved in a new formulation and dosage in 2021 for **chronic weight management** in adults with obesity or overweight with at least one weight-related condition, in addition to a reduced calorie diet and increased physical activity. Semaglutide was originally approved in 2017 and is marketed as Ozempic injection and Rybelsus tablets to improve blood sugar levels in adults with type 2 diabetes.
- **Zimhi** (naloxone hydrochloride) [see also Kloxxado on page 31] injection to treat **opioid overdose** was approved as a single-shot injection in 2021.
- **Zynrelef** (bupivacaine and meloxicam) extended-release solution, a combination of two approved drugs, was approved in 2021 to **relieve pain for up to 72 hours in the postsurgical setting for certain procedures**. Zynrelef delivers a fixed-dose combination of the local anesthetic bupivacaine and a low dose of the nonsteroidal anti-inflammatory drug meloxicam.

Drugs in brackets refer to other treatments for the same or similar disease.

Conclusion

Reviewing drug applications and deciding to approve therapies is a well-coordinated and cross-disciplinary collaboration among our physicians, safety evaluators, chemists, biologists, biostatisticians, nurses, pharmacists, pharmacologists, epidemiologists, regulatory and policy experts. These professionals worked as a well-integrated team to bring safe and effective drug therapies to the American public as efficiently as possible in 2021 — which we hope will help patients in need for years to come.

On a broader level, the work in bringing new drugs to market is something that goes beyond CDER and FDA. CDER collaborates with stakeholders across the medical community, including academia, industry, patients and their caregivers, patient advocacy groups, and state and other federal agencies, to help ensure patients have safe and effective therapies for a wide range of medical conditions. We listen to their concerns and strive to see their perspectives. We know it is important to understand the needs of our key constituencies and take actions that will benefit as many Americans as possible.

This report provides valuable examples of the ways CDER approves a wide range of drugs to enhance patient health.

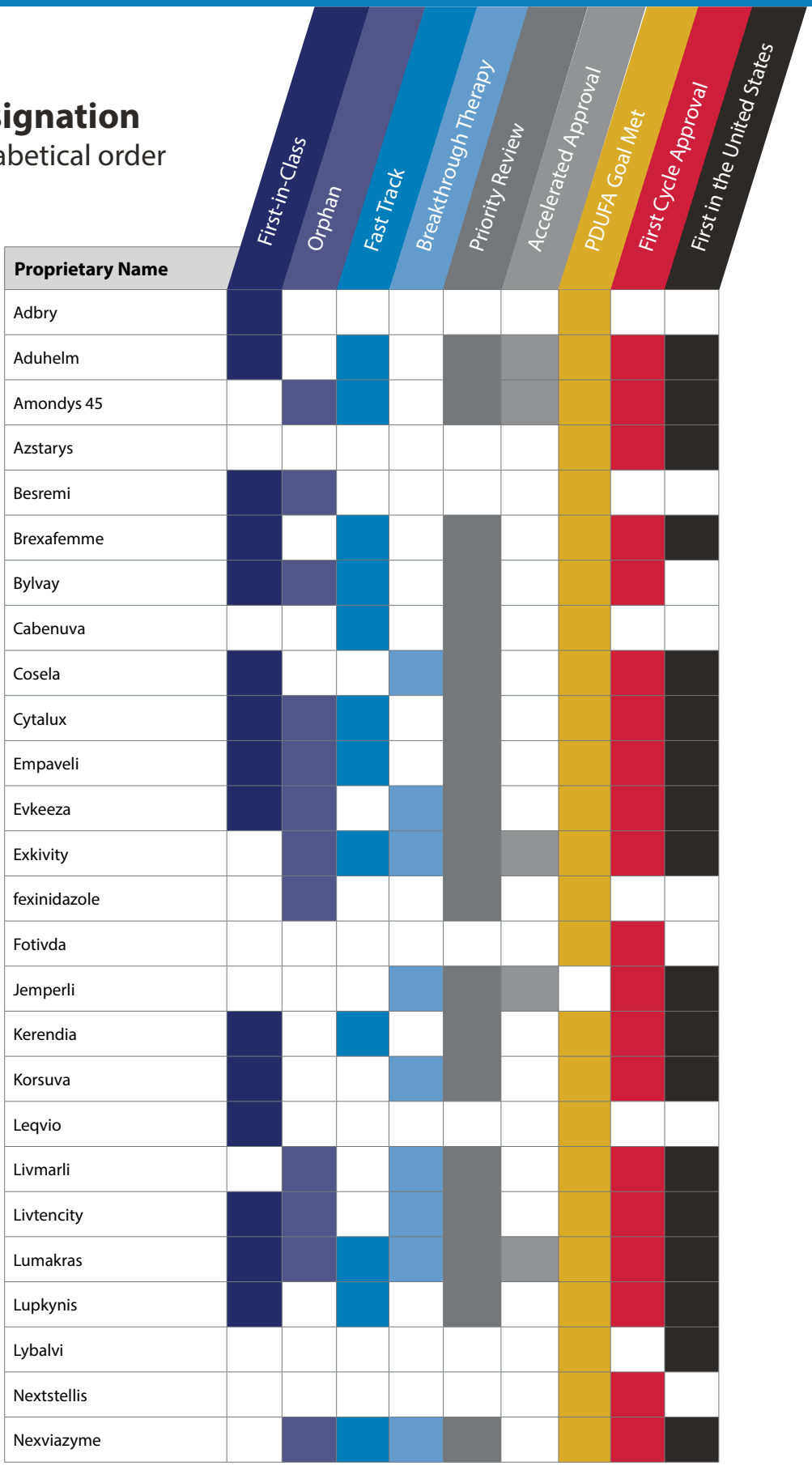
Appendix A:
CDER's Novel Approvals of 2021 (in alphabetical order)

For information about vaccines, allergenic products, blood and blood products, cellular and gene therapy products go to 2021 Biological License Application Approvals.

Approval date	Trade name	Active ingredient(s)	Summary of FDA-approved use on approval date (see Drugs@FDA for complete indication)	Dosage form
12/27/2021	Adbry	tralokinumab-ldrm	To treat moderate-to-severe atopic dermatitis	Injection
6/7/2021	Aduhelm	aducanumab-avwa	To treat Alzheimer's disease	Injection
2/25/2021	Amondys 45	casimersen	To treat Duchenne muscular dystrophy	Injection
3/2/2021	Azstarys	serdexmethylphenidate and dexmethylphenidate	To treat attention deficit hyperactivity disorder	Capsule
11/12/2021	Besremi	ropeginterferon alfa-2b-njft	To treat polycythemia vera	Injection
6/1/2021	Brexafemme	ibrexafungerp	To treat vulvovaginal candidiasis	Tablet
7/20/2021	Bylvay	odevixibat	To treat pruritus in progressive familial intrahepatic cholestasis	Capsule and Oral Pellet
1/21/2021	Cabenuva	cabotegravir and rilpivirine (co-packaged)	To treat HIV	Injection
2/12/2021	Cosela	trilaciclib	To mitigate chemotherapy-induced myelosuppression in small cell lung cancer	Injection
11/29/2021	Cytalux	pafolacianine	To use for ovarian cancer imaging	Injection
5/14/2021	Empaveli	pegcetacoplan	To treat paroxysmal nocturnal hemoglobinuria	Injection
2/11/2021	Evkeeza	evinacumab-dgnb	To treat homozygous familial hypercholesterolemia	Injection
9/15/2021	Exkivity	mobocertinib	To treat types of locally advanced or metastatic non-small cell lung cancer	Capsule
7/16/2021		fexinidazole	To treat human African trypanosomiasis	Tablet
3/10/2021	Fotivda	tivozanib	To treat renal cell carcinoma	Capsule
4/22/2021	Jemperli	dostarlimab-gxly	To treat endometrial cancer	Injection
7/9/2021	Kerendia	finerenone	To reduce the risk of kidney and heart complications in chronic kidney disease associated with type 2 diabetes	Tablet
8/23/2021	Korsuva	difelikefalin	To treat moderate-to-severe pruritus in chronic kidney disease	Injection
12/22/2021	Leqvio	inclisiran	To treat heterozygous familial hypercholesterolemia or clinical ASCVD	Injection
9/29/2021	Livmarli	maralixibat	To treat cholestatic pruritus in Alagille syndrome	Oral Solution
11/23/2021	Livtencity	maribavir	To treat cytomegalovirus infection	Tablet
5/28/2021	Lumakras	sotorasib	To treat types of non-small cell lung cancer	Tablet
1/22/2021	Lupkynis	voclosporin	To treat lupus nephritis	Capsule
5/28/2021	Lybalvi	olanzapine and samidorphan	To treat schizophrenia and aspects of bipolar I disorder	Tablet

Approval date	Trade name	Active ingredient(s)	Summary of FDA-approved use on approval date (see Drugs@FDA for complete indication)	Dosage form
4/15/2021	Nextstellis	drospirenone and estetrol	To prevent pregnancy	Tablet
8/6/2021	Nexviazyme	avalglucosidase alfa-ngpt	To treat late-onset Pompe disease	Injection
2/26/2021	Nulibry	fosdenopterin	To reduce the risk of mortality in molybdenum cofactor deficiency type A	Injection
2/26/2021	Pepaxto	melphalan flufenamide	To treat relapsed or refractory multiple myeloma	Injection
3/18/2021	Ponvory	ponesimod	To treat relapsing forms of multiple sclerosis	Tablet
5/26/2021	Pylarify	piflufolastat F 18	To identify prostate-specific membrane antigen-positive lesions in prostate cancer	Injection
4/2/2021	Qelbree	viloxazine	To treat attention deficit hyperactivity disorder	Capsule
9/28/2021	Qulipta	atogepant	To prevent episodic migraines	Tablet
7/16/2021	Rezurock	belumosudil	To treat chronic graft-versus-host disease after failure of at least two prior lines of systemic therapy	Tablet
5/21/2021	Rybrevant	amivantamab-vmjw	To treat types of non-small cell lung cancer	Injection
6/30/2021	Rylaze	asparaginase erwinia chrysanthemi (recombinant)-rywn	To treat acute lymphoblastic leukemia and lymphoblastic lymphoma in patients who are allergic to E. coli-derived asparaginase products, as a component of chemotherapy	Injection
7/30/2021	Saphnelo	anifrolumab-fnia	To treat moderate-to severe systemic lupus erythematousus along with standard therapy	Injection
10/29/2021	Scemblix	asciminib	To treat Philadelphia chromosome-positive chronic myeloid leukemia	Tablet
8/25/2021	Skytrofa	lonapegsomatropin-tcgd	To treat short stature due to inadequate secretion of endogenous growth hormone	Injection
10/7/2021	Tavneos	avacopan	To treat severe active anti-neutrophil cytoplasmic autoantibody-associated vasculitis in combination with standard therapy, including glucocorticoids	Capsule
2/3/2021	Tepmetko	tepotinib	To treat types of non-small cell lung cancer	Tablet
12/27/21	Tezspire	tezepelumab-ekko	To treat severe asthma as an add-on therapy	Injection
9/20/2021	Tivdak	tisotumab vedotin-tftv	To treat recurrent or metastatic cervical cancer with disease progression on or after chemotherapy	Injection
5/28/2021	Truseltiq	infigratinib	To treat cholangiocarcinoma	Capsule
2/5/2021	Ukoniq	umbralisib	To treat marginal zone lymphoma and follicular lymphoma	Tablet
1/19/2021	Verquvo	vericiguat	To mitigate the risk of cardiovascular death and hospitalization for chronic heart failure	Tablet
11/19/2021	Voxzogo	vosoritide	To improve growth in children five years of age and older with achondroplasia and open epiphyses	Injection
12/17/2021	Vyvgart	efgartigimod alfa-fcab	To treat generalized myasthenia gravis	Injection
8/13/2021	Welireg	belzutifan	To treat von Hippel-Lindau disease	Tablet
3/22/2021	Zegalogue	dasiglucagon	To treat severe hypoglycemia	Injection
4/23/2021	Zynlonta	loncastuximab tesirine-lpyl	To treat types of relapsed or refractory large B-cell lymphoma	Injection

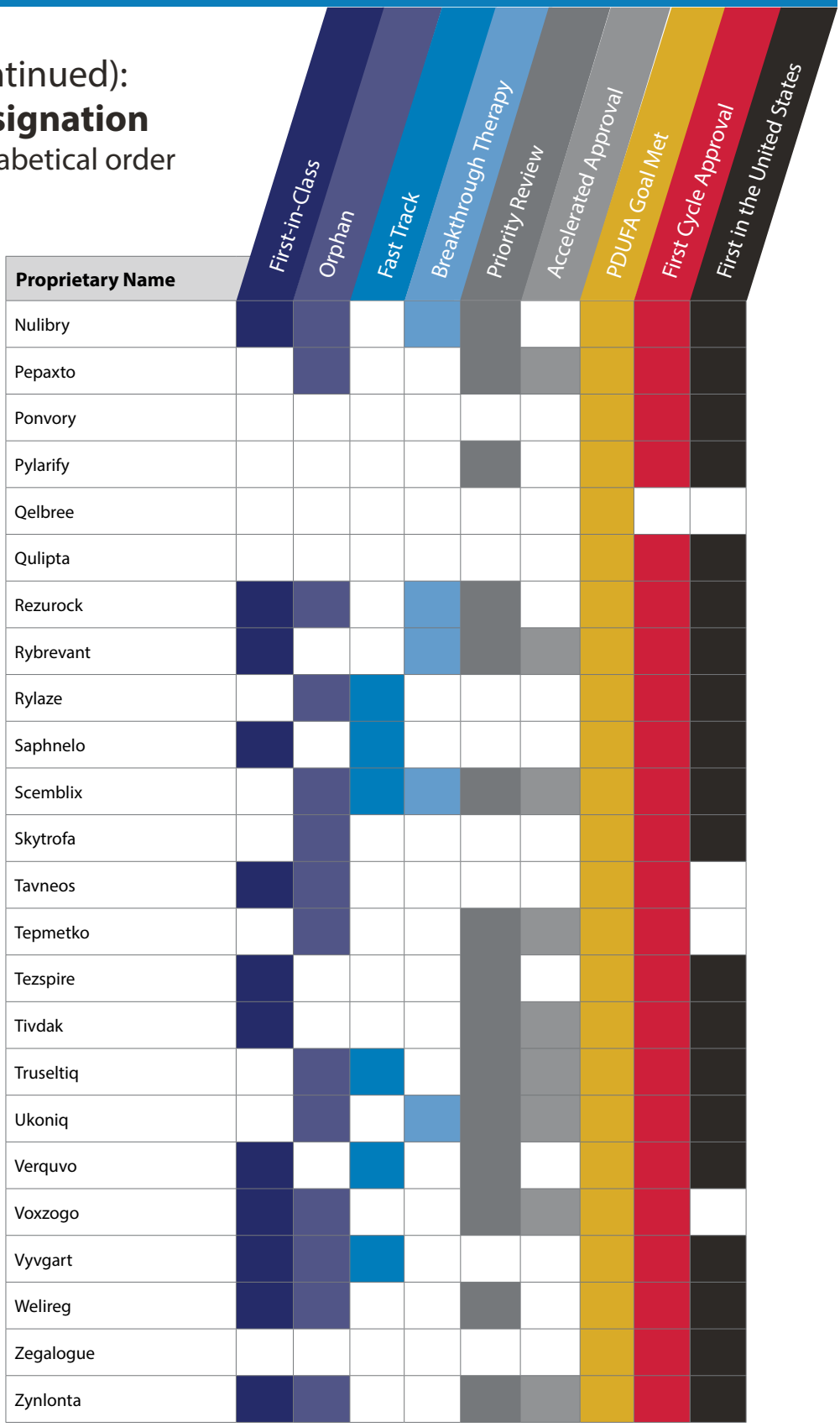
Appendix B:
Novel Drug Designation
Drugs listed in alphabetical order



Proprietary Name
Adbry
Aduhelm
Amondys 45
Azstarys
Besremi
Brexafemme
Bylvay
Cabenuva
Cosela
Cytalux
Empaveli
Evkeeza
Exkivity
fexinidazole
Fotivda
Jemperli
Kerendia
Korsuva
Leqvio
Livmarli
Livtencity
Lumakras
Lupkynis
Lybalvi
Nextstellis
Nexviazyme

Appendix B (continued): **Novel Drug Designation**

Drugs listed in alphabetical order



Proprietary Name
Nulibry
Pepaxto
Ponvory
Pylarify
Qelbree
Qulipta
Rezurock
Rybrevant
Rylaze
Saphnelo
Scemblix
Skytrofa
Tavneos
Tepmetko
Tezspire
Tivdak
Truseltiq
Ukoniq
Verquvo
Voxzogo
Vyvgart
Welireg
Zegalogue
Zynlonta

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