News

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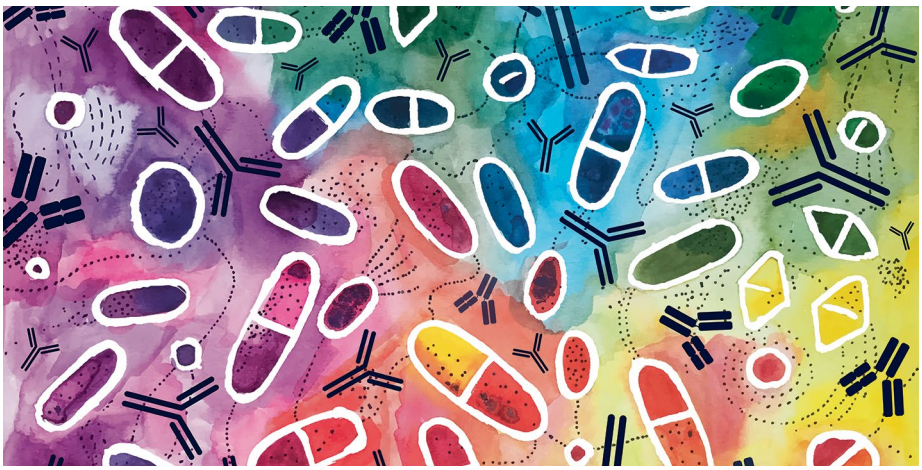
2022 FDA approvals

By Asher Mullard

The FDA approved 37 novel drugs in 2022, the fewest to pass regulatory scrutiny since 2016.



Last year the FDA's Center for Drug Evaluation and Research (CDER) approved 37 novel drugs. This is a drop from the highs of the past 5 years, and brings the rolling 5-year average down to 49 drugs per year. But the 2022 approval number remains above the historic average since 1993, of 34 drugs per year (Fig. 1, Table 1).

Approvals by the Center for Biologics Evaluation and Research (CBER) — which regulates vaccines, cell and gene therapies, and blood products — bump the number higher, and underline the uptick in gene therapy submissions (Table 2). Two novel products secured Emergency Use Authorizations (EUAs), an expedited regulatory pathway that rose to prominence during COVID-19 but that is now seeing less use (Table 3).

Cancer drugs continue to dominate CDER's approval list, with ten new oncology drugs accounting for 27% of CDER's approval cohort. Approval numbers for dermatology and non-malignant haematology indications were above their 5-year averages, while infectious diseases and neurology saw fewer approvals than in recent years (Fig. 2).

Biologics continue their ascendance, accounting for 41% of CDER's approvals last year. This is the highest percentage of biologics to date. Antibody-based therapeutics — monoclonal antibodies (mAbs), bispecifics and antibody–drug conjugates (ADCs) — accounted for 30% of the approvals, another high-water mark (Fig. 3).

57% of the new approvals received priority review, for therapies that the FDA expects to offer 'significant improvements' over the standard of care (Fig. 4). 35% received breakthrough designation, for drugs that could confer 'substantial improvements' over available therapies. 54% had orphan designation, for diseases that affect fewer than 200,000 individuals in the USA. 16% received accelerated approval, with a green light based on improvements on surrogate endpoints that the FDA deems as 'reasonably likely' to predict clinical benefit.

Analysts at Boston Consulting Group (BCG) predict average peak sales of the new CDER and CBER approvals to reach US$1.6 billion, above the longer-term average of $1.4 billion. The median forecasted peak sales for the newly approved products is $0.6 billion.

The mega-blockbusters

Several noteworthy approvals showcased new target space, new clinical opportunities and untapped commercial potential.

Eli Lilly's tirzepatide, for example, is a peptidic drug that mimics two gut hormones — glucagon-like peptide 1 (GLP1) and glucose-dependent insulinotropic polypeptide (GIP) — to control blood sugar levels in patients with type 2 diabetes. Synthetic versions of GLP1 were first approved in 2005, but Lilly's co-agonist agent is the first to mimic GIP as well.

In five pivotal trials of the drug — SURPASS-1, -2, -3, -4 and -5 — single-agent or combination use of tirzepatide outperformed active

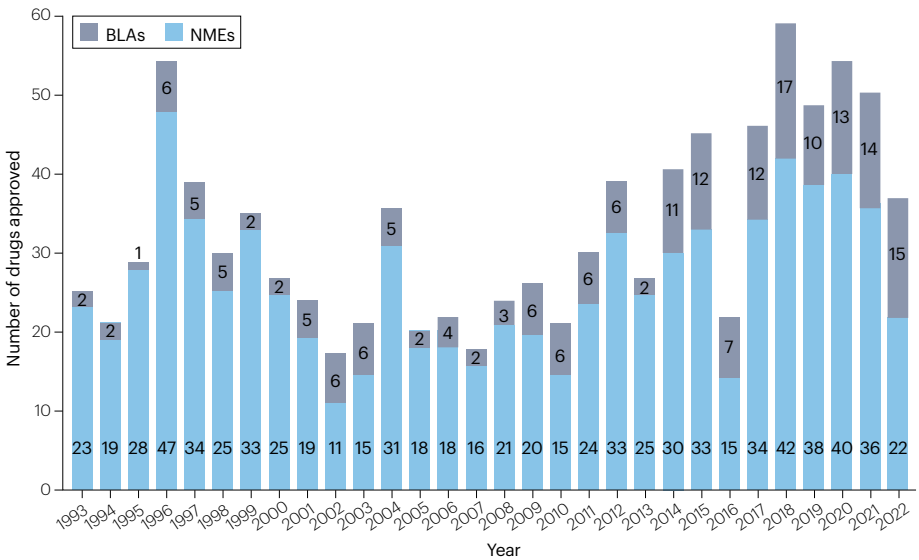


Fig. 1 | Novel FDA approvals since 1993. Annual numbers of new molecular entities (NMEs) and biologics license applications (BLAs) approved by the FDA's CDER. See Table 1 for new approvals in 2022. Products approved by CBER, including vaccines and gene therapies, are not included in this drug count (Table 2). Source: FDA.

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Table 1 | CDER approvals in 2022

Drug (brand name)	Sponsor	Properties	Indication	Review
Daridorexant (Quviviq)	Idorsia	Orexin receptor antagonist	Insomnia	S
Abrocitinib (Cibinqo)	Pfizer	JAK inhibitor	Atopic dermatitis	P, B
Tebentafusp (Kimmtrak)[a]	Immunocore	gp100 peptide–HLA×CD3 bispecific T-cell engager	Uveal melanoma	P, O, B
Faricimab (Vabysmo)[a]	Roche/Genentech	VEGF×ANG2 bispecific antibody	nAMD and DME	S
Sutimlimab (Enjaymo)[a]	Bioverativ	C1s-targeted mAb	RBC transfusion due to haemolysis in CAD	P, O, B
Mitapivat (Pyrukynd)	Agios	Pyruvate kinase activator	Haemolytic anaemia due to PK deficiency	P, O
Pacritinib (Vonjo)	CTI Biopharma	JAK2 inhibitor	Myelofibrosis	P, O, A
Ganaxolone (Ztalmy)	Marinus	$GABA_A$ receptor positive allosteric modulator	Seizures associated with CDD	P, O
Relatlimab; nivolumab (Opdualag)[a]	Bristol Myers Squibb	LAG3-targeted mAb plus PD1-targeted mAb	Melanoma	P, O
Lutetium Lu-177 vipivotide tetraxetan (Pluvicto)	Novartis	PSMA-binding radioligand therapeutic agent	PSMA-positive prostate cancer	P, B
Oteseconazole (Vivjoa)	Mycovia	Azole antifungal	Vulvovaginal candidiasis	P
Mavacamten (Camzyos)	Bristol Myers Squibb	Cardiac myosin inhibitor	Classes of obstructive HCM	S, O, B
Vonoprazan; amoxicillin; clarithromycin (Voquezna Triple Pak)	Phathom	Potassium-competitive acid blocker plus a penicillin class antibacterial plus a macrolide antimicrobial	*Helicobacter pylori* infection	P
Tirzepatide (Mounjaro)	Eli Lilly	GIP receptor and GLP1 receptor agonist	Type 2 diabetes	S
Tapinarof (Vtama)	Dermavant	Aryl hydrocarbon receptor agonist	Plaque psoriasis	S
Vutrisiran (Amvuttra)	Alnylam	TTR-targeted siRNA	Polyneuropathy of hereditary TTR-mediated amyloidosis	S, O
Olipudase alfa (Xenpozyme)[a]	Sanofi/Genzyme	Acid sphingomyelinase ERT	Acid sphingomyelinase deficiency	P, O, B
Spesolimab (Spevigo)[a]	Boehringer Ingelheim	IL-36R-targeted mAb	Generalized pustular psoriasis flares	P, O, B
DaxibotulinumtoxinA (Daxxify)[a]	Revance	Botulinum toxin	Glabellar lines	S
Deucravacitinib (Sotyktu)	Bristol Myers Squibb	TYK2 inhibitor	Plaque psoriasis	S
Eflapegrastim (Rolvedon)[a]	Spectrum	Leukocyte growth factor	Incidence of infection in non-myeloid malignancies, with myelosuppressive drugs	S
Terlipressin (Terlivaz)	Mallinckrodt	Vasopressin receptor agonist	Kidney function in hepatorenal syndrome	P, O
Gadopiclenol (Elucirem)	Guerbet	Gadolinium-based contrast agent	Lesions with abnormal vascularity	P
Omidenepag isopropyl (Omlonti)	Santen	Prostaglandin E2 receptor agonist	Intraocular pressure in open-angle glaucoma or ocular hypertension	S
Sodium phenylbutyrate; taurursodiol (Relyvrio)	Amylyx	Mechanism unknown	Amyotrophic lateral sclerosis	P, O
Futibatinib (Lytgobi)	Taiho Oncology	FGFR kinase inhibitor	FGFR2-aberrant intrahepatic cholangiocarcinoma	P, O, B, A
Tremelimumab (Imjudo)[a]	AstraZeneca	CTLA4-targeted mAb	Hepatocellular carcinoma	S, O
Teclistamab (Tecvayli)[a]	J&J	BCMA×CD3 bispecific antibody	Multiple myeloma	P, O, B, A
Mirvetuximab soravtansine (Elahere)[a]	ImmunoGen	FRα-targeted antibody–drug conjugate	Ovarian cancer	P, O, A
Teplizumab (Tzield)[a]	Provention Bio	CD3-targeted antibody	Delay onset of type 1 diabetes	P, B
Olutasidenib (Rezlidhia)	Rigel/Forma	IDH1 inhibitor	*IDH1*-mutated AML	S, O
Adagrasib (Krazati)	Mirati	KRAS-G12C inhibitor	$KRAS^{G12C}$-mutated NSCLC	S, O, B, A
Lenacapavir (Sunlenca)	Gilead	HIV-1 capsid inhibitor	HIV-1 infection	P, B
Mosunetuzumab (Lunsumio)[a]	Roche/Genentech	CD20×CD3 bispecific antibody	Follicular lymphoma	P, O, B, A

Table 1 (continued) | CDER approvals in 2022

Drug (brand name)	Sponsor	Properties	Indication	Review
Xenon Xe 129 hyperpolarized (Xenoview)	Polarean	Hyperpolarized contrast agent	MRI-evaluation of lung ventilation	S
Ublituximab (Briumvi)[a]	TG Therapeutics	CD20-targeted mAb	Relapsing forms of multiple sclerosis	S
Anacaulase (NexoBrid)[a]	Mediwound	Proteolytic enzymes from pineapple plants	Eschar removal after thermal burns	S, O

[a]Biologic approval. A, accelerated; AML, acute myeloid leukaemia; ANG2, angiopoetin 2; B, breakthrough; BCMA, B cell maturation antigen; C1s, complement protein component 1, s subcomponent; CAD, cold agglutinin disease; CDD, cyclin-dependent kinase-like 5 deficiency disorder; DME, diabetic macular edema; ERT, enzyme replacement therapy; FGFR, fibroblast growth factor receptor; FRα; folate receptor α; $GABA_A$, gamma-aminobutyric acid type A; GIP, glucose-dependent insulinotropic polypeptide; GLP1, glucagon-like peptide 1; HCM, hypertrophic cardiomyopathy; HLA, human leukocyte antigen; IDH1, isocitrate dehydrogenase 1; IL-36R, interleukin-36 receptor; JAK, Janus kinase; J&J, Johnson & Johnson; mAb, monoclonal antibody; MRI, magnetic resonance imaging; nAMD; neovascular age-related macular degeneration; NSCLC, non-small-cell lung cancer; O, orphan; P, priority; PK, pyruvate kinase; PSMA, prostate-specific membrane antigen; RBC, red blood cell; S, standard; siRNA, small interfering RNA; TTR, transthyretin; TYK2, tyrosine kinase 2; VEGF, vascular endothelial growth factor. Source: Drugs@FDA.

comparators on blood sugar lowering activity. The newly approved drug also offered weight loss benefits, of around 6.5–14% across dose levels.

"This is the most effective drug yet approved for the treatment of type 2 diabetes," said Daniel Drucker, a clinician scientist and endocrinologist at the Lunenfeld-Tanenbaum Research Institute at The Mount Sinai Hospital. "I think it will be welcomed with enthusiasm."

Ongoing trials of the drug could unlock an approval in obesity, a historically challenging indication. In the SURMOUNT-1 trial in over 2,500 patients who are obese or overweight but who do not have diabetes, tirzepatide recipients lost 15–21% of their body weight at 72 weeks, compared with 3% on placebo. An approval in this setting could come in 2023.

Peak global sales of this drug could reach US$10.8 billion (all forecasts are from BCG's analysis of EvaluatePharma data, unless otherwise noted).

Bristol Myers Squibb's (BMS's) deucravacitinib also covers various scientific, clinical and commercial bases. The drug is the first TYK2 inhibitor, the first inhibitor of a pseudokinase domain and the first de novo deuterated drug to market. "It's a real tour de force. Three firsts in a single molecule — that's just showing off really," said University of Melbourne molecular biologist Andrew Wilks, who discovered the JAK proteins, which are related to TYK2.

In two phase III trials of the drug — POETYK PSO-1 and PSO-2 — nearly 1,700 psoriasis patients were randomized to deucravacitinib, Amgen's PDE4 inhibitor apremilast or placebo. Both trials met both co-primary endpoints, which measured the severity of disease versus placebo. Deucravacitinib beat its apremilast active comparator handily too, and is now set to unseat Amgen's $2 billion per year drug.

BMS is developing deucravacitinib for other indications, including psoriatic arthritis and systemic lupus erythematosus.

Peak sales could reach nearly $1.7 billion.

Months after the approval of BMS's drug, Takeda acquired Nimbus's TYK2 inhibitor — another pseudokinase-targeted drug — for $4 billion plus milestones.

Moderna's mRNA-based COVID-19 vaccine Spikevax also secured full FDA approval from CBER in 2022. The pioneering mRNA vaccine secured an EUA in December 2020. Moderna expected sales of up to $19 billion in 2022 for the vaccine.

Table 2 | Selected CBER approvals in 2022

Biologic name (brand)	Sponsor	Properties	Indication
COVID-19 vaccine, mRNA (Spikevax)	Moderna	mRNA vaccine	COVID-19 immunization
Ciltacabtagene autoleucel (Carvykti)	Legend Biotech/J&J	BCMA-targeted genetically modified autologous T-cell immunotherapy	Multiple myeloma
Measles, mumps and rubella vaccine live (Priorix)	GSK	Live, attenuated vaccine	Measles, mumps and rubella vaccination
Betibeglogene autotemcel (Zynteglo)	bluebird bio	β-globin-encoding lentiviral vector for autologous haematopoietic stem cell gene therapy	β-thalassaemia
Elivaldogene autotemcel (Skysona)	bluebird bio	*ABCD1*-encoding lentiviral vector for autologous haematopoietic stem cell gene therapy	Neurologic dysfunction in CALD
Fecal microbiota, live (Rebyota)	Rebiotix/ Ferring	Faecal microbiota suspension for rectal enema	Recurrence of *Clostridioides difficile* infection
Etranacogene dezaparvovec (Hemgenix)	CSL Behring	Factor IX-encoding adeno-associated virus vector gene therapy	Haemophilia B
Nadofaragene firadenovec (Adstiladrin)	Ferring	Interferon α-2b-encoding adenovirus vector gene therapy	BCG-unresponsive non-muscle invasive bladder cancer

ABCD1, ATP binding cassette subfamily D member 1; BCG, Bacillus Calmette–Guérin; BCMA, B cell maturation antigen; CALD, cerebral adrenoleukodystrophy; J&J, Johnson & Johnson. Source: Drugs@FDA.

Table 3 | Selected EUAs in 2022

Biologic name	Sponsor	Properties	Indication
Novavax COVID-19 vaccine, adjuvanted	Novavax	Subunit vaccine, adjuvanted	COVID-19 prevention
Bebtelovimab[a]	Eli Lilly	Spike-targeted mAb	Mild-to-moderate COVID-19

[a]EUA granted in Feb 2022, revoked due to inactivity against circulating variants in November 2022. EUA, Emergency Use Authorization; mAb, monoclonal antibody.

Cancer clinchers

Several cancer approvals also broke new target, modality, clinical and commercial ground.

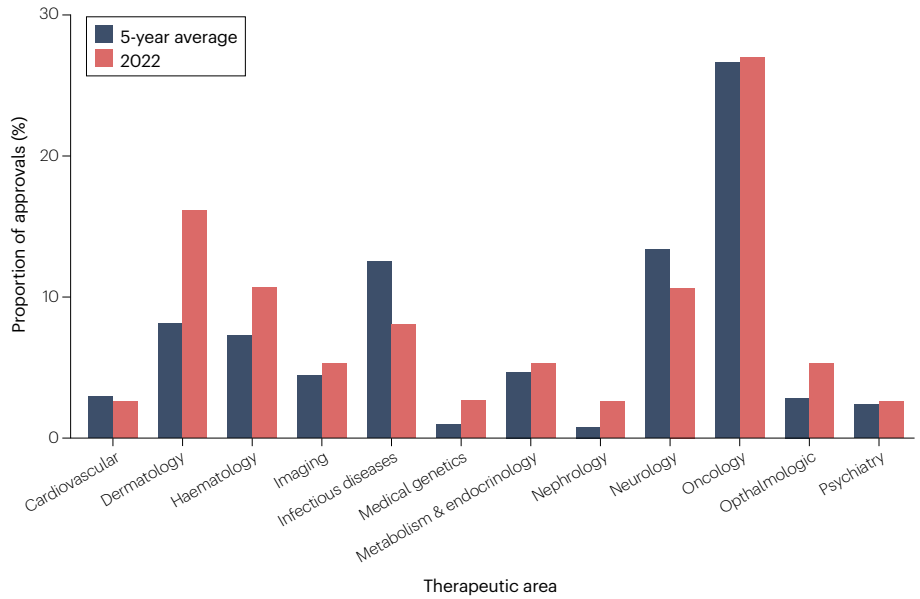

Fig. 2 | CDER approvals by therapeutic area. Indications that span multiple disease areas are classified under only one. Source: *Nature Reviews Drug Discovery*, FDA.

BMS's LAG3 blocker relatlimab, for example, secured a long-awaited expansion of the immune checkpoint inhibitor class. Like CTLA4 and PD1/PDL1-targeted agents that launched the immuno-oncology revolution over a decade ago, LAG3-targeted drugs unleash the immune system on cancer cells. The FDA approved the first-in-class relatlimab in combination with BMS's PD1-directed nivolumab for advanced melanoma based on the results of the phase II/III RELATIVITY-047 trial, in which the antibody combination provided better median progression-free survival than nivolumab alone.

Prior to these results "there was a big question mark about whether or not modulators of any of these other checkpoints would have any activity whatsoever," said Jason Luke, a medical oncologist at the University of Pittsburgh Medical Center.

Relatlimab plus nivolumab will now compete with the established standard of care, nivolumab plus the CTLA4 blocker ipilimumab. A head-to-head trial of these combinations has not been done, and overall survival data from relatlimab plus nivolumab is not yet mature. But data to date suggest that the new combination option might offer comparable efficacy and lower toxicity.

Peak sales of the relatlimab plus nivolumab combination could reach $2.3 billion.

AstraZeneca's CTLA4 blocker tremelimumab meanwhile highlighted the difficult path for validated checkpoint inhibitor targets. The FDA approved BMS's first-in-class CTLA4 blocker ipilimumab in 2011, a foundational regulatory green light for immune checkpoint inhibitors. Tremelimumab was in phase III trials then, but took another 11 years to make it past regulators. It is just the second anti-CTLA4 mAb to market in the USA. The FDA approved tremelimumab for unresectable hepatocellular carcinoma, on the basis of the Himalaya trial results.

With the approval of Immunocore's tebentafusp, a new iteration of bispecific T-cell-engaging biologics has arrived. Most bispecific T-cell engagers rely on antibody domains to bring cancer cells into proximity to T cells. But tebentafusp fuses a gp100–HLA-targeted T cell receptor (TCR) domain to bind cancer cells and a CD3-binding antibody domain to recruit T cells. The FDA approved the biologic on the basis of the phase III IMCgp100-202 trial, in previously untreated patients with metastatic uveal melanoma.

TCRs bind to MHC–peptide antigens, rather than cell-surface-expressed proteins, and so stand to open new doors in oncology. "The target space is massively expanded," says Carsten Reinhardt, chief development officer at Immatics, one of several companies developing the TCR therapy pipeline.

Another bispecific T-cell engager takes on the popular BCMA target. Johnson & Johnson's (J&J's) teclistamab uses a BCMA-targeted antibody arm to bind multiple myeloma cells and a CD3-targeted arm to engage T cells. It was approved on the basis of the phase I/II MajesTEC-1 trial, in patients with triple-class-exposed relapsed or refractory multiple myeloma. The 'off-the-shelf' biologic will compete with highly effective but hard to manufacture BCMA-targeted CAR-T therapies, including J&J's newly CBER-approved ciltacabtagene autoleucel.

GSK's ADC belantamab mafodotin was the first BCMA-targeted therapy to secure FDA approval, in 2020, but the company pulled it from the market in 2022 after a confirmatory phase III trial failed to show benefit.

Roche/Genentech's bispecific antibody mosunetuzumab, by contrast, binds CD20 on the surface of lymphoma cells and CD3 on T cells. The FDA approved this bispecific antibody on the basis of a phase II trial in patients with relapsed or refractory follicular lymphoma who had received at least two prior therapies, including a prior anti-CD20 mAb. A phase III trial of the bispecific antibody plus lenalidomide versus rituximab plus lenalidomide is ongoing in follicular lymphoma, as are other phase II trials in other cancer settings.

BCMA and CD20 top the list of targets for T-cell-engaging bispecific agents in late-stage development.

Mirati's KRAS-G12C-targeted small molecule adagrasib notched up another green light for a covalent inhibitor of the once-undruggable KRAS GTPase. The FDA approved Mirati's drug on the basis of the phase II KRYSTAL-1 trial, in patients with locally advanced or metastatic non-small-cell lung cancer (NSCLC) with $KRAS^{G12C}$ mutations. A crowded pipeline of follow-on KRAS-G12C inhibitors are in the clinic, and drug developers hope to improve both the depth and durability of the effect of these treatments via an abundance of ongoing combination trials.

Close calls

One of the most-watched regulatory rulings of the year was the FDA's review of Amylyx's AMX0035 – a fixed-dose combination of sodium phenylbutyrate plus taurursodiol – for the deadly motor neuron disease amyotrophic lateral sclerosis (ALS). The mechanism of action of this therapy is unknown, but Amylyx hypothesizes that it may prevent neuronal death by mitigating endoplasmic reticulum stress and mitochondrial dysfunction.

In 2020, results from a phase II trial of this drug in 177 people with ALS suggested that it provided some benefit over placebo on the Amyotrophic Lateral Sclerosis Functional Rating Scale–Revised, which measures physical function. A linked Editorial at the time called

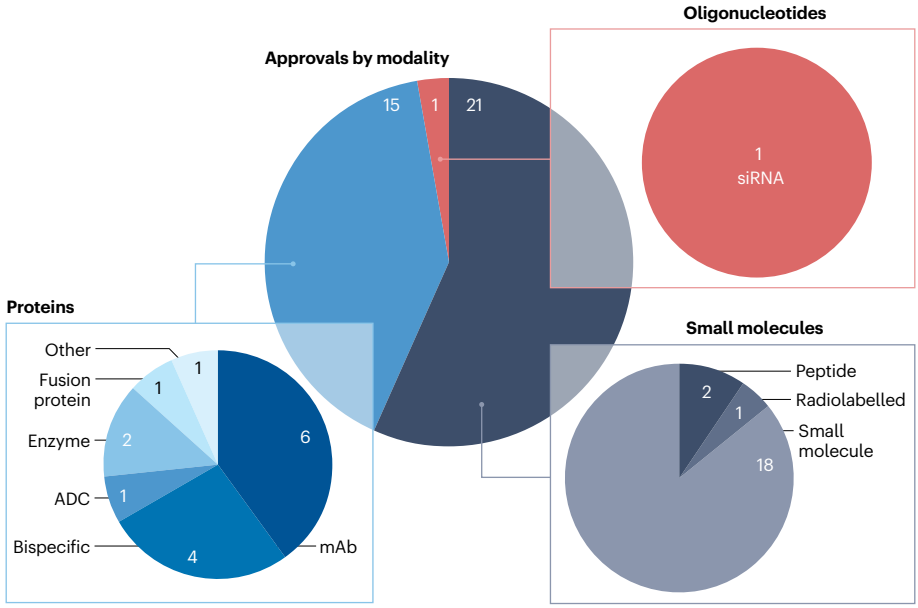

Fig. 3 | CDER approvals by modality. Small molecules, including peptides of up to 40 amino acids in length, and oligonucleotides are approved as new molecular entities (NMEs). Protein-based candidates are approved through biologics license applications (BLAs). ADC, antibody–drug conjugate; mAb, monoclonal antibody; siRNA, small interfering RNA. Source: *Nature Reviews Drug Discovery*.

the efficacy "incremental", "modest" and "a cause for hope", and flagged up the need for confirmatory phase III data. When Amylyx initially approached the FDA about approval for the therapy on the basis of these results, the agency said that a second trial would be needed to confirm that the signal was real. In the summer of 2021, following the controversial approval of a first amyloid-lowering drug for Alzheimer disease, the FDA reversed course and accepted Amylyx's drug for review.

The FDA gathered its independent advisors to discuss the drug twice over the course of 2022, with differing outcomes. In March, panellists voted 6 to 4 that the data did not show that the treatment was effective in ALS. FDA reviewers and independent experts alike questioned the trial's small size, missing data, the drug's modest effect size, the statistical analyses and more. When the panel was reconvened in September to discuss the data again, it voted 7 to 2 in favour of the drug's efficacy.

A phase III trial of the drug is ongoing, with results due in 2024.

Amylyx is charging $158,000 per year for the drug. Peak sales could reach $1.3 billion.

Provention Bio's teplizumab, for the prevention of type 1 diabetes had a long development path.

This CD3-targeted antibody is a humanized version of OKT3, the first ever mAb to secure FDA approval, in 1986. Researchers have suspected for decades that immune-modulating CD3-targeted antibodies might stop T cells from killing insulin-producing cells, slowing the course of autoimmune type 1 diabetes.

A phase III trial of teplizumab in patients with type 1 diabetes failed over a decade ago, missing a composite primary endpoint of improved insulin use and blood sugar levels. In 2019, however, an NIH-sponsored phase II trial in 76 individuals at risk of the disease showed that the antibody delayed the median time to diagnosis of type 1 diabetes by around 2 years.

When the FDA convened its independent advisors to assess the antibody, in 2021, they voted 10 to 7 in favour of approval. But several panellists questioned whether the data package and small phase II trial provided sufficiently robust data. "I do think this is a promising paradigm-shifting therapy that really needs to move forward, at least scientifically. I'm excited about it. But I have a lot of scepticism about the entire body of data," said Michael Blaha, a cardiologist from Johns Hopkins Medicine. Blaha voted for approval, but for a narrower setting than was granted.

The FDA initially rejected the drug in 2021, due to manufacturing concerns, and approved it upon resubmission in 2022.

A phase III trial of the antibody in adolescents who have been recently diagnosed with type 1 diabetes is ongoing, with results due in the second half of 2023.

Provention has partnered with Sanofi to copromote the antibody, at a cost of around $194,000 per course. Peak sales could reach $1 billion.

Gene therapies get into a groove

CBER's regulatory rulings highlight the rise of gene therapies.

Three of these new gene therapies address aberrant protein expression for rare, genetic diseases.

Bluebird bio's betibeglogene autotemcel uses a lentiviral vector to transduce haematopoietic stem cells ex vivo with β-globin, for the treatment of β-thalassaemia. The company's elivaldogene autotemcel uses the same ex vivo platform to enable ABCD1 expression for the treatment of cerebral adrenoleukodystrophy. CSL Behring's etranacogene dezaparvovec uses an adeno-associated virus vector to correct factor IX expression directly in patients with haemophilia A.

These one-off therapies are priced, respectively, at $2.8 million, $3 million and $3.5 million — making them the three most expensive drugs in the USA. Peak sales could reach $390 million, $21 million and $172 million, respectively.

CBER has now approved five gene therapies for rare genetic diseases, all in the past 5 years.

It also approved Ferring's gene therapy nadofaragene firadenovec for high-risk Bacillus

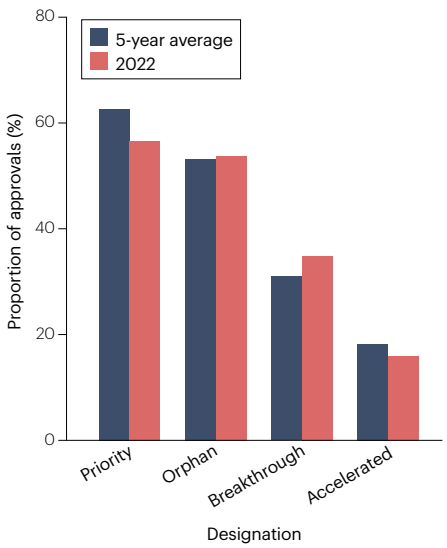

Fig. 4 | CDER approvals trends by designation. Source: *Nature Reviews Drug Discovery*, FDA.

Table 4 | Selected rejected drugs of 2022

Drug	Sponsor	Properties	Indication
Sintilimab	Innovent Biologic	PD1-targeted mAb	NSCLC
Toripalimab	Coherus BioSciences	PD1-targeted mAb	Nasopharyngeal cancer
Bulevirtide	Gilead	NTCP-mediated cell-entry inhibitor	Hepatitis D
Omburtamab	Y-mAbs Therapeutics	Radiolabelled B7-H3-targeted mAb	Brain cancer

mAb, monoclonal antibody; NSCLC, non-small-cell lung cancer; NTCP, Na^+-taurocholate cotransporting polypeptide. Source: BioMedTracker.

Calmette-Guérin-unresponsive non-muscle-invasive bladder cancer. This product consists of a non-replicating adenoviral vector-based gene therapy that encodes interferon-α-2b, an immune-boosting cytokine.

CBER also granted a green light to Ferring/Rebiotix's RBX2660, a consortium of faecal microbes that is delivered via rectal enema to reduce the recurrence of *Clostridioides difficile* infection. This therapy is the first microbiome-based drug to get regulatory approval in the USA. The FDA's independent experts voted in favour of approval for this therapy in September, despite concerns over the magnitude of benefit and the design of the drug's pivotal trial.

Try again

Drug developers also received several complete response letters in 2022 (Table 4). The FDA rejected two PD1 blockers – Lilly/Innovent Biologic's sintilimab and Coherus's toripalimab, both of which were developed primarily in China. These rejections followed an FDA advisory panel meeting on the approvability of drugs developed in just one foreign country, typically China.

Gilead's HIV-1 capsid inhibitor lenacapavir also received a complete response letter, due to manufacturing issues. The FDA approved the first-in-class drug later in the year.

Several notable new drugs are potentially up for approval in 2023, including two amyloid-targeting antibodies for Alzheimer disease, two respiratory syncytial virus vaccines, a haemophilia A gene therapy and a first-in-modality CRISPR-based therapeutic (Table 5).

Table 5 | Selected approvals to watch for in 2023

Biologic name	Sponsor	Properties	Indication	Timing
Lecanemab	Eisai/Biogen	Amyloid-β-targeted mAb	Alzheimer disease	January
Bercolagene telserpavec	Krystal Biotech	Topical, redosable gene therapy	Dystrophic epidermolysis bullosa	February
Donanemab	Eli Lilly	Amyloid-β-targeted mAb	Alzheimer disease	February
Efanesoctocog alfa	Sanofi/Amunix	Factor VIII therapy	Haemophilia A	February
Valoctocogene roxaparvovec	BioMarin	Factor VIII gene therapy	Haemophilia A	March
SER-109	Seres	Purified Firmicutes spores	*Clostridium difficile* infection	April
Tofersen	Biogen/Ionis	SOD1 antisense agent	*SOD1*-mutated ALS	April
GSK3844766A	GSK	Adjuvanted RSV vaccine	RSV in older adults	May
RSVpreF	Pfizer	RSV vaccine	RSV in older adults	May
SRP-9001	Sarepta	Micro-dystrophin gene therapy	Duchenne muscular dystrophy	May
Momelotinib	GSK/Sierra Oncology	ALK2, JAK1 and JAK2 inhibitor	Myelofibrosis	June
Olorofim	F2G	Dihydroorotate dehydrogenase inhibitor	Fungal infections	June
Nedosiran	Novo Nordisk	LDH-targeted siRNA	Hyperoxaluria	September
Concizumab	Novo Nordisk	TFPI-targeted mAb	Haemophilia A and B	September
Zuranolone	Sage/Biogen	$GABA_A$ receptor positive allosteric modulator	MDD and postpartum depression	December
Talquetamab	J&J	GPRC5D×CD3 bispecific antibody	Multiple myeloma	December
Repotrectinib	Bristol Myers Squibb/Turning Point	ROS1 inhibitor	*ROS1*$^+$ NSCLC	2023
Exagamglogene autotemcel	Vertex	Ex vivo CRISPR–Cas9 gene-edited therapy	SCD and β-thalassaemia	2023

ALK2, activin receptor-like kinase 2; ALS, amyotrophic lateral sclerosis; $GABA_A$, gamma-aminobutyric acid type A; JAK, Janus kinase; J&J, Johnson & Johnson; LDH, lactate dehydrogenase; mAb, monoclonal antibody; MDD, major depressive disorder; NSCLC, non-small-cell lung cancer; RSV, respiratory syncytial virus; SCD, sickle cell disease; siRNA, small interfering RNA; SOD1, superoxide dismutase 1; TFPI, tissue factor pathway inhibitor. Source: BioMedTracker.