2019 FDA drug approvals

The FDA approved 48 new drugs last year, keeping up the momentum of recent years.

Asher Mullard

The FDA's Center for Drug Evaluation and Research (CDER) approved 48 novel drugs in 2019 (TABLE 1). Although this approval count falls short of CDER's record 59 approvals of 2018, it still comes in as the third biggest approval class in the past 25 years (FIG. 1).

CDER's 5-year rolling approval average now stands at 44 new drugs per year, double the nadir of 22 in 2009.

Regulatory designations were in line with recent levels too (FIG. 2). CDER approved 28 (58%) priority review products, for therapies that are expected to offer significant improvements over standards. It approved 21 (44%) products with orphan drug designation, addressing rare diseases that affect fewer than 200,000 people in the USA. Breakthrough designees, offering substantial improvements over available therapies, accounted for 13 (27%) approvals. And 9 (19%) products received accelerated approval, on the basis of improvements on surrogate endpoints rather than clinical ones.

There were a few key differences against precedent by therapeutic area (FIG. 3). Cancer remained the dominant therapeutic area, accounting for 11 (23%) of the approvals and on a par with the 25% 5-year average. But neurological products did better than usual, picking up 9 (19%) approvals, as did non-cancer haematology products, with 6 (13%) approvals. Infectious disease products were down, at 5 (10%) approvals, as were metabolism and endocrinology products, with no approvals.

New and emerging modalities continued to accumulate CDER approvals in 2019 (FIG. 4), with a first approval for a nanobody and a burst of antibody–drug conjugate (ADC) activity.

The Center for Biologics Evaluation and Research (CBER) also added some much-awaited new approvals in 2019, including another gene therapy (TABLE 2).

This diverse set of approved products includes multiple possible blockbuster wins. There are five products that could each earn nearly US$3 billion or more per year in annual global sales, suggest consensus sales forecasts collected by the Clarivate Analytics' Cortellis platform (TABLE 3).

The combined and average projected peak sales of this cohort are less compelling, though. Analysts at Boston Consulting Group forecast combined peak sales of $44 billion for this year's newly approved drugs, corresponding to average projected peak sales of $900 million per drug and a median of $400 million. This is below the 20-year average of $1.2 billion per drug and the median of $500 million.

Sales forecasts are notoriously unreliable, however, and can miss actual revenue numbers by more than 40%.

A handful of candidates received complete response letters in 2019 (TABLE 4), some of which might make comebacks in 2020.

Big hitters

Topping the new approvals by expected revenue is Vertex Pharmaceuticals' Trikafta for the treatment of cystic fibrosis.

Trikafta consists of three agents that mitigate the effects of disease-causing mutations in the gene encoding the CFTR

Table 1 | **CDER approvals in 2019**

Drug (brand name)	Sponsor	Properties	Indication	Review[b]
PrabotulinumtoxinA (Jeuveau)[a]	Evolus	Acetylcholine release inhibitor and a neuromuscular blocking agent	Glabellar lines associated with corrugator and/or procerus muscle activity	S
Caplacizumab (Cablivi)[a]	Sanofi/Ablynx	vWF-directed nanobody	ATTP	P, O
Triclabendazole (Egaten)	Novartis	Anthelmintic	Fascioliasis	P, O
Brexanolone (Zulresso)	Sage Therapeutics	$GABA_A$ receptor-positive modulator	Postpartum depression	P, B
Solriamfetol (Sunosi)	Jazz	Dopamine and noradrenaline reuptake inhibitor	Excessive sleepiness due to narcolepsy or obstructive sleep apnoea	S, O
Siponimod (Mayzent)	Novartis	S1P receptor modulator	Relapsing forms of multiple sclerosis	S
Romosozumab (Evenity)[a]	Amgen	Sclerostin inhibitor	Osteoporosis	S
Erdafitinib (Balversa)	Janssen /J&J	FGFR inhibitor	Bladder cancer	P, B, A
Risankizumab (Skyrizi)[a]	AbbVie	IL-23 antagonist	Plaque psoriasis	S
Tafamidis (Vyndaqel)	Pfizer/Foldrx	Transthyretin stabilizer	Heart disease caused by ATTR-CM	P, O, B
Alpelisib (Piqray)	Novartis	PI3K inhibitor	Breast cancer	P
Polatuzumab vedotin (Polivy)[a]	Roche	CD79b-directed ADC	Diffuse large B-cell lymphoma	P, O, B, A
Bremelanotide (Vyleesi)	Amag	Melanocortin receptor agonist	Hypoactive sexual desire disorder	S
Selinexor (Xpovio)	Karyopharm Therapeutics	XPO1 inhibitor	Multiple myeloma	P, O, A
Cilastatin; imipenem; relebactam (Recarbrio)	Merck & Co.	A renal dehydropeptidase inhibitor, a penem antibacterial and a β-lactamase inhibitor	Complicated urinary tract and complicated intra-abdominal infections	P
Ferric maltol (Accrufer)	Shield Therapeutics	Iron replacement product	Iron deficiency anaemia	S
Darolutamide (Nubeqa)	Bayer	Androgen receptor inhibitor	Prostate cancer	P
Pexidartinib (Turalio)	Daiichi Sankyo	CSF1R, KIT and FLT3 inhibitor	Tenosynovial giant cell tumour	P, O, B
Pitolisant (Wakix)	Harmony	H_3 receptor antagonist/inverse agonist	Excessive sleepiness due to narcolepsy	P, O
Pretomanid (Pretomanid)	Pfizer/Mylan	Antimycobacterial	Tuberculosis	P, O
Entrectinib (Rozlytrek)	Roche	TRKA, TRKB, TRKC, ROS1 and ALK inhibitor	NTRK fusion-positive solid tumours and ROS1-positive NSCLC	P, O, B, A
Upadacitinib (Rinvoq)	AbbVie	JAK inhibitor	Rheumatoid arthritis	S
Fedratinib (Inrebic)	Celgene/BMS	JAK2 and FLT3 inhibitor	Myelofibrosis	P, O
Lefamulin (Xenleta)	Nabriva	Pleuromutilin antibacterial	CABP	P
Gallium dotatoc Ga-68	UIHC PET Imaging Center	Radioactive diagnostic	Localization of somatostatin receptor-positive neuroendocrine tumours	S, O
Istradefylline (Nourianz)	Kyowa Kirin	Adenosine receptor antagonist	Parkinson disease, 'off' episodes	S
Tenapanor (Ibsrela)	Ardelyx	NHE3 inhibitor	IBS with constipation	S
Trifarotene (Aklief)	Galderma	Retinoic acid receptor agonist	Acne vulgaris	S
Brolucizumab (Beovu)[a]	Novartis	VEGF inhibitor	Wet age-related macular degeneration	S
Afamelanotide (Scenesse)	Clinuvel	Melanocortin 1 receptor agonist	Erythropoietic protoporphyria	P, O
Fluorodopa F-18	Feinstein Institutes	Radioactive diagnostic	Diagnosis of parkinsonian syndromes	S
Lasmiditan (Reyvow)	Eli Lilly	Serotonin (5-HT) 1F receptor agonist	Migraine with or without aura	S
Tezacaftor, elexacaftor, ivacaftor (Trikafta)	Vertex	Two CFTR correctors and a CFTR potentiator	Most common gene mutation that causes cystic fibrosis	P, O, B
Air polymer-type A (ExEm Foam)	Giskit	Ultrasound contrast agent	Assess fallopian tube patency in women with known or suspected infertility	S
Luspatercept (Reblozyl)[a]	Celgene/BMS	Erythroid maturation agent	Anaemia in β-thalassaemia	P, O
Cefiderocol (Fetroja)	Shionogi	Cephalosporin antibacterial	Complicated urinary tract infections	P
Zanubrutinib (Brukinsa)	BeiGene	BTK inhibitor	Mantle cell lymphoma	P, O, B, A
Crizanlizumab (Adakveo)[a]	Novartis	P-selectin blocker	Painful complications of SCD	P, O, B
Givosiran (Givlaari)	Alnylam	ALAS1-directed siRNA	Acute hepatic porphyria	P, O, B
Cenobamate (Xcopri)	SK Life Science	Unknown	Partial onset seizures	S

Table 1 (cont.) | **CDER approvals in 2019**

Drug (brand name)	Sponsor	Properties	Indication	Review[b]
Voxelotor (Oxbryta)	Global Blood Therapeutics	Haemoglobin S polymerization inhibitor	SCD	P, O, B, A
Golodirsen (Vyondys 53)	Sarepta	Exon 53 skipping antisense	Duchenne muscular dystrophy	P, O, A
Enfortumab vedotin (Padcev)[a]	Astellas	Nectin-4-directed ADC	Urothelial cancers	P, B, A
Brilliant Blue G (Tissueblue)	Dutch Ophthalmic Research	Brilliant Blue G dye	Staining the internal limiting membrane	P, O
Lemborexant (Dayvigo)	Eisai	Orexin receptor antagonist	Insomnia	S
Trastuzumab deruxtecan (Enhertu)[a]	Daiichi Sankyo/ AstraZeneca	HER2-directed ADC	HER2-positive breast cancer	P, B, A
Lumateperone (Caplyta)	Intra-Cellular Therapies	Atypical antipsychotic	Schizophrenia	S
Ubrogepant (Ubrelvy)	Allergan	CGRP receptor antagonist	Migraine with or without aura	S

A, accelerated; ADC, antibody–drug conjugate; ATTP, acquired thrombotic thrombocytopenic purpura; ATTR-CM, transthyretin amyloid cardiomyopathy; ALAS1, aminolevulinate synthase; B, breakthrough; BMS, Bristol-Myers Squibb; BTK, Bruton's tyrosine kinase; CABP, community-acquired bacterial pneumonia; CGRP, calcitonin gene-related peptide; CFTR, cystic fibrosis transmembrane conductance regulator; FGFR, fibroblast growth factor receptor; H3, histamine 3; HER2, human epidermal growth factor receptor 2; IBS, irritable bowel syndrome; NHE3, sodium/hydrogen exchanger 3; NSCLC, non-small-cell lung cancer; O, orphan; P, priority; PI3K, phosphoinositide 3-kinase; S1P, sphingosine 1-phosphate; SCD, sickle cell disease; vWF, von Willebrand factor; XPO1, exportin 1. [a]Biologic approval. [b]Products that received priority reviews as a result of the use of priority review vouchers, rather than because the FDA deemed these drugs to offer significant advances, are classified as having received standard reviews. Source: Drugs@FDA.

ion channel: ivacaftor, a CFTR 'potentiator', helps keep the channel in an open state; and tezacaftor and elexacaftor, two CFTR 'correctors', facilitate trafficking of the protein to the cell surface. The FDA first approved ivacaftor in 2012 and tezacaftor in 2018, but elexacaftor had not been approved before.

With this approval, Vertex has nearly tamed cystic fibrosis. Whereas ivacaftor on its own was approved initially for only around 5% of patients with cystic fibrosis, the triple combination could help around 90% of patients.

Analysts forecast annual average global sales for this combination of $4.5 billion by 2025. The company is already using the proceeds from its cystic fibrosis franchise to broaden its pipeline to other indications.

Trikafta's approval also showcased how fast drug development can be when the conditions are just right. Vertex first synthesized elexacaftor in 2016, just 3.5 years before the drug was approved. And the FDA approved the combination 5 months ahead of its anticipated Prescription Drug User Fee Act (PDUFA) date. Vertex credits its speed with Trikafta to its deep understanding and experience with cystic fibrosis biology and biomarkers.

AbbVie — looking to change things up as its $20 billion per year TNF blocker adalimumab approaches a 2023 patent cliff — meanwhile scored two potentially lucrative drug approvals.

Analysts forecast that its IL-23 antagonist risankizumab, approved for the treatment of psoriasis, will earn nearly $4.1 billion in sales by 2025. In a phase III head-to-head trial of risankizumab versus adalimumab in 605 patients with moderate to severe plaque psoriasis, the IL-23 blocker outperformed the TNF blocker when it came to skin clearance, without raising any additional safety concerns, AbbVie and partner Boehringer Ingelheim reported in *The Lancet* last year.

The drug is still in development for other indications including Crohn's disease,

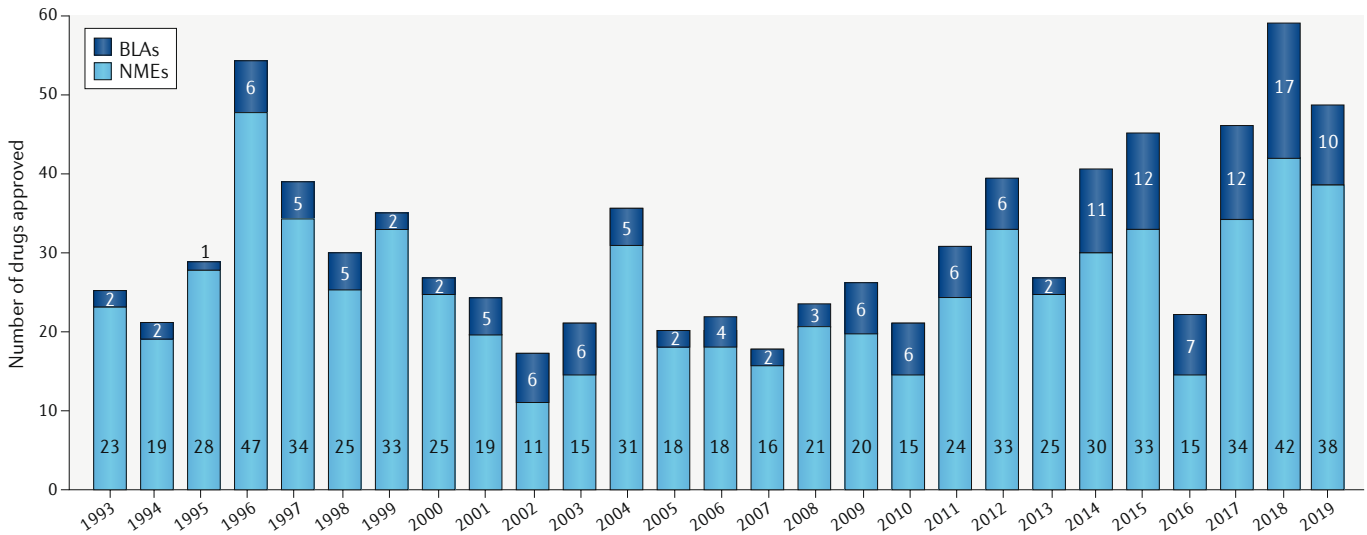

Fig. 1 | **Novel FDA approvals since 1993.** Annual numbers of new molecular entities (NMEs) and biologics license applications (BLAs) approved by the FDA's Center for Drug Evaluation and Research (CDER). See TABLE 1 for new approvals in 2019. Approvals of products such as vaccines and gene therapies by the Center for Biologics Evaluation and Research (CBER) are not included in this drug count (see TABLE 2). Source: Drugs@FDA.

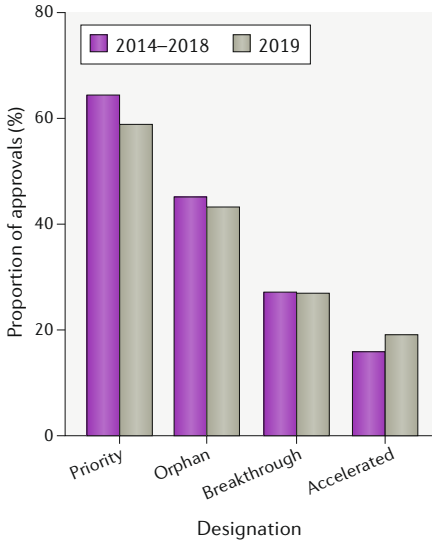

Fig. 2 | **CDER approvals trends.** For 2019 data, products that received priority reviews as a result of the use of priority review vouchers, rather than because the FDA deemed these drugs to offer significant advances, are classified as having received standard reviews. Source: *Nature Reviews Drug Discovery*, FDA.

psoriatic arthritis, ulcerative colitis and asthma. IL-23 is part of the IL-17–T_H17 pathway, however, where a competitive pipeline of candidates are vying for autoimmune market share.

AbbVie's newly approved JAK inhibitor upadacitinib could also earn $3.6 billion in annual sales, for inflammatory and autoimmune indications, by 2025. The JAK inhibitor space is crowded too, with five JAK inhibitors now approved. But whereas Incyte's first-in-class JAK inhibitor ruxolitinib, Pfizer's second-to-market tofacitinib and Lilly and Incyte's third-to-market baricitinib are non-selective JAK family inhibitors, AbbVie's upadacitinib is the first JAK1-selective agent to be approved.

Upadacitinib is being developed for other immune and anti-inflammatory indications, including psoriatic arthritis and ulcerative colitis.

Bristol-Myers Squibb's JAK inhibitor fedratinib, approved on the same day as upadacitinib, is selective for JAK2 over other members of the JAK family. It was developed and approved for myelofibrosis, and is not currently listed as in development in other indications.

Analysts also expect that a novel formulation of an already approved product could provide an attractive windfall. Novo Nordisk's oral GLP1 agonist semaglutide, for type 2 diabetes, is forecast to earn $3.8 billion annually by 2025. The GLP1 agonist market is currently worth around $7.7 billion, and analysts expect that the ease and convenience of this oral formulation of semaglutide will enable Novo Nordisk to continue to dominate this class.

The oral formulation of peptide and biologic therapeutics remains extremely challenging, but Novo Nordisk's success here could prompt renewed re-investment in these efforts.

Novartis's potential mega-blockbuster onasemnogene abeparvovec was approved by the agency's CBER division. The FDA approved the gene therapy for treatment of spinal muscular atrophy, making it the second gene therapy to receive regulatory approval in the USA. The agency approved the first — Spark Therapeutics' voretigene neparvovec, for an inherited form of vision loss — in December 2017. A wave of other gene therapy candidates is now approaching the market.

Onasemnogene abeparvovec uses an adeno-associated virus vector to deliver a fully functional copy of the human *SMN* gene to a patient's motor neuron cells. Analysts forecast average annual sales of $2.9 billion by 2025.

Novartis picked up an impressive six approvals last year, but its roll out of onasemnogene abeparvovec has hit some road bumps. With a list price of $2.1 million for a one-off injection, the potentially curative gene therapy is also the world's most expensive drug, drawing fire from drug pricing critics. Novartis also got into hot water with the FDA for its delayed disclosure of fraudulent data handling during the development of the gene therapy.

Modality moves

With the approval of Sanofi's caplacizumab, for the treatment of acquired thrombotic thrombocytopenic purpura, the industry added a novel modality to its toolbox.

Caplacizumab, a single-domain antibody fragment, is the first nanobody to make it to market. Nanobodies, typically in the 12–30 kDa range, have long promised a range of benefits over traditional ≥150 kDa monoclonal antibodies. The smaller format can have target specificity similar to that of full-length antibodies, while also opening up new routes of administration, the ability to bind to targets that are out of reach to full-length candidates, and cheap and fast manufacturing, say advocates.

Few of those benefits have been realized as yet, but several experimental domain antibodies could reinvigorate interest in this type of therapeutics.

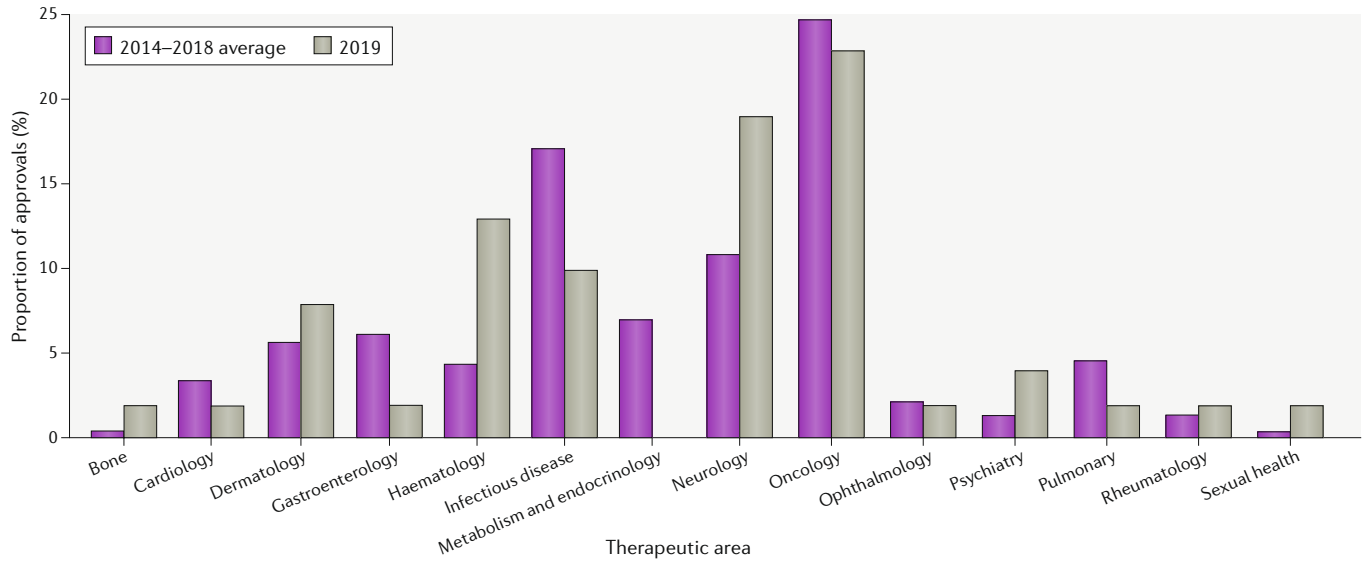

Fig. 3 | **CDER approvals by selected therapeutic areas.** Source: *Nature Reviews Drug Discovery*, FDA.

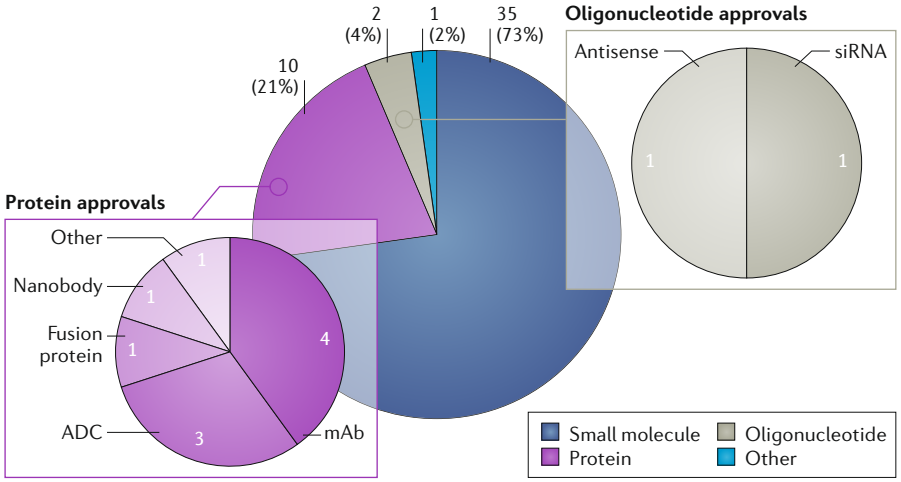

Fig. 4 | **CDER approvals by modality.** 'Small molecules' includes all peptides of up to 40 amino acids in length. Small molecules and oligonucleotides are approved as new molecular entities (NMEs). Protein-based candidates are approved as biologics license applications (BLAs). ADC, antibody–drug conjugate; mAb, monoclonal antibody. Source: *Nature Reviews Drug Discovery*.

The FDA's approval of Alnylam Pharmaceuticals' givosiran, meanwhile, marked the second approval for an RNAi-based candidate. Givosiran is an siRNA therapeutic that induces RNAi-based degradation of aminolevulinic acid synthase 1 (*ALAS1*) mRNA in the liver, for the treatment of acute hepatic porphyria (AHP).

The first RNAi-based candidate to make it to market was Alnylam's patisiran, approved by the FDA in 2018 for hereditary transthyretin-mediated amyloidosis.

The FDA also approved three ADCs in 2019 — Roche's polatuzumab vedotin, Astellas's enfortumab vedotin and Daiichi Sankyo's trastuzumab deruxtecan (partnered with AstraZeneca) — bringing the total number of ADC approvals to eight.

The agency approved a first ADC in 2000, giving a green light to Wyeth's gemtuzumab ozogamicin for acute myeloid leukaemia, but its new owner Pfizer withdrew it from the market in 2010. The FDA approved only five ADCs from 2011 to 2018, including a re-approval for Pfizer's gemtuzumab ozogamicin, at a lower recommended dose and in a different patient population from the first time around.

At least three ADCs — including GlaxoSmithKline's BCMA-targeted ADC belantamab mafodotin — are under regulatory review for potential approval in 2020.

Adding options

The FDA approved two new drugs that could transform the treatment of sickle cell disease (SCD), in which abnormally shaped red blood cells can restrict blood flow, limit the delivery of oxygen to the body's tissues and cause severe pain and organ damage.

Global Blood Therapeutics' voxelotor is an anti-sickling agent that increases haemoglobin's affinity for oxygen, reducing its propensity for sickling and polymerization. The agency granted accelerated approval to the drug on the basis of its effect on haemoglobin levels in patients. The company will run a post-approval study to confirm that this results in a therapeutic benefit, focusing on the risk of stroke, a life-threatening complication associated with SCD.

Analysts forecast annual average sales of $1.5 billion by 2025 for the drug, based on hopes that it will provide therapeutic benefit for a broad population of patients with the disease.

The FDA also approved Novartis's P-selectin-targeted antibody crizanlizumab, which blocks the cell adhesion protein to prevent the multicellular interactions that can lead to painful and dangerous vaso-occlusive crises. Analysts forecast lower annual sales for this drug, however, based on its likely roll out in only a subset of patients with SCD who have a history of acute vaso-occlusive crises.

With the FDA's approval of Johnson & Johnson's esketamine for treatment-resistant depression, the agency green-lit the first antidepressant in a new class in decades.

Esketamine is an enantiomer of the analgesic ketamine, and so was approved as

Table 2 | **Selected CBER approvals in 2019**

Biologic	Sponsor	Properties	Indication
Jynneos	Bavarian Nordic	Modified Vaccinia Ankara	Prevention of smallpox and monkeypox
Onasemnogene abeparvovec (Zolgensma)	Novartis/AveXis	AAV-based *SMN* gene therapy	Spinal muscular atrophy
Dengvaxia	Sanofi Pasteur	Live, attenuated tetravalent vaccine	Prevention of dengue disease
Esperoct	Novo Nordisk	Pegylated recombinant factor VIII	Haemophilia A
Ervebo	Merck & Co.	Live, attenuated vaccine	Prevention of Ebola virus disease

AAV, adeno-associated virus. Source: FDA.

Table 3 | **Selected potential blockbuster approvals**

Drug	Sponsor	Forecast (US$ billions)
Tezacaftor, elexacaftor, ivacaftor[a]	Vertex	4.5
Risankizumab	AbbVie	4.1
Oral semaglutide	Novo Nordisk	3.8
Upadacitinib	AbbVie	3.6
Onasemnogene abeparvovec[a]	Novartis	2.9
Tafamidis[a]	Pfizer	1.7
Brolucizumab	Novartis	1.6
Voxelotor[a]	Global Blood Therapeutics	1.5
Esketamine[a]	Johnson & Johnson	1.5
Polatuzumab vedotin[a]	Roche	1.2

[a]Drugs with breakthrough therapy designation. Sales forecasts are average, annual, global consensus estimates for candidates that are expected to reach blockbuster status by 2025, as reported in Clarivate Analytics' Cortellis database on 31 December 2019.

Table 4 | **Selected Complete Response Letters in 2019**

Drug	Sponsor	Properties	Indication	Status
Sacituzumab govitecan	Immunomedics	TROP2-directed ADC	Breast cancer	Re-submitted
ALKS 5461	Alkermes	μ-Opioid antagonist plus buprenorphine	MDD	Suspended
Iclaprim (IV)	Motif Bio	Microbial dihydrofolate reductase inhibitor	SSSI	Phase III data needed
Sotagliflozin	Lexicon Pharmaceuticals	Dual SGLT1 and SGLT2 inhibitor	Type 1 diabetes	Appeal anticipated
Quizartinib	Daiichi Sankyo	FLT3, PDGFR and KIT inhibitor	AML	Undisclosed
RVT-802	Enzyvant Therapeutics	Allogeneic thymic-tissue based therapy	Congenital athymia	Undisclosed
Cabotegravir and rilpivirine	ViiV Healthcare	Integrase strand transfer inhibitor and non-nucleoside reverse transcriptase inhibitor	HIV-1 infection	Undisclosed

ADC, antibody–drug conjugate; AML, acute myeloid leukaemia; IV, intravenous; MDD, major depressive disorder; SSSI, skin and skin structure infections. Source: BioMedTracker.

a new active ingredient rather than as a new chemical entity. Psychiatrists and patients have been awaiting this approval because of the need for fast-acting drugs for patients who do not respond to other antidepressants.

Researchers are still trying to understand esketamine's mechanism of action. Whereas most other antidepressants modulate signalling through the monoamine neurotransmitters serotonin, dopamine and noradrenaline, esketamine's effect was initially linked to its activity as an NMDA receptor antagonist. That theory has since been questioned, and a slew of would-be competitor NMDA-modulating candidates from companies including Pfizer, AstraZeneca and Merck & Co. have failed in the clinic.

Analysts forecast average annual sales of $1.5 billion for esketamine by 2024.

The agency's CBER also approved Merck & Co's Ervebo, a first vaccine for the prevention of Ebola infection. Ervebo is a live recombinant viral vaccine that consists of a vesicular stomatitis virus (VSV) backbone deleted for the VSV envelope glycoprotein and substituted with the envelope glycoprotein of the Zaire ebolavirus.

On the horizon

2020's approval cohort could be another big one, with several novel, promising and potentially lucrative candidates already under review (TABLE 5).

Aimmune Therapeutics' Palforzia and DBV Technologies' Viaskin Peanut could be the first two therapies — made of peanut protein — for peanut allergy. GlaxoSmithKline's ADC belantamab mafodotin and Bristol-Myers Squibb's CAR-T therapy idecabtagene vicleucel could score first green lights in the crowded anti-BCMA space. Intercept Pharmaceuticals' obeticholic acid could pick up a first approval in the red-hot race to be first to market for non-alcoholic steatohepatitis (NASH). And Biogen could file its anti-amyloid-β aducanumab for Alzheimer disease. Biogen first said that this antibody had failed in pivotal trials, but later announced that it could slow cognitive decline, setting the stage for what could be a much-watched regulatory decision for a beleaguered class of drugs.

Table 5 | **Selected potential approvals for new drugs in 2020**

Drug	Sponsor	Properties	Indication	Expected PDUFA date
Palforzia (AR-101)[a,b]	Aimmune Therapeutics	Peanut protein	Peanut allergy	January
Avapritinib[a,b]	Blueprint Medicines	PDGFRα -D816V inhibitor	GIST	February
Risdiplam[b]	Roche	*SMN2* gene splicing modulator	SMA	May
Ozanimod	BMS/Celgene	S1P receptor modulator	Multiple sclerosis	March
Selumetinib[a]	AstraZeneca/Merck & Co.	MEK inhibitor	Neurofibromatosis	Q2 2020
Satralizumab[a]	Roche	IL-6 receptor antibody	NMO	Q2 2020
Sacituzumab govitecan[a,b]	Immunomedics	TROP2-directed ADC	Breast cancer	June (second review)
Obeticholic acid (Ocaliva)[a,b]	Intercept	Farnesoid X receptor agonist	NASH	June (sNDA)
Viaskin Peanut[a]	DBV Technologies	Peanut protein	Peanut allergy	August
Belantamab mafodotin[a]	GlaxoSmithKline	BCMA-directed ADC	Multiple myeloma	August
Lisocabtagene maraleucel[a]	BMS/Celgene/Juno	Anti-CD19 CAR T-cell therapy	DLBCL	August
Valoctocogene roxaparvovec[a,b]	BioMarin	AAV-based factor VIII gene therapy	Haemophilia A	August
Evinacumab[a]	Regeneron	ANGPTL3 antibody	HOFH	Potential filing
Idecabtagene vicleucel[a]	BMS/Celgene	Anti-BCMA CAR-T cell therapy	Multiple myeloma	Potential filing
Lumasiran[a]	Alnylam	HAO1-directed siRNA	Hyperoxaluria	Potential filing
Aducanumab[b]	Biogen	Amyloid-β antibody	Alzheimer disease	Potential filing

[a]Breakthrough designated drug. [b]Blockbuster sales forecasted by 2025, according to Cortellis database. AAV, adeno-associated virus; ADC, antibody–drug conjugate; BMS, Bristol-Myers Squibb; DLBCL, diffuse large B-cell lymphoma; GIST, gastrointestinal stromal tumours; HOFH, homozygous familial hypercholesterolaemia; NASH, non-alcoholic steatohepatitis; NMO, neuromyelitis optica; PDUFA; Prescription Drug User Fee Act; SMA, spinal muscular atrophy; sNDA, supplemental new drug application. Sources: BioMedTracker and Cortellis database.