2020 FDA drug approvals

The FDA approved 53 novel drugs in 2020, the second highest count in over 20 years.

Asher Mullard

Despite the disruptions caused by COVID-19, the FDA's Center for Drug Evaluation and Research (CDER) approved 53 novel therapeutics in 2020. This is the second highest total ever, falling just short of 2018's all-time high of 59, and tying with the 1996 approval cohort (FIG. 1).

This bumper crop (TABLE 1) raises the 5-year average to 46 approvals per year. This is more than double where it stood a decade ago, from 2006–2010, at 22 approvals per year.

These counts do not include approvals from the FDA's Center for Biologics Evaluation and Research (CBER; TABLE 2) or candidates that received Emergency Use Authorization in 2020 (BOX 1).

Continuing the trend of recent years, cancer products dominated the approval list (FIG. 2). Industry's focus on cancer was even more notable than usual in 2020. The FDA approved 18 (34%) cancer products in 2020, the most ever on both an absolute and a relative basis. The 5-year running average for cancer approvals is 25%.

Neurology products made up the second biggest therapeutic area, with 8 (15%) approvals. Infectious diseases came in third, with 6 (11%) approvals. These are both near their 5-year running averages.

On the modality front, antibody-based and oligonucleotide-based therapeutics continue to broaden the therapeutic landscape (FIG. 3). Twelve antibody-based therapeutics secured approval, tying with 2018 for the all-time high for such products. The 5-year rolling average for antibody approvals now sits at ten per year. In the period 2006–2010, by contrast, the FDA approved only two new antibodies per year on average.

It was a standout year for products with orphan and breakthrough designations, as well as for accelerated approvals (FIG. 4). The FDA approved 31 products (58%) for rare diseases, up from a 5-year average of 46%. It approved 22 (42%) with breakthrough designations, for products that might offer substantial improvements over other available options for serious diseases. This is up from a 5-year average of 28%. And it granted accelerated approval, on the basis of improvements on surrogate end points that are thought to be reasonably likely to predict clinical benefit, to 12 (23%) products, up from a 5-year average of 16%. Priority reviews, for products that would offer significant improvements in safety or effectiveness, were down, however.

Eleven products are on track for blockbuster sales by 2026, show sales forecasts from EvaluatePharma (TABLE 3). These include four products with potential for annual sales of more than US$2 billion.

But the overall financial prospects for newly approved agents remains below average, shows an analysis by Boston Consulting Group. The average projected peak sales of a newly approved drug in 2020 was $700 million, and the median was $400 million, they found. This is below a long-term average of $1.3 billion and a median of $500 million.

Antibodies on the rise

The 12 approvals for antibody-based therapies were supported by a broadening technology base and target space. Antibody–drug conjugates (ADCs) aimed at novel targets, for instance, notched up two approvals.

Immunomedics's sacituzumab govitecan is a TROP2-targeted ADC for the treatment of triple-negative breast cancer. The company first submitted this therapeutic to the FDA in 2018, but the agency rejected it in 2019. Immunomedics said at the time that the delay was due to manufacturing issues, and it resubmitted the drug that year. After the

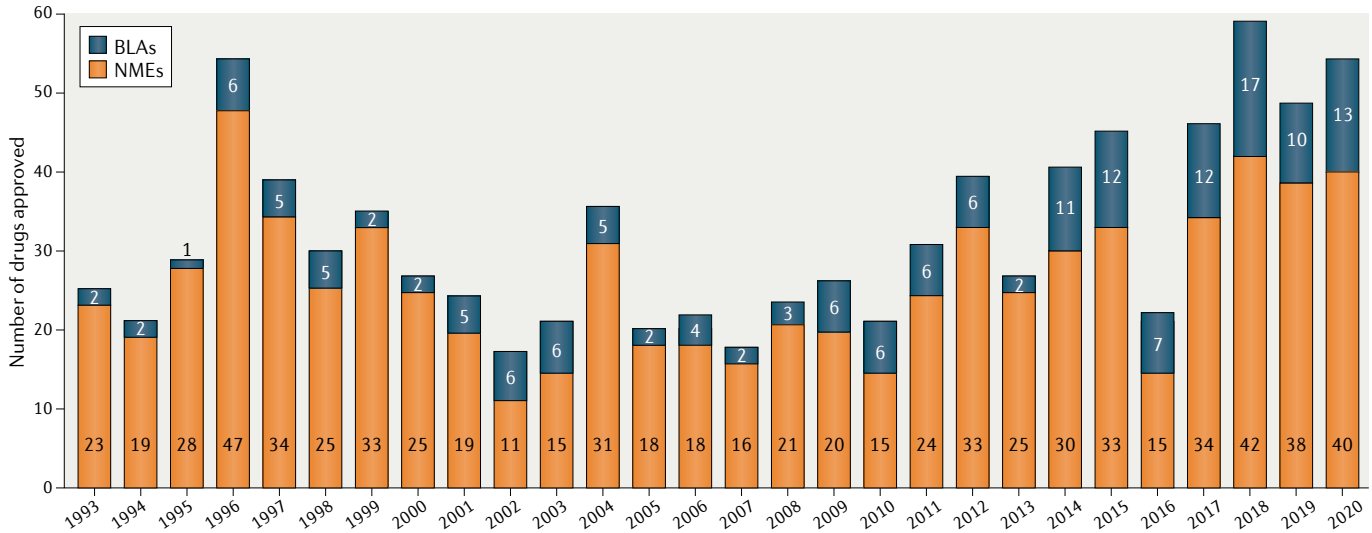

Fig. 1 | **Novel FDA approvals since 1993.** Annual numbers of new molecular entities (NMEs) and biologics license applications (BLAs) approved by the FDA's Center for Drug Evaluation and Research (CDER). See TABLE 1 for new approvals in 2020. Approvals by the Center for Biologics Evaluation and Research (CBER), for products such as vaccines and gene therapies, are not included in this drug count (see TABLE 2). Source: FDA.

Table 1 | **CDER approvals in 2020**

Drug (brand name)	Sponsor	Properties	Indication	Review
Avapritinib (Ayvakit)	Blueprint Medicines	PDGFRA, PDGFRA mutants and KIT kinase inhibitor	GIST with PDGFRA exon 18 mutations	P, O, B
Teprotumumab (Tepezza)[a]	Horizon Therapeutics	IGF1R-directed mAb	Thyroid eye disease	P, O, B
Tazemetostat (Tazverik)	Epizyme	EZH2 inhibitor	Epithelioid sarcoma	P, O, A
Lactitol (Pizensy)	Braintree Labs	Osmotic laxative	Chronic idiopathic constipation	S
Eptinezumab (Vyepti)[a]	Lundbeck	CGRP-directed mAb	Migraine	S
Bempedoic acid (Nexletol)	Esperion Therapeutics	ACL inhibitor	HeFH or atherosclerotic cardiovascular disease	S
Amisulpride (Barhemsys)	Acacia	Dopamine D_2 receptor antagonist	Nausea and vomiting after surgery	S
Rimegepant (Nurtec ODT)	Biohaven	CGRP receptor antagonist	Migraine	S
Isatuximab (Sarclisa)[a]	Sanofi	CD38-directed mAb	Multiple myeloma	S, O
Osilodrostat (Isturisa)	Recordati Rare Diseases	Cortisol synthesis inhibitor	Cushing disease	S, O
Ozanimod (Zeposia)	Celgene/Bristol Myers Squibb	S1P receptor modulator	Multiple sclerosis	S
Selumetinib (Koselugo)	AstraZeneca	MEK1/2 kinase inhibitor	Neurofibromatosis type 1	P, O, B
Tucatinib (Tukysa)	Seagen	HER2 kinase inhibitor	HER2-positive breast cancer	P, O, B
Pemigatinib (Pemazyre)	Incyte	FGFR1-3 kinase inhibitor	Cholangiocarcinoma	P, O, B, A
Sacituzumab govitecan (Trodelvy)[a]	Immunomedics/Gilead	TROP2-directed ADC, with topoisomerase inhibitor	Triple-negative breast cancer	P, B, A
Opicapone (Ongentys)	Neurocrine	COMT inhibitor	Parkinson disease	S
Capmatinib (Tabrecta)	Novartis	MET kinase inhibitor	NSCLC	P, O, B, A
Selpercatinib (Retevmo)	Eli Lilly/Loxo Oncology	RET kinase inhibitor	RET fusion-positive NSCLC and thyroid cancer	P, O, B, A
Ripretinib (Qinlock)	Deciphera	KIT and PDGFRA kinase inhibitor	GIST	P, O, B
Fluoroestradiol F-18	Zionexa	Radioactive diagnostic	Imaging, breast cancer	S
Artesunate (Artesunate)	Amivas	Artemisinin antimalarial	Severe malaria	P, O, B
Flortaucipir F-18	Eli Lilly	Radioactive diagnostic	Imaging, tau in Alzheimer disease	P
Inebilizumab (Uplizna)[a]	Viela Bio	CD19-directed mAb	NMOSD	S, O, B
Lurbinectedin (Zepzelca)	Jazz	Alkylating drug	Small-cell lung cancer	P, O, A
Triheptanoin (Dojolvi)	Ultragenyx	Medium-chain triglyceride	LC-FAODs	S, O
Fostemsavir (Rukobia)	ViiV Healthcare	Attachment inhibitor	HIV	P, B
Remimazolam (Byfavo)	Acacia	Benzodiazepine	Procedural sedation	S
Cedazuridine; decitabine (Inqovi)	Otsuka	Cytidine deaminase inhibitor; nucleoside metabolic inhibitor	Myelodysplastic syndromes	P, O
Abametapir (Xeglyze)	Dr Reddy's	Metalloproteinase inhibitor	Head lice	S
Tafasitamab (Monjuvi)[a]	MorphoSys	CD19-directed mAb	DLBCL	P, O, B, A
Belantamab mafodotin (Blenrep) [a]	GlaxoSmithKline	BCMA-directed ADC, with microtubule inhibitor	Multiple myeloma	P, O, B, A
Nifurtimox (Lampit)	Bayer	Nitrofuran antiprotozoal	Chagas disease	P, O, A
Oliceridine (Olinvyk)	Trevena	Opioid receptor agonist	Acute pain	S
Risdiplam (Evrysdi)	Roche/Genentech	SMN2 splicing modifier	Spinal muscular atrophy	P, O
Viltolarsen (Viltepso)	Nippon Shinyaku	Dystrophin splicing modifier	Duchenne muscular dystrophy	P, O, A
Satralizumab (Enspryng)[a]	Roche/Genentech	IL-6R-directed mAb	NMOSD	S, O, B
Clascoterone (Winlevi)	Cassiopea SpA	Androgen receptor inhibitor	Acne vulgaris	S
Somapacitan (Sogroya)[a]	Novo Nordisk	Growth hormone analogue	Growth hormone deficiency	S
Copper dotatate Cu-64	Radiomedix	Radioactive diagnostic	Imaging, cancer	P, O
Pralsetinib (Gavreto)	Blueprint Medicines/Roche	RET kinase inhibitor	RET fusion-positive NSCLC	P, O, B, A
Atoltivimab; odesivimab; maftivimab (Inmazeb)[a]	Regeneron	Cocktail of Ebola glycoprotein-directed mAbs	Ebola virus	P, O, B
Remdesivir (Veklury)	Gilead	Nucleotide analogue RNA polymerase inhibitor	COVID-19	P

Table 1 (cont.) | **CDER approvals in 2020**

Drug (brand name)	Sponsor	Properties	Indication	Review
Lonafarnib (Zokinvy)	Eiger	Farnesyltransferase inhibitor	HGPS	P, O, B
Lumasiran (Oxlumo)	Alnylam	HAO1-directed siRNA	Hyperoxaluria type 1	P, O, B
Naxitamab (Danyelza)[a]	Y-mAbs Therapeutics	GD2-directed mAb	High-risk neuroblastoma	P, O, B, A
Setmelanotide (Imcivree)	Rhythm	MC_4 receptor agonist	Rare genetic diseases of obesity	P, O, B
PSMA-11 Ga-68	UCLA	Radioactive diagnostic	Imaging, prostate cancer	S
Berotralstat (Orladeyo)	BioCryst	Plasma kallikrein inhibitor	Hereditary angioedema	S, O
Tirbanibulin (Klisyri)	Athenex	Microtubule inhibitor	Actinic keratosis	S
Margetuximab (Margenza)[a]	MacroGenics	HER2-directed mAb	HER2-positive breast cancer	S
Relugolix (Orgovyx)	Myovant Sciences	GnRH receptor antagonist	Prostate cancer	P
Ansuvimab (Ebanga)[a]	Ridgeback	Ebola glycoprotein-directed mAb	Ebola virus	P, O, B
Vibegron (Gemtesa)	Urovant Sciences	β_3-adrenoceptor agonist	Overactive bladder	S

[a]Biologic approval. A, accelerated; ACL, adenosine triphosphate-citrate lyase; ADC, antibody–drug conjugate; B, breakthrough; COMT, catechol-*O*-methyltransferase; DLBCL, diffuse large B cell lymphoma; GIST, gastrointestinal stromal tumour; GnRH, gonadotropin-releasing hormone; HeFH, heterozygous familial hypercholesterolaemia; HGPS, Hutchinson-Gilford progeria syndrome; LC-FAODs, long-chain fatty acid oxidation disorders; mAb, monoclonal antibody; MC_4, melanocortin 4; NSCLC, non-small-cell lung cancer; NMOSD, neuromyelitis optica spectrum disorder; O, orphan; P, priority; siRNA, small interfering RNA; UCLA, University California Los Angeles. Source: Drugs@FDA.

FDA approved the ADC, Gilead acquired Immunomedics for $21 billion, primarily for access to this agent.

Analysts forecast $2.4 billion in annual sales for sacituzumab govitecan by 2026.

GlaxoSmithKline meanwhile scored a first-mover advantage in the highly competitive race to bring BCMA-targeted cancer therapies to market.

BCMA is overexpressed on multiple myeloma cells. Solid biological validation, limited risk of off-tissue toxicity and strong commercial potential have driven a bonanza of interest in BCMA. Drug developers are developing more than a dozen CAR-T cell therapies, ADCs, bispecific antibodies and other BCMA-directed therapeutics.

Bespoke BCMA-targeted CAR-T cell therapies have shown striking efficacy, but these may face manufacturing and distribution bottlenecks. GlaxoSmithKline instead went for an off-the-shelf approach with its ADC belantamab mafodotin, an agent that could offer broad efficacy across patients.

Analysts forecast annual sales of $1.3 billion by 2026.

The FDA has now approved nine ADCs. It granted five of these approvals in the past 2 years. Two ADCs are currently under review by the FDA, with decisions due in 2021.

2020 also saw the second and third approval for monoclonal antibody (mAb) products that target viral antigens. These went to Regeneron's cocktail of atoltivimab, odesivimab and maftivimab (counted as a single approval) and to Ridgeback's ansuvimab, both for Ebola. Multiple mAbs that target SARS-CoV-2 are in the clinic.

Some other novel mAbs are taking on established competitors. Lundbeck's eptinezumab is the fourth antibody to target CGRP or the CGRP receptor, for example, for migraine. Biohaven's rimegepant, which also secured approval in 2020, is the second small-molecule CGRP receptor antagonist to be approved.

Small molecules, big impacts

Small molecules are also opening up new biological and therapeutic opportunities. Roche and Genentech's risdiplam showcases the potential of small molecules that bind RNA targets.

Spinal muscular atrophy (SMA) is a rare neuromuscular disorder that results in the progressive destruction of motor neurons. It is caused by defects in *SMN1*, which codes for the survival motor neuron (SMN) protein. In 2016, the FDA approved Biogen and Ionis's nusinersen, the first disease-modifying therapy for SMA. This antisense oligonucleotide therapeutic modulates the splicing of pre-mRNA from *SMN2*, promoting the inclusion of exon 7 and thereby increasing production of functional SMN protein.

Risdiplam, developed by Genentech in collaboration with the SMA Foundation and PTC Therapeutics, is a small-molecule drug that also modulates the splicing of *SMN2* pre-mRNA to increase levels of the full-length SMN protein. Whereas nusinersen is administered intrathecally in the clinic, risdiplam is orally available and can be administered at home.

SMA has been a case study in modality innovation in recent years. In addition to the FDA's approval of nusinersen, in 2019 the agency approved Novartis's gene therapy onasemnogene abeparvovec, which uses an adeno-associated virus vector to introduce a functional *SMN1* gene into motor neurons.

Analysts forecast annual sales of $2 billion for risdiplam by 2026, highlighting the potential for small molecules to compete against emergent modalities for rare diseases.

Other companies are also targeting RNA with small molecules, focusing on opportunities beyond splice modulation.

Table 2 | **Selected CBER approvals in 2020**

Biologic	Sponsor	Properties	Indication
Palforzia	Aimmune Therapeutics	Peanut allergen powder	Peanut allergic reactions
Sevenfact	LFB	Coagulation FVIIa, recombinant	Bleeding episodes in haemophilia A or B
MenQuadfi	Sanofi Pasteur	Meningococcal conjugate vaccine	Invasive meningococcal disease
Brexucabtagene autoleucel (Tecartus)	Gilead/Kite	CD19-directed CAR-T cell therapy	Mantle cell lymphoma

CAR, chimeric antigen receptor; FVIIa, factor VIIa. Source: FDA.

Box 1 | **COVID-19 and Emergency Use Authorizations in 2020**

In an attempt to get a handle on the COVID-19 pandemic, the FDA has relied on Emergency Use Authorizations (EUAs) to facilitate rapid roll out of a few potentially helpful COVID-19 vaccine and drug candidates. These authorizations are for products that "may be effective", a lower level of evidence than the "effectiveness" standard that the agency otherwise uses for approval. EUAs are not intended as long-term alternatives to obtaining FDA approval, however, and sponsors are expected to continue to develop their products for full regulatory review.

Most notably, two vaccine candidates secured EUAs in December, just a year after the SARS-CoV-2 virus emerged. Both Pfizer and BioNTech's BNT162b2 and mRNA-1273 are mRNA vaccines, using lipid nanoparticle-encapsulated oligonucleotides to express an antigen of choice in vaccine recipients. First phase III results suggest that both of these vaccines have efficacy rates of around 95%.

Pfizer and Moderna both plan to file their vaccines for full approval in 2021, paving the way for possible approvals by the end of the year.

Gilead's track record with remdesivir shows how quickly the agency can convert an EUA into an approval. The FDA first granted the EUA to remdesivir in May, and approved it in October.

The agency has also granted EUAs to two novel antibody-based products: Regeneron's combination of casirivimab and imdevimab, and Eli Lilly's bamlanivimab. These therapeutic antibodies target the spike protein of SARS-CoV-2. They are authorized for patients who are SARS-CoV-2 positive and at high risk for progressing to severe COVID-19 and/or hospitalization.

But the FDA's use of EUAs also highlighted the perils of rapid drug development, and stoked fears around the politicization of the regulatory process. Most notably, the FDA granted an EUA to the antimalarials chloroquine and hydroxychloroquine in March, despite little evidence of their efficacy in COVID-19. The FDA revoked this EUA in June, noting that these drugs "are unlikely to be effective in treating COVID-19".

Keeping up with the kinases

Small-molecule kinase inhibitors are also still going strong. The FDA approved eight kinase inhibitors last year, and these accounted for just under half of the novel oncology approvals.

Despite the competition in the kinase space, prospects are still good for agents with the right pharmacological profiles.

With the FDA's approval of Blueprint Medicines' PDGFR inhibitor avapritinib for gastrointestinal stromal tumours (GISTs), for example, the company will take on Novartis's pioneering small-molecule kinase inhibitor imatinib in a narrow patient population.

Imatinib is one of a few multikinase inhibitors with activity against PDGFR that is already used for GIST patients. According to Blueprint, however, around 6% of these patients have PDGFRA exon 18 mutations that respond particularly poorly to imatinib. Blueprint advanced avapritinib on the basis of its activity against both wild-type PDGFRA and PDGFRA mutants, and the drug is the first therapy approved for patients with GISTs carrying PDGFRA exon 18 mutations.

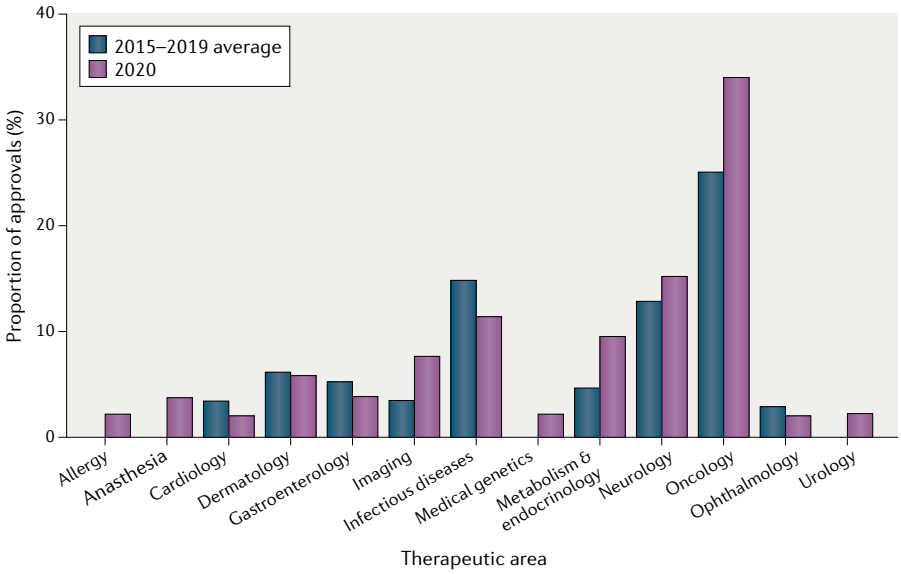

Fig. 2 | **CDER approvals by selected therapeutic areas.** Source: *Nature Reviews Drug Discovery*, FDA.

If estimates of around 3,000 GIST cases per year in the USA are accurate, this amounts to around 180 potential avapritinib patients per year. Blueprint is working towards additional GIST approvals, as well as approvals in systemic mastocytosis.

Analysts forecast sales of $1 billion for the drug by 2026.

Eli Lilly secured an approval for a first RET-selective kinase inhibitor, selpercatinib. Multikinase inhibitors such as Sanofi's vandetanib and Exelixis's cabozantinib have activity against RET, but the safety and durability of these drugs is thought to be limited at least in part owing to their activity against other kinases. Loxo Oncology set out to target RET specifically, noting that around 2% of cancers carry mutations or abnormalities in this kinase. Eli Lilly gained selpercatinib in its $8 billion acquisition of Loxo in 2019.

The first approval for selpercatinib is in non-small-cell lung cancer, one of the most prevalent forms of cancer, and in two forms of thyroid cancer, in which RET alterations are particularly common. Lilly might apply for tissue-agnostic approvals for this agent in the future.

The FDA also approved Blueprint Medicines and Roche's RET-selective inhibitor pralsetinib in non-small-cell lung cancer.

Interesting times

Gilead's remdesivir scored a first approval for the treatment of COVID-19, moving through its development and regulatory milestones at unprecedented speed.

Remdesivir is an RNA polymerase inhibitor that mimics an RNA nucleotide to stall viral RNA synthesis. Initially discovered for hepatitis C and respiratory syncytial virus applications, the small molecule was repurposed as a potential treatment for Ebola during the 2014–2016 outbreak of that disease in West Africa. These trials helped establish a safety database for remdesivir, but it proved ineffective in this setting.

With the emergence of SARS-CoV-2, the virus that causes COVID-19, Gilead quickly advanced remdesivir into trials. First trials of remdesivir in COVID-19 started in February. By May, the FDA had granted it Emergency Use Authorization, enabling the distribution of an unapproved candidate. In October, the FDA approved the drug on the basis of one NIH-sponsored trial and two Gilead-sponsored trials. A large, multi-armed trial led by the World Health Organization found "little or no effect on hospitalized patients with COVID-19," however.

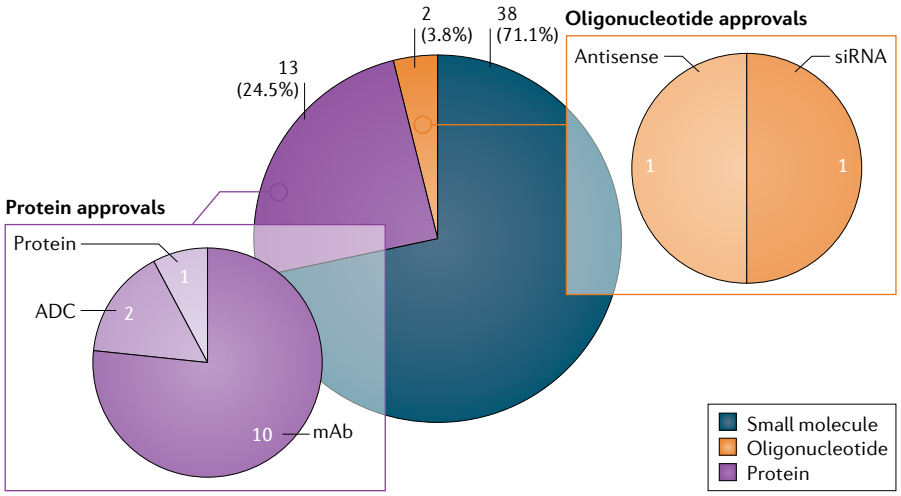

Fig. 3 | **CDER approvals by modality.** 'Small molecules' includes all peptides of up to 40 amino acids in length. Small molecules and oligonucleotides are approved as new molecular entities (NMEs). Protein-based candidates are approved through biologics license applications (BLAs). ADC, antibody–drug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

Analysts are currently forecasting peak sales of nearly $1.5 billion for remdesivir in 2021, declining to $500 million by 2025. But these forecasts are falling fast, and exemplify the pitfalls of sales projections. In June 2020, some analysts were forecasting peak annual sales as high as $7 billion.

The FDA also granted Emergency Use Authorizations to several other novel COVID-19 candidates, including vaccines and therapeutic antibodies (BOX 1).

Epizyme's tazemetostat is the first inhibitor of the epigenetic writer protein EZH2, which methylates histones to modulate transcriptional activity. The FDA approved tazemetostat for epithelioid sarcoma.

Eiger BioPharmaceuticals' lonafarnib is a first-in-class farnesyltransferase inhibitor. Whereas drug developers worked on this target decades ago with anti-cancer aspirations, Eiger's approval was for a rare premature aging disorder called Hutchinson-Gilford progeria syndrome.

Trevena's μ-opioid receptor agonist oliceridine, approved for moderate-to-severe acute pain, faces stiff competition. This drug was once heralded as the poster child of biased GPCR agonists, drugs that can preferentially activate only a subset of a receptor's signalling pathways. Trevena had hoped that oliceridine would have a cleaner safety profile than traditional opioid receptor agonists, but the agency says oliceridine's safety profile "is similar to other opioids".

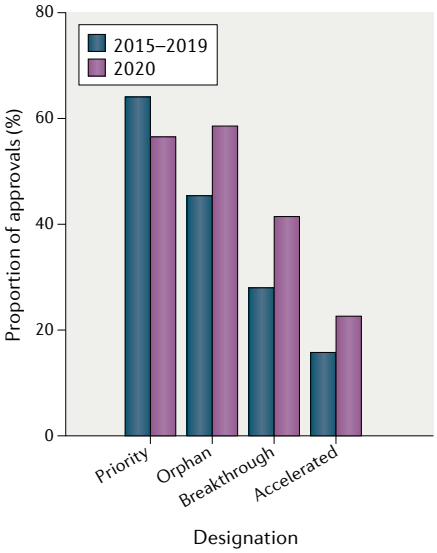

Fig. 4 | **CDER approvals trends.** Products that received priority review due to the use of a priority review voucher are classified as having received standard review. Source: *Nature Reviews Drug Discovery*, FDA.

CBER's approval of Gilead's brexucabtagene autoleucel marked the third green light for a CD19-targeted CAR-T cell therapy. It is the first CAR-T cell therapy to be approved for mantle cell lymphoma.

Not all good news

Several drug developers suffered regulatory setbacks in 2020, receiving complete response letters from the FDA (TABLE 4).

AbbVie, Allergan and Molecular Partners hoped that their VEGF-targeted agent abicipar pegol would be approved for wet age-related macular degeneration. This would have been a first approval for a DARPin (designed ankyrin repeat protein), a low-molecular-weight biologic modality that aims to compete with mAbs. But the FDA rejected the candidate, citing intraocular inflammation concerns.

The FDA rejected Gilead's JAK inhibitor filgotinib for rheumatoid arthritis. Analysts had previously projected peak sales of nearly $1.5 billion for the anti-inflammatory drug. But the FDA asked for additional safety data from ongoing studies.

The EMA approved the drug in 2020.

The FDA also rejected Novartis and The Medicines Company's inclisiran, a small interfering RNA agent that lowers PCSK9 production, for hyperlipidaemia. If approved, the oligonucleotide-based drug would have competed with two FDA-approved mAbs that target PCSK9. Whereas these mAbs are administered once every 2–4 weeks, inclisiran is dosed twice yearly. Novartis acquired The Medicines Company for $9.7 billion in 2019 for access to this therapeutic, licensed from Alnylam Pharmaceuticals.

Novartis says the rejection was due to "unresolved facility inspection-related conditions".

The EMA approved inclisiran in 2020.

Table 3 | **Selected potential blockbuster approvals in 2020**

Drug	Sponsor	2026 forecast (US$ billions)
Teprotumumab	Horizon Therapeutics	3.4
Ozanimod	Bristol Myers Squibb	2.5
Sacituzumab govitecan	Immunogenics/Gilead	2.4
Risdiplam	Roche	2
Rimegepant	Biohaven Pharmaceuticals	1.6
Ripretinib	Deciphera Pharmaceuticals	1.6
Lurbinectedin	Jazz Pharmaceuticals	1.5
Belantamab mafodotin	GlaxoSmithKline	1.3
Tucatinib	Seagen	1.2
Avapritinib	Blueprint Medicines	1
Tazemetostat	Epizyme	1

Source: EvaluatePharma.

Table 4 | **Selected Complete Response Letters in 2020**

Drug	Sponsor	Properties	Indication
Abicipar pegol	Molecular Partners/AbbVie	VEGF-directed DARPin	Wet AMD
Obeticholic acid (Ocaliva)[a]	Intercept Pharmaceuticals	Farnesoid X receptor agonist	NASH
Viaskin Peanut	DBV Technologies	Peanut allergen	Peanut allergy
Filgotinib[b]	Gilead	JAK1 inhibitor	Rheumatoid arthritis
Valoctocogene roxaparvovec	BioMarin Pharmaceutical	Factor VIII gene therapy	Haemophilia A
Sutimlimab	Sanofi	Complement C1-directed mAb	Autoimmune haemolytic anaemia
ALKS 3831	Alkermes	Antipsychotic drug combination	Schizophrenia and bipolar I disorder
Inclisiran[b]	Novartis/The Medicines Company	PCSK9-directed siRNA	Hyperlipidaemia

[a]Previously approved for primary biliary cholangitis. [b]Approved by the EMA. AMD, age-related macular degeneration; mAb, monoclonal antibody; DARPin, designed ankyrin repeat protein; NASH, non-alcoholic steatohepatitis; siRNA, small interfering RNA. Source: BioMedTracker.

Intercept's farnesoid X receptor agonist obeticholic acid was first approved by the FDA for primary biliary cholangitis in 2016, and so a supplementary approval in non-alcoholic steatohepatitis (NASH) would not have qualified for inclusion on the FDA's novel approval list. But there were hopes that this drug would secure a first approval for NASH, an indication that has attracted many drug developers over the past decade. The FDA rejected the application, however, noting that "the predicted benefit … remains uncertain and does not sufficiently outweigh the potential risks."

A new year

It remains to be seen whether industry and the FDA can keep this approval pace up, in the face of COVID-19-related disruptions. "Although CDER has been meeting most of its user fee commitments, it is possible that our ability to do so may change due to the extended length of the pandemic," an FDA spokesperson said. The FDA typically discloses in December how many novel drugs sponsors have filed over the course of the year, but it had not yet done so as *Nature Reviews Drug Discovery* went to press.

Several notable potential approvals are slated for 2021 (TABLE 5), some of which were originally scheduled for 2020.

Bristol Myers Squibb's lisocabtagene maraleucel, for example, could become the fourth CAR-T cell therapy to make it to market. Whereas the other three FDA-approved CAR-T cell therapies are all directed at CD19-expressing cells, lisocabtagene maraleucel takes aim at BCMA. Bristol Myers Squibb acquired Celgene in 2019 for $74 billion, in part to access this therapeutic and Celgene/Juno Therapeutics' CAR-T cell expertise.

A regulatory decision on lisocabtagene maraleucel was originally set for November 2020. The FDA deferred action on the application, however, owing to the challenges of inspecting manufacturing facilities during the COVID-19 pandemic.

The FDA is expected to make a decision on Biogen's amyloid-β-targeted antibody aducanumab for Alzheimer disease by the end of March 2021. Biogen initially reported that aducanumab had failed in its pivotal trials, but the company changed course in 2019 after re-analysing its clinical data. In November, an independent advisory panel voted against approving the antibody. The FDA is not obliged to follow this recommendation.

Amgen's KRAS-G12C inhibitor sotorasib is under review for non-small-cell lung cancer, leading a deep pipeline against this holy grail of cancer targets.

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

Drug	Sponsor	Properties	Indication	Expected PDUFA
Lisocabtagene maraleucel[a,b]	Bristol Myers Squibb	CD19-directed 4-1BB CAR-T cell therapy	DLBCL	Pending
Vericiguat[b]	Merck & Co./Bayer	sGC stimulator	Congestive heart failure	January
Evinacumab[a]	Regeneron	ANGPTL3-directed mAb	Hypercholesterolaemia	February
Trilaciclib[a,b]	G1 Therapeutics	CDK4/6 inhibitor	Small-cell lung cancer	February
Idecabtagene vicleucel[a,b]	Bristol Myers Squibb	BCMA-directed CAR T cell	Multiple myeloma	March
Aducanumab[b]	Biogen	Amyloid-β-directed mAb	Alzheimer disease	March
Tanezumab	Pfizer/Eli Lilly	NGF-directed mAb	Osteoarthritis pain	March
Roxadustat[b]	AstraZeneca	HIF prolyl hydroxylase inhibitor	Anaemia of CKD	March
Tralokinumab	AstraZeneca	IL-13-directed mAb	Atopic dermatitis	2Q2021
Abrocitinib[a]	Pfizer	JAK1 inhibitor	Atopic dermatitis	April
PF-06482077[a]	Pfizer	Pneumococcal conjugate vaccine	Pneumococcal vaccine	June
Teplizumab	Provention Bio	CD3-directed mAb	Type 1 diabetes	July
Amivantamab[a]	Johnson & Johnson	EGFR and MET bispecific antibody	NSCLC	August
Sotorasib (AMG 510)[a]	Amgen	KRAS-G12C inhibitor	NSCLC	August
V114[a,b]	Merck & Co.	Pneumococcal conjugate vaccine	Pneumococcal vaccine	November
BNT162b2	Pfizer/BioNTech	COVID-19 mRNA vaccine	COVID-19	BLA filing in 2021
mRNA-1273	Moderna	COVID-19 mRNA vaccine	COVID-19	BLA filing in 2021

[a]Breakthrough designated drug. [b]Forecasted blockbuster sales by 2026, according to Cortellis database. BLA, Biologics License Application; DLBCL, diffuse large B cell lymphoma; CAR, chimeric antigen receptor; CKD, chronic kidney disease; mAb, monoclonal antibody; NSCLC, non-small-cell lung cancer; PDUFA, Prescription Drug User Fee Act; sGC, soluble guanylate cyclase. Sources: BioMedTracker and Cortellis database.