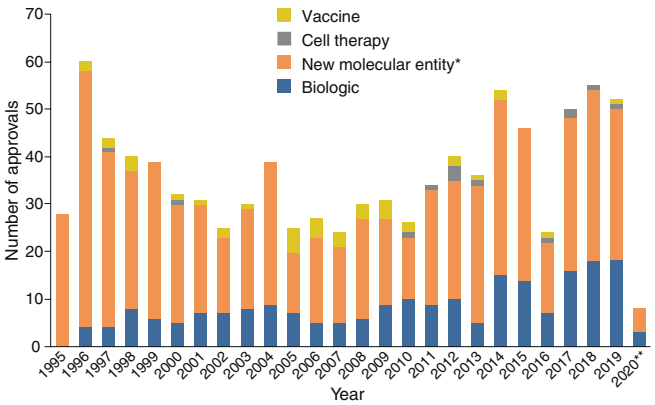
DATA PAGE

Drug pipeline 1Q20

The US Food and Drug Administration (FDA) kept up its pace with nine approvals. Notable firsts include Tazverik for epithelial sarcoma (the first small-molecule inhibitor of the histone methyltransferase EZH2) and Tepezza for thyroid eye disease (the first approved monoclonal antibody (mAb) targeting insulin-like growth factor receptor; IGF-1R). Mesoblast's mesenchymal stem cell therapy (remestemcel-L) for pediatric graft-versus-host disease and GlaxoSmithKline's first-in-class small molecule HIV attachment inhibitor targeting glycoprotein 120 (gp120) come before the FDA next quarter. Clinical trial results of two oligonucleotide drugs showed a cholesterol-lowering antisense oligonucleotide drug and a small-interfering RNA (siRNA) drug gave improvements over statin alone. The COVID-19 pandemic is affecting the drug pipeline; Bristol-Myers Squibb's Zeposia is among several drug launches delayed.

Historic US regulatory approvals by drug class

Biologics approvals held steady in 2019.



*New molecular entity (NME) class includes mainly small-molecule drugs, but also steroid, synthetic peptide, and mixed compounds, excluding new formulations. **Partial year to March 31.Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com).

Upcoming catalysts (3Q20)

Drug/company	Indication	Drug information
Fostemsavir tromethamine/ GlaxoSmithKline	HIV/AIDS	8/5/2020 FDA PDUFA date for this small-molecule HIV attachment inhibitor that interferes with viral gp120 protein binding to $CD4^+$ cells
Lisocabtagene maraleucel/ Bristol-Myers Squibb	Diffuse large B-cell lymphoma, non-Hodgkin's lymphoma	8/17/2020 FDA PDUFA date for these autologous chimeric antigen receptor (CAR) modified T cells with 1:1 ratio of $CD4^+$ and $CD8^+$ cells
Margetuximab/ MacroGenics	Breast cancer	8/19/2020 FDA PDUFA date for this chimeric Fc modified IgG1 mAb targeting epidermal growth factor receptor 2 (EGFR-2)
Valoctocogene roxaparvovec/ BioMarin	Hemophilia A	8/12/2020 FDA PDUFA date for adeno-associated virus 5 gene therapy vector containing a B-domain-deleted factor VIII gene with a liver-specific promoter
Inebilizumab/ Viela Bio	Neuromyelitis optica (Devic's syndrome	6/13/2020 FDA PDUFA date for this humanized IgG1-κ mAb against CD38
Satralizumab/ Roche	Neuromyelitis optica (Devic's syndrome)	5/31/2020 FDA PDUFA date for this humanized IgG2 mAb against interleukin-6 receptor
Remestemcel-L/ Mesoblast	Graft-versus-host disease	9/30/2020 FDA PDUFA date for mesenchymal stem cells isolated from the bone marrow of autologous donors

Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com)

Notable clinical trial results

Drug/company	Indication	Drug information
Inclisiran/ The Medicines Company	Dyslipidemia/ hypercholesterolemia	3/18/2020 In three phase 3 trials of this siRNA targeting proprotein convertase subtilisin–kexin type 9 mRNA, twice-yearly dosing led to durable low-density lipoprotein C reductions compared with placebo (*N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa1912387, 2020)
Pelacarsen/ Novartis (Ionis)	Cardiovascular disease	1/1/2020 In a randomized, double-blind, placebo-controlled, dose-ranging phase 2 trial of patients with established heart disease, this *N*-acetylgalactosamine-conjugated 2′-*O*-methoxyethyl phosphorothioate antisense oligonucleotide designed to suppress lipoprotein(a) mRNA resulted in dose-dependent decreases in lipoprotein levels (80% at highest dose compared with 6% in controls) (*N. Engl. J. Med.* **382**, 244–255, 2020)
Nemolizumab/ Galderma	Pruritus	2/20/2020 In a 12-week, randomized, double-blind, phase 2 trial of humanized IgG2 mAb directed against interleukin-31 receptor-α, which blocks signaling from IL-31, patients on drug had 53% reduction in severity compared with 20% with placebo (*N. Engl. J. Med.* **382**, 706–716, 2020)
PTI-125/Cassava Sciences	Alzheimer's disease	2/7/2020 In a phase 2a open-label trial of this small-molecule binder of filamin A (a scaffolding protein required for the toxic signaling of β-amyloid), multiple biomarkers showed improvement after 28 days (*J. Prev. Alzheimers Dis.* https://doi.org/10.14283/jpad.2020.6 2020)
RV521/ReViral	Respiratory syncytial virus (RSV)	1/27/2020 In a randomized trial, this small-molecule viral fusion inhibitor of RSV F protein reduced viral load and disease severity in healthy adults challenged with RSV (*Antimicrob. Agents Chemother.* **64**, e01884-19, 2020)

Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com)

Notable drug approvals

Drug/company	Indication	Drug information
Tazverik (tazemetostat)/Royalty Pharma, Epizyme	Epithelial sarcoma	1/23/2020 FDA granted accelerated approval for this first-in-class small molecule inhibitor of methyltransferase EZH2, which catalyzes the trimethylation of Lys27 on histone H3
Ayvakit (avapritinib)/ Blueprint Medicines	Gastrointestinal stromal tumor	1/9/2020 FDA approved this selective inhibitor of KIT and platelet-derived growth factor-α (PDGFRα) for patients harboring *PDGFRA* exon 18 mutations, including PDGFRA D842V mutation.
Tepezza (teprotumumab)/ Horizon Therapeutics	Thyroid eye disease	1/21/2020 FDA approved this human IgG1 mAb that targets IGF-1R
Nexletol (bempedoic acid)/Esperion Therapeutics	Dyslipidemia/ hypercholesterolemia	2/21/2020 FDA approved this small molecule inhibitor of ATP citrate lyase, upstream from statins
Nurtec ODT (rimegepant)/Biohaven Pharmaceuticals	Migraine and other headaches	2/27/2020 FDA approved this small-molecule, orally dissolving calcitonin gene-related peptide (CGRP) receptor antagonist
Isturisa (osilodrostat)/ Recordati	Cushing's syndrome	3/6/2020 FDA approved this small-molecule inhibitor of aldosterone synthase
Sarclisa (isatuximab)/ Sanofi	Multiple myeloma	3/2/2020 FDA approved this humanized IgG1 mAb against CD38
Zeposia (ozanimod)/ Bristol-Myers Squibb	Multiple sclerosis	3/25/2020 FDA approved this selective sphingosine 1-phosphate 1 (S1PR1) and 5 (S1PR5) receptor modulator

Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com)

Notable regulatory setbacks

Drug/company	Indication	Drug information
AXO-AAV-GM2/ Axovant	GM2 gangliosidoses (Tay-Sachs disease, Sandhoff disease, AB variant)	1/13/2020 FDA put a clinical hold on this adeno-associated virus (AAV) serotype 2 gene therapy that delivers β-hexosaminidase α and β subunit genes (*HEXA* and *HEXB*) via two coadministered AAVrh8 vectors delivered directly to the central nervous system due to CMC and device-related issues.
PledOx/Pled Pharma	Chemotherapy-induced peripheral neuropathy	1/23/2020 FDA put a clinical hold on phase 3 clinical trial of this manganese superoxide dismutase mimic due to a few adverse effects, while trials continue in Europe and Asia
LB-0001/LogicBio Therapeutics	Organic acidemias	2/10/2020 FDA put a clinical hold on this recombinant adeno-associated viral vector with a human methylmalonyl-CoA mutase gene for unspecified clinical and non-clinical reasons
Concizumab/ Novo Nordisk	Hemophilia A and B	3/16/2020 FDA put a clinical hold on a two phase 3 and one phase 2 trial of this humanized IgG4 mAb specific for the K2 domain of tissue factor pathway 1 (TFP1) inhibitor owing to three non-fatal thombic events — the fifth such TFP1 inhibitor to fail.

Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com)

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