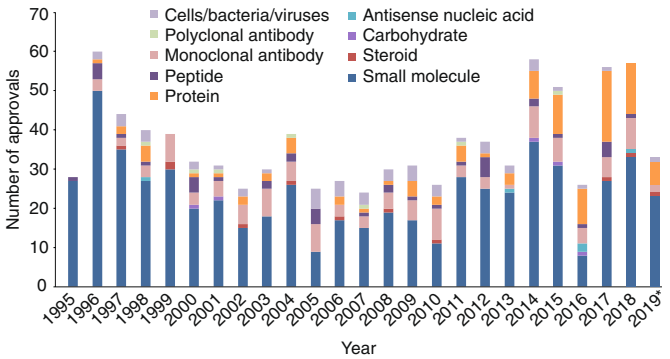
DATA PAGE

Drug pipeline 3Q19

The third quarter saw US Food and Drug Administration approvals for two anti-infectives. Pretomanid, indicated for drug-resistant tuberculosis (TB), is only the third TB drug approved over the past 50 years and the first antibiotic to be developed by a non-profit, the TB Alliance. Elsewhere, MSD Merck got the green light for Recarbrio, which is approved for intra-abdominal and for urinary and reproductive tract infections. Two new cancer drugs were approved through the agency's accelerated approval pathway: Karyopharm's Xpovio and Roche/Genentech's Rozlytrek. In early 2020, the FDA will review two sickle cell anemia drugs working through novel mechanisms. Meanwhile, Sarepta's second exon-skipping antisense drug for muscular dystrophy got pushback from the regulator; its predecessor, Exondys 51, was approved in 2016.

FDA approvals by drug type

Another productive year for drug approvals.



*As of September 30, 2019. Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com).

Notable clinical trial results (3Q19)

Drug/company	Indication	Drug information
Roxadustat/ AstraZeneca	Anemia	7/24/2019 In phase 3 double-blind, placebo-controlled trial conducted at 27 sites in China, this small-molecule second-generation hypoxia-inducible factor prolyl hydroxylase inhibitor produced a statistically significant increase in hemoglobin for 26 weeks (*N. Engl. J. Med.* **381**, 1001–1010, 2019)
Waylivra (volanesorsen)/ Akcea Therapeutics	Dyslipidemia / hypercholesterolemia	8/8/2019 In a phase 3 double-blind, randomized, placebo-controlled trial of this 2′-*O*-methoxyethyl antisense oligonucleotide that targets apolipoprotein CIII mRNA, patients with familial chylomicronemia syndrome saw a statistically significant mean reduction in triglycerides of 77% from baseline at three months whereas patients on placebo had an 18% increase (*N. Engl. J. Med.* **381**, 531–542, 2019)
Inebilizumab/ Viela Bio	Neuromyelitis optica (NMO or Devic's syndrome)	9/6/2019 In a randomized, placebo-controlled, double-blind phase 2/3 trial, this humanized, Fc-afucosylated IgG1 mAb against CD19 reduced attacks, risk of disability worsening, hospitalizations, and new magnetic resonance imaging lesions in NMO compared with placebo (*Lancet* **394**, 1352–1363, 2019)

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

Notable drug approvals (3Q19)

Drug/company	Indication	Drug information
Xpovio (selinexor)/ Karyopharm Therapeutics	Multiple myeloma	7/3/2019 US FDA accelerated approval for this small-molecule selective inhibitor of nuclear export mediated by binding to exportin-1/ CRM1/XPO1
Recarbrio (imipenem cilastatin relebactam)/MSD Merck	Intra-abdominal and urinary and reproductive tract bacterial infections	7/16/2019 US FDA approved this drug containing a new small-molecule class A and C lactamase inhibitor
Turalio (pexidartinib)/ Daiichi Sankyo	Pigmented villonodular synovitis	8/2/2019 US FDA approved this small-molecule CSF-1/ Flt3/Kit/SL cytokine ligand inhibitor that downregulates immune cells
Pretomanid/TB Alliance and Mylan	Drug-resistant tuberculosis infections	8/14/2019 US FDA approved this small-molecule nitroimidazole, which both inhibits mycolic acid cell wall synthesis and acts as a respiratory poison following nitric oxide release.
Rozlytrek (entrectinib)/ Roche-Genentech	Non-small-cell lung cancer/*NTRK*-mutated solid tumors	8/15/2019 US FDA accelerated approval for this small-molecule inhibitor of anaplastic lymphoma kinase, tyrosine kinases TRKA, TRKB and TRKC, and proto-oncogene tyrosine protein kinase ROS1
Wakix (pitolisant)/ Bioproject Pharma	Narcolepsy	8/14/2019 US FDA approved this small-molecule selective histamine H3-receptor antagonist that enhances histaminergic brain receptor signaling
Nourianz (istradefylline)/ Kyowa Kirin	Parkinson's disease	8/27/2019 US FDA approved this small molecule selective adenosine A2 receptor antagonist for patient's experiencing 'off' episodes with levodopa
Ibsrela (tenapanor)/ Ardelyx	Irritable bowel syndrome	9/12/2019 US FDA approved this first-in-class sodium–hydrogen exchanger isoform 3 inhibitor

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

Upcoming catalysts (1Q20)

Drug/company	Indication	Drug information
Crizanlizumab/Novartis	Sickle cell anemia	1/1/2020 FDA PDUFA date for this humanized IgG2 monoclonal antibody (mAb) against P-selectin
Tazemetostat/Epizyme	Sarcoma	1/23/2020 US PDUFA date for this small-molecule selective inhibitor of methyltransferase EH2, a silencer of gene promoters, which is overexpressed in tumors.
Givosiran/Alnylam	Acute hepatic porphyria	2/4/2020 FDA PDUFA date for this subcutaneous *N*-acetylgalactosamine-conjugated siRNA targeting aminolevulinate synthase 1
Avapritinib/Blueprint Medicines	Gastrointestinal stromal tumor	2/14/2019 FDA PDUFA date for this small-molecule selective inhibitor of PDGFR-α D816V, PDGFR-α D842 and KIT exon 17 mutants
Voxelotor/Global Blood Therapeutics	Sickle cell anemia	2/26/2020 FDA PDUFA date for this small- molecule allosteric modifier of the hemoglobin α-chain to prevent abnormal polymer formation and increase oxygen affinity
Enfortumab Vedotin/ Astellas Pharma	Bladder cancer	3/13/2020 FDA PDUFA date for this conjugate of monomethyl auristatin and an IgG1 mAb against nectin-4
Teprotumumab/Horizon Therapeutics	Grave's disease	3/6/2020 FDA PDUFA date for this human IgG1 mAb against insulin-like growth factor receptor 1

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

Notable regulatory setbacks (3Q19)

Drug/company	Indication	Drug information
Golodirsen/Sarepta	Duchenne muscular dystrophy	8/19/2019 FDA issued a complete response letter for this exon-skipping antisense phosphorodiamidate morpholino owing to renal toxicity seen in preclinical tests
EB-101/Abeona Therapeutics	Recessive dystrophic epidermolysis bullosa	9/23/2019 FDA put a clinical hold on this ex vivo gene therapy used to prepare type VII collagen gene-corrected skin grafts because of lack of information on stability of therapy during transport to clinical sites.
ACE-083/Acceleron	Muscular dystrophy	9/16/2019 Company is discontinuing development of cysteine-knot ligand trap for TGF-β owing to lack of improvement in functional tests
AMG-176/Amgen	Acute myelogenous leukemia, multiple myeloma	9/12/2019 Company put a voluntary hold on clinical trials because of toxicity signal from AMG-397, which targets the same pathway as AMG-176: myeloid cell leukemia 1, a Bcl-2 family member

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

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