

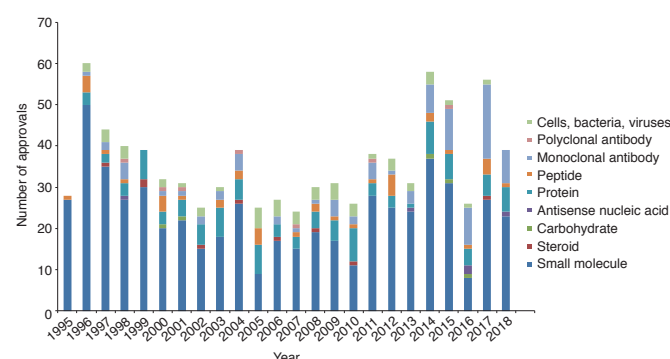
Drug pipeline 3Q18

Laura DeFrancesco

The third quarter saw a raft of first-in-class approvals, including the first RNA interference (RNAi) drug, the first nanobody, and a novel immunotoxin combining a CD22 Fv antibody fragment and an exotoxin. RNAi, antisense and small molecules achieved clinical

FDA approvals by drug type

2017 saw close to record approvals. 2018 is on track for another big year.



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

Notable approvals (3Q18)

Drug/company	Indication	Drug information
Tegsedi (inotersen)/Akcea Therapeutics	Hereditary transthyretin amyloidosis with polyneuropathy	7/11/2018 EMA, 10/5/2018 FDA approved this 2'-O-methoxyethyl antisense oligonucleotide (generation 2+) that blocks production of mutant and wild-type human transthyretin
Tpoxx (tecovirimat)/SIGA Technologies	Smallpox	7/13/2018 FDA approved this oral small molecule inhibitor of orthopoxvirus VP37 envelope wrapping protein
Tibsovo (ivosidenib)/Agios Pharmaceuticals	Acute myelogenous leukemia	7/20/2018 FDA approved this inhibitor of isocitrate dehydrogenase 1
Onpatro (patisiran)/Alnylam	Hereditary transthyretin amyloidosis with polyneuropathy	8/10/2018 FDA approved this 21-mer double-stranded small interfering RNA (siRNA) oligonucleotide containing 2'-O-methyl modified and unmodified ribonucleosides
Oxervate (cenegermin-bkbj)/Dompé	Ophthalmic wound healing	8/22/2018 FDA approved this recombinant human nerve growth factor
Takhzyro (lanadelumab-flyo)/Shire	Hereditary angioedema	8/23/2018 FDA approves this fully human IgG1 monoclonal antibody (mAb) against kallikrein
Lumoxiti (moxetumomab pasudotex-tldf)/Astrazeneca	Hairy cell leukemia	9/13/2018 FDA approves this recombinant immunotoxin comprising an anti-CD22 Fv fragment covalently fused to a 38-kDa fragment of <i>Pseudomonas</i> exotoxin A
Cablivi (caplacizumab)/Sanofi	Thrombotic thrombocytopenic purpura	8/31/2018 EMA approved this bivalent nanobody against von Willebrand factor that prevents thrombus formation in blood vessels
Galafold (migalastat hydrochloride)/Amicus Therapeutics	Fabry's disease	8/10/2018 FDA accelerated approval of small molecule binder to the misfolded enzyme α -galactosidase
Copiktra (duvelisib)/Verastem Oncology	Indolent non-Hodgkin's lymphoma, including follicular lymphoma, and chronic lymphocytic leukemia	9/24/2018 FDA accelerated approval in non-Hodgkin's lymphoma of small molecule inhibitor of phosphoinositide-3-kinase (PI3K)- δ and PI3K- γ
Libtayo (cemiplimab-rwlc)/Regeneron Pharmaceuticals	Skin cancer, squamous cell carcinoma	9/28/2018 FDA approves this human mAb targeting the checkpoint inhibitor programmed cell death receptor 1 (PD-1)
Diacomit (stiripentol)/Laboratoires Biocodex	Dravet syndrome (epilepsy)	8/20/2018 FDA approves this small molecule with direct and indirect actions on GABA A receptor and cytochrome P450s, respectively
Emgality (galcanezumab-gnlm)/Eli Lilly	Migraine and other headaches	9/28/2018 FDA approves this anti-CGRP (calcitonin gene-related peptide) IgG4 mAb
Ajovy (fremanezumab-vfrm)/Teva Pharmaceutical Industries	Migraine and other headaches	9/14/2018 FDA approves this anti-CGRP IgG1 mAb

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milestones in hereditary transthyretin amyloidosis for both neuropathy and cardiomyopathy. Disappointing trial data presented a major setback for indoleamine 2,3-dioxygenase inhibitors in immunoncology.

Upcoming catalysts (1Q19)

Drug/company	Indication	Drug information
Evenity (romosozumab)/Amgen	Osteoporosis, osteopenia	1/11/2019 FDA PDUFA date for this humanized IgG2 mAb against sclerostin
Sacituzumab (isacituzumab govitecan)/Immunomedics	Triple-negative breast cancer	1/18/2019 FDA PDUFA date for this antibody-drug conjugate, a humanized IgG1 anti-Trop-2 (epithelial glycoprotein-1) mAb (hRS7) conjugated with the active metabolite of irinotecan, SN-38
Ravulizumab (ALXN1210)/Alexion Pharmaceuticals	Paroxysmal nocturnal hemoglobinuria	2/18/2019 FDA PDUFA date for this second-generation, long-acting anti-complement 5 IgG2 mAb, which differs in four amino acids from predecessor Solaris
Elzonris (tagraxofusp)/Stemline Therapeutics	Blastic plasmacytoid dendritic cell neoplasm	2/21/2019 FDA PDUFA date for recombinantly expressed fusion protein comprising human interleukin-3 and diphtheria toxin
Scenesse (afamelanotide)/Clinuvel Pharmaceuticals	Porphyria	2/25/2019 FDA PDUFA date for synthetic peptide analog of the α -melanocyte-stimulating hormone
Turoctocog alfa pegol (N8-GP)/Novo Nordisk	Hemophilia A	2/27/2019 FDA PDUFA date for this recombinant factor VIII, glycopegylated on the truncated B-domain for longer half life
Siponimod/Novartis	Multiple sclerosis	12/1/2018 FDA PDUFA date for this small molecule modulator of sphingosine-1-phosphate receptor

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Clinical trials (3Q18)

Drug/company	Indication	Drug information
Tegsedi (inotersen)/Akcea Therapeutics	Hereditary transthyretin amyloidosis with polyneuropathy (familial amyloid polyneuropathy)	7/5/2018 Phase 3 randomized, double blind, placebo-controlled trial of 2'-O-methoxyethyl antisense oligonucleotide showed improvement in quality of life and neurological dysfunction over control (<i>N. Engl. J. Med.</i> 379 , 22–23, 2018)
Vyndaqel/Pfizer	Transthyretin amyloid cardiomyopathy (wild type or hereditary)	8/27/2018 Phase 3 placebo-controlled, randomized, double-blind trial of a small-molecule stabilizer of protein transthyretin (TTR) reduced mortality and frequency of cardiac events compared with placebo (<i>N. Engl. J. Med.</i> 379 , 1007–1016, 2018)
Xofluza (baloxavir marboxil)/Roche	Influenza (excluding vaccines)	9/6/2018 Phase 3 randomized, placebo-controlled, double-blind trial of mRNA cap-dependent endonuclease inhibitor reduced time to improvement compared with placebo and Tamiflu (<i>N. Engl. J. Med.</i> 379 , 913–923, 2018)
Onpatro (patisiran)/Alnylam	Hereditary transthyretin amyloidosis with polyneuropathy (familial amyloid polyneuropathy)	9/14/2018 Phase 3 randomized, double-blind, placebo-controlled trial of systemically delivered 2'-O-methyl ribonucleoside siRNA encapsulated in amino lipid (DLin-MC3-DMA/cholesterol/DSPC/PEG2000-C-DMG) nanoparticle improved markers of cardiomyopathy compared with placebo (https://doi.org/10.1161/CIRCULATIONAHA.118.035831)

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Setbacks (3Q18)

Drug/company	Indication	Drug information
Domagrozumab/Pfizer	Duchenne muscular dystrophy	8/30/2018 The company terminated two clinical studies of this humanized IgG1 mAb against growth differentiation factor 8 because the primary endpoint (change in stair climb) was not met relative to placebo
Waylivra (volanesorsen)/Akcea Therapeutics	Dyslipidemia, hypercholesterolemia	8/27/2018 FDA issued complete response letter for antisense against apolipoprotein C-III due to serious thrombocytopenia even though triglycerides were reduced 77% compared to placebo
Epacadostat/Incyte	Solid tumors	6/4/2018 Company suspended development of this indoleamine 2,3-dioxygenase inhibitor in combination with checkpoint inhibitor Keytruda after phase 3 trial showed no improvement compared to Keytruda alone, prompting 3 other companies working with the same target to alter their plans.

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

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