Drug pipeline 3Q18

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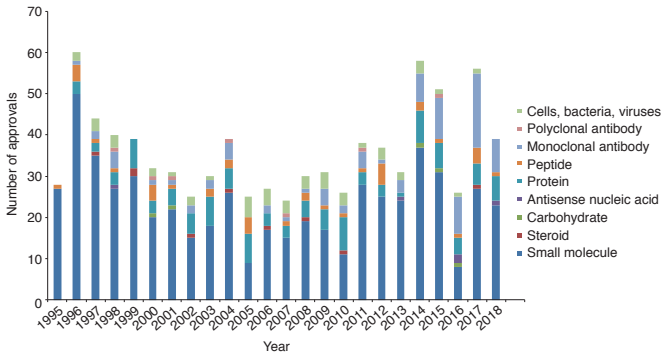
The third quarter saw a raft of first-in-class approvals, including the first RNA interference (RNAi) drug, the first nanobody, and a novel immunotoxin combining a CD22 Fv antibody fragment and an exotoxin. RNAi, antisense and small molecules achieved clinical milestones in hereditary transthyretin amyloidosis for both neuropathy and cardiomyopathy. Disappointing trial data presented a major setback for indoleamine 2,3-dioxygenase inhibitors in immuno-oncology.

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
Onpattro (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 (cenegerminbkbj)/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 pasudotoxtdfk)/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 *Pseudomonas* 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 (cemiplimabrwlc)/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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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 (*N. Engl. J. Med.* **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 (*N. Engl. J. Med.* **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 (*N. Engl. J. Med.* **379**, 913–923, 2018)
Onpattro (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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