Drug pipeline: 4Q17

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The US Food and Drug Administration (FDA) approved an almost record-setting 56 drugs in 2017, including December's first approval for an adeno-associated virus (AAV) gene therapy (Luxturna) and October's registration for a second chimeric antigen receptor T-cell (CAR-T) therapy (Yescarta). Promising results were reported for bluebird bio's

lentiviral-based gene therapy in adrenomyeloneuropathy, two of four monoclonal antibodies (mAbs) against calcitonin gene-related peptide (CGRP) in migraine, and Vertex's combination of its small-molecule cystic fibrosis transmembrane regulator (CFTR) corrector therapy with Kalydeco.

Historic US regulatory approvals by lead indication

Source: Biomed Tracker, a service of Sagient research (www.biomedtracker.com)

Notable clinical trial results (4Q17)

Drug/company	Indication	Summary
Spinraza (nusinersen)/ Biogen	Spinal muscular atrophy	11/1/2017 In phase 3 trial of 2'-O-methoxyethyl phosphorothioate antisense drug, 51% of patients had motor milestone responses versus 0% in untreated. (<i>N. Engl. J. Med.</i> 377 , 1723–1732, 2017)
Exondys 51 (eteplirsen)/ Sarepta	Duchenne muscular dystrophy (DMD)	12/27/2017 In phase 2b trial of exon-skipping phosphorodiamidate morpholino oligo drug, 12 patients treated over 5 years achieved a significant reduction in pulmonary decline. (<i>J. Neuromuscul. Dis.</i> doi:10.3233/JND-170272, 2017)
Aimovig (erenumab)/ Amgen	Migraine and other headaches	11/30/2017 In a phase 3 trial of 955 patients, 50% of patients receiving human IgG2 mAb against the receptor of CGRP achieved 50% or greater reduction in mean number of migraine days per month versus 26.6% in placebo group. (<i>N. Engl. J. Med.</i> 377 , 2123–2132, 2017)
Fremanezumab/ Teva Pharmaceutical	Migraine and other headaches	11/30/2017 In a phase 3 preventive trial of 1,130 patients, 50% receiving fully humanized IgG-kappa mAb against CGRP ligand had lower frequency of headaches in 12 weeks versus 18% on placebo. (<i>N. Engl. J. Med.</i> 377 , 2113–2122, 2017)
Lenti-D (elivaldogene tavalentiv)/ bluebird bio	Adrenomyeloneuropathy	10/4/2017 In phase 2/3 trial, all 17 patients receiving autologous hematopoietic stem cells engineered with a lentiviral vector encoding human <i>ABCD1</i> cDNA gene therapy had engrafted cells with no safety issues, 88% free of disabilities. (<i>N. Engl. J. Med.</i> 377 , 1630–1638, 2017)
VX-661 (tezacaftor)/ Vertex	Cystic fibrosis	11/3/2017 In a randomized, placebo-controlled phase 3 trial, small-molecule that corrects trafficking of Phe508del CFTR was efficacious in combination with CFTR potentiator Kalydeco (ivacaftor) in patients heterozygous for Phe508del mutation and CFTR mutation with residual function. (<i>N. Engl. J. Med.</i> 377 , 2024–2035, 2017)

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

Catalysts (Q218)

Drug/company	Indication	Summary
Ibalizumab/ Theratechnologies	HIV/AIDS	4/3/2018 FDA PDUFA date for this first-in-class humanized IgG4 mAb against CD4
KRN23 (burosumab)/ Ultragenyx	X-Linked hypophosphatemia	4/17/2018 FDA PDUFA date for this fully human IgG1 mAb against fibroblast growth factor 23 (FGF 23)
Aimovig (erenumab)/ Amgen	Migraine and other headaches	5/17/2018 FDA PDUFA date against this fully human IgG2 mAb against CGRP receptor
Mogamulizumab/ Kyowa Hakko Kirin	Cutaneous T-cell lymphoma	6/4/2018 FDA PDUFA date for this humanized IgG1 afucosylated mAb against CC-motif chemokine receptor 4 (CCR4) expressed on malignant T cells
Fremanezumab/Teva Pharmaceutical	Migraine and other headaches	6/15/2018 FDA PDUFA date for humanized IgG-kappa mAb against CGRP
Tavalisse (fostamatinib disodium)/Rigel	Immune thrombocytopenic purpura	4/17/2018 PDUFA date for this oral Syk kinase inhibitor
Plazomicin/Achaogen	Urinary tract and reproductive tract infections	6/26/2018 FDA PDUFA date for this novel neoglycoside with broad activity against MRSA and other drug-resistant Gram-negative bacteria

Source: BioMedTracker, a service of Sagient Research (<http://www.biomedtracker.com>) PDUFA, the Prescription Drug User Fee Act; MRSA, methicillin-resistant *Staphylococcus aureus*

Notable regulatory approvals (4Q17)

Drug/company	Indication	Drug information
Yescarta (axicabtagene ciloleucel)/Gilead	Diffuse large B-cell lymphoma	10/18/2017 FDA approved autologous CAR-Ts engineered with a γ -retroviral vector, encoding anti-CD19 single-chain antigen-recognition domain (ARD) with CD28 and CD3-zeta intracellular signaling domains
Prevymis (letermovir)/ Merck	Cytomegalovirus infection	11/8/2018 FDA approved this small-molecule first-in-class quinazoline inhibitor of viral terminase
Fasenra (benralizumab)/ AstraZeneca	Asthma	11/14/2017 FDA approved this humanized IgG1 mAb targeting the interleukin-5 receptor alpha
Mepesvii (vestronidase alfa-yjbk)/Ultragenyx	Mucopolysaccharidosis VII	11/15/2017 FDA approved this recombinant human β -glucuronidase protein replacement therapy
Hemlibra (emicizumab-kxwh)/Roche	Hemophilia A	11/16/2017 FDA approved this humanized bispecific IgG4 mAb targeting factors IXa and Xb
Rhopressa (netarsudil)/ Aerie	Glaucoma/ocular hypertension	12/18/2017 FDA approved this small-molecule inhibitor of Rho kinase and the norepinephrine transporter with three modes of action.
Luxturna (voretigene neparovec-rzyl)/Spark	Leber's congenital amaurosis	12/19/2017 FDA approved an AAV serotype 2 vector delivering RPE65 to retinal cells

Biosimilars

Ogivri (trastuzumab-dkst)/Mylan	Gastric cancers	12/01/2017 FDA approved the first Herceptin mAb biosimilar
Admelog/Sanofi	Diabetes mellitus, types I and II	12/11/2017 FDA approved first Humalog follow-on biologic
Trastuzumab/Samsung Bioepis	Breast cancer	11/20/2017 EMA approved second Herceptin mAb biosimilar

Breakthrough drug

MOR208/Morphosys	Diffuse large B-cell lymphoma	10/23/2017 Humanized IgG1 mAb against CD-19
Valoctocogene roxaparvec/BioMarin	Hemophilia A	10/26/2017 AAV serotype 5 vector delivering factor VIII gene therapy
GSK2857916/ GlaxoSmithKline	Multiple myeloma	11/2/2017 Humanized and afucosylated IgG1 anti-B-cell maturation antigen (BCMA) antibody-drug conjugate (ADC) via uncleavable linker
bb2121/Celgene/bluebird	Multiple myeloma	11/16/2017 Autologous CAR-Ts engineered with a lentiviral vector encoding an anti-BCMA ARD with 4-1BB and CD3-zeta intracellular signaling domains

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

Notable regulatory setbacks (4Q17)

Drug/company	Indication	Drug information
Tirasemtiv/Cytokinetics	Amyotrophic lateral sclerosis	11/21/2017 Company suspended phase 3 trial of small-molecule troponin activator because primary endpoint was not met
REGN910-3/ Regeneron	Diabetic macular edema, diabetic retinopathy, wet AMD	11/27/2017 Company suspended trials of combination of Eylea (aflibercept) and fully human IgG1 angiopoietin 2 mAb because the combination showed no improvement over Eylea alone
Apilidin (plitidepsin)/ PharMar	Multiple myeloma	12/14/2017 CHMP issued a negative opinion on this cyclodepsipeptide derived from the marine tunicate <i>Apilidium albicans</i> due to negligible improvement in survival
GED 0301/Celgene	Crohn's disease	10/19/2017 Company suspended phase 3 trial of gastro-resistant (pH-dependent) tablet containing 21-base phosphorothioate antisense oligo (containing 5-methyl modifications at cytosine at residues 3 and 16 to reduce immunogenic CpG tracts) against human Smad7 mRNA following interim analysis by Data Monitoring Committee

MD, age-related macular degeneration; CHMP, The Committee for Medicinal Products for Human Use. Source: BioMedTracker, a service of Sagient Research (<http://www.biomedtracker.com>)

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