Drug pipeline: 4Q16

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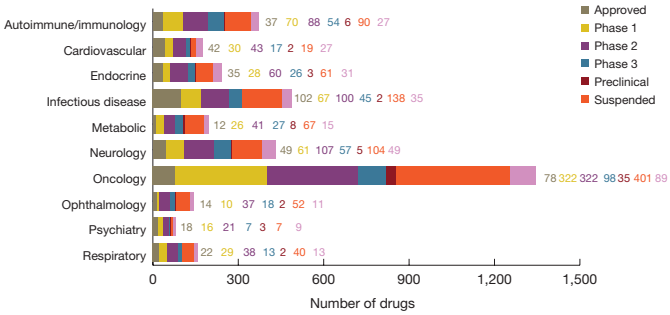
Although approvals were down year-on-year, December saw a rash of drug registrations, which included innovative products like MACI (autologous chondrocytes on an implantable artificial matrix), the antisense molecule Spinraza (nusinersen), and Zinplava, a fully human monoclonal antibody that targets *Clostridium difficile* toxin B. However, complete response letters predominated more than in previous quarters, with setbacks for Cempra's solithera and Regeneron's sarilumab. Decisions on several biosimilars are on the horizon.

Historic US regulatory approvals by lead indication



Notable clinical trial results (4Q16)

Drug/company	Indication	Summary
Ocrevus (ocrelizumab)/ Roche	Multiple sclerosis	12/21/2016 In a phase 3 randomized placebo-controlled trial of 732 patients, those receiving anti-CD20 humanized mAb had lower rates of clinical and MRI progression than controls. (*N. Engl. J. Med.* http://dx.doi.org/10.1056/NEJMoa1606468, 2016)
Biosimilar trastuzumab/Mylan	Breast cancer	12/27/2016 In a randomized clinical trial, the overall response rate to trastuzumab biosimilar plus taxane was similar to that for trastuzumab plus taxane at 24 weeks (69.6% versus 64%). (*J. Am. Med. Assoc.* **317**, 37–47, 2017)
Anifrolumab/ AstraZeneca	Systemic lupus erythematosus	11/14/2016 A phase 2 clinical trial of the fully human mAb to subunit 1 of type 1 interferon met primary endpoints of SLE responder Index of 4 and reduction in corticosteroid use. (*Arthr. Rheumatol.* http://dx.doi.org/10.1002/art.39962, 2016)
Zmapp/Mapp Biopharmaceutical	Ebola	10/12/2016 In a randomized controlled trial with 71 patients, 40% fewer deaths resulted among those receiving the standard of care plus three humanized mAbs targeting Ebola mucin-like domain and 6D31 and core epitopes of glycoprotein 1 manufactured in transgenic *Nicotiana benthamiana* lacking plant-specific N-glycan residues. (*N. Engl. J. Med.* **375**, 1448–1456, 2016)
LMTX (leucomethyl-thioninium)/TauRx	Alzheimer's disease (AD)	11/15/2016 In a 15-month randomized double-blind phase 3 trial of prodrug tau aggregation inhibitor, patients with mild to moderate AD showed no improvement in disease assessment scale or cognitive subscale. (*Lancet* **388**, 2873–2884, 2016)
Crizanlizumab/ Novartis	Sickle cell anemia	12/3/2016 In a phase 2 double-blind placebo-controlled randomized trial with humanized monoclonal antibody to P-selectin, the rate of crises was 45% lower and the time to crisis was longer than in patients receiving placebo. (*N. Engl. J. Med.* http://dx.doi.org/10.1056/NEJMoa1611770, 2016)
Eravacycline/ Tetraphase	Intra-abdominal bacterial infections	11/16/2016 In a phase 3 trial, this broad-spectrum Gram-negative synthetic fluorocycline antibiotic exceeded the non-inferiority margin compared with ertapenam (*JAMA Surg.* http://dx.doi.org/10.1001/jamasurg.2016.4237, 2016)
LEE011 (ribociclib)/Novartis	Breast cancer	10/10/2016 In a phase 3 study of this cyclin-dependent kinase 4/6 inhbitor (breakthrough designated drug) with letrozol, the risk of progression was reduced 44% compared with that for letrozol alone. (*N. Engl. J. Med.* **375**, 1738–1748, 2016)

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

Notable regulatory approvals (4Q16)

Drug/company	Indication	Drug information
Lartruvo (olaratumab)/ Eli Lilly	Sarcoma	10/19/2016 FDA, 11/20/2016 EMA approved this fully human IgG1 mAb against platelet-derived growth factor receptor-α
Rekovelle (follitropin-d)/ Ferring	Reproductive disorder	10/28/2016 EMA approved this recombinant follicle-stimulating hormone expressed by human retinal cell line PER.C6
Zinplava (bezlotoxumab)/ Merck	*Clostridium difficile*–associated diarrhea/infection	10/21/2017 FDA approved this fully human mAb to *C. difficile* toxin B
Parsabiv (velcalcetide)/ Amgen	Hyperparathyroidism (secondary)	11/11/2016 EMA approved this peptide protein kinase C (PKC)-ε inhibitor
MACI (matrix-induced autologous chondrocyte implant)/Vericel	Cartilage and joint repair	12/13/2016 FDA approved this autologous chondrocyte implant, with *in vitro*–expanded cells seeded on collagen membrane
Eucrisa (crisaborole)/ Pfizer	Atopic dermatitis (eczema)	12/14/2016 FDA approved this topical phosphodiesterase-4 inhibitor
Rubraca (rucaparib)/ Clovis Oncology	Ovarian cancer	12/19/2016 FDA approved the second PARP inhibitor

Notable regulatory approvals (4Q16) continued

Drug/company	Indication	Drug information
Spinraza (nusinersen)/ Biogen	Spinal muscular atrophy	12/23/2016 FDA approved this 18-mer 2'-O-methoxyethyl (2'-MOE) phosphorothioate antisense oligonucleotide
Breakthrough drug		
NiCord (stem and progenitor cells)/Gamida	Hematologic cancer	10/11/2016 Umbilical-cord-blood-derived and *ex vivo*–expanded stem and progenitor cell treatment
Velusetrag/Theravance	Gastroparesis therapy	12/06/2016 Small-molecule selective serotonin 5-HT4 receptor agonist
Nerixia (neridronic acid)/ Grunenthal	Chronic pain	12/16/2016 Amino-bisphosphonate
Dupixent (dupilumab)/ Regeneron	Atopic dermatitis (eczema)	10/13/2016 Human mAb targeting interleukin-4 receptor-α subunit
JCAR017/Juno	Diffuse large B cell lymphoma (NHL)	12/20/2016 Autologous chimeric antigen receptor modified T cell, with CD4 and CD8 in a 1:1 ratio
Alecensa (alectinib)/ Roche	Non-small-cell lung cancer	10/3/2016 Small-molecule inhibitor of anaplastic lymphoma kinase

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

Notable regulatory setbacks (4Q16)

Drug/company	Indication	Drug information
Sarilumab/Regeneron	Rheumatoid arthritis	10/28/2016 FDA issued a complete response letter for this fully human mAb to IL-6α receptor owing to manufacturing deficiencies
ERY-ASP/Erytech	Acute lymphocytic leukemia	11/14/2016 The company withdrew its marketing authorization application (MAA) from EMA for this erythrocyte-enclosed asparaginase because of the short time frame for providing requested data
Biosimilar pegfilgrastim/Gedeon Richter	Neutropenia/ leukopenia	11/16/2016 The company withdrew its MAA from the EMA for its biosimilar because of a negative opinion from CHMP
Lutathera/Advanced Accelerator	Neuroendocrine tumors	12/21/2016 FDA issued a complete response letter for radiolabeled somatostatin owing to incompleteness of the application and a request for subgroup analysis
Solithera/Cempra	Community-acquired pneumonia (antibacterial)	12/29/2016 FDA issued a complete response letter for fluoroketolide macrolide because of manufacturing deficiencies and a risk of hepatotoxicity
Parsabiv/Amgen	Hyperparathyroidism	8/24/2016 FDA issued a complete response letter for this peptide protein kinase C ε inhibitor

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

Notable upcoming regulatory decisions (1Q17)

Drug/company	Indication	Summary
Translarna/PTC Therapeutics	Muscular dystrophy	1/16/2017 EMA will be reviewing its conditional approval of small molecule that increases ribosome read-through at stop codons
Terrosa/Stada	Osteoporosis/osteopenia	1/16/2016 FDA PDUFA for Forteo (parathyroid hormone receptor) biosimilar
Plecanatide (guanilib)/Synergy Pharmaceuticals	Chronic idiopathic constipation	1/27/2017 FDA PDUFA for this 16 amino acid analog of uroguanylin, an agonist of guanylate cyclase-C
Truxima (rituximab)/ Teva	Chronic lymphocytic leukemia/ small cell lymphocytic lymphoma, rheumatoid arthritis, ANCA vasculitis, indolent non-Hodgkin's lymphoma	2/20/2017 EMA decision on first anti-CD-20 mAb, Rituxan biosimilar
Filgrastim/Apotex	Neutropenia/leukopenia	2/28/2016 FDA PDUFA date for this recombinant human G-CSF, Neupogen biosimilar, previously approved by EMA
Telotristat ethyl/ Lexicon	Neuroendocrine tumors	2/28/2017 FDA PDUFA date for this small-molecule tryptophan hydroxylase inhibitor that suppresses peripheral serotonin synthesis
Biosimilar Pegfilgrastim/Apotex	Neutropenia/leukopenia	3/31/2017 FDA PDUFA date for this pegylated recombinant human G-CSF, Neulasta biosimilar
Dupixent (dupilumab)/Regeneron	Atopic dermatitis (eczema)	3/29/2017 FDA PDUFA date for this human mAb targeting interleukin-4 receptor-α subunit, antagonizing IL-4 and IL-13 pathways
Biosimilar Infliximab/ Samsung Bioepis	Rheumatoid arthritis, axial spondyloarthritis, Crohn's disease, ulcerative colitis, psoriatic arthritis, psoriasis	3/31/2017 FDA PDUFA date for this Remicade biosimilar previously approved by EMA
Brineura (cerliponase alfa)/BioMarin	Neuronal ceroid lipofuscinosis	3/31/2017 CHMP Panel review of this recombinant human tripeptidyl peptidase-1
Biosimilar Insulin Glargine (Merck)	Diabetes mellitus, type 2	3/22/2017 FDA PDUFA for this long-acting insulin glargine biosimilar

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

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