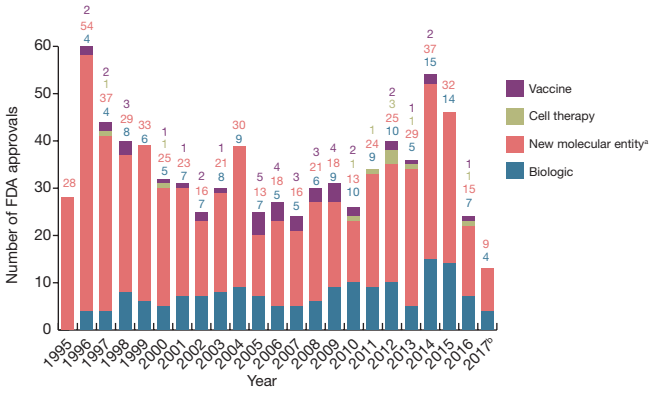
Drug pipeline: 1Q17

Laura DeFrancesco

The first quarter saw a rash of approvals. Among the most noteworthy small molecules are the first new drug for Parkinson's disease in a decade and a compound specific for STAT/JAK 1 and 2 in rheumatoid arthritis. Whereas the EMA approved the arthritis drug, the FDA is asking the company for more trial data. First-in class monoclonals were registered that target B-cell epitope CD20 for primary progressive multiple sclerosis, interleukin (IL)-4 receptor for advanced eczema and IL-17 receptor for psoriasis. Positive trial results were also announced for Kite Pharma's chimeric antigen receptor (CAR)-T cell therapy against CD19 in lymphoma.

Historic US regulatory approvals by drug class

Reversing last year's trend, when the first quarter was a slow one at the FDA, this year approvals are back up, perhaps to 2014 rates.



[a]New molecular entity (NME) class includes mainly small-molecule drugs, but also steroid, synthetic peptide and mixed compounds, excluding non-NME and new formulation.[b]Partial year to March 31. Source: US Food and Drug Administration

Notable clinical trial results 4Q16

Drug/company	Indication	Drug information
Pacritinib/CTI	Myelofibrosis	3/20/2017 In phase 3 randomized trial of this small-molecule JAK1/2 inhibitor in 327 patients, 19% had reduced spleen volume versus 5% in controls (*Lancet Haematology* http://dx.doi.org/10.1016/S2352-3026(17)30027-3, 2017)
Imprime PGG poly-(1-6)-β-glucotriosyl-(1-3)-β-glucopyranose β-glucan/Biothera	Non-small-cell lung cancer	3/16/2017 In randomized phase 2 study +/- cetuximab of beta-1,3–1,6 glucan immunomodulator, 47% had an objective response rate versus 25% with cetuximab alone (*Invest. New Drugs* http://dx.doi.org/10.1007/s10637-017-0450-3, 2017)
Sacituzumab govitecan/Seattle Genetics	Breast cancer	3/14/2017 In phase 2 single-arm trial of this humanized IgG1 mAb targeted against Trop-2 conjugated to 7-ethyl-10-hydroxycamptothecin, 69% (48/69) of patients had reduced tumor volume (*J. Clin. Oncol.* http://dx.doi.org/10.1200/JCO.2016.70.8297, 2017)
CIM331 (nemolizumab)/Galderma	Atopic dermatitis (eczema)	3/2/2017 In phase 2 randomized double-blind, placebo-controlled multi-dose trial of 216 patients, humanized IgG2 anti-IL-31 receptor A mAb gave significant improvements in puritis scores (*N. Engl. J. Med.* **376**, 826-835, 2017)
Axicabtagene ciloleucel/Kite Pharma	Diffuse large B-cell lymphoma	4/2/2017 In this phase 2b trial of 111 patients, 82% overall response rate with a single infusion of autologous peripheral blood monocytes retrovirally transfected with chimeric antigen receptor (FMC63 Fc domain/CD28 costimulator) against CD19 (*Am. Assoc. Cancer Res.* Abstract CT019, April 2, 2017)
Xilonix/Xbiotech	Colorectal cancer	1/13/2017 In a phase 3 double-blind, placebo-controlled trial of a natural IgG4/kappa anti-IL-1 mAb autoantibody clone, 33% achieved endpoint versus 19% in control group (*Lancet Oncol.* **18**, 192–201, 2017)

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

Notable regulatory setbacks (4Q16)

Drug/company	Indication	Drug information
Custirsen/OncoGenex	Prostate cancer	3/7/2017 Company suspended work on this 2′-methoxyethyl modified phosphorothioate antisense oligonucleotide against clusterin mRNA after phase 3 randomized controlled trial showed no benefit
Bococizumab/Pfizer	Dyslipidemia/hypercholesterolemia	3/20/2017 Company suspended work on humanized IgG4 anti-PCSK9 mAb after lipid reduction attenuated over time and immunogenicity not seen with similar agents
Biosimilar Pegfilgrastim (Sandoz)/Novartis	Neutropenia/leukopenia	1/18/2017 Company withdrew marketing application from EMA after regulatory agency asked for additional studies
Translarna (ataluren)/PTC Therapeutics	Cystic fibrosis	3/6/2017 Company suspended development of exon-skipping small molecule after phase 3 double-blind, placebo-controlled trial failed to meet primary and secondary endpoints

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

Notable regulatory approvals (1Q17)

Drug/company	Indication	Drug information
Bavencio (avelumab)/Merck KGaA	Merkel cell carcinoma	03/23/2017 FDA granted accelerated (conditional) approval for a fully human IgG1 anti-PD-L1 mAb
Parsabiv (etelcalcitide)/Amgen	Hyperparathyroidism (secondary) for adults on dialysis	2/7/2017 FDA approved this long-acting peptide agonist of the calcium-sensing receptor, which inhibits release of parathyroid hormone
Siliq (brodalumab)/Valeant	Psoriasis	2/15/2017 FDA approved this human IgG2 anti-IL-17 receptor A mAb
Kisqali (ribociclib)/Novartis	Breast cancer	3/17/2017 FDA approved this cyclin-dependent kinase 4/6 small-molecule inhibitor
Xadago (safinomide)/Newron Pharmaceuticals	Parkinson's disease	3/21/2017 FDA approved this multi-targeted small-molecule inhibitor of monoamine oxidase-B, glutamate release, dopamine uptake, sodium and calcium channels
Dupixent (dupilumab)/Regeneron	Atopic dermatitis (eczema)	3/28/2017 FDA approved this first-in-class human IgG4 anti-IL-4 receptor mAb for severe eczema
Ocrevus (ocrelizumab)/Roche	Multiple sclerosis (MS)	3/28/2017 FDA approved this glycosylated humanized IgG1 anti-CD20 mAb for primary progressing and relapsing remitting MS
Truxima (rituximab)/Teva	Chronic lymphocytic leukemia/small cell lymphocytic lymphoma, antineutrophil cytoplasmic antibodies associated vasculitis, indolent non-Hodgkin's lymphoma, rheumatoid arthritis (RA)	1/20/2017 EMA approved the first Rituxan biosimilar
Baricitinib/Eli Lilly	RA	2/13/2017 EMA approved this specific STAT/JAK 1 and 2 small-molecule inhibitor
Xermelo (telotristat ethyl)/Lexicon	Neuroendocrine tumors	2/28/2017 FDA approved this small-molecule tryptophan hydroxylase inhibitor for patients with carcinoid syndrome with diarrhea
Translarna/PTC Therapeutics	Duchenne muscular dystrophy	1/1/2017 EMA renewed conditional marketing authorization for exon-skipping small molecule
Breakthrough therapy designations		
AMT-060/UniQure	Hemophilia B	1/30/2017 Adeno-associated virus (AAV) serotypes 2/5 encoding Factor IX
Toca 511/TocaGen	Brain cancer (malignant glioma, anaplastic astrocytoma and glioblastoma)	2/23/2017 Replication-competent murine leukemia viral vector encoding *Saccharomyces cerevisiae*-derived cytosine deaminase gene in combination with an extended-release formulation of 5-fluorouracil prodrug, 5-fluorocytosine

mAb, monoclonal antibody; FDA, US Food and Drug Administration; EMA, European Medicines Agency. Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com)

Notable regulatory decisions 2Q17

Drug/company	Indication	Drug information
Brigatinib/Takeda	Non-small-cell lung cancer	4/28/2017 FDA PDUFA date for this small-molecule ALK inhibitor for patients with the ALK-L1196 mutation
Nonacog Beta Pegol/Novo Nordisk	Hemophilia B	5/16/2017 FDA PDUFA for glyco-PEGylated derivative of recombinant factor IX
Durvalumab/AstraZeneca	Bladder cancer	6/30/2017 FDA PDUFA for this human IgG1 anti-PD-L1 and L2 mAb
Retacrit/The Galencia Group	Anemia due to chronic renal failure and chemotherapy	6/1/2017 FDA PDUFA date for Epogen (Amgen) biosimilar
Midostaurin/Novartis	Mastocytosis, AML	6/26/2017 FDA PDUFA date for semi-synthetic staurosporine multi-target protein kinase inhibitor
Brineura (cerliponase alfa)/BioMarin Pharmaceuticals	Neuronal ceroid lipofuscinosis	4/27/2017 FDA PDUFA date for tripeptidyl peptidase 1 enzyme replacement therapy
Anamorelin/Helsinn Healthcare	Cachexia/weight loss	4/15/2017 EMA decision on this small-molecule ghrelin mimetic
Cx601/TiGenix	Crohn's disease	5/31/2017 EMA decision on allogeneic fat-derived stem cells treated with collagenase I expanded *in vitro* and then trypsinized

FDA, US Food and Drug Administration; PDUFA, Prescription Drug User Fee Act; mAb, monoclonal antibody; AML, acute myeloid leukemia; EMA, European Medicines Agency. Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com)

Laura DeFrancesco is Senior Editor at Nature Biotechnology.