Drug pipeline: 1Q18

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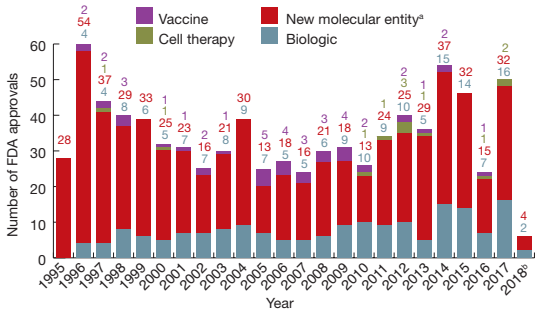
Approvals were down last quarter. Vertex (Cambridge, MA, USA) got a green light for its small-molecule combination to combat cystic fibrosis; Theratechnologies (Montreal, Quebec, Canada) and Sun Pharmaceuticals (Mumbai, India) received registrations for monoclonal antibodies (mAbs) to treat HIV and psoriasis, respectively. A gene therapy suffered a clinical setback in Duchenne muscular dystrophy. Decisions await several new therapeutic modalities, including short-interfering RNA (siRNA) and ASO therapies against transthyretin-related (TTR)-hereditary amyloidosis; an antibody–drug conjugate for hairy cell leukemia, a nanobody against thrombotic thrombocytopenic purpura and the first new anti-malarial in 60 years.

Historic US regulatory approvals by drug class

A slow first quarter may be due to a rash of approvals at the end of last year.



[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 regulatory approvals (1Q18)

Drug/company	Indication	Drug information
Symdeko (tezacaftor-ivacaftor)/Vertex	Cystic fibrosis (CF)	2/12/2018 FDA approved this fixed-dose combination therapy of a novel corrector of the cystic fibrosis transmembrane conductance regulator (CFTR) trafficking defect, and an approved CFTR potentiator
Trogarzo (ibalizumab-uiyk)/Theratechnologies	HIV/AIDS	3/6/2018 FDA approved this humanized IgG4 anti-CD4 mAb that blocks viral entry into T cells
Ilumya (tildrakizumab-asmn)/Sun Pharmaceuticals	Psoriasis	3/21/2018 FDA approved this humanized IgG1k mAb against the p19 subunit of IL-23
Breakthrough therapy designation		
Maribavir/Shire	Cytomegalovirus infection	1/4/2018 Small-molecule benzimidazole L-ribonucleoside inhibitor of UL97 kinase, DNA synthesis and capsid maturation
Voxelotor/Global Blood Therapeutics	Sickle cell anemia	1/9/2018 Small-molecule allosteric modifier of hemoglobin structure
Balovaptan/Roche	Autism spectrum disorders	1/29/2018 Small-molecule antagonist of V1A vasopressin receptors
SPK-8011/Spark Therapeutics	Hemophilia A	2/20/2018 Adeno-associated virus containing an optimized B-domain-deleted coagulation factor VIII cassette
ALN-GO1/Alnylam	Hyperoxaluria	3/12/2018 *N*-acetyl galactosamine (GalNAc)-conjugated siRNA targeting glycolate oxidase
PTI-428/Proteostasis	Cystic fibrosis	3/12/2018 Small-molecule 'mutation-agonistic' amplifier of CFTR
Erdafitinib/Johnson & Johnson	Bladder cancer	3/15/2018 Small-molecule pan-fibroblast growth factor receptor tyrosine kinase inhibitor
Enfortumab vedotin/Astellas	Bladder cancer	3/26/2018 Antibody–drug conjugate (ADC) comprising a fully human IgG1k mAb against nectin-4 conjugated to monomethyl auristatin E (MMAE) via an enzyme-cleavable linker

FDA, US Food and Drug Administration. Source: BioMedTracker, a service of Sagient Research (http://biomedtracker.com)

Notable regulatory setbacks (1Q18)

Drug/company	Indication	Drug information
SGT-001/Solid Biosciences	Duchenne muscular dystrophy	3/14/2018 FDA placed a hold on phase 1/2 trial of AAV9 vector-mediated gene therapy encoding micro-dystrophin 5 gene under control of muscle-specific promoter creatine kinase 8 due to unexpected serious adverse reaction (decreased platelet count) in first patient dosed.
Vobarilizumab/Ablynx	Systemic lupus erythematosus	3/26/2018 The company suspended phase 2 randomized, placebo-controlled, double-blind trial of sequence-optimized humanized nanobody to IL-6 receptor due to lack of dose response at 24 weeks
Solanezumab/Lilly	Alzheimer's disease	1/25/2018 Company suspended double-blind, placebo-controlled, phase 3 trial of antibody against beta-amyloid (targeting a portion in the middle of the molecule) in patients with mild dementia when cognitive decline was not significantly affected.
Axalimogene filolisbac/Advaxis	Cervical and head and neck cancer	3/9/2018 FDA put a clinical hold on this immunotherapy of attenuated Listeria monocytogenes lacking master transcriptional regulator protein-related factor A and engineered to express a truncated, non-hemolytic listeriolysin O fused with the E7 oncoprotein of human papilloma virus 16 due to a patient death.

FDA, US Food and Drug Administration. Source: BioMedTracker, a service of Sagient Research (http://biomedtracker.com)

Notable clinical trial results (1Q18)

Drug/company	Indication	Drug information
GS010/GenSight Biologics	Leber's hereditary optic neuropathy	2/6/2018 Open label, phase 1/2 clinical trial demonstrated that a recombinant, replication-defective, adeno-associated virus serotype 2 (AAV2) vector containing a modified cDNA encoding human wild-type mitochondrial NADH protein subunit 4 (ND4) provided sustained improvement in visual acuity of patients with ND4 G11778A mutation at two years. (*Ophthalmol.* doi:10.1016/j.ophtha.2017.12.036, 2017)
Lebrikizumab/Dermira	Atopic dermatitis	1/15/2018 In placebo-controlled, randomized double-blind phase 2 trial of humanized IgG4 mAb against IL-13, 84% of patients receiving drug showed improvement in eczema area severity index versus 62% in placebo arm. (*J. Am. Acad. Dermatol.* doi:10.1016/j.jaad.2018.01.017, 2018)
SCIB1/ScanCell	Melanoma	2/12/2018 In a phase 1/2 trial of an electroporated DNA plasmid encoding two cancer epitopes (tyrosine-related protein 2 (TRP-2180-188) and glycoprotein 100; gp100174-190) within the complementarity-determining region of a human IgG1 mAb, dose-dependent T-cell responses were induced in 88% of patients after five doses, with 7 of 15 patients achieving stable disease. (*OncoImmunol.* doi:10.1080/2162402X.2018.1433516, 2018)
NGM282/NGM Biopharmaceuticals	Non-alcoholic steatohepatitis	3/5/2018 In randomized, double-blind, placebo-controlled, phase 2 study of an engineered variant of the human fibroblast growth factor 19, 70% of treated patients had significant reductions in liver fat content versus 7% in placebo group. (*The Lancet* **391**, 1174–1185, 2018. Doi: 10.1016/S0140-6736(18)30474-4)
Larotrectinib/Loxo Oncology	Solid tumors	3/29 2018 In phase 1/2 dose-escalating trial of a small molecule targeting TRK for pediatric patients with TRK fusion-positive tumors, 93% had objective responses. (*Lancet Oncol.* doi:10.1016/S1470-2045(18)30119-0, 2018)
IdeS/Hans Medical	Kidney transplant rejection	3/21/2018 In a phase 2 open-label trial, *Streptococcus pyogenes* endopeptidase, which cleaves human IgG at the hinge region producing F(ab')2 and Fc fragments, eliminated IgG (and other immune markers) in sensitized chronic kidney patients, including one patient who received a transplant maintained for three years. (*Am. J. Transplant.* doi:10.1111/ajt.14733)
BAF312 (siponimod)/Novartis	Multiple sclerosis	3/22/2018 In a randomized, placebo-controlled, phase 3 trial, small-molecule sphingosine-1-phosphate receptor modulator reduced confirmed disability progression by 21% compared with controls. (*The Lancet* **391**, 1263–1273, 2018)
Venclexta (venetoclax)/AbbVie	Mantle cell lymphoma	3/29/2018 In phase 2 trial of small-molecule Bcl-2 selective inhibitor with Imbruvica (Bruton's kinase inhibitor), patients had a 42% complete response rate compared with historical data of 21% and 24% with each drug alone. (*N. Engl. J. Med.* doi:10.1056/NEJMoa1715519, 2018)

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

Notable upcoming catalysts (3Q18)

Drug/company	Indication	Drug information
Galcanezumab/Lilly	Migraine and other headaches	9/27/2018 FDA PDUFA date for humanized IgG4 mAb against calcitonin gene-related peptide
Inotersen (ISIS-TTRRx)/Ionis	TTR-hereditary amyloidosis (familial amyloid polyneuropathy)	7/6/2018 FDA PDUFA date for second-generation 2′-*O*-(2-methoxyethyl; MOE) modified ASO gapmer against transthyretin precursor mRNA.
Moxetumomab pasudotox/AstraZeneca	Hairy cell leukemia	9/1/2018 FDA PDUFA date for recombinant immunotoxin comprising the disulfide-stabilized Fv portion of an anti-CD22 mouse mAb covalently fused via a 7-mer linker to a 38-KDa fragment of *Pseudomonas* exotoxin-A
Patisiran/Alnylam	TTR-related hereditary amyloidosis (FAP)	8/10/2018 FDA PDUFA date for this systemically delivered second-generation lipid nanoparticle with small-interfering RNA against transthyretin
Galafold (migalastat)/Amicus	Fabry disease	8/13/2018 FDA PDUFA date for this small-molecule 1-deoxygalactonojirimycin, which acts as a chaperone when bound to mutated alpha galactosidase, restoring folding and activity
Volanesorsen/Akcea	Dyslipidemia/hypercholesterolemia	8/30/2018 FDA PDUFA date for this second-generation 2'MOE chimeric ASO against apolipoprotein C3 mRNA
Caplacizumab/Ablynx	Thrombotic thrombocytopenic purpura	7/31/2018 PDUFA date for this combination of systemic and subcutaneous bivalent, humanized nanobody (single variable-domain immunoglobulins) against von Willebrand factor
Tafenoquine/GlaxoSmithKline	Malaria	7/27/2018 FDA PDUFA date for this non-NME small-molecule 8-aminoquinoline that triggers Ca2+ entry, oxidative stress and possibly activation of casein kinase in erythrocytes, the first drug for malaria in 60 years
ATIR101/Kiadis Pharma	Graft-versus-host disease	9/30/2018 European decision for photosensitizing small molecule used in ex vivo depletion of auto-reactive T cells in allogeneic grafts before transplantation

PDUFA, Prescription Drug User Fee Act. Source: BioMedTracker, a service of Sagient Research (http://biomedtracker.com)

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