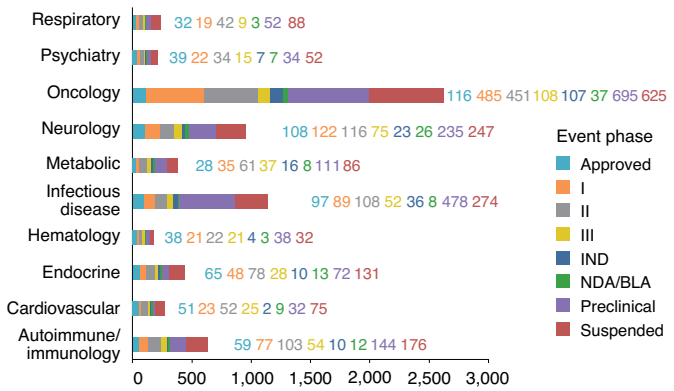
DATA PAGE

Drug pipeline 4Q20

Approvals rolled on, with some notable firsts: the first ever FDA-approved drug for Hutchison–Gilford progeria and European approval for a small-interfering RNA (siRNA) in a blockbuster indication—Novartis/Alnylam's cholesterol-lowering Leqvio (inclisiran), targeting proprotein convertase subtilisin kexin type 9 (PCSK9). Another siRNA drug, Oxlumo (lumasiran) for hyperoxaluria, was also registered at the FDA. Several gene and cell-based therapies ran into problems, mainly due to manufacturing issues or an inability to inspect third-party manufacturing sites. In infectious disease, registrations came for two new Ebola monoclonal antibody (mAb) treatments, one a cocktail of three recombinant molecules and the other a mAb derived from the plasma of a survivor of the 2015 outbreak; interim reporting on COVID-19 trials is ramping up, with more to come in the coming quarters.

Top ten disease groups by pipeline size

Oncology still leads in all stages of drug development, but infectious diseases and neurology pipelines are growing, a sign of the pandemic and aging populations.



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

Notable clinical trial results (4Q20)

Drug/company	Indication	Drug information
Evinacumab/ Regeneron	Dyslipidemia/ hypercholesterolemia	12/10/2020 In a double-blind, placebo-controlled, phase 2 trial, a fully human IgG4 mAb against angiopoietin-like 3 reduced low-density lipoprotein cholesterol by more than 50% at the maximum dose (*N. Engl. J. Med.* **383**, 2307–2319, 2020)
Nadofaragene firadenovec/FKD Therapies Oy	Bladder cancer	11/27/2020 In a phase 3, open label, multi-dose trial, over 50% of patients receiving this adenoviral serotype 5 vector carrying an interferon-α 2b transgene with a polyamide surfactant excipient (Syn3) for enhanced transduction of the bladder epithelium had a complete response at 3 months (*Lancet* https://doi.org/10.1016/S1470-2045(20)30540-4)
Imetelstat/Geron	Myelodysplastic syndrome	10/27/2020 In this phase 2/3 trial, this 13-mer N3′–P5′ thio-phosphoramidate (NPS) oligonucleotide covalently attached to a palmitoyl lipid moiety caused durable transfusion independence in heavily transfused patients (*J. Clin. Oncol.* **39**, 48–56, 2021)
Lirentelimab/ Allakos	Gastroenteritis	10/22/2020 In a phase 2 randomized, placebo-controlled trial, this anti-Siglec-8 IgG1 mAb reduced gastrointestinal eosinophils (*N. Engl. J. Med.* **383**, 1624–1634, 2020)

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

Notable drug approvals (4Q20)

Drug/company	Indication	Drug information
Inmazeb (atoltivimab/ maftivimab/ odesivimab-ebgn)/ Regeneron Pharmaceuticals	Ebola virus infection	10/14/2020 FDA approves cocktail of 3 human IgG1 mAbs directed against 3 Ebola glycoprotein epitopes: atoltivimab combines neutralization and antibody-dependent effector function via FcγRIIIa, maftivimab is a neutralizing antibody that blocks viral entry, and odesivimab is a non-neutralizing antibody that induces FcγRIIIa signaling
Veklury (remdesivir)/ Gilead Sciences	COVID-19	10/22/2010 FDA approves this broad-spectrum antiviral targeting viral RNA-dependent RNA polymerase
Zokinvy (lonafarnib)/Eiger BioPharmaceuticals	Hutchinson–Gilford progeria syndrome	11/23/2020 FDA approves this small-molecule farnesyltransferase inhibitor
Oxlumo (lumasiran)/ Alnylam	Hyperoxaluria	11/23/2020 FDA approves this triantennary *N*-acetylgalactosamine-conjugated phosphorothioate, 2′-*O*- methyl, 2′-fluoro and 2′-deoxy-modified siRNA targeting glycolate oxidase
Danyelza (naxitamab-gqgk)/Y-mAbs Therapeutics	Neuroendocrine tumors	11/25/2020 FDA granted accelerated approval to this humanized IgG3 3F8 mAb targeting ganglioside GD2 and the T cell receptor invariant chain CD3
Imcivree (setmelanotide)/ Rhythm Pharmaceuticals	Metabolic disease	11/25/2020 FDA approved this peptide agonist with specificity for melanocortin-4 receptor
Orladeyo (berotralstat)/ BioCryst Pharmaceuticals	Hereditary angioedema	12/4/2020 FDA approves this first-in-class oral small-molecule plasma kallikrein inhibitor
Leqvio (inclisiran)/ Novartis/Alnylam	Hypercholesterolemia	12/11/2020 EMA approves this triantennary *N*-acetylgalactosamine-conjugated phosphorothioate, 2′-*O*- methyl, 2′-fluoro and 2′-deoxynucleic acid-modified siRNA targeting proprotein convertase subtilisin kexin type 9 (PCSK9) mRNA
Klisyri (tirbanibulin)/ Almirall	Actinic keratoses	12/14/2020 FDA approves this small-molecule Src kinase (non-ATP-competitive) and tubulin polymerization inhibitor
Ebanga (ansuvimab-zykl)/ Ridgeback Biotherapeutics	Ebola virus infection	12/21/2020 FDA approved this lyophilized IgG1 mAb with both neutralizing and FcγRIIIa binding activity, isolated from immortalized B cells from a survivor of the 1995 outbreak, that targets a cap region epitope in Ebola virus glycoprotein
Margenza (margetuximab)/ MacroGenics	Breast cancer	12/16/2020 FDA approved this Fc-optimized chimeric IgG1 mAb against the human epidermal growth factor receptor 2

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

Notable regulatory setbacks (4Q20)

Drug/company	Indication	Drug information
Ryoncil (remestemcel-L)/ Mesoblast	Graft-versus-host disease	10/5/2020 FDA issued a complete response letter for this autologous mesenchymal stem cell treatment, asking for more data and better rationale for potency metrics
Omburtamab/ Y-mAbs Therapeutics	Neuroblastoma	10/5/2020 FDA issued a refuse to file letter for this radiolabeled (^{131}I) humanized IgG1-svFv mAb against B7-H3 due to CMC issues
VY-HTT01/ Voyager Therapeutics	Huntington's disease	10/13/2020 FDA put a clinical hold due to CMC issues on this AAV1 gene therapy encoding a miR-451a-based artificial microRNA targeting huntingtin mRNA
Betibeglogene autotemcel/ bluebird bio	Sickle cell disease	11/5/2020 Because of quality control demands from the FDA, the company is delaying filing for its self-inactivating HIV-1-derived lentiviral vector encoding a T87Q-mutated form of the human hemoglobin subunit-β (*HBB*, β-globin) gene under the control of a human β-globin promoter and a 3′ β-globin enhancer
Lisocabtagene maraleucel/Bristol Myers Squibb	B cell lymphoma	11/16/2020 FDA was unable to inspect third-party manufacturing facility of autologous T cells engineered ex vivo with a lentiviral vector encoding an anti-CD19 chimeric antigen receptor (CAR) and truncated epidermal growth factor receptor (tEGFR) (a selection marker), which will mean a missed PDUFA date
NurOwn/ BrainStorm Cell Therapeutics	Amyotrophic lateral sclerosis	11/17/2020 Company announced that top-line results of phase 3 trial of mesenchymal stem cells failed to meet statistical significance
Etranacogene dezaparvovec/ uniQure	Hemophilia B	12/21/2020 FDA put a clinical hold due to liver cancer in one patient possibly connected to treatment with this AAV5 vector encoding the Padua variant of factor IX
Odronextamab/ Regeneron	B cell non-Hodgkin lymphomas	12/14/2020 FDA put a partial hold on phase 1/2 clinical trials of this IgG4 bispecific mAb, requesting that the company amend the trial protocols to reduce the incidence of cytokine release syndrome

CMC: chemistry, manufacturing and controls Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com)

Notable clinical trials for COVID-19 products

Drug/company	Indication	Drug information
Avigan (favipiravir)/ Dr. Reddy's Laboratories	COVID-19	11/16/2020 In a phase 3 randomized trial, an oral small-molecule RNA polymerase inhibitor produced significant improvement in time to clinical cure (*Int. J. Infect. Dis.* **103**, 62–67, 2021)
Bamlanivimab/ Eli Lilly	COVID-19	10/28/2020 In a phase 2 randomized, placebo-controlled double-blind trial of a neutralizing humanized IgG1κ mAb targeting an epitope on the spike (S) protein of SARS-CoV-2, one of the doses reduced viral load by 3.4-fold (*N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa2029849)
Olumiant (baricitinib)/ Eli Lilly	COVID-19	12/22/2020 In a phase 3 trial, this small-molecule JAK/STAT inhibitor combined with remdesivir reduced time to recovery compared with remdesivir alone (*N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa2031994)
Actemra (tocilizumab)/ Roche	COVID-19	12/17/2020 In a randomized, placebo-controlled trial, this humanized IgG1κ mAb targeting IL-6R receptor reduced by 7.3% progression to mechanical ventilation or death compared with placebo and shortened the median time to hospital discharge during the 28-day study period by 1.5 days (*N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa2030340)
REGN-COV2 (casirivimab/ imdevimab)/ Regeneron	COVID-19	12/17/2020 In an ongoing phase 1–3 double-blind clinical trial of outpatients, a cocktail of two neutralizing human IgG1 mAbs targeting S protein epitopes reduced viral load in unhospitalized patients who lacked antibodies and had a high viral load and reduced medically attended visits in this population from 15% to 6% compared with placebo (*N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa2035002)

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

Upcoming catalysts (2Q21)

Drug/company	Indication	Drug information
Lenti-D/bluebird bio	Adrenoleukodystrophy	3/1/2021 EMA CHMP opinion on autologous hematopoietic stem cells transduced ex vivo with a lentiviral vector carrying human *ABCD1* cDNA
Tralokinumab/AstraZeneca	Atopic dermatitis	3/1/2021 FDA PDUFA date for this humanized IgG4 mAb against interleukin-13 receptor (IL-13R)
Vosoritide/BioMarin Pharmaceutical	Achondroplasia	4/1/2021 EMA CHMP opinion for this stabilized analog of human C-type natriuretic peptide
Abrocitinib/Pfizer	Atopic dermatitis	4/30/2021 FDA PDUFA date for this first-in-class (for indication) small-molecule JAK/STAT inhibitor
Avalglucosidase alfa/Sanofi	Pompe disease	5/18/2021 FDA PDUFA date for this highly phosphorylated recombinant human α-glucosidase enzyme replacement therapy
Loncastuximab tesirine/ADC Therapeutics	Diffuse large B cell lymphoma/NHL	5/21/2021 FDA PDUFA date for this humanized IgG1 mAb targeting CD19 conjugated to tesirine (a SG3199 warhead with a pyrrolobenzodiazepine dimer linker)
Bimekizumab/UCB	Psoriasis	4/1/2021 EMA CHMP opinion on this humanized IgG1 mAb that neutralizes both IL-17A and IL-17F
Fosdenopterin/BridgeBio Pharma	Molybdenum cofactor deficiency	4/9/2021 FDA PDUFA date for this cyclic pyranopterin monophosphate (cPMP) substrate replacement therapy in an unmet need
Pegunigalsidase alfa/Chiesi Farmaceutici	Fabry's disease	4/27/2021 FDA PDUFA date for this PEGylated recombinant α-galactosidase A produced in a carrot (*Daucus carota*) expression system
Lumevoq/GenSight Biologics	Leber's hereditary optic neuropathy	6/1/2021 EMA CHMP opinion on this recombinant adeno-associated viral vector serotype 2 (AAV2) containing the wild-type *ND4* gene
PF-06482077/Pfizer	*Streptococcus pneumoniae* vaccine	5/1/2021 FDA PDUFA date for this 20-valent pneumococcal conjugate vaccine
Arimoclomol/Orphazyme	Niemann–Pick disease	6/17/2021 FDA PDUFA date for this small-molecule activator of molecular chaperones

EMA, European Medicines Agency; CHMP, Committee for Medicinal Products for Human Use; PDUFA, Prescription Drug User Fee Act. Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com)

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Published online: 9 February 2021
https://doi.org/10.1038/s41587-021-00818-6