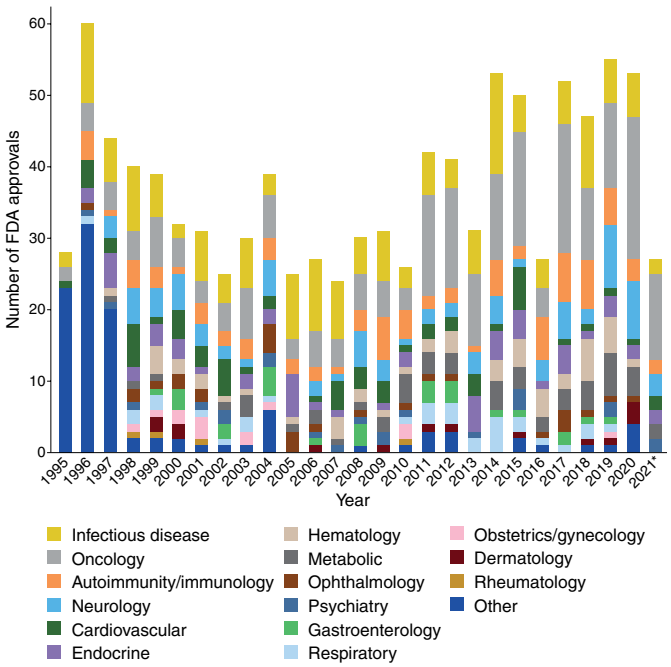
DATA PAGE

Drug pipeline 2Q21—accelerated approvals to the fore

Accelerated, rather than full, approvals were prominent. As usual, cancer registrations predominated—including Amgen's Lumakras, a first-in-class covalent targeter of KRAS in lung cancer. The other big news was the controversial go-ahead from the US Food and Drug Administration (FDA) for Biogen's Alzheimer's monoclonal antibody (mAb) Aduhelm, which later was given a narrower label by the agency; the approval prompted calls by the acting FDA head for a federal investigation into interactions between the drug developer and regulators. Less prominent, but also notable, was the approval of Truseltiq, a drug from the multi-asset play BridgeBio, providing validation for its business model. There were setbacks for two COVID-19 products, as well as the gene therapy timrepigene emparvovec for the eye disease choroideremia. FDA decisions coming up include new disease-modulating drugs in cervical cancer, myasthenia gravis and leukopenia.

Historic US regulatory approvals by disease group

Oncology continues as the perennial leader.



*Partial year to 30 June.

Upcoming catalysts (4Q21)

Drug / company	Indication	Drug information
Tisotumab vedotin / Seagen	Cervical cancer	10/8/2021 FDA PDUFA date for this antibody–drug conjugate of a human IgG1κ mAb targeting human tissue factor conjugated to monomethyl auristatin E
Plinabulin / BeyondSpring	Neutropenia, leukopenia	11/30/2021 FDA PDUFA date for this small-molecule halimide derivative with selective immunomodulating microtubule-binding agent properties derived from marine *Aspergillus* sp.
Palovarotene / Ipsen	Fibrodysplasia ossificans progressiva	11/30/2021and 11/01/2021 FDA PDUFA and CHMP opinion dates for this selective small-molecule agonist of retinoic acid receptor-γ
Efgartigimod / Argenx	Myasthenia gravis	12/17/2021 FDA PDUFA date for this human IgG1 Fc fragment optimized to bind neonatal Fc receptor delivered using recombinant human hyaluronidase enzyme
Balstilimab / Agenus	Cervical cancer	12/16/2021 FDA PDUFA date for this fully human IgG4 mAb against programmed death ligand 1 (PD -1)

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

Notable regulatory setbacks (2Q21)

Drug / company	Indication	Drug information
Pegunigalsidase alfa / Chiesi Farmaceutici	Fabry's disease	4/28/2021 FDA issued a complete response letter for this PEGylated recombinant α-galactosidase A produced in a carrot (*Daucus carota*) expression system because travel restrictions caused delays in inspection
CD24Fc / Merck	COVID-19 treatment	4/15/2021 Because of an FDA request for more clinical data, company halted development of this recombinant fusion protein comprising the extracellular domain of human CD24 linked to the human IgG1 Fc domain, which binds to DAMPs (danger-associated molecular patterns) in cellular debris, preventing their interaction with Toll-like receptors
Arimoclomol citrate / Orphazyme	Niemann–Pick disease	6/18/2021 FDA issued a complete response letter for this small-molecule (*N*-[(2*R*)-2-hydroxy-3-(1-piperidyl)propoxy] pyridine-3-carboximidoyl chloride, 1-oxide) activator of molecular chaperones, requesting more information on the interpretation of the 5-domain clinical severity scale
AdCovid / Altimmune	COVID prevention	6/29/2021 Company suspended trials of this intranasally administered replication-defective adenovirus 5 vector encoding S protein vaccine due to a low immune response
Timrepigene emparvovec / Biogen	Choroideremia	6/14/2021 Company suspended trials of this adeno-associated virus serotype 2 (AAV-2) vector containing *CHM*, which encodes the Rab escort protein-1, as it failed to meet primary endpoint of better than 15-letter improvement in visual acuity

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

Notable clinical trial results (2Q21)

Drug / company	Indication	Drug information
Efgartigimod / Argenx	Myasthenia gravis	6/16/2021 In a phase 3 double-blind, placebo-controlled trial, patients receiving this human IgG1 Fc antibody fragment that binds neonatal Fc receptor, delivered using recombinant human hyaluronidase, had at least a two-point improvement in daily living score (*Lancet Neurol.* **20**, 526–536, 2021)
Tezepelumab / Amgen	Asthma	5/13/2021 In a phase 3 double-blind, placebo-controlled trial of this human IgG2 mAb targeting thymic stromal lymphopoietin, patients with severe asthma had fewer exacerbations and better lung function and quality of life (*N. Engl. J. Med.* **384**, 1800–1809, 2021)
Sutimlimab / Sanofi	Autoimmune hemolytic anemia	4/7/2021 In an open-label trial of this humanized IgG4 mAb against complement factor C1s, upstream inhibition of complement pathway halted hemolysis, increased hemoglobin levels and reduced fatigue (*N. Engl. J. Med.* **384**, 1323–1334, 2021)
Omidubicel / Gamida Cell	Bone marrow transplant and stem cell transplant	6/22/2021 In a phase 3 trial of umbilical cord blood–derived stem and progenitor cells expanded ex vivo using nicotinamide (a sirtuin-1 modulator), transplant patients had faster hematopoietic recovery and fewer transplant-related complications than those treated with standard of care (umbilical cord blood) (*Blood* https://doi.org/10.1182/blood.2021011719, 2021)
Upadacitinib / AbbVie	Atopic dermatitis	5/20/2021 In randomized placebo-controlled trials of this small-molecule preferential JAK1 or JAK1/3 inhibitor, all primary and secondary endpoints were met with treatment combined with topical steroids compared with placebo plus topical steroids (*Lancet* https://doi.org/10.1016/S0140-6736(21)00588-2, 2021)
Xeljanz / Pfizer	COVID-19 treatment	6/16/2021 In this randomized, placebo-controlled trial of hospitalized patients not yet on ventilator, patients receiving this orally active small-molecule inhibitor of JAKs 1, 2 and 3 had significantly reduced rate of progression to respiratory failure or death (18.1% versus 29.0%) (*N. Eng. J. Med.* https://doi.org/10.1056/NEJMoa2101643, 2021)

JAK, Janus-activated kinase. Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com)

Notable drug approvals (2Q21)

Drug / company	Indication	Drug information
Jemperli (dostarlimab-gxly) / GlaxoSmithKline	Uterine (endometrial) cancer	4/22/2021 FDA granted accelerated approval to this humanized IgG4 mAb against PD1
Zynlonta (loncastuximab tesirine-lpyl) / ADC Therapeutics	Diffuse large B-cell lymphoma, non-Hodgkin's lymphoma	4/23/2021 FDA granted accelerated approval to humanized IgG1 mAb targeting CD19 conjugated to tesirine (a SG3199 warhead with a pyrrolobenzodiazepine dimer linker)
Rybrevant (amivantamab-vmjw) / Johnson & Johnson	Non-small-cell lung cancer	5/21/2021 FDA granted accelerated approval for this human IgG1 bispecific mAb targeting epidermal growth factor receptor and cMet
Lumakras (sotorasib) / Amgen	Non-small-cell lung cancer	5/28/2021 FDA granted accelerated approval for this first-in-class small-molecule covalent KRAS GTPase inhibitor for patients with a G12C mutation
Truseltiq (infigratinib) / BridgeBio Pharma	Biliary tract cancer	5/28/2021 FDA granted accelerated approval to this small molecule ATP competitive tyrosine kinase inhibitor of fibroblast growth factor receptor 1
Aduhelm (aducanumab) / Biogen	Alzheimer's disease	6/7/2021 FDA granted accelerated approval to this fully human IgG1 mAb against a conformational epitope on β-amyloid plaques

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

Laura DeFrancesco
Senior Editor, Nature Biotechnology.

Published online: 10 August 2021
https://doi.org/10.1038/s41587-021-01013-3