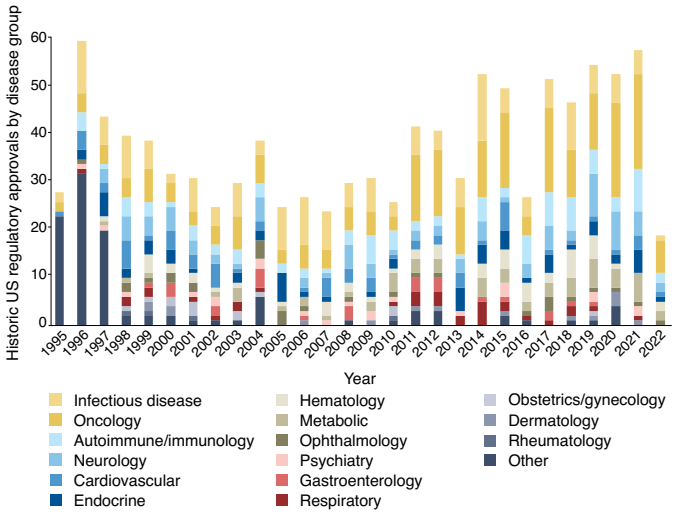
DATA PAGE

Drug pipeline 2Q22 — a downturn in approvals

Amid a slow quarter for approvals, Alnylam got its fifth approval in as many years with Amvuttra (vutrisiran), a next-generation RNA interference (RNAi) drug for the rare disease hereditary transthyretin-mediated (hATTR) amyloidosis. It offers more convenient subcutaneous delivery than the company's own drug for the same indication, Onpattro (patisiran), which requires frequent infusions. Also notable is Bristol Myers Squibb's first-in-class therapy for hypertrophic cardiomyopathy, Camzyos (mavacamten), which is a unique disease-modifying intervention for this indication. Garnering the most attention, however, was Lilly's drug Olumiant (baricitinib), the first systemic drug for hair loss, which adds to an existing set of indications (including COVID-19) for the Janus kinase/signal transducer and activator of transcription (JAK/STAT) inhibitor. In the coming months, the US Food and Drug Administration will assess a slew of monoclonal antibodies — mostly, but not exclusively, for cancer indications.

Historic US regulatory approvals by disease group

A relatively slow quarter for drug approvals.



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

Notable regulatory setbacks (4Q20)

Drug/company	Indication	Drug information
Tolebrutinib/ Sanofi	Multiple sclerosis and myasthenia gravis	6/30/2022 FDA placed holds on four phase 3 clinical trials of this brain-penetrating small molecule Bruton's tyrosine kinase inhibitor owing to concerns over liver injury
AT845/Astellas Pharma	Pompe disease	6/26/2022 FDA put a clinical hold on this AAV8 vector-based gene therapy, encoding a functional copy of the *GAA* gene, following the occurrence of a serious adverse event of peripheral sensory neuropathy in one of the trial participants.
Fosgonimeton/ Athira	Alzheimer's disease	6/22/2022 The company announced that this stimulator of hepatocyte growth factor missed the primary endpoint in a phase 2 study of mild-to-moderate disease
SRP-5051/ Sarepta	Duchenne muscular dystrophy	6/23/2022 FDA put a hold on a trial of this non-disclosed cell-penetrating peptide conjugated to a PMO following a serious adverse event of hypomagnesemia in one patient

AAV8, adeno-associated virus serotype 8 GAA, acid α-glucosidase; PMO, phosphorodiamidate morpholino oligomer. Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com)

Upcoming catalysts (4Q22)

Drug/company	Indication	Drug information
Mirvetuximab soravtansine/ImmunoGen	Ovarian cancer	11/28/2022 FDA PDUFA date for this anti-folate receptor ADC, formed by the humanized IgG1 mAb covalently conjugated to a maytansinoid derivative (DM4; *N*2′-deacetyl-*N*2′-(4-mercapto-4-methyl-1-oxopentyl)-maytansine) payload via a cleavable *N*-hydroxysuccinimidyl-4-(2-pyridyldithio)butanoate (sulfo-SPDB) linker
Penpulimab/Akeso	Nasopharyngeal cancer	11/30/2022 FDA PDUFA date for this engineered IgG1 anti-PD-1 mAb, which lacks the Fc gamma receptor
Omburtamab/Y-mAbs Therapeutics	Brain cancer (neuroblastoma, leptomeningeal cancer, medulloblastoma and ependymoma)	11/30/2022 FDA PDUFA date for this ^{131}I-radiolabeled mouse IgG1 mAb targeting B7-H3-expressing immune cells
Ublituximab/TG Therapeutics	Multiple sclerosis	12/28/2022 FDA PDUFA date for this chimeric anti-CD20 IgG1 mAb directed towards the CD20 antigen with the glycosylation profile of LFB-R603 for enhanced ADCC
Tremelimumab/ AstraZeneca	Hepatocellular cancer (including secondary metastases)	10/01/2022 FDA PDUFA date for this fully human IgG2 against CTLA4
Etranacogene dezaparvovec/CSL	Hemophilia B	11/01/2022 FDA PDUFA date for this viral gene therapy consisting of AAV5 vector carrying the human factor IX Padua mutant gene
Sparsentan/Travere Therapeutics	IgA nephropathy (Berger's disease)	11/17/2022 FDA PDUFA date for this dual-acting angiotensin and endothelin receptor antagonist that blocks the vasoconstrictive and mitogenic agents angiotensin II and endothelin 1

AAV5, adeno-associated virus serotype 5; ADCC, antibody-dependent cell-mediated cytotoxicity; ADC, antibody drug conjugate; B7-H3, B7 homolog 3 protein; CD20, cluster of differentiation 20; CTLA4, cytotoxic T lymphocyte-associated antigen 4; Fc, immunoglobulin crystallizable fragment; IgA, immunoglobulin A; LFB-R603, anti-CD20 mAb; PD-1, programmed cell death protein 1; PDUFA, Prescription Drug User Fee Act. Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com).

Notable drug approvals (2Q22)

Drug/company	Indication	Drug information
Camzyos (mavacamten)/BMS and Myokardia	Cardiomyopathy	4/28/2022 FDA approves this allosteric small-molecule inhibitor of myosin that decreases the adenosine triphosphatase activity of cardiac myosin heavy chain, inhibiting the formation of myosin–actin cross bridges, reducing contractility and improving cardiac filling pressures
Mounjaro (tirzepatide)/ Eli Lilly	Diabetes mellitus type 2	5/13/2022 FDA approves this peptide agonist of GIP receptor and GLP-1 receptor
Vtama (tapinarof)/ Roivant Sciences	Psoriasis	5/23/2022 FDA approves this small-molecule aryl hydrocarbon receptor-modulating agent in a topical cream with an unknown mechanism
Amvuttra (vutrisiran)/ Alnylam	Hereditary transthyretin amyloidosis with polyneuropathy	6/13/2022 FDA approves this double-stranded 2′-fluoro, 2′-methoxy-modified phosphorothioate siRNA–GalNAc conjugate that causes degradation of mutant and wild-type *TTR* mRNA through RNA interference
Skyrizi (risankizumab-rzaa)/ AbbVie	Crohn's disease	6/16/2022 FDA approves this humanized IgG1 mAb that selectively binds to the p19 subunit of human IL-23 cytokine and inhibits its interaction with the IL-23 receptor
Olumiant (baricitinib)/ Eli Lilly	Alopecia areata	6/13/2022 FDA approves this small-molecule inhibitor of Janus kinase (JAK) subtypes JAK1 and JAK2

GalNAc, *N*-acetylgalactosamine; GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide-1; IgG, immunoglobulin G; IL-23, interleukin-23; mAb, monoclonal antibody; siRNA, small interfering RNA. Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com).

Notable clinical trial results (4Q20)

Drug/company	Indication	Drug information
Lenacapavir/ Gilead Sciences	Multi-drug resistant HIV	5/12/2022 In a phase 3 trial of this small-molecule HIV capsid inhibitor, those receiving the drug had a 71% better response than those on placebo (*N. Engl. J. Med.* **386**, 1793–1803 (2022))
BI 1015550/ Boehringer	Idiopathic pulmonary fibrosis	6/9/2022 In a phase 3 randomized placebo-controlled trial of this oral, small-molecule phosphodiesterase 4B inhibitor, treatment prevented a decrease in lung function (*N. Engl. J. Med.* **386**, 2178–2187 (2022))
Fazirsiran/Takeda (Arrowhead)	α1 antitrypsin deficiency (A1AD or AATD)	6/25/2022 In an open label, phase 2 clinical trial, FDA approved this subcutaneously administered GalNAc-conjugated double-stranded 1′-de(6-amino-9H-purin-9-yl)-, 2′-deoxy-2′-fluoro), 3′-(*O*-(*cis*-4-((3S,8S)-17-((2-(acetylamino)-2-deoxy-β-D-galactopyranosyl) oxy)-3,8-bis(((2-(2-((2-(acetylamino)-2-deoxy-β-D-galactopyranosyl)oxy)ethoxy) ethyl)amino)carbonyl)-1,6,11-trioxo-15-oxa-2,7,12-triazaheptadec-1-yl)cyclohexyl) hydrogen-modified phosphorothioate siRNA that blocks *SERPINA1* mRNA and inhibits AAT was found in all patients to lower mutant AAT protein in the liver and decrease glomerular burden (*N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa2205416, 2022)

AAT, α1 antitrypsin; GalNAc, *N*-acetylgalactosamine; RNAi, RNA interference; *SERPINA1*, serpin family A member 1. Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com)

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