Data page

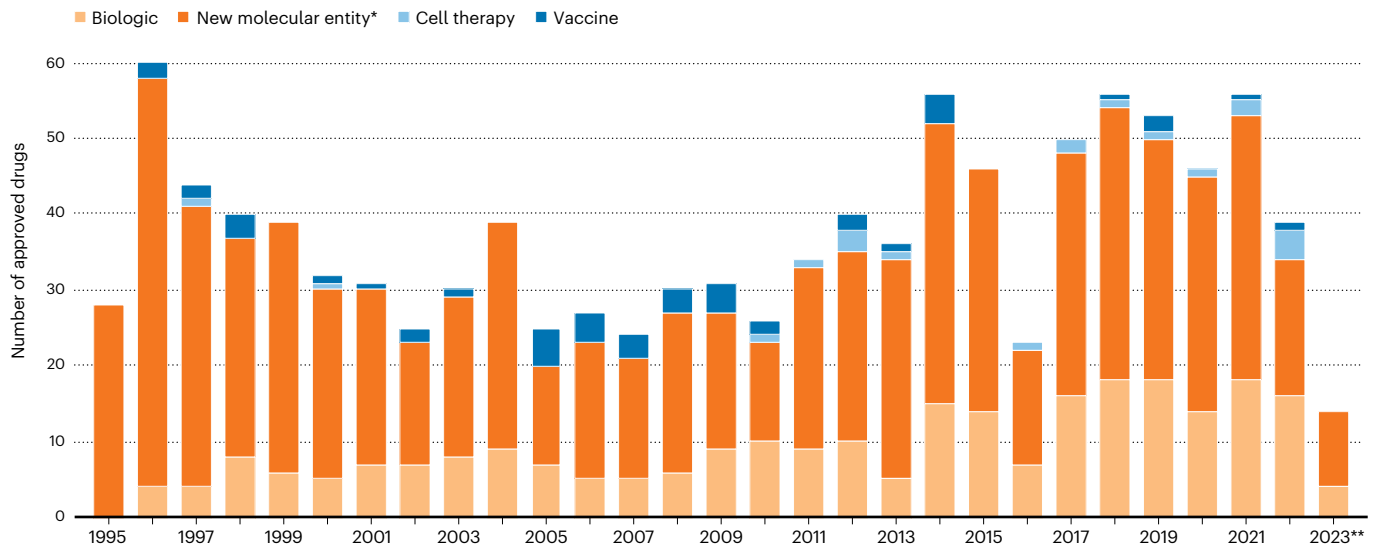
Drug pipeline 1Q23 — Everything everywhere all over the place

John Hodgson

Regulatory paths are rarely straightforward, especially for complex modalities in complex diseases. The plight of anti-amyloid antibodies in Alzheimer's disease remains unpredictable after two FDA decisions in January: FDA asked Eli Lilly for more data from patients with year-long exposure to donanemab before it would consider approval, but gave Biogen and Eisai's lecanemab an accelerated approval. There were three approvals for treatments for rare or ultra-rare diseases in the first quarter of 2023: Chiesi Farmaceutici's α-mannosidase replacement enzyme Lamzede and small-molecule treatments for Rett syndrome (Daybue from Acadia Pharma) and Friedreich's ataxia (Skyclarys from Reata Pharmaceuticals). The blood-clotting market is undergoing fast technological change: Sanofi's once-weekly factor VIII analog Altuviiio received FDA approval in February while Novo Nordisk's antibody prophylactic for hemophilia A or B and BioMarin's Roctavian factor VIII gene therapy both have PDUFA dates in the next several months. But there were setbacks for Graphite Bio's gene-edited sickle cell disease treatment and Sarepta's microdystrophin gene therapy.

Historic US regulatory approvals by drug class

Approvals on course to surpass 2022 total.



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

Notable drug approvals (1Q23)

Drug/company	Indication	Drug information
Lamzede (velmanase alfa)/ Chiesi Farmaceutici	α-mannosidosis	2/16/2023 FDA approves this recombinant human α-mannosidase replacement enzyme
Leqembi (lecanemab)/Eisai, Biogen	Alzheimer's disease	1/6/2023 FDA gives accelerated approval to this humanized monoclonal IgG1 antibody against amyloid-β plaques
Daybue (trofinetide)/ Acadia Pharmaceuticals	Rett syndrome	3/10/2023 FDA approves this analog of the amino-terminal tripeptide (glycine–proline–glutamate) of IGF-1
Skyclarys (omaveloxolone)/ Reata Pharmaceuticals	Friedreich's ataxia	2/28/2023 FDA approves this small-molecule activator of Nrf2, which activates genes that promote mitochondrial function
Altuviiio (efanesoctocog alfa)/Sanofi	Hemophilia A	2/23/2023 FDA approves this fully recombinant extended-half-life factor VIII protein that can be dosed once-weekly

Notable drug approvals (1Q23) (continued)

Drug/company	Indication	Drug information
Jaypirca (pirtobrutinib)/Eli Lilly	Mantle cell lymphoma – non-Hodgkin lymphoma	1/27/2023 FDA grants accelerated approval for this small-molecule BTK inhibitor that binds reversibly to the kinase target, potentially limiting the emergence of drug resistance
Brenzavvy (bexagliflozin)/ TheracosBio	Diabetes mellitus, type 2	1/23/2023 FDA approves this sodium–glucose co-transporter 2 (SGLT2) inhibitor in adults. In 2022, FDA approved it for diabetes in cats
Zynyz (retifanlimab-dlwr)/Incyte	Merkel cell carcinoma	3/22/2023 FDA gives accelerated approval for this humanized IgG4κ anti-PD-1 mAb
Jesduvroq (daprodustat)/GSK	Anemia due to dialysis-dependent chronic kidney disease	2/1/2023 FDA approves this oral small-molecule prolyl hydroxylase inhibitor that stabilizes hypoxia-inducible factors, leading to erythropoietin gene transcription and the correction of anemia

IgG, immunoglobulin G; IGF-1, insulin like growth factor 1; Nrf2, nuclear factor erythroid 2–related factor 2; BTK, Bruton's tyrosine kinase; PD-1, programmed cell death 1; mAb, monoclonal antibody; SGLT2, sodium–glucose transporter 2. Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com).

Upcoming catalysts (3Q23)

Drug/company	Indication	Drug information
Bimekizumab (Bimzelx)/UCB	Psoriatic arthritis	04/01/2023 FDA PDUFA date for this humanized bispecific IgG1 mAb that neutralizes IL-17A and IL-17F
Ryoncil (remestemcel-L)/ Mesoblast	Graft-versus-host disease	08/02/2023 FDA PDUFA date for this adult allogeneic, bone-marrow-derived mesenchymal stem cell treatment
Lumevoq/GenSight Biologics	Leber's hereditary optic neuropathy	7/1/2023 EMA CHMP opinion for this AAV-2 gene therapy encoding the wild-type *ND4* gene
Concizumab/Novo Nordisk	Hemophilia A and B	09/01/2023 FDA PDUFA date for this humanized IgG4 mAb specific for the K2 domain of TF1 inhibitor peptide
Nedosiran/Novo Nordisk	Hyperoxaluria	09/01/2023 FDA PDUFA date for this second-generation siRNA created using GalXC technology, with an extended Dicer substrate siRNA (DsiRNA-EX) that silences the *LDHA* gene
Roctavian/BioMarin	Hemophilia A	06/30/2023 FDA PDUFA date for this AAV5-based gene therapy vector that expresses a recombinant version of human factor VIII under the control of a liver-specific promoter
Pozelimab/Regeneron	CHAPLE syndrome	08/20/2023 FDA PDUFA date for this fully human monoclonal antibody to human complement C5 produced with IgG4P Fc domains
Olorofim/F2G	Fungal infections	6/1/2023 FDA PDUFA date for this orotomide inhibitor of dihydroorotate dehydrogenase

Il-15, interleukin-15; AAV, adeno-associated virus; ND4, NADH dehydrogenase 4 gene; TF-1, tissue factor pathway 1; siRNA, short interfering RNA; PDUFA, Prescription Drug User Fee Act; EMA, European Medicines Agency; CHMP, Committee for Medicinal Products for Human Use. Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com).

Notable regulatory setbacks (1Q23)

Drug/company	Indication	Drug information
Donanemab/Eli Lilly	Alzheimer's disease	1/19/2023 FDA issues a CRL for the application for accelerated approval for this humanized IgG1 mAb targeting amyloid-β_{p3-42}, the N-terminally truncated pyroglutamate-3 isoform, because of the small number of patients with 12 months of drug exposure
Omecamtiv mecarbil/Cytokinetics	Chronic heart failure	2/28/2023 FDA issues a CRL for this small-molecule cardiac myosin activator because of lack of substantial evidence that risk of heart failure was reduced; the company will conduct no further clinical trials
Delandistrogene moxeparvovec/Sarepta	Duchenne muscular dystrophy	3/16/2023 FDA announces plans to hold an advisory committee meeting for this AAVrh74.MHCK7.micro-dystrophin gene therapy on 12 May 2023
Hypericin/Soligenix	Cutaneous T cell lymphoma	2/14/2023 FDA issues a refuse-to-file letter for this small-molecule synthetic photosensitizer as a result of an incomplete NDA
Nula-cel/Graphite Bio	Sickle cell anemia	1/5/2023 Company discontinues phase 1/2 trial of nulabeglogene autogedtemcel (nula-cel) for sickle cell disease owing to a serious adverse event in the first patient dosed. The company will restructure, reducing workforce by around 50%.

CRL, complete response letter; IgG, immunoglobulin G; mAb, monoclonal antibody; NDA, New Drug Application. Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com).

Notable clinical trial results (1Q23)

Drug/company	Indication	Drug information
PEGylated interferon lambda/Eiger BioPharmaceuticals	COVID-19 treatment	2/8/2023 In a randomized, controlled, adaptive trial of vaccinated people with COVID-19, 2.7% of treated required hospitalization versus 5.6% receiving placebo (*N. Engl. J. Med.* **388**, 518–528, 2023)
Momelotinib/GSK	Myelofibrosis	1/27/2023 In a randomized, controlled, double-blind phase 3 study, this inhibitor of JAK1/2 and ACVR1 provided significant improvement in symptoms compared to standard of care (*Lancet* https://doi.org/10.1016/S0140-6736(22)02036-0, 2023)
Nirogacestat/GSK	Desmoid tumors	3/8/2023 In a phase 3 double-blind, randomized, placebo-controlled trial, this selective, reversible, non-competitive small-molecule inhibitor of γ-secretase yielded a significant increase in progression-free survival over placebo (*N. Engl. J. Med.* **388**, 898–912, 2023)
Leriglitazone/Minoryx Therapeutics	Adrenoleukodystrophy	1/19/2023 A multi-center, double-blind, placebo-controlled trial of this small-molecule PPAR-γ inhibitor met secondary endpoints of balance, quality of life and tolerability, and no treated patients had progressive disease (*Lancet* https://doi.org/10.1016/S1474-4422(22)00495-1, 2023)
Garadacimab/CSL Behring	Hereditary angioedema	2/28/2023 In a double-blind, randomized, placebo-controlled, multicenter, parallel-group study of this fully human recombinant factor XIIa antagonist monoclonal antibody, patients taking garadacimab (*N* = 39) experienced a statistically lower monthly attack rate compared to placebo over the 6-month study (*Lancet* https://doi.org/10.1016/S0140-6736(23)00350-1, 2023)

JAK1/2, Janus kinase 1 and 2; ACVR1, activin A receptor type I; PPAR, peroxisome proliferator-activated receptor. Source: BioMedTracker, a service of Sagient Research (http://www.biomedtracker.com).

John Hodgson
Cambridge, UK.