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PERSPECTIVES

Antibodies to watch in 2024

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ABSTRACT

The 'Antibodies to Watch' article series provides an annual summary of commercially sponsored monoclonal antibody therapeutics currently in late-stage clinical development, regulatory review, and those recently granted a first approval in any country. In this installment, we discuss key details for 16 antibody therapeutics granted a first approval in 2023, as of November 17 (lecanemab (Leqembi), rozanolixizumab (RYSTIGGO), pozelimab (VEOPOZ), mirikizumab (Omvoh), talquetamab (Talvey), elranatamab (Elrexfio), epcoritamab (EPKINLY), glofitamab (COLUMVI), retifanlimab (Zynyz), concizumab (Alhemo), lebrikizumab (EBGLYSS), tafolecimab (SINTBILO), narlumosbart (Jinlitai), zuberitamab (Enrexib), adebrelimab (Arelili), and divozilimab (Ivlizi)). We briefly review 26 product candidates for which marketing applications are under consideration in at least one country or region, and 23 investigational antibody therapeutics that are forecast to enter regulatory review by the end of 2024 based on company disclosures. These nearly 50 product candidates include numerous innovative bispecific antibodies, such as odronextamab, ivonescimab, linvoseltamab, zenocutuzumab, and erfonrilimab, and antibody–drug conjugates, such as trastuzumab botidotin, patritumab deruxtecan, datopotamab deruxtecan, and MRG002, as well as a mixture of two immunocytokines (bifikafusp alfa and onfekafusp alfa). We also discuss clinical phase transition and overall approval success rates for antibody therapeutics, which are crucial to the biopharmaceutical industry because these rates inform decisions about resource allocation. Our analyses indicate that these molecules have approval success rates in the range of 14–32%, with higher rates associated with antibodies developed for non-cancer indications. Overall, our data suggest that antibody therapeutic development efforts by the biopharmaceutical industry are robust and increasingly successful.

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Introduction

In this 15th installment of the annual 'Antibodies to Watch' article series, we review commercially sponsored monoclonal antibody therapeutics currently in late-stage clinical development, regulatory review, and those granted a first approval in any country in 2023. While we collect data for antibody therapeutics year-round, most details included here were collected during August 1 to November 1, 2023, although major transitions that occurred through mid-December were incorporated as possible. Due to the persistence of the trend toward first marketing application submission and approval antibody therapeutics in regions outside the United States (US) or European Union (EU) (Figure 1), the format for 'Antibodies to Watch in 2024' differs from past versions, which are freely available online (www.tandfonline.com/journals/kmab20/collections/antibodies-to-watch). Here, data are presented in a country-agnostic manner, i.e., only one section of 'Antibodies to Watch in 2024' is devoted to antibody therapeutics granted a first global approval in 2023 and only one section focuses on investigational antibody therapeutics for which marketing applications are undergoing a first review in any country. We do not include summaries for any antibody therapeutics approved before 2023, regardless of whether marketing applications for these are undergoing review by the US Food and Drug Administration (FDA), European Medicines Agency (EMA), or any other regulatory agency, such as the National Medicinal Product Administration (NMPA) in China, the Ministry of Health, Labour and Welfare in Japan, Swissmedic, Health Canada, Australian Therapeutic Goods Administration, or the UK's Medicines and Healthcare products Regulatory Agency. However, in addition to data for antibody therapeutics first approved in 2023, data for all antibodies approved in the US or EU in 2023 are included in Supplemental Table S1. Data for investigational antibody therapeutics currently in regulatory review in the US or EU regardless of whether they are approved elsewhere, are found in Supplemental Table S2.

Key details for 16 antibody therapeutics granted a first approval in 2023, as of mid-November, and 26 product candidates for which marketing applications are under consideration in at least one country or region are summarized below. In addition, we discuss 23 investigational antibody

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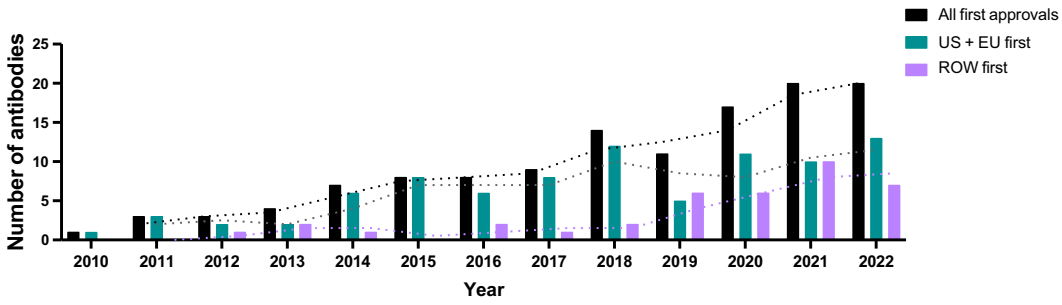

Figure 1. Annual first approvals for antibody therapeutics during 2010–2022.

therapeutics that are forecast to enter regulatory review by the end of 2024 based on company disclosures. With the waning of the pandemic, only two molecules that are intended for COVID-19 patients are included here. Notably, FDA issued an emergency use authorization (EUA) for the use of anti-complement C5a vilobelimab (Gohibic) for treatment of COVID-19 symptoms in April 2023, and we mention below that an EUA may be sought by AstraZeneca for anti-SARS-CoV-2 AZD3152 for the prevention of COVID-19. This may seem surprising because the public health emergency (PHE) declaration in the US expired in May 2023, but, due to the provisions in the relevant federal regulations, an EUA may remain in effect and new EUAs may continue being issued beyond the duration of the PHE declaration if all other statutory conditions are met.

While the focus of this report is the currently active late-stage clinical pipeline, our full dataset includes details for investigational antibody therapeutics sponsored by commercial firms that entered clinical study during 2000 to the present. Critically, this allows us to calculate approval success and clinical phase transition rates for these molecules based on factors such as their period of clinical development, the diseases for which they are developed and their molecular characteristics. Since the rates typically do not dramatically change from year to year, we assess success rates only periodically. The success rates presented here update the rates provided in 'Antibodies to Watch in 2019'. Overall, our data suggest that past work on well-validated targets such as CD20, HER2, PD-1, PD-L1, combined with intensive research on innovative antibody formats, has yielded dividends in the form of higher success rates, numerous approved antibody therapeutics, and expanded choices for treatment of patients.

Within the current dataset, we identified over 130 antibody therapeutics undergoing evaluation in pivotal Phase 2, Phase 2/3, or Phase 3 studies, referred to here as 'late-stage' clinical studies because data derived from them may be used to support marketing applications submitted to regulatory agencies. Extensive data for this late-stage commercial pipeline are found in Supplemental Table S3. Due to the large volume of literature for the molecules, we cite only publications and other disclosures made public during January 1 to November 17, 2023, in the summaries below. See Note added in proof at the end of this article for updated major events that occured around or within two weeks after the December 10, 2023 submission for publication.

Approval success rates

Accurate approval success rates for antibody therapeutics are crucial because they inform decisions about resource allocation within the biopharmaceutical industry. Such decisions affect individual company portfolios, as well investments by financial institutions in companies developing the drugs. We previously reported clinical phase transition and approval success rates for antibody therapeutics sponsored by commercial firms that entered clinical study during the 15-y period from January 1, 2000, to December 31, 2014.[1] The rates, calculated for molecules that entered clinical study during two overlapping periods (2000–2009 and 2005–2014), showed that 21% and 22%, respectively, of these antibody therapeutics were granted approvals in either the US or EU, based on the data available at the time. However, because clinical development periods can be lengthy, e.g., 10–12 y, final fates (approval or complete termination) were known for only 76% and 58% of the molecules in the 2000–2009 and 2005–2014 cohorts, respectively, when the calculations were made.

As part of our ongoing work tracking trends in commercial development of innovative antibody therapeutics, we have continued to monitor the status of these molecules and collect data for new antibody therapeutics that entered clinical study since the end of 2014. Data are collected from publicly available sources such as company pipelines, press releases and presentations, clinical trials registries, the World Health Organization's lists of recommended international nonproprietary names (INN), and an open-access database of therapeutic antibodies (IMGT/mAb-DB, www.imgt.org/mAb-DB/). In keeping with our past practice, molecules with at least one binding site derived from an antibody gene are included, but Fc only and Fc fusion proteins are excluded. Antibody therapeutics developed solely by noncommercial organizations, e.g., National Institutes of Health, and all biosimilar antibodies are excluded.

To update and expand our previous study of success rates, during January to June 2023, we extracted data for antibody therapeutics that entered clinical study in the 20-year period from January 1, 2000, to December 31, 2019, and then cross-checked our data with those from the public domain and two commercial databases (Beacon, GlobalData). Based on the totality of the evidence, we assigned each of the 1,358 molecules included in the dataset one of the two therapeutic areas (cancer, non-cancer) and one of the nine possible phases of development (Phase 1, 2, or 3 clinical study; regulatory review;

approved; all development terminated at Phase 1, 2, or 3, or during regulatory review), where each phase represents the most advanced phase of development achieved by the molecule. Success was defined as the first marketing approval in any country; no subsequent supplemental approvals were included in calculations. Clinical phase transition and approval success rates were calculated for antibody therapeutics that entered clinical study in three overlapping periods (2000–2009, 2005–2014, and 2010–2019), and we separately calculated rates for all antibody therapeutics (Figure 2), antibody therapeutics for non-cancer indications (Figure 3), and antibody therapeutics for cancer (Figure 4). In each of these three cases, we calculated rates both when success was defined broadly, i.e., an approval granted in any country or region, and when success was narrowly defined as an approval granted only in either the US or EU. Final fates were known for 90%, 84%, and 59% of the molecules included in the 2000–2009, 2005–2014, and 2010–2019 cohorts, respectively.

Regardless of whether all data were included or whether the data were stratified by therapeutic area, the phase transition

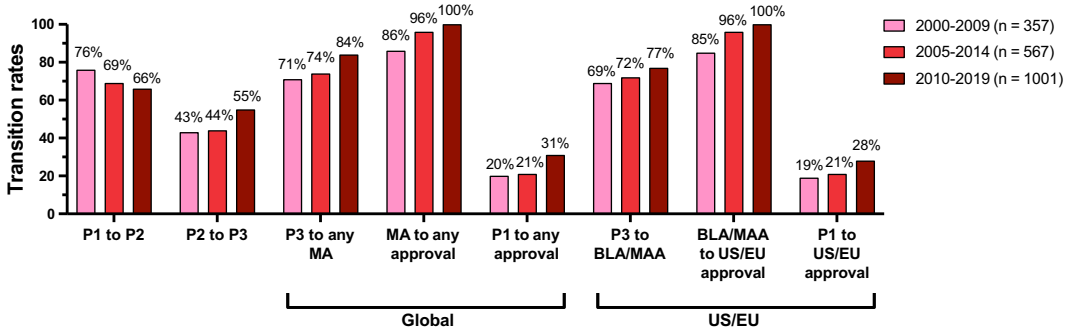

Figure 2. Clinical phase transition and approval success rates for antibody therapeutics for any therapeutic area that entered clinical study during 3 periods. Pink bars, clinical entry during 2000–2009. Red bars, clinical entry during 2005–2014. Brick red bars, clinical entry during 2010–2019. Cohorts included only novel antibody therapeutics in clinical studies sponsored by commercial firms; biosimilars were excluded. Final fates (approval or termination) are known for 90%, 84% and 59% of the molecules that entered clinical study during 2000–2009, 2005–2014, and 2010–2019, respectively. Mabs in phase 1/2 studies were classified as phase 2; mAbs that advanced to phase 2/3 were classified as phase 3. Transitions occurring between phase 1 to 2 and phase 2 to 3 clinical studies conducted world-wide were included. Global approval refers to a first approval granted in any country or region; US/EU approval refers to a first approval in only the US or EU; supplemental approvals of any kind were not included. Single-step transition rates were calculated as the number of antibody therapeutics that transitioned from a given phase to the next divided by the sum of the number that transitioned and the number that were terminated at that phase at the time of the calculation. Phase 1 to approval rates were calculated by multiplying the four relevant single-step transition rates. Abbreviations: BLA, biologics license application submission to the US Food and Drug Administration; MA, marketing application submission to any regulatory agency; MAA, marketing authorization application submission to the European medicines agency.

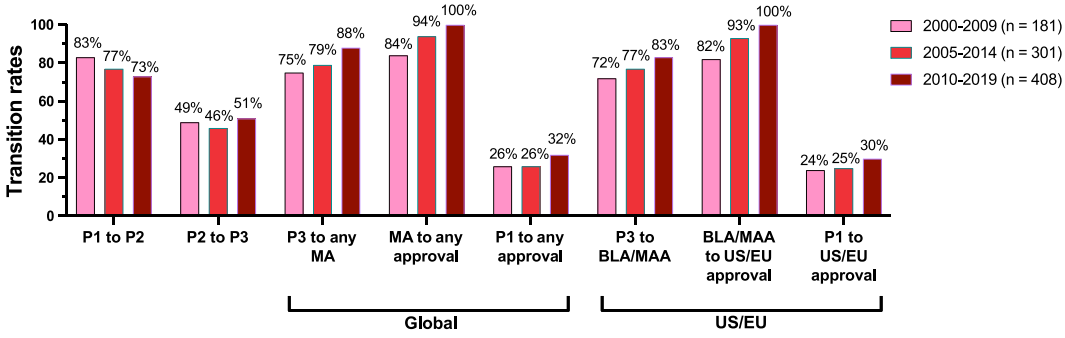

Figure 3. Clinical phase transition and approval success rates for antibody therapeutics for non-cancer indications that entered clinical study during 3 periods. Pink bars, clinical entry during 2000–2009. Red bars, clinical entry during 2005–2014. Brick red bars, clinical entry during 2010–2019.

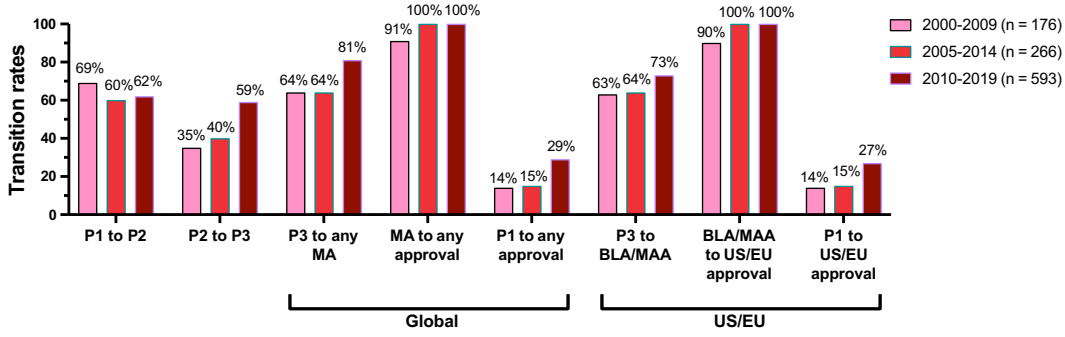

Figure 4. Clinical phase transition and approval success rates for antibody therapeutics for cancer that entered clinical study during 3 periods. Pink bars, clinical entry during 2000–2009. Red bars, clinical entry during 2005–2014. Brick red bars, clinical entry during 2010–2019.

rates followed an overall pattern that is typical of drug development, i.e., the Phase 2 to 3 and the marketing application submission to approval transition rates were lowest and highest, respectively. Phase 3 studies tend to be complex, lengthy, and expensive; hence, if preliminary evidence of safety and efficacy from Phase 2 studies is not suitable, companies are most likely to terminate programs at Phase 2. Similarly, preparation of marketing applications is complex and resource-intensive, and submission is expensive (e.g., $3.1 million fee for biologics license applications (BLAs) that include clinical data submitted to FDA); hence, in general, companies tend not to submit applications unless their data would seem to support approval.

For all molecules (Figure 2), the phase transitions for the 2000–2009 and 2005–2014 cohorts were similar, with offsetting minor differences in the Phase 1 to 2 and application submission to approval transition rates resulting in nearly identical overall approval success rates (20% and 21% for global approval, respectively; 20% and 21% for US/EU only approval, respectively). This stability in the rates is notable, considering that the 2005–2014 cohort is 59% larger than the 2000–2009 cohort. Similarly, the 2010–2019 cohort is larger than the 2005–2014 cohort (by 77%) and the 2000–2009 cohort (by 181%), reflecting the biopharmaceutical industry's increased interest in antibody therapeutics development over this 20-y period (Figure 5). With the exception of the Phase 1 to 2 transition rate, the 2010–2019 cohort had higher rates for every phase transition compared to the two previous periods, resulting in substantially higher approval success rates (31% and 28% for global approval and for US/EU only approval, respectively). It should be noted, however, that a greater degree of uncertainty is associated with the rates calculated for this cohort because it includes the largest number of molecules that remain in active development. Rates may vary as the final fates of these molecules are decided in the future.

Stratification of the data into the therapeutic areas (non-cancer, cancer) revealed dramatic differences in the phase transition rates between the two cohorts (Figures 3, 4). With one exception (Phase 2 to 3 transition, 2010–2019 cohort), rates for transitions between Phase 1 to marketing application submission were higher for antibody therapeutics for non-cancer indications compared to those for cancer. As a consequence of this, and despite the higher marketing application to approval transition rates for the cancer cohort, antibody therapeutics for non-cancer indications had substantially higher Phase 1 to global approval success rates for the 2000–2009 and 2005–2014 cohorts compared to those for cancer (26% and 26% vs 14% and 15%, respectively), as well as a marginally higher Phase 1 to global approval success rate for the 2010–2019 cohort (32% vs 29%). Similarly, the Phase 1 to US/EU-specific approval success rates were also higher for the antibody therapeutics for non-cancer indications (24–30%) compared to those for cancer (14–27%) in the three periods we examined.

When comparing data for the three periods, the rates for antibody therapeutics for cancer, in particular the Phase 2 to 3 and Phase 3 to any marketing application submission rates, showed the most remarkable differences (Figure 4). Compared to the 2000–2009 cohort, the Phase 2 to 3 and Phase 3 to any marketing application submission rates for the 2010–2019 cohort increased by 70% and 25%, respectively. These increases caused an apparent doubling of the Phase 1 to global approval rate between these periods, from 14% for the 2000–2009 cohort to 29% for the 2010–2019 cohort. This result was likely due to the substantial increase in the number of antibody therapeutics targeting well-validated antigens, in particular PD-1, PD-L1, HER2, and CD20, that entered clinical development during 2010–2019. When combined, the number of antibodies targeting these four antigens in clinical development during 2000–2009 and 2010–2019 grew from fewer than 20 to over 140. Those that entered clinical development during 2010–2019 have been remarkably successful so far, with nearly 40 PD-1, PD-L1, HER2, and CD20-targeting antibodies from this cohort now in regulatory review or already approved as of October 2023. It should also be noted that ~40% are still in development. We look forward to reevaluating success rates for this cohort after the fates for more molecules are known.

The Biotechnology Innovation Organization (BIO) recently released a report on monoclonal antibody clinical phase transition and approval success rates based on a study of individual drug program phase transitions from January 1, 2011, to November 30, 2020.[2] Their data were extracted from the commercially available database Biomedtracker. Their method, however, differed substantially from ours. The BIO study included data for all phase transitions for all diseases for which each molecule was evaluated in clinical studies during the designated period, and success was defined as an approval only by the FDA. Their method was intended to broadly reflect company resource utilization directed toward US approvals and thus includes more terminations and excludes non-US approvals, resulting in an approval Success rate for monoclonal

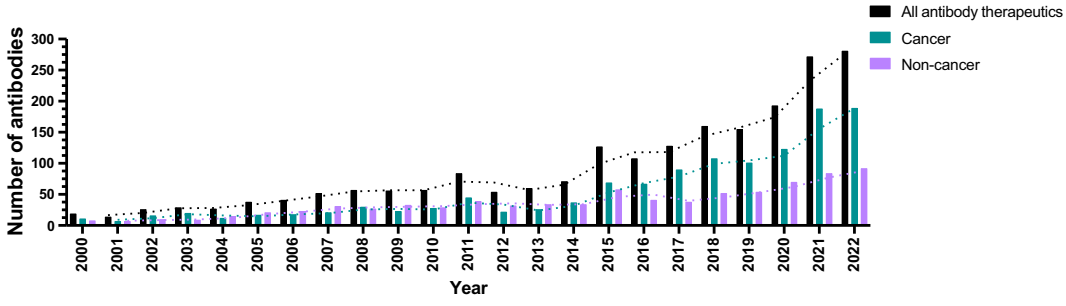

Figure 5. Annual number of antibody therapeutics entering clinical study, 2000–2022. Black bars, all antibody therapeutics. Green bars, antibody therapeutics for non-cancer indications only. Purple bars, antibody therapeutics for cancer only. Dotted lines, 2-y moving averages. Totals include only antibody therapeutics sponsored by commercial firms; those sponsored solely by government, academic or nonprofit organizations were excluded. Biosimilar antibodies and fc fusion proteins were also excluded.

antibodies that is substantially lower than ours. A similar study on clinical development success rates for the period 2006–2015 that was released by BIO in 2016 reported similar results (11.6% vs 12.1% for the 2011–2020 period).[3] We note, however, that our approach was designed to answer a different question (i.e., what percentage of commercially sponsored antibody therapeutics that enter clinical study are ultimately granted at least one marketing approval?) and thus yielded approval success rates in the range of 20–31% and 19–28% for antibody therapeutics approved in at least one country and specifically in the US/EU, respectively, for the three periods we examined.

Antibody therapeutics granted a first approval in 2023

As detailed in Table 1 and the summaries below, a total of 16 new antibody therapeutic products were granted a first approval in 2023, as of November 17. Subsequent approvals that occurred in other countries in 2023 are also noted. Of the 16 products, the majority were approved in the US (9/16), with 5 granted approvals in China and the EU and 4 each granted approvals in Japan and Canada. An equal number are products for cancer (8) as are for non-cancer indications (8). Summaries of key details for the products are provided below, in the order they appear in Table 1.

Lecanemab (Eisai Co., Ltd., Biogen, Inc.)

Lecanemab (BAN2401, LEQEMBI®) is a humanized IgG1κ monoclonal antibody that targets soluble and insoluble amyloid β_{1-42} (Aβ) aggregates. Initially developed by BioArctic, lecanemab was licensed to Eisai in a collaboration agreement, enabling joint development. Under an agreement with Biogen, Eisai and Biogen are responsible for commercializing and promoting lecanemab together. On January 6, 2023, the FDA granted lecanemab-irmb accelerated approval for the treatment of Alzheimer's disease (AD).[4] Lecanemab was approved in Japan in September 2023. Marketing applications for lecanemab are undergoing review in the EU, UK, and China.

FDA's accelerated approval was based on Phase 2 data that demonstrated that lecanemab reduced the accumulation of Aβ plaques in the brain, a defining pathophysiological feature of AD. On July 6, 2023, the FDA converted lecanemab to a traditional approval based on the Phase 3 data from Eisai's large, global Charity AD clinical trial (NCT03887455), a multicenter, randomized, double-blind, placebo-controlled, parallel-group study that enrolled 1,795 patients with AD.[5] The results demonstrated that lecanemab reduced clinical decline on Clinical Dementia Rating Sum of Boxes by 27% at 18 months compared to placebo. The recommended dosage for lecanemab is 10 mg/kg via intravenous infusion every 2 weeks (Q2W). Treatment with lecanemab should be initiated in patients with mild cognitive impairment or mild dementia stage of disease, the population in which treatment was evaluated in clinical trials.

Several other clinical studies of lecanemab are currently ongoing or recruiting participants, including a Phase 2 study (NCT01767311), the Phase 2/3 DIAN-TU-001 (Tau NexGen; NCT05269394) study for individuals with AD-causing genetic mutations, and the Phase 3 AHEAD 3–45 study (NCT04468659) for patients with preclinical AD and elevated amyloid or early preclinical AD and intermediate amyloid.

Rozanolixizumab (UCB)

Rozanolixizumab (UCB7665, RYSTIGGO®) is a humanized IgG4κ monoclonal antibody that binds to the neonatal Fc receptor (FcRn). On June 27, 2023, rozanolixizumab-noli was approved by the FDA for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AchR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive.[6] MG is an autoimmune disease caused primarily by autoantibodies attacking proteins located in the neuromuscular junction, which disrupts the

Table 1. Commercially sponsored monoclonal antibody therapeutics granted a first approval in any country during 2023.

INN (brand name)	Target; format	Indication first approved	Country/region of approval in 2023*
Lecanemab (Leqembi)	Amyloid beta protofibrils; Humanized IgG1κ	Early Alzheimer's disease	US, Japan
Rozanolixizumab (RYSTIGGO)	FcRn; Humanized IgG4κ	Generalized myasthenia gravis	US, Japan
Pozelimab (VEOPOZ)	Complement C5; Human IgG4κ	CHAPLE disease	US
Mirikizumab (Omvoh)	IL-23p19; Humanized IgG4κ	Ulcerative colitis	US, EU, Japan, Australia, UK, Canada, Israel
Talquetamab (Talvey)	GPCR5D, CD3; Humanized IgG4κ	Multiple myeloma	US, EU, UK, Switzerland
Elranatamab (Elrexfio)	BCMA, CD3; Humanized IgG2κ bispecific	Multiple myeloma	US, EU, Switzerland, Brazil
Epcoritamab (EPKINLY)	CD20, CD3; Humanized IgG1κ/λ bispecific	Diffuse large B-cell lymphoma	US, Japan, UK, Canada
Glofitamab (COLUMVI)	CD20, CD3e; IgG1κ/λ bispecific	Diffuse large B-cell lymphoma	US, EU, Australia, Canada, UK, China
Retifanlimab (Zynyz)	PD-1; Humanized IgG4κ	Merkel cell carcinoma	US
Concizumab (Alhemo)	Tissue factor pathway inhibitor; Humanized IgG4κ	Hemophilia A or B with inhibitors	Canada, Australia, Switzerland
Lebrikizumab (EBGLYSS)	IL-13; Humanized IgG4κ	Atopic dermatitis	EU
Tafolecimab (SINTBILO)	PCSK9; Human IgG2κ	Primary hypercholesterolemia and mixed dyslipidemia	China
Narlumosbart (Jinlitai)	RANKL; Human IgG4κ	Giant cell tumor of bone	China
Zuberitamab (Enrexib)	CD20; Chimeric IgG1κ	Diffuse large B-cell lymphoma	China
Adebrelimab (Arelili)	PD-L1; Humanized IgG4κ	Extensive-stage small cell lung cancer	China
Divozilimab (Ivlizi)	CD20; Humanized IgG1κ	Multiple sclerosis	Russia

*Subsequent approvals that occurred in 2023 in other countries are noted; the table includes information publicly available as of November 17, 2023. Abbreviations: BCMA, B cell maturation antigen; EU, European Union; GRCR5D, G protein-coupled receptor class C group 5 member D; PCSK9, proprotein convertase subtilisin/kexin type 9; PD-L1, programmed cell death protein ligand 1; RANKL, receptor activator of nuclear factor kappa-B ligand. See supplemental table S1 for more details about each antibody; updated data available at: https://www.antibodysociety.org/antibody-therapeutics-product-data/.

transmission of signals from nerves to muscles, leading to muscle weakness and fatigue. Two pivotal proteins, AchR and MuSK, are targeted by autoantibodies. By binding to FcRn, rozanolixizumab lowers total IgG levels, leading to decreased levels of AchR and MuSK autoantibodies.[7]

Rozanolixizumab was subsequently approved in Japan in September 2023 for the treatment of gMG in adult patients who inadequately respond to steroids or other immunosuppressants. On November 9, 2023, EMA's Committee for Medicinal Products (CHMP) adopted a positive opinion and recommended the granting of a marketing authorization for Rystiggo for the treatment of gMG. The European Commission's decision is normally issued 67 d from adoption of the opinion.

The approvals of rozanolixizumab were supported by data from the Phase 3 MycarinG study (NCT03971422), a multicenter, randomized, double-blind, placebo-controlled study. A total of 200 patients were randomized 1:1:1 to receive weight-tiered doses of rozanolixizumab ($n = 133$), equivalent to ≈7 mg/kg ($n = 66$) or ≈10 mg/kg ($n = 67$), or placebo ($n = 67$). The study met the primary endpoint, with a statistically significant difference favoring rozanolixizumab at day 43 in the Myasthenia Gravis Activities of Daily Living (MG-ADL) total score change from baseline (−3.4 points in rozanolixizumab-treated group at either dose vs −0.8 points in the placebo-treated group ($p < 0.001$)). The secondary endpoint, which was the change between treatment groups from baseline to day 43 in the Quantitative Myasthenia Gravis (QMG), was also met. The recommended dosage depends on the patient's body weight and is administered as a subcutaneous infusion Q1W for 6 weeks. Patients below 50 kg receive a dose of 420 mg; those between 50 kg and 100 kg are given 560 mg, while patients weighing 100 kg and above get 840 mg.[6]

Several multinational Phase 3 and Phase 2 studies are currently ongoing or recruiting patients for various autoimmune diseases, including gMG, myelin oligodendrocyte glycoprotein antibody-associated disease, leucine-rich glioma inactivated 1 autoimmune encephalitis, and severe fibromyalgia syndrome.[8]

Pozelimab (Regeneron Pharmaceuticals, Inc.)

Pozelimab (Veopox™, REGN3918) is a human IgG4κ mAb that targets complement factor 5 (C5) to help prevent diseases mediated by the complement pathway. Pozelimab was derived from Regeneron's proprietary *VelocImmune*® transgenic mouse technology. The FDA granted Rare Pediatric Disease designation to pozelimab for treatment of CD55-deficient protein-losing enteropathy (CHAPLE) and Orphan Drug for the treatment of CHAPLE and paroxysmal nocturnal hemoglobinuria (PNH). Pozelimab was also granted Fast Track designation by FDA.

On August 18, 2023, the FDA approved pozelimab-bbfg for the treatment of children (>1 y) and adults with CHAPLE disease.[9] This approval is based on the results from a Phase-2/3 open-label trial (NCT04209634) that evaluated the efficacy and safety of pozelimab in 10 patients aged 3 to 19 y (median age of 8.5 y) with CHAPLE. Patients received a single loading dose of 30 mg/kg IV pozelimab on Day 1, and then subsequent weekly weight-based doses of SC pozelimab. All patients achieved normalization of serum albumin and serum IgG concentrations within 12 weeks, and this was maintained through at least 72 weeks of treatment. Common adverse events were upper respiratory tract infection, fracture, urticaria, and alopecia, and the prescribing information for pozelimab also includes a Boxed Warning regarding the risk of serious meningococcal infections in patients treated with complement inhibitors. All patients included in the clinical trial received meningococcal vaccination prior to treatment as well as antibacterials as a prophylactic treatment.

Pozelimab is also being investigated in combination with cemdisiran, a siRNA C5 inhibitor, in development by Alnylam Pharmaceuticals, Inc. The Phase 3 study (NCT05070858) is evaluating the efficacy and safety of pozelimab and cemdisiran combination therapy in adult patients with symptomatic generalized myasthenia gravis, and the Phase 3 NCT05744921 and NCT05133531 studies are evaluating this combination in patients with PNH. Regeneron anticipates additional marketing application submissions for pozelimab with or without cemdisiran in 2025 or later.[10]

Mirikizumab (Eli Lilly and Company)

Mirikizumab (LY3074828, Omvoh®) is a humanized anti-IL-23p19 IgG4 monoclonal antibody developed as a treatment for ulcerative colitis (UC) and Crohn's disease. Several mutations were incorporated to stabilize the hinge region (S228P), reduce FcγR and C1q binding (F234A, L235A), and abrogate the heterogeneity at the C-terminal end (K447> del). UC and Crohn's disease both belong to the category of inflammatory bowel disease (IBD) characterized by recurring inflammation of the digestive tract. Targeting the p19 subunit of IL-23, mirikizumab inhibits the IL-23 pathway involved in the pathogenesis of these diseases.

On March 27, 2023, mirikizumab was approved in Japan for use as induction and maintenance therapy in patients with moderate-to-severe UC who have an inadequate response to conventional therapy or therapies. The approval establishes mirikizumab as the first IL-23p19 inhibitor for this indication.[11] On May 26, 2023, mirikizumab was approved in the EU for the treatment of adult patients with moderately to severely active UC who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic treatment. Mirikizumab was subsequently approved in Australia for moderately to severely active UC in September 2023. On October 26, 2023, mirikizumab-mrkz was approved by FDA for the treatment of moderately to severely active UC in adults.[12] Mirikizumab is administered through IV infusion (300 mg every 4 weeks) during the induction therapy and by subcutaneous injection (200 mg every 4 weeks), either via an autoinjector or a syringe, during the maintenance therapy.

The approvals were based on the results of the LUCENT clinical trials program. Mirikizumab was evaluated in three Phase 3 studies, LUCENT-1, LUCENT-2, and LUCENT-3, that included UC patients. LUCENT-1 (NCT03518086) is a multicenter, randomized, double-blind, placebo-controlled induction study with an enrollment of more than 1,100 patients with moderately-to-severely active UC, who

previously failed conventional and/or biologic therapies and/or JAK inhibitors, who were randomized 3:1 to intravenous 300 mg mirikizumab or placebo Q4W for 12 weeks. Patients ($n = 544$) who completed the 12-week LUCENT-1 induction study were re-randomized to receive mirikizumab (200 mg) subcutaneously, or placebo Q4W for an additional 40 weeks in LUCENT-2 (NCT03524092), a multicenter, randomized, double-blind, placebo-controlled maintenance study. LUCENT-3 (NCT03519945) is an open-label extension study to evaluate the long-term efficacy and safety of mirikizumab in participants with moderately to severely active UC.

For LUCENT-1 and -2, the primary outcome measures were percentage of participants with clinical remission at Week 12 and Week 40, respectively. In the LUCENT-1 study, patients treated with mirikizumab achieved significantly superior rates (45.5%, $n = 395/868$) of clinical remission (primary endpoint) compared to the rate from the patients taking placebo (27.9%, $n = 82/294$, $p < 0.001$). Results from the LUCENT-2 study showed that 63.6% ($n = 91/143$) of the patients who achieved clinical remission at 12 weeks were able to maintain clinical remission at 1 y with the treatment of mirikizumab, while the rate is only about one-third in patients receiving placebo (36.9%, $n = 24/65$, $p < 0.001$). Bowel urgency, measured using the Urgency Numeric Rating Scale (0–10), was assessed in both studies, and results showed that a significantly higher proportion of patients administered mirikizumab versus placebo achieved clinically meaningful improvement in this secondary outcome measure at Weeks 12 and 52.[13]

Mirikizumab is also being evaluated as a treatment for Crohn's disease in the Phase 3 VIVID-1 study (NCT03926130) and the long-term extension VIVID-2 study (NCT04232553). Lilly recently announced that co-primary and all major secondary endpoints were met in the VIVID-1 study, which evaluated mirikizumab vs placebo or an active control (ustekinumab) in patients with moderately to severely active Crohn's disease. Based on the study results, Lilly plans to submit a BLA for mirikizumab in Crohn's disease to FDA and submissions to other regulatory agencies in 2024.[14]

Talquetamab (Janssen Research & Development, LLC)

Talquetamab (TALVEY™, JNJ-64407564) is a humanized IgG4κ/λ bispecific T cell-engaging antibody that binds to G protein-coupled receptor class C group 5 member D (GPCR5D) as well as to CD3 on T cells. GPRC5D is highly expressed on the surface of myeloma cells, with minimal expression on B cells. OmniAb's transgenic mouse and Genmab's bispecific Duobody technologies were applied in the development of talquetamab.

On August 9, 2023, talquetamab-tgvs was granted accelerated approval by the FDA for the treatment of relapsed or refractory (RR) multiple myeloma (MM) in adult patients who have received at least four prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody.[15] Also, in August 2023, talquetamab was granted conditional marketing authorization by the European Commission as a monotherapy for the treatment of RRMM in adult patients who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody, and who have demonstrated disease progression in their last therapy.[16]

These approvals were based on the positive results from the Phase 1/2 MonumenTAL-1 study (Phase 1: NCT03399799, Phase 2: NCT04634552), which were recently presented at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting held in Chicago on June 2–6, 2023.[17] Patients in the Phase 1/2 MonumenTAL-1 study were treated with either 0.8 mg/kg SC talquetamab Q2W or 0.4 mg/kg SC talquetamab weekly (QW), and the overall response rate was similar across both doses (73.6% overall response rate (CI range: 63.0–82.4) for Q2W, 73% overall response rate (CI range: 63.2–81.4) for QW). The median duration of response (DOR) was not reached for patients on the Q2W dose, while the DOR for patients on the QW dose was 9.5 months (range: 6.7–13.3). The 12-month progression-free survival (PFS) rates were 54.4% and 34.9% for the Q2W and QW dose, respectively. There was a low discontinuation rate due to adverse events (8% for Q2W and 5% for QW), with the most common adverse events being cytokine release syndrome, dysgeusia, and skin-related adverse events. Adverse reactions leading to treatment discontinuation were mainly due to immune effector cell-associated neurotoxicity syndrome or weight loss.

Talquetamab is currently also being evaluated in combination with other therapies, such as the anti-BCMA T-cell engager teclistamab (TECVAYLI) for the treatment of RRMM (NCT04586426), teclistamab and anti-CD38 daratumumab for MM (NCT04108195), an anti-PD1 inhibitor for RRMM (NCT05338775), carfilzomib, daratumumab, lenalidomide, and pomalidomide for MM (NCT05050097), and daratumumab, pomalidomide, and dexamethasone in treatment-resistant MM (NCT05455320).

Elranatamab (Pfizer Inc.)

Elranatamab (Elrexfio™, PF-06863135) is a humanized IgG2κ bispecific T cell-engaging antibody targeting CD3 on the surface of T cells and B-cell maturation antigen (BCMA), which is highly expressed on the surface of myeloma cells.

On August 14, 2023, the FDA granted accelerated approval to elranatamab for the treatment of RRMM in adult patients who have had at least four prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.[18] Elranatamab was subsequently approved in Switzerland in September 2023. The FDA review was conducted under Project Orbis, which is a framework for concurrent submission and review of oncology drugs to potentially expedite approvals among international partners (Switzerland, Brazil, Canada, Australia, and Singapore). In December 2023, the European Commission granted conditional marketing authorization for elranatamab for the treatment of adult patients with relapsed and refractory multiple myeloma (RRMM) who have received at least three prior therapies, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.

The approvals were based on positive results from the Phase 2 MagnetisMM-3 trial (NCT04649359), in which patients were

given two priming doses of 12 mg and 32 mg SC elranatamab during the first week of treatment, and then subsequently dosed with 76 mg SC elranatamab weekly. This study included a total of 123 patients who had failed to respond to at least three prior lines of therapy. Sixty-one percent (95% CI: 51.8–69.6%) of these patients had a confirmed objective response after a median follow-up of 14.7 months, with 35% of patients achieving a complete response or better.[19] After six cycles, patients who had a partial response or better lasting at least 2 months switched to a Q2W dosing interval instead of weekly. Of the patients who switched to Q2W dosing, 80% of patients still maintained response at least 6 months after the switch. The most common adverse effects were cytokine release syndrome, hematologic-related events, and infections.

The full approval of elranatamab by the FDA is dependent on positive data from the confirmatory Phase 3 study (MagnetisMM-5) which is designed to test elranatamab alone and as a combination therapy with daratumumab for the treatment of RRMM compared to the standard treatment combination of daratumumab, pomalidomide, and dexamethasone (NCT05020236). The study is expected to include up to 854 adults with RRMM and is anticipated to have a primary completion date in August 2026.

Epcoritamab (Genmab, AbbVie)

Epcoritamab (GEN3013, EPKINLY™) is an IgG1k/λ T-cell engager targeting CD20 and CD3. Jointly owned by Genmab and AbbVie, it was developed using Genmab's DuoBody® platform. This method exploits controlled Fab-arm exchange, which involves the production, purification, and recombination of two IgG1 antibodies, each containing a single matched point mutation (K409R; F405L) in the third constant region (CH3). The mutations are selected to weaken the non-covalent CH3–CH3 interaction in the parental IgG1 mAbs and ensure a unidirectional process for the dissociation of heavy-light (HL) chain homodimers and the formation of a strongly favored heterodimeric HL interaction.[20] On May 19, 2023, FDA granted accelerated approval to epcoritamab-bysp for the treatment of adult patients with RR diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL from indolent lymphoma, and high-grade B-cell lymphoma after two or more lines of systemic therapy.

The effectiveness of epcoritamab was evaluated in EPCORE NHL-1 (NCT03625037), an open-label, multi-cohort, multicenter, single-arm trial in patients with CD20+ DLBCL. The overall response and complete response (CR) rates were 61% (95% CI, 53–69) and 38%, respectively, and the estimated median duration of response was 15.6 months in heavily pretreated RR DLBCL patients. Epcoritamab is administered through subcutaneous injections in 28-d cycles until disease progression or unacceptable toxicity. The prescribing information comes with a Boxed Warning for serious or life-threatening cytokine release syndrome and life-threatening or fatal immune effector cell-associated neurotoxicity syndrome.[21,22]

Epcoritamab is currently under evaluation by AbbVie and Genmab in an ongoing Phase 3 trial (NCT04628494) as a monotherapy in patients with RR DLBCL. The companies are also evaluating EPKINLY combination regimens in two Phase 3 trials in patients with newly diagnosed DLBCL (NCT05660967) and RR follicular lymphoma (FL) (NCT05409066). Commercial responsibilities of EPKINLY in the US and Japan will be shared by AbbVie and Genmab. AbbVie is also responsible for further global commercialization.[21]

Glofitamab (Hoffmann-La Roche)

Glofitamab (RO7082859, CD20-TCB, RG6026, COLUMVI™) is a full-length IgG1κ/λ bispecific monoclonal antibody that simultaneously binds to CD20 on malignant B cells and CD3 on T cells. Developed by Roche, glofitamab was engineered to have a 2:1 structure using the CrossMab technology, in which bivalent binding to CD20 is achieved by fusing a second CD20 arm to the CD3ε binding arm via a flexible linker. Glofitamab also possesses PG LALA mutations in the Fc region to eliminate binding to FcγRs and C1q. On March 25, 2023, Glofitamab received its first approval (with conditions) in Canada for the treatment of adult patients with RR DLBCL not otherwise specified, DLBCL arising from FL, or primary mediastinal B-cell lymphoma, who have received two or more lines of systemic therapy and are ineligible to receive or cannot receive CAR T-cell therapy or have previously received CAR T-cell therapy.[23] It was subsequently granted accelerated approval by the FDA on June 15, 2023, conditional marketing authorization by EMA on July 7, 2023,[24,25] as well as approvals in other countries (Table 1).

The approval was based on the positive results from the Phase 1/2 NP30179 study (NCT03075696), an open-label, multicenter, single-arm trial that included 132 patients with RR DLBCL after two or more lines of systemic therapy. The overall response rate for the patients treated with fixed-duration glofitamab was 56% (95% CI, 47–65) and 43% achieved complete responses. The median time to first response was 42 d. The estimated median duration of response was 18.4 months. Following a single dose of anti-CD20 obinutuzumab (1,000 mg) on Cycle 1 Day 1, glofitamab is administered to patients by intravenous infusions for a maximum of 12 cycles (2.5 mg on Day 8, 10 mg on Day 15 of Cycle 1; and 30 mg on Day 1 of each subsequent 21-d cycle). The most common adverse events among patients who received glofitamab in the study were cytokine release syndrome (70%).[24]

A Phase 3 study (STARGLO, NCT04408638) evaluating the efficacy and safety of glofitamab in combination with gemcitabine + oxaliplatin (GemOx) versus rituximab in combination with GemOx in patients with relapsed/refractory DLBCL is ongoing. The study's estimated primary completion date is in April 2025.

Retifanlimab (Incyte Corporation, Macrogenics, Zai Lab)

Retifanlimab (INCMGA00012, MGA012, ZL-1306, ZYNYZ™) is a humanized IgG4κ monoclonal antibody that binds to the PD-1 receptor and blocks interaction with its ligands. On

March 22, 2023, the FDA granted accelerated approval to retifanlimab-dlwr for adult patients with metastatic or recurrent locally advanced Merkel cell carcinoma (MCC).

The approval was based on the efficacy evaluation from the POD1UM–201 study (NCT03599713), an open-label, single-arm study in patients with metastatic or recurrent locally advanced MCC who had not received prior systemic therapy for their advanced disease. The primary endpoint was objective response rate (ORR) as determined by independent central review (ICR) using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. Among chemotherapy-naïve patients ($n = 65$) who received retifanlimab monotherapy, the ORR was 52% (95% CI, 40–65). Twelve patients (18%) showed complete response, while partial response was observed in 22 patients (34%). Twenty-six (76%) of the responding patients had a duration of response (DOR) of 6 months or longer, and 21 experienced a DOR of 12 months or longer. The recommended dosage of retifanlimab is 500 mg administered as an intravenous infusion over 30-min Q4W until disease progression, unacceptable toxicity, or up to 24 months. The most common (≥10%) adverse reactions are fatigue, musculoskeletal pain, pruritus, diarrhea, rash, pyrexia, and nausea.[26,27]

Multiple ongoing clinical trials are evaluating retifanlimab as a treatment for various cancer types, including non-small cell lung cancer (NSCLC), penile squamous cell cancer, and pancreatic or ampullary adenosquamous carcinoma. Additionally, retifanlimab is being investigated in combination with various other treatments, such as pemigatinib, palbociclib, and pelareorep, for different malignancies.[28]

Concizumab (Novo Nordisk)

Concizumab (NNC172–2021, NN7415, Alhemo™) is a humanized, hinge-stabilized (S228P mutation) IgG4κ monoclonal antibody that selectively binds to the Kunitz-2 domain of the tissue factor pathway inhibitor (TFPI). By binding to TFPI, concizumab decreases its inhibitory activity on the activated Factor X (Factor Xa), an essential component of the extrinsic coagulation cascade, and improves the efficiency of blood clot formation. On March 10, 2023, concizumab received its first approval in Canada for the treatment of adolescent and adult patients (12 y of age or older) with hemophilia B who have Factor IX inhibitors and require routine prophylaxis to prevent or reduce the frequency of bleeding episodes. Concizumab was subsequently approved in Australia and Switzerland in July and August 2023, respectively. Marketing applications for concizumab are undergoing regulatory review in the EU, US, and Japan.[29] In April 2023, Novo Nordisk announced that they received a complete response letter from the FDA requesting additional information related to the monitoring and dosing of patients and the manufacturing process.[30]

Concizumab is administered subcutaneously once daily using a single-patient-use prefilled multi-dose pen. The recommended dosing regimen of concizumab includes a loading dose of 1 mg/kg on day 1, followed by a once-daily dose of 0.20 mg/kg on day 2 and subsequent days until individual maintenance dose setting. The maintenance dose is determined based on the concizumab pre-dose plasma concentration measured at 4 weeks after starting treatment.

The efficacy and safety of concizumab were evaluated in the Phase 3 explorer7 trial (NCT04083781). A total of 133 patients were enrolled, with 52 randomized to receive on-demand therapy with bypassing agents (arm 1) or concizumab prophylaxis (arm 2). A further 81 nonrandomized patients received concizumab to assess the overall safety. The study was paused due to the occurrence of thromboembolic events associated with concizumab treatment and later resumed with an adjusted dosing regimen. The efficacy results obtained after the study pause showed that an 86% reduction in treated spontaneous and traumatic bleeds was achieved in patients who received concizumab, compared with those who received on-demand treatment with bypassing agents. In the concizumab prophylaxis arm ($n = 33$), the estimated mean annualized bleeding rate (primary endpoint) was lower at 1.7 (95% CI, 1.01–2.87) compared to 11.8 (95% CI, 7.03–19.86) in the on-demand treatment arm ($n = 19$).[1]

Concizumab is also undergoing evaluation in two Phase 3 trials, explorer8 (NCT04082429) in male adolescents and adults aged ≥12 y with hemophilia A and B without inhibitors and explorer10 (NCT05135559) in male children aged <12 y with hemophilia A and B and male patients of any age with hemophilia A and B with and without inhibitors.[29]

Lebrikizumab (Almirall S.A., Eli Lilly and Company)

Lebrikizumab (Ebglyss) is a humanized, hinge-stabilized (S228P mutation) IgG4κ antibody that targets IL-13, a key mediator of the pro-inflammatory response and enhances neuronal responses to the persistent itch stimuli in atopic dermatitis. Lebrikizumab was originally developed by F. Hoffmann-La Roche Ltd and Genentech, Inc., a member of the Roche Group. In 2017, the exclusive, worldwide rights to lebrikizumab were obtained by Dermira (acquired by Eli Lilly in 2020) to develop and commercialize it for atopic dermatitis and all other indications. Roche retained certain rights, including the exclusive rights for the development and promotion of lebrikizumab for interstitial lung diseases. The exclusive rights to develop and commercialize lebrikizumab in Europe for certain indications including atopic dermatitis were acquired by Almirall in 2019.

On November 16, 2023, the European Commission approved lebrikizumab for the treatment of adult and adolescent patients (12 y and older with a body weight of at least 40 kg) with moderate-to-severe atopic dermatitis (AD), who are candidates for systemic therapy.[31] Lilly submitted a BLA for lebrikizumab, the treatment for atopic dermatitis to the FDA in the third quarter of 2022. FDA subsequently issued a complete response letter citing deficits that Lilly plans to address.

The approval in the EU was based on results from three phase 3 trials evaluating the safety and efficacy of lebrikizumab in adults and adolescents >12 y of age with atopic dermatitis. Advocate 1 (NCT04146363) and Advocate 2 (NCT04178967) are randomized, double-blind, placebo-controlled, parallel-group studies in which patients with moderate-to-severe atopic dermatitis received either an initial dose of 500 mg of

lebrikizumab followed by 250 mg lebrikizumab Q2W or placebo for a 16-week treatment period. Following the 16 weeks, patients who received a clinical response to lebrikizumab were re-randomized to receive lebrikizumab Q2W or Q4W, or placebo, for another 36 weeks. The primary endpoints were an Investigator Global Assessment (IGA) score of clear or almost clear (0 or 1, respectively) skin with reduction of at least two points from baseline and at and least 75% reduction in the Eczema Area and Severity Index (EASI-75) score. Both Advocate 1 and Advocate 2 met their primary endpoints, with the IGA outcome being achieved in 43.1% of the lebrikizumab cohort ($n = 283$) compared to 12.7% in placebo cohort ($n = 141$) for Advocate 1 and 33.2% of the lebrikizumab cohort ($n = 281$) compared to 10.8% in the placebo cohort ($n = 146$) for Advocate 2.[32] The third Phase 3 study, Adhere (NCT04250337), is a 16-week randomized, double-blind, parallel-group study which investigated the efficacy of lebrikizumab in combination with topical corticosteroids in 211 patients with AD. Patients were randomized 2:1 to receive either 250 mg SC lebrikizumab Q2W after an initial loading dose of 500 mg, or placebo, in combination with topical steroids, either mid-potency (0.1% triamcinolone acetonide cream) or low-potency (1% hydrocortisone cream). After 16 weeks, IGA of 0 or 1 with a 2 or more-point reduction from baseline was achieved by 41.2% of the lebrikizumab cohort compared to 22.1% of the placebo cohort, with statistical significance being reached as early as 8 weeks.[33] There was also a significantly greater proportion of patients achieving EASI-75 responses.

Tafolecimab (Innovent Biologics, Inc.)

Tafolecimab (SINTBILO®) is a human IgG2κ antibody targeting the proprotein convertase subtilisin/kexin type 9 (PCSK9). In August 2023, Innovent Biologics, Inc. announced that NMPA approved tafolecimab for the treatment of primary hypercholesterolemia and mixed dyslipidemia in adult patients.[34] The approved dosing regimens of SINTBILO® include 150 mg Q2W, 450 mg Q4W, and 600 mg Q6W, all of which were shown in Phase 3 studies to be effective in reducing low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), non-high-density lipoprotein cholesterol (non-HDL-C), apolipoprotein B (ApoB), and lipoprotein a (Lp(a)).

NMPA's approval is based on the results of three placebo-controlled Phase 3 clinical studies, CREDIT-1 (NCT04289285), CREDIT-2 (NCT04179669), and CREDIT-4 (NCT04709536). The CREDIT-1 and CREDIT-2 studies assessed the efficacy and safety of tafolecimab in Chinese subjects with non-familial hypercholesterolemia and heterozygous familial hypercholesterolemia, respectively. The CREDIT-4 study included patients with either type of hypercholesterolemia. Patients who received tafolecimab were subcutaneously administered either 450 mg Q4W or 600 mg Q6W for 48 weeks (CREDIT-1), 150 mg Q2W or 450 mg Q4W for 24 weeks (CREDIT-2), or 450 mg Q4W for 12 weeks (CREDIT-4); in each study tafolecimab showed a favorable safety profile and significant lipid-lowering efficacy in patients who received the drug vs. placebo.[35–37]

Narlumosbart (CSPC Pharmaceutical Group Limited)

Narlumosbart (Jinlitai, 津立泰) is a human IgG4κ mAb targeting receptor activator of nuclear factor-κB ligand (RANK-L) developed by Shanghai JMT-BioTechnology Co., Ltd., a subsidiary of CSPC Pharmaceutical Group Limited. In September 2023, CSPC announced that NMPA approved narlumosbart for the treatment of giant cell tumor of bone (GCTB) that is unresectable or where surgical resection is likely to result in severe morbidity.[38]

NMPA's approval of narlumosbart was based on data from two clinical studies, the single-arm, open-label pivotal Phase 2 JMT103CN03 study (NCT04255576), and the observational JMT103CN03-1 Real-World Study (NCT05402865). The Phase 2 study enrolled 139 participants, and eligible patients received 2 mg/kg narlumosbart administrated subcutaneously every 4 weeks with a loading dose on Days 8 and Day 15 of the first 4 weeks of therapy. The observational study, which served as the control arm for the pivotal Phase 2 study, evaluated the efficacy and safety of anti-RANK-L denosumab and non-denosumab therapies in the treatment of Chinese populations of surgically unsalvageable or severe post-surgery morbidity associated with GCTB. The results of the studies showed better clinical efficacy in patients who received narlumosbart, with a tumor response rate of 93.5% and a trend higher than that of the denosumab group.[38]

Narlumosbart is also being evaluated in a multi-center, randomized, double-blind, active-controlled study Phase 3 study (NCT05813665, CTR20231025) in an estimated 146 patients with unresectable or surgically difficult GCTB. Patients will receive narlumosbart 120 mg or denosumab 120 mg SC Q4W. The primary outcome measure of the study is the percentage of patients with tumor response.

The efficacy and safety of narlumosbart is currently also being assessed in osteoporosis in a randomized placebo/positive-controlled Phase 2 study (NCT05278338) that is enrolling an estimated 200 postmenopausal women with osteoporosis. Participants will be randomized to receive either 60 or 90 mg narlumosbart, 60 mg denosumab, or placebo. All therapeutic interventions will be administered as a single SC injection at the beginning of the treatment phase and 6 months following the initial dose. The primary endpoint is the change rate of lumbar bone mineral density from baseline at 12 months of treatment. The estimated primary completion date is in December 2023.

Zuberitamab (BioRay Pharmaceutical Co., Ltd.)

Zuberitamab (HS006, 安瑞昔®) is a human-mouse chimeric IgG1κ anti-CD20 monoclonal antibody that kills B cells via antibody-dependent cell-mediated cytotoxicity (ADCC) and complement-mediated cytotoxicity. On May 12, 2023, zuberitamab was approved by China's NMPA for the treatment of CD20-positive DLBCL, which is one of the most common types of non-Hodgkin lymphoma (NHL) in adults.[39] In China, DLBCL is estimated to represent around 40% of all cases of NHL.

NMPA's approval was based on the results from a Phase 3 study conducted by BioRay. In this multi-center, randomized,

non-inferiority trial (REFLECT) in China, 487 patients were enrolled and treated with six cycles of either zuberitamab + CHOP or rituximab + CHOP. The results showed that individuals who received the treatment of zuberitamab + CHOP exhibited a higher CR rate compared to those in the rituximab + CHOP group (85.66% vs 77.34%, $P = 0.0378$). Additionally, the zuberitamab group also showed superior PFS rate (3-y PFS rate 78.03% vs 70.90%) and overall survival (OS) rate (3-y OS rate 87.70% vs 83.14%) over the rituximab group. Particularly, for patients with the germinal center B-cell subtype, the zuberitamab demonstrated significantly better CR rates, event-free survival rates, and OS rates compared to those in the rituximab group. Furthermore, the safety profile of the patients receiving zuberitamab did not significantly differ from that of the rituximab group.[40]

Adebrelimab (Jiangsu Hengrui Medicine Co., Ltd.)

Adebrelimab (Arelili®) is a humanized anti-PD-L1 IgG4κ antibody developed by Jiangsu Hengrui Medicine Co. Ltd. In March 2023, the company announced that the NMPA approved adebrelimab in combination with chemotherapy as a first-line treatment for extensive-stage small cell lung cancer (SCLC).[41]

NMPA's approval of adebrelimab for marketing is based on results from the placebo-controlled Phase 3 CAPSTONE-1 study (NCT03711305) conducted in 47 study sites in China. Eligible SCLC patients ($n = 462$) were randomly assigned (1:1) to receive four to six cycles of carboplatin and etoposide with either adebrelimab (20 mg/kg, day 1 of each cycle) or matching placebo, followed by maintenance therapy with adebrelimab or placebo. The study showed that, compared with the placebo combined with chemotherapy, adebrelimab combined with chemotherapy significantly improved the OS of patients (median 15.3 months (95% CI 13.2–17.5) vs 12.8 months (11.3–13.7)).[42] The OS rate was 62.9% vs 52.0% at 12 months and 31.3% vs 17.2% at 24 months. PFS per independent review committee (IRC) was 5.8 months (95% CI 5.6–6.9) with adebrelimab + chemo vs 5.6 months (95% CI 5.5–5.7) with placebo + chemo (HR 0.67, 95% CI 0.54–0.83); PFS rate was 49.4% vs 37.3% at 6 months and 19.7% vs 5.9% at 12 months.

Adebrelimab is being evaluated in additional Phase 3 studies in lung cancer, in combination with chemo-radiotherapy in SCLC patients (NCT04691063); in combination with chemotherapy as perioperative treatment of resectable Stage II or III NSCLC (NCT04316364), as well as in early-stage clinical studies of patients with other solid tumors.

Divozilimab (BIOCAD)

Divozilimab (BCD-132, Ivlizi®) is an afucosylated, humanized anti-CD20 IgG1κ monoclonal antibody developed by BIOCAD. The Ministry of Health of the Russian Federation approved divozilimab for the treatment of multiple sclerosis in March 2023. Multiple sclerosis is an autoimmune disorder in which the immune system attacks the myelin sheath and disrupts the normal transmission of nerve signals. Divozilimab binds CD20 receptors on B cells and leads to the depletion of these cells. With the reduced number of B cells, the inflammatory process can be dampened, potentially slowing down the progression of the disease and decreasing the frequency and severity of relapses.[43]

Divozilimab is administered intravenously once every 6 months. The efficacy and safety of divozilimab in the treatment of patients with relapsing multiple sclerosis was evaluated in the Phase 3 MIRANTIBUS study (NCT05385744) using an active reference drug (teriflunomide). To evaluate the long-term efficacy and safety, patients from Phase 2 and Phase 3 studies continue to receive divozilimab in an extended Phase 3 and the EXTENSION study.[43] BIOCAD is also evaluating divozilimab in the treatment of systemic sclerosis (scleroderma) and neuromyelitis optica spectrum disorders in two Phase 3 studies (NCT05726630 and NCT05730699, respectively).

Antibody therapeutics undergoing first regulatory review

As of November 1, 2023, marketing applications for 26 investigational (i.e., not approved for marketing in any country) antibody therapeutics are undergoing review by at least one regulatory agency (Table 2). Of these molecules, applications for 16 are undergoing review solely in China, while 10 are undergoing review in either the US or EU. Antibodies intended as treatments for non-cancer indications slightly outnumber those for cancer (14 vs. 12, respectively). Relevant details for these molecules are summarized below, in the order they appear in Table 2.

Donanemab (Eli Lilly and Company)

Donanemab (LY3002813) is a humanized IgG1κ monoclonal antibody that targets Aβ (p3–42), a pyroglutamate form of amyloid beta that is aggregated in amyloid plaques. Donanemab was granted Breakthrough Therapy designation by FDA for the treatment of Alzheimer's disease (AD). In October 2021, Eli Lilly announced that they initiated rolling submission of a biologics license application for the accelerated approval of donanemab for the treatment of early symptomatic AD. In January 2023, the FDA issued a complete response letter due to the limited number of patients with at least 12 months of drug exposure that were included in the Phase 2 TRAILBLAZER-ALZ clinical study (NCT03367403) on which the application was based.[44] In the second quarter of 2023, based on Phase 3 clinical study data, Eli Lilly submitted BLA for traditional approval, with FDA action expected by the end of the year.[45] In mid-August 2023, EMA began evaluation of a marketing authorization application (MAA) for donanemab.

In July 2023, results were published from the landmark Phase 3 trial, TRAILBLAZER-ALZ 2 (NCT04437511), in which 1736 patients with early symptomatic AD with amyloid and low/medium or high tau pathology were randomized 1:1 to receive IV donanemab ($n = 860$) or placebo ($n = 874$) Q4W for 72 weeks.[46] The primary outcome of this study was a change in the Integrated Alzheimer's Disease Rating Scale (iADRS) from baseline to 76 weeks. This study demonstrated that donanemab significantly slowed cognitive and functional

Table 2. Commercially sponsored investigational monoclonal antibody therapeutics with marketing applications in regulatory review in any country.

INN or drug code	Target; format	Indication under review	Country/region of review
Donanemab	Amyloid β; Humanized IgG1κ	Early Alzheimer's disease	US, EU, Japan
Crovalimab	Complement C5; Humanized IgG1κ	Paroxysmal nocturnal hemoglobinuria	US, EU, Japan, China
Vilobelimab	Complement C5a; Chimeric IgG4κ	SARS-CoV-2 induced septic acute respiratory distress syndrome	EU
Marstacimab	TF pathway inhibitor; Human IgG1λ	Hemophilia	EU
Garadacimab	Factor XIIa; Human IgG4λ	Hereditary angioedema	EU
Narsoplimab	MASP-2; Human IgG4λ	Hematopoietic stem cell transplant-associated thrombotic microangiopathy	US
Cosibelimab	PD-L1; Human IgG1λ	Squamous cell carcinoma	US
Zolbetuximab	Claudin 18.2; Chimeric IgG1κ	HER2-negative gastric or gastroesophageal junction adenocarcinoma	US, EU, Japan, China
Odronextamab	CD20, CD3; Human IgG4κ bispecific	Diffuse large B-cell lymphoma	US, EU
Trastuzumab duocarmazine	HER2; Humanized IgG1κ ADC	HER2+ breast cancer	US
Suciraslimab	CD22; Chimeric IgG1κ	Rheumatoid arthritis	China
Batoclimab	FcRn; Human IgG1λ	Generalized myasthenia gravis	China
Ebdarokimab	IL-12/23p40; Humanized IgG1κ	Psoriasis	China
Xeligekimab	IL-17A; Human IgG4κ	Psoriasis	China
Vunakizumab	IL-17A; Humanized IgG1κ	Psoriasis	China
Ebronucimab	PCSK9; Human IgG1λ	Primary hypercholesterolemia and mixed hyperlipidemia, heterozygous familial hypercholesterolemia	China
Recaticimab	PCSK9; Humanized IgG1κ	Hypercholesterolemia	China
Ongericimab	PCSK9; Humanized IgG4κ	Hypercholesterolemia	China
Trastuzumab botidotin	HER2; Humanized IgG1κ ADC	HER2+ breast cancer	China
Enlonstobart	PD-1; Human IgG4κ	Cervical cancer	China
Iparomlimab	PD-1; Humanized/chimeric IgG4κ	Cancer	China
Iparomlimab, Tuvonralimab	PD-1, CTLA-4; mixture	Cancer	China
Ivonescimab	PD-1, VEGF-A; IgG1κ-[scFv]2 bispecific	Lung cancer	China
Socazolimab	PD-L1; Human IgG1λ	Cervical cancer	China
Benmelstobart	PD-L1; Humanized IgG1κ	Small cell lung cancer	China
Tagitanlimab	PD-L1; Humanized IgG1κ	Nasopharyngeal cancer, solid tumor indications	China

The table includes information found in the public domain as of December 8, 2023. Abbreviations: ADC, antibody–drug conjugate; HER2, human epidermal growth factor receptor 2; IL, interleukin; MASP, mannan-binding lectin-associated serine protease; PD-1, programmed cell death protein 1. See supplemental table S2 for more details about each antibody; updated data available at: https://www.antibodysociety.org/antibody-therapeutics-product-data/.

decline by 22% based on iADRS, with specific subgroups of patients having a greater response, i.e., in patients with low-medium levels of tau ($n = 1182$), donanemab treatment slowed decline by 35% on iADRS.

Donanemab also met all the primary and secondary endpoints for the six-month primary outcome analysis for the Phase 3 TRAILBLAZER-ALZ 4 study (NCT05108922). This study is the first active comparator study that compares the efficacy of donanemab to anti-amyloid beta aducanumab in early, symptomatic AD.[47] In the six-month analysis, brain amyloid clearance was achieved in 37.9% of patients treated with donanemab compared with 1.6% of patients treated with aducanumab. This study is ongoing and will have further analyses at 12 months and at 18 months.

Crovalimab (Chugai Pharmaceuticals, Genentech, F. Hoffmann-La Roche Ltd.)

Crovalimab (SKY59, RG6107, RO7112689), a complement C5 inhibiting, humanized IgG1κ antibody without effector functions that was engineered (M428L/N434A) to have enhanced affinity to FcRn at an acidic pH to extend its plasma half-life, was developed by Chugai Pharmaceuticals as a treatment for PNH. Based on Chugai's Recycling Antibody® technology, crovalimab is engineered to bind its antigen repeatedly, enabling sustained complement inhibition at a low dose administered subcutaneously (SC) Q4W. Moreover, crovalimab binds a different epitope of C5 compared to existing antibody drugs, suggesting that it represents an alternative option for patients with PNH with a specific C5 gene mutation. Roche is responsible for the development of crovalimab outside of Japan and Taiwan.

Crovalimab was granted Breakthrough Therapy for PNH by NMPA in July 2021. In August 2022, Chugai announced that the NMPA accepted a marketing application for crovalimab for PNH. This submission to NMPA, which included data from the China-specific Phase 3 COMMODORE 3 study (NCT04654468), was accepted under Priority Review. Based on the results of the Phase 3 COMMODORE 1 (NCT04432584) and 2 (NCT04434092) studies, Genentech and Chugai have filed marketing applications in the US, EU, China, and Japan.[48]

COMMODORE 3 was a multicenter single-arm trial studying crovalimab in C5 inhibitor-naive patients with PNH in China. Patients ($n = 51$) received crovalimab according to a weight-based dosing schedule, including loading (intravenous dose on Days 1 and 4, weekly subcutaneous doses starting from Day 2) and subcutaneous maintenance doses (every 4 weeks starting from Week 5); treatment continued after 24 weeks in patients with clinical

benefit. The co-primary efficacy endpoints of hemolysis control and transfusion avoidance (TA) were met. The mean proportion of participants with hemolysis control from Week 5 through to Week 25 was 78.7% (95% CI: 67.8%, 86.6%). The difference between the proportion of participants with TA within 24 weeks prior to screening (0.0%) and the proportion of participants with TA from baseline through to Week 25 (51.0%) was statistically significant ($p < 0.0001$).[49]

The global Phase 3 COMMODORE 1 (NCT04432584) and 2 (NCT04434092) studies assessed the efficacy and safety of crovalimab versus eculizumab in participants with PNH that are C5 inhibitor-experienced patients or not previously treated with complement inhibitors, respectively. COMMODORE 1 assessed safety, pharmacokinetics (PK), pharmacodynamics (PD), and exploratory efficacy of crovalimab. Data from the study support the favorable benefit – risk profile of crovalimab, including allowing for SC administration with the option to self-administer.[50] Data from the COMMODORE 2 study presented at European Hematology Association (EHA) meeting in June 2023 in Frankfurt, Germany, demonstrated that SC crovalimab Q4W was non-inferior in disease control to IV eculizumab Q2W with comparable safety for patients who have not been treated with C5 inhibitors.[51]

Vilobelimab (InflaRx N.V.)

Vilobelimab (Gohibic) is a chimeric IgG4κ antibody targeting complement C5a developed by InflaRx N.V. as a treatment for diseases mediated by the complement pathway. FDA has granted InflaRx Fast Track and Orphan Drug designations, and EMA has granted Orphan Drug designation, for vilobelimab for the treatment of ulcerative pyoderma gangrenosum.

In April 2023, FDA issued an EUA for the use of Gohibic (vilobelimab) injection for the treatment of COVID-19 in hospitalized adults when initiated within 48 h of receiving invasive mechanical ventilation or extracorporeal membrane oxygenation (artificial life support).[52] The EUA was granted based on results from the Phase 3 PANAMO (NCT04333420) clinical trial of critically ill, mechanically ventilated COVID-19 patients in which Gohibic treatment reduced mortality by 23.9% vs. placebo.[53] For this indication, vilobelimab is administered as an IV infusion over 30–60 min in up to 6 doses of 800 mg Gohibic over the course of 22 d.

On August 30, 2023, InflaRx N.V. announced an MAA for vilobelimab for the treatment of adult patients with SARS-CoV -2-induced septic acute respiratory distress syndrome (ARDS) receiving invasive mechanical ventilation or extracorporeal membrane oxygenation was submitted to and validated by EMA. The MAA submission is based on the results of the Phase 3 PANAMO trial.[54]

Vilobelimab is also being evaluated in a Phase 3 study (NCT05964413) as a treatment for pyoderma gangrenosum. The study started in August 2023 and has an expected enrollment of 90 patients and estimated primary completion date in February 2026.

Marstacimab (Pfizer, Inc.)

Marstacimab (PF-06741086) is a human IgG1λ antibody targeting the Kunitz 2 domain of tissue factor pathway inhibitor, which is a single-chain polypeptide that can reversibly inhibit Factor Xa and thereby prevent the formation of blood clots. Pfizer is developing marstacimab as a prophylactic to prevent or reduce the frequency of bleeding in people with hemophilia. FDA granted Fast Track designation to marstacimab for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in hemophilia A with inhibitors or hemophilia B with inhibitors and Orphan Drug designation for the treatment of hemophilia A and hemophilia B patients with or without inhibitors. EMA granted Orphan Drug designation to marstacimab for treatment of hemophilia. In August 2023, Pfizer announced that they plan to discuss Phase 3 clinical trial data with regulatory authorities, with the goal of initiating regulatory filings in the coming months.[55] EMA's CHMP started evaluation of a marketing application for marstacimab as an antihemorrhagic agent on October 26, 2023.[56]

The open-label Phase 3 BASIS study (NCT03938792) is evaluating annualized bleed rate (ABR) through 12 months on treatment with marstacimab in ~145 participants (12 to <75 y) with severe hemophilia A (defined as FVIII < 1%) or moderately severe to severe hemophilia B (defined as FIX activity ≤2%), with or without inhibitors. This study compares results from the patients' prescribed factor replacement (FVIII or FIX) therapy or bypass therapy during a 6-month Observational Phase with those from a 12-month Active Treatment Phase, during which participants receive prophylaxis (a 300 mg SC loading dose of marstacimab, followed by 150 mg SC once weekly) with potential for dose escalation to 300 mg once weekly. In May 2023, Pfizer announced that the study met its primary endpoints, showing that administration of marstacimab resulted in a statistically significant and clinically relevant reduction in the ABR. In the patient group treated with on-demand factor replacement therapy in the Observational Phase, marstacimab demonstrated superiority ($P < 0.0001$; 92% reduction in bleeds). The results also showed superiority ($p = 0.0376$; 35% reduction in ABR) with marstacimab compared to prophylaxis.[57]

Garadacimab (CSL Ltd.)

Garadacimab (CSL312) is a hinge-stabilized (S228P mutation) human IgG4λ antibody targeting Factor XIIa for the treatment of hereditary angioedema, a rare autosomal dominant disorder characterized by potentially life-threatening, recurrent episodes of severe swelling. Factor XIIa is a key initiator of the plasma kallikrein-kinin system which can lead to increased vascular permeability, vasodilation, chemotaxis, and subsequent extravasation of fluids into interstitial tissues. Garadacimab has been granted Orphan Drug designations for hereditary angioedema by both the FDA and EMA. EMA's CHMP started the evaluation of an MAA for garadacimab on November 23, 2023. CSL aims to launch garadacimab in fiscal year 2024.[58]

The safety and efficacy of garadacimab were evaluated in the randomized, double-blind Phase 3 VANGUARD trial (NCT04656418) which included 65 eligible patients with type I or type II hereditary angioedema. Patients were randomized 3:2 to receive a 400 mg SC loading dose of garacidimab, followed by monthly doses of 200 mg SC garacidimab, or placebo. The study met its primary and secondary efficacy objectives and also demonstrated favorable safety and tolerability.[59] The estimated median time to first angioedema attack was 11 d in the placebo group, whereas the majority of patients in the garacidimab group did not have any attacks in the 6-month treatment period. Long-term safety and efficacy data is also being investigated in the open-label extension study (NCT04739059).

Narsoplimab (Omeros Corporation)

Narsoplimab (OMS721) is a human IgG4λ hinge-stabilized (S228P mutation) monoclonal antibody that targets mannan-binding lectin-associated serine protease-2 (MASP-2), which is part of the lectin pathway of the complement system. Narsoplimab is being developed by Omeros Corporation for hematopoietic stem cell transplant-associated thrombotic microangiopathy (TA-TMA). Narsoplimab has been granted Breakthrough Therapy designation and Orphan Drug designation by the FDA for the treatment of TA-TMA, the prevention of complement-mediated TMAs, and the treatment of IgA nephropathy. The FDA has also granted narsoplimab Fast Track designation for the treatment of atypical hemolytic uremic syndrome (aHUS). It has also been granted Orphan Medicinal Product designation for IgA nephropathy and TA-TMA by EMA.

The FDA granted priority review to a BLA for narsoplimab for the treatment of TA-TMA in January 2021, then in October 2021, the agency issued a complete response letter that requested additional information to support regulatory approval. Omeros submitted a Formal Dispute Resolution request to the FDA in June 2022. The request was denied, but FDA proposed a path forward for the resubmission of the BLA based on the data from the completed pivotal trial versus a historical control group, i.e., comparing the existing response data from the trial to a threshold defined from an independent literature analysis. As of November 2023, Omeros expects a BLA resubmission that includes additional information supporting approval.[60]

The results were reported for patients ($n = 15$) who received narsoplimab via Omeros' compassionate use program. Narsoplimab was IV administered at a dose of 4 mg/kg, with a maximum dose of 370 mg, twice weekly for at least eight doses. Eleven patients responded to treatment (73%), based on the achievement of transfusion independence (10 patients) and clinical and laboratory improvement, which occurred in all responders. One-hundred-day survival was 80% in the study population and 100% for responders.[61]

Cosibelimab (Checkpoint therapeutics, Inc.)

Cosibelimab (CK-301) is a human anti-PD-L1 IgG1λ antibody discovered at the Dana-Farber Cancer Institute and licensed by Checkpoint Therapeutics, Inc. in 2015. In January 2023, Checkpoint Therapeutics announced that they had submitted a BLA to the FDA for the approval of cosibelimab for the treatment of patients with metastatic cutaneous squamous cell carcinoma (cSCC) or locally advanced cSCC. The goal date for a first action by FDA is January 3, 2024.[62]

The BLA includes results from a registration-enabling Phase 1 trial (NCT03212404) that evaluated the efficacy and safety of fixed doses of cosibelimab administered as either 800 mg Q2W or 1200 mg Q3W, in patients with select recurrent or metastatic cancers, including metastatic or locally advanced cSCC. The primary endpoint was ORR by independent central review using RECIST V.1.1. For the cohort administered cosibelimab at 800 mg Q2W, the ORR was 47.4% (95% CI: 36.0–59.1%) with median follow-up of 15.4 (range 0.4–40.5) months. As of the data cutoff date, the median DOR was not reached (range: 1.4+ to 34.1+ months), with response ongoing in 73.0% of participants. This study continues to enroll patients to evaluate cosibelimab as a treatment for patients with locally advanced cSCC and to evaluate cosibelimab administered at 1200 mg Q3W.[63]

Zolbetuximab (Astellas Pharma Inc.)

Zolbetuximab (IMAB362) is a chimeric IgG1κ antibody targeting Claudin 18.2 (CLDN18.2). The expression of this antigen is confined to tight junctions of the gastric mucosa in healthy tissues, but certain epitopes are exposed on the surface of gastric cancer cells due to changes in their cell polarity. Zolbetuximab's BLA has been granted a Priority Review by the FDA for the treatment of patients with CLDN18.2-positive, locally advanced unresectable, or metastatic HER2-negative gastric or gastroesophageal junction (mG/GEJ) adenocarcinoma. FDA's first action on the BLA is expected by January 12, 2024.[64] EMA, Japan's Ministry of Health, Labour and Welfare, and the NMPA have accepted marketing applications for zolbetuximab for the same patient cohort as the FDA, with the outcomes expected to be determined in 2024.[65,66]

These marketing application submissions were based on results from the Phase 3 SPOTLIGHT (NCT03504397) and GLOW clinical trials (NCT03653507). The SPOTLIGHT trial is a global, randomized, placebo-controlled, double-blind trial that included 565 patients with CLDN18.2-positive, HER2-negative, locally advanced unresectable, or mG/GEJ adenocarcinoma randomized to receive either zolbetuximab (800 mg/m^2 loading dose followed by 600 mg/m^2 every 3 weeks) plus mFOLFOX6 (283 patients) or placebo plus mFOLFOX6 (282 patients).[67] The patients receiving zolbetuximab had a significant reduction in the risk of disease progression or death, with the median PFS being 10.61 months (95% CI: 8.9–12.48) for the zolbetuximab group compared to 8.67 months (95% CI: 8.21–10.28) for the placebo group. The most common adverse events (>Grade 3) were nausea, vomiting, and decreased appetite. The GLOW study, which was also randomized and placebo-controlled, evaluated zolbetuximab plus capecitabine and oxaliplatin (CAPOX) as first-line treatment for CLDN18.2-positive, HER2-negative, locally advanced unresectable, or mG/GEJ adenocarcinoma. The primary endpoint

of PFS (median, 8.21 months versus 6.80 months with zolbetuximab versus placebo; hazard ratio (HR) = 0.687; 95% confidence interval (CI), 0.544–0.866; $P = 0.0007$) was met, as was the key secondary endpoint of overall survival (median, 14.39 months versus 12.16 months; HR = 0.771; 95% CI, 0.615–0.965; $P = 0.0118$).[68]

Odronextamab (Regeneron Pharmaceuticals, Inc)

Odronextamab (REGN1979) is a hinge-stabilized, bispecific human IgG4κ antibody targeting CD20 and CD3 with an Fc that was modified to reduce Fc receptor binding. The antibody was derived from Regeneron's VelocImmune® technology and Veloci-Bi® platform and is being developed for the treatment of RR B-cell NHL. In 2020, Regeneron granted Zai Lab rights to develop and exclusively commercialize odronextamab in oncology in mainland China, Hong Kong, Taiwan, and Macau. Odronextamab received Fast Track designation from FDA and Orphan Drug designations by the FDA and EMA for the treatment of patients with FL and DLBCL, which are subtypes of NHL. Regeneron has submitted marketing applications for odronextamab for RR FL and DLBCL to FDA and EMA. FDA's target date for a first action on the BLA is March 31, 2024.

The marketing applications include results from the Phase 1 ELM-1 (NCT02290951) and pivotal Phase 2 ELM-2 (NCT03888105) studies. The dose-escalation, dose-expansion ELM-1 study evaluated the safety and tolerability of odronextamab in 145 patients with RR B cell malignancies who had previously received CD20-antibody therapy.[69] The ORR was 51% (72 of 142), but, in patients with FL who received odronextamab at 5 mg or higher, the ORR was 91% (29 of 32).

In the ongoing, open-label ELM-2 study, odronextamab is IV administered in patients with FL, DLBLC, mantle cell lymphoma, marginal zone lymphoma, or B-cell NHL. The primary end point of the trial is ORR. Secondary endpoints include CR, PFS, OS, and duration of response. Results from a pre-specified analysis in DLBCL showed ORR and CR rate were 53% (48/90) and 37% (33/90), respectively, with a median study follow-up duration of 17.1 months.[70]

Trastuzumab duocarmazine (Byondis B.V., medac GmbH)

[vic-]trastuzumab duocarmazine (SYD985) is an antibody–drug conjugate in which the cleavable linker-drug valine-citrulline-seco-duocarmycin-hydroxybenzamide-azaindole (vc-seco-DUBA) is attached to the anti-HER2 IgG1κ antibody trastuzumab. Once internalized into HER2-expressing cancer cells, the linker is cleaved by proteolysis, and the inactive cytotoxin is activated to induce DNA damage. In January 2018, [vic-]trastuzumab duocarmazine received Fast Track designation from the FDA based on Phase 1 data (NCT02277717) which included heavily pre-treated last-line HER2-positive metastatic breast cancer patients.

In July 2022, FDA and EMA accepted marketing applications for the use of [vic-]trastuzumab duocarmazine in patients with HER2-positive, unresectable locally advanced or metastatic breast cancer. However, in May 2023, the FDA issued a complete response letter and suspended the decision on the product's approvability.[71] According to the company, the FDA requested additional information that requires time and resources that extend beyond the current evaluation period. In September 2023, Byondis withdrew the MAA submitted to EMA because it could not address EMA's concerns within the required time limit.[72]

The marketing applications were based on the Phase 3 TULIP® study (NCT03262935), which included 437 patients who were diagnosed with advanced-stage breast cancer that had been pre-treated with either two or more lines of anti-HER2 therapy or [ado-]trastuzumab emtansine (KADCYLA®). Patients were randomized to 1.2 mg/kg of IV [vic-]trastuzumab duocarmazine every 21 d ($n = 291$) or physician's choice treatment ($n = 146$), which included lapatinib plus capecitabine or trastuzumab plus either capecitabine, vinorelbine, or eribulin. This study met its primary endpoint of PFS, with a statistically improved improvement of 2.1 months over physician's choice therapy.[73] The study results were not found in the peer-reviewed literature as of October 2023.

Suciraslimab (SinoMab BioScience Limited)

Suciraslimab (SM03, 舒西利单抗) is a chimeric anti-CD22 IgG1κ antibody developed by SinoMab BioScience Limited for the treatment of auto-immune diseases, including RA. The target is an inhibitory coreceptor of the BCR, present in human B lymphocytes. SM03 disturbs the CD22 configuration, inducing its internalization from the cell surface of human B cells and facilitates trans binding between CD22 to human autologous cells, leading to a decrease of human B cells activation and proliferation.[74] In September 2023, the NMPA accepted a BLA for suciraslimab as a treatment of RA.[75]

In April 2023, SinoMab reported that the SM03-RA-III Phase 3 study (NCT04312815) of suciraslimab achieved the primary endpoint.[76] The randomized, placebo-controlled, double-blind SM03-RA-III study assessed the efficacy and safety of suciraslimab compared to placebo in patients with moderate-to-severe active RA receiving methotrexate (MTX). Patients were randomized to receive suciraslimab at 600 mg IV or placebo + MTX 7.5–20 mg/wk. The primary endpoint was the percentage of participants with ACR20, American College of Rheumatology 20% (ACR20) response at Week 24, defining by at least a 20% improved compared with baseline in both tender joint counts and swollen joint counts as well as a 20% improvement in 3 of the 5 additional measurements (disease activity assessed using visual analog scale by physician and patient, patient's assessment of pain, Health Assessment Questionnaire, level of C-reactive protein). As of September 2023, study results have not been published.

Batoclimab (CSPC Pharmaceuticals Co., Ltd., Harbour Biomed)

Batoclimab (HBM9161, 巴托利单抗), a human IgG1λ anti-FcRn antibody that induces the degradation of IgG, is in development as a treatment for IgG-mediated autoimmune

diseases. Initially developed by HanAll Biopharma, batoclimab was licensed to Harbour BioMed for development, manufacturing, and commercialization in Greater China, and to Immunovant Sciences Ltd. for development in certain other regions. In 2022, Harbour BioMed then transferred these exclusive rights to CSPC NBP Pharmaceuticals Co., Ltd., a wholly owned subsidiary of CSPC Pharmaceutical Group Limited. Batoclimab received a Breakthrough Therapy designation by the NMPA for the treatment of adult patients with generalized gMG. In June 2023, NMPA accepted a BLA for batoclimab for the treatment of gMG.

Positive top-line results of a Harbour BioMed-sponsored, randomized, placebo-controlled Phase 3 study (NCT05039190) to confirm the efficacy of HBM9161 subcutaneous injection for the treatment of gMG in Chinese patients were reported.[77] During the initial 5-week treatment period of this study, patients received six doses of the study drug (HBM9161 680 mg or matching placebo) by subcutaneous injection, once a week (QW). After the 5-week treatment period, patients were assessed weekly. After the completion of the first treatment cycle, a second cycle of treatment was started if re-treatment criteria were met. Batoclimab was well tolerated, and the study met its primary and key secondary endpoints.

Ebdarokimab (Akeso Inc.)

Ebdarokimab (AK101, 依若奇单抗) is a human IgG1κ antibody targeting Interleukin-12/Interleukin-23 p40 subunit developed by Akeso for the treatment of moderate-to-severe plaque psoriasis. In August 2023, NMPA accepted an NDA for ebdarokimab for the treatment of adult patients with moderate-to-severe plaque-type psoriasis.[78]

The NDA included results from two Phase 3 studies. In the randomized, placebo-controlled Phase 3 clinical study (NCT05120297), patients with moderate-severe plaque psoriasis were randomized to receive ebdarokimab or placebo SC at Week 0 and Week 4, with a follow-up to Week 16. The primary outcome measurements were the percentage of patients who achieved at least 75% reduction in psoriasis area and severity score from baseline (PASI 75) and the percentage of patients who achieved static physical global assessment (sPGA) clearance or very slight (0/1). The second Phase 3 (NCT05509361) study evaluated the long-term safety and efficacy of ebdarokimab by assessing the occurrence of treatment-emergent adverse event up to 52 weeks as the first endpoint. Clinical results showed that ebdarokimab has significant efficacy at both 16 and 52 weeks with favorable safety profile.[78]

Xeligekimab (Chongqing Genrix Biopharmaceutical Co., Ltd.)

Xeligekimab (GR1501, 赛立奇单抗) is a human anti-IL-17A IgG4 monoclonal antibody developed by Chongqing Genrix Biopharmaceutical Co., Ltd. for immune-mediated disorders, including psoriasis and arthritis. In March 2023, the NMPA accepted a marketing application for xeligekimab as a treatment for moderate and severe plaque psoriasis.[79]

The placebo-controlled Phase 3 CTR20210246 study evaluated the effectiveness and safety of xeligekimab in patients with moderate and severe plaque psoriasis. Patients were administered subcutaneous injections of 200 mg each time over a period of 48 weeks. The study's primary endpoints were the proportion of subjects reaching PASI75 and the proportion of subjects reaching PGA (0/1) at Week 12. Longer-term effects were included as secondary endpoints. Study results were not reported as of September 2023.

Xeligekimab is also being evaluated in a Phase 3 study (NCT05881785, CTR20220952) as a treatment for axial spondyloarthritis. In this study, 465 patients were randomly assigned 1:1:1 to receive 100 mg xeligekimab injection, 200 mg xeligekimab injection, or placebo. After a 16-week period, subjects in the active drug groups continued to be administered xeligekimab injection, and those in the placebo group were randomly assigned 1:1 to the 100 mg xeligekimab injection and 200 mg xeligekimab injection. The primary outcome measure is the proportion of participants who achieve an ASAS 20 response at Week 16, with ASAS20 response defined as an improvement of ≥20% and ≥1 units in at least three of the four ASAS main domains. Longer-term effects were included as secondary endpoints. Study results were not reported as of September 2023.

Vunakizumab (Jiangsu Hengrui Pharmaceuticals Co., Ltd.)

Vunakizumab (SHR-1314, 夫那奇珠单抗) is a humanized IgG1κ monoclonal antibody targeting IL17A, a cytokine involved in the inflammatory processes in several autoimmune diseases. Vunakizumab is being developed by Jiangsu Hengrui Pharmaceuticals Co., Ltd. for the treatment of moderate-to-severe plaque psoriasis. Hengrui's pipeline indicates that an NDA/BLA was submitted for vunakizumab as a single agent to treat moderate-to-severe plaque psoriasis.[80] The NMPA's Center for Drug Evaluation database indicates the application was accepted in April 2023.

Hengrui conducted a multicenter, randomized, double-blind, placebo-controlled Phase 3 trial (NCT04839016) in order to assess the efficacy, safety, pharmacokinetics, and immunogenicity of SC vunakizumab in patients with moderate-to-severe plaque psoriasis. Patients were randomized to receive SC vunakizumab 240 mg or placebo at Weeks 0, 2, 4, and 8. At Week 12, patients initially assigned placebo were switched to receive vunakizumab 240 mg (Weeks 12, 14, 16, and Q4W thereafter) and patients in the vunakizumab arm continued to receive SHR-1314 Q4W with an additional dose of placebo given at Week 14) through Week 52. The primary measures include the percentage of subjects who achieve at least 90% improvement in PASI score (PASI 90) and the Static Physicians Global Assessment (sPGA) of 0 or 1 response at Week 12. At Week 12, the proportion of patients achieving the primary endpoints of PASI 90 (76.8% (95% CI 72.7–80.5) vs 0.9% (95% CI 0.2–3.1)) and sPGA 0/1 (71.8% (95% CI 67.5–75.8) vs 0.4% (95% CI 0.1–2.4)) were significantly higher with vunakizumab than with placebo. During the maintenance period, the response rates of PASI 90 and sPGA 0/1 were sustained through Week 52

in patients on continuous vunakizumab. Up to Week 12, adverse events were mostly mild, with comparable overall incidence rates between groups (69.1% with vunakizumab vs 71.6% with placebo). Data demonstrated the efficacy and tolerability of vunakizumab at Week 12 and Week 52 for patients with psoriasis.[81]

Ebronucimab (Akeso Inc.)

Ebronucimab (AK102, 伊努西单抗) is a human IgG1λ PCKS9 inhibitor jointly developed by Akeso and AD Pharmaceuticals. In June 2023, NMPA accepted an NDA for ebronucimab for two indications: 1) primary hypercholesterolemia and mixed hyperlipidemia and 2) heterozygous familial hypercholesterolemia.

The marketing application included data from pivotal Phase 3 studies conducted in patients with primary hypercholesterolemia, mixed hyperlipidemia, and heterozygous familial hypercholesterolemia. Three dosing regimens were evaluated, including Q6W, which is expected to provide enhanced patient benefits such as longer dosing intervals. The efficacy results from these studies showed a significant reduction in LDL-C levels from baseline (maximum reduction of more than 65%), lower (total cholesterol) TC, non-HDL-C and ApoB levels, and increased HDL-C and ApoA-I levels.[82]

Recaticimab (Jiangsu Hengrui Pharmaceuticals Co., Ltd.)

Recaticimab (SHR-1209, 瑞卡西单抗) is a humanized, anti-PCSK9 IgG1κ monoclonal antibody developed by Jiangsu Hengrui Pharmaceuticals Co., Ltd. for the treatment of dyslipidemia, including hypercholesterolemia and hyperlipidemia. Hengrui's pipeline indicates that an NDA/BLA was submitted for recaticimab as a single agent for primary hypercholesterolemia and mixed hyperlipidemia and heterozygous familial hypercholesterolemia and for primary hypercholesterolemia and mixed hyperlipidemia with poor lipid control in combination with lipid-lowering drugs.[80] The NMPA's Center for Drug Evaluation database indicates the application was accepted in June 2023.

The Phase 3 REMAIN-1 (NCT04849000) study evaluated recaticimab as monotherapy in patients with primary hypercholesterolemia and mixed hyperlipidemia. This study had a primary outcome measure of the percentage change in LDL-C relative to baseline at 12 weeks or 16 weeks of treatment. Results of the study were presented at the 2023 European Society of Cardiovascular Annual Meeting held in Amsterdam, the Netherlands in August 2023. A total of 703 patients who met the criteria were randomly assigned to receive recaticimab (157 patients in the 150 mg Q4W group, 156 patients in the 300 mg Q8W group, and 155 patients in the 450 mg Q12W group) or placebo (78 patients in the 150 mg Q4W group, 300 mg 79 patients in the Q8W group, and 78 patients in the 450 mg Q12W group). Compared with placebo, after 12 weeks of treatment with 150 mg Q4W, LDL-C was reduced by 49.6% (95% CI, 44.2–54.9) compared with baseline; after 16 weeks of treatment with 300 mg Q8W, LDL-C was reduced by 49.6% compared with baseline. Baseline reduction was 52.8% (95% CI, 48.3–57.2) and LDL-C was reduced by 45.0% (95% CI, 41.0–49.0) from baseline after 12 weeks of 450 mg Q12W treatment ($P < 0.0001$ for each group vs. placebo).[83]

Hengrui has also sponsored two randomized, placebo-controlled Phase 3 studies of recaticimab in combination with lipid-lowering drugs as a treatment of dyslipidemia. The Phase 3 NCT04885218 study assessed the efficacy and safety of recaticimab combined with lipid-lowering agents in the stable treatment of patients with hypercholesterolemia and hyperlipidemia. The study enrolled 692 patients and evaluated high, medium, and low doses of recaticimab. The primary outcome measure was the percentage change in LDL-C relative to baseline at 24 weeks of treatment. The Phase 3 NCT04844125 study evaluated recaticimab in patients with hypercholesterolemia background lipid-lowering therapy in combination with recaticimab or placebo. The study enrolled 144 patients and has a primary outcome measure 12 weeks percentage change in LDL-C relative to baseline at 12 weeks.

Ongericimab (Junshi Biosciences)

Ongericimab (JS002, 昂戈瑞西单抗) is a humanized, hinge-stabilized anti-PCSK9 IgG4κ monoclonal antibody developed by Junshi Biosciences for the treatment of primary hypercholesterolemia, including familial and non-familial heterozygous, mixed dyslipidemia and homozygous familial hypercholesterolemia. In April 2023, an NDA for ongericimab for hypercholesterolemia was accepted by the NMPA.

The efficacy and safety of ongericimab were evaluated in two Phase 3 studies, JS002–003 (NCT04781114) and JS002–006 (NCT05532800). JS002–003 is a randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy, as well as immunogenicity of repeat dosing of JS002 in patients with primary hypercholesterolemia and mixed hyperlipidemia when combined with statin therapy. Participants (n = 806) were randomized in a 2:1 ratio of JS002 SC (at 150 Q2W or 300 mg Q4W) or placebo. The primary outcome measure was the percentage change in LDL-C relative to baseline at Week 24. The JS002–006 study assessed the efficacy and safety of ongericimab SC 150 mg Q2W dosed via prefilled syringes and prefilled autosyringes in the same indication. Patients (n = 255) received ongericimab SC in prefilled syringes or placebo or ongericimab SC in prefilled autosyringes or placebo. The primary endpoints were the percentage change in LDL-C relative to baseline at week 12. The primary endpoints were met in these two Phase 3 clinical studies.[84]

Trastuzumab botidotin (Sichuan Kelun-Biotech Biopharmaceutical Co Ltd.)

Trastuzumab botidotin (A166) is an ADC composed of an anti-HER2 IgG1κ antibody site-specifically conjugated to the tubulin inhibitor Duostatin-5 via a cleavable valine-citrulline linker. In May 2023, Sichuan Kelun-Biotech Biopharmaceutical Co Ltd. submitted a marketing application to NMPA for A166 for third-line+ advanced HER2+ breast cancer based on positive results of a pivotal Phase 2 study.

The single-arm pivotal Phase 2 CTR20212088 study evaluated A166 in patients with HER2-positive unresectable locally

advanced, recurrent, or metastatic breast cancer who failed previous second-line or above anti-HER2 therapy. Patients received A166 for injection at a dose of 4.8 mg/kg. The infusion interval was 21 (±3) d. The primary endpoint was the objective response rate as assessed by the Independent Review Committee (IRC) using RECIST 1.1 efficacy evaluation criteria. The primary endpoint of the study was met.[85]

Sichuan Kelun-Biotech Biopharmaceutical Co Ltd is also evaluating A166 as second-line+ treatment in a Phase 3 study (CTR20231740) for HER2-positive unresectable or metastatic breast cancer that started in July 2023. Additional early-phase clinical studies are exploring the therapeutic potential of A166 for other advanced HER2+ solid tumors, including gastric and colorectal cancer.

Enlonstobart (CSPC Pharmaceutical Group Ltd.)

Enlonstobart (SG001, Enshuxing, 恩朗苏拜单抗) is a recombinant human anti-PD-1 IgG4κ monoclonal antibody developed by CSPC Pharmaceutical Group Ltd. In March 2023, a marketing application for conditional approval of enlonstobart for the treatment of recurrent or metastatic cervical cancer patients with positive PD-L1 expression who have failed at least first-line platinum-based chemotherapy was accepted by NMPA.[86]

A Phase 3 confirmatory study in first-line cervical cancer has started. The randomized, double-blind, placebo-controlled, multicenter Phase 3 trial (NCT05715840/CTR20230132) will evaluate the efficacy and safety of enlonstobart plus platinum-containing chemotherapy with or without bevacizumab in the first-line treatment of PD-L1-positive (CPS ≥1) recurrent or metastatic cervical cancer. Participants ($n = 368$) will be randomized to receive enlonstobart 360 mg IV Q3W or placebo, in addition to paclitaxel 175 mg/m^2, cisplatin 50 mg/m^2 or carboplatin (AUC = 5) with or without bevacizumab 15 mg/kg. Primary endpoints include safety lead-in with the incidence and grade of the adverse events, PFS and OS. The estimated primary completion of the study is July 2024.

Iparomlimab (Qilu Puget Sound Biotherapeutics)

Iparomlimab (PSB103, QL1604, 艾帕洛利单抗) is a monoclonal antibody targeting PD-1 developed by Qilu Puget Sound Biotherapeutics as a treatment for solid tumors. In September 2023, the NMPA accepted a marketing application for QL1604.[87]

Results of a placebo-controlled Phase 2 study (NCT04864782) of iparomlimab plus paclitaxel-cisplatin /carboplatin as a first-line treatment in patients with recurrent or metastatic cervical cancer were reported at the ESMO Asia Congress held in Singapore on December 2–4, 2022.[88] In this study, patients received QL1604 (200 mg, IV) or placebo plus investigator choice of paclitaxel (175 mg/m2) and cisplatin (70 mg/m2)/carboplatin (AUC 6) at day 1 of each 21-d cycle for up to 6 cycles. Patients subsequently continued to receive QL1604 maintenance treatment (200 mg Q3W) until disease progression, intolerable toxicity, or other discontinuation events. The primary efficacy endpoint was ORR by investigators per RECIST v1.1 and iRECIST. ORR and iORR were 58.7% (27/46) and 60.9% (28/46). The median PFS was 8.1 months (95% CI: 5.7, NE); median follow-up time for PFS was 6.23 months (range: 0 to 14 months).

Iparomlimab, tuvonralimab (Qilu Puget Sound Biotherapeutics)

Iparomlimab and tuvonralimab (PSB205, QL1706) comprise a mixture of antibodies derived from the MabPair technology platform, which simultaneously produces two engineered monoclonal antibodies in a single cell at a ratio of approximately 2:1. The mixture of iparomlimab, a hinge-stabilized anti-PD-1 IgG4 antibody, and tuvonralimab, an anti-CTLA-4 IgG1 antibody is being developed by Qilu Puget Sound Biotherapeutics as a treatment for solid tumors. In August 2023, the NMPA accepted a marketing application for QL1706.[87]

In a Phase 1/1b study, QL1706 was well tolerated and demonstrated promising antitumor activity.[89] For immunotherapy-naive patients, treatment with QL1706 resulted in ORRs of 24.2%, 38.7%, and 28.3% in NSCLC, nasopharyngeal carcinoma, and cervical cancer patients, respectively. QL1706 is currently being evaluated in randomized Phase 2 (NCT05576272, NCT05179317) and Phase 3 (NCT05446883, NCT05487391) trials of patients with these types of cancers.

Ivonescimab (Akeso Inc.)

Ivonescimab (AK112, 依沃西单抗, SMT112) is a tetravalent, humanized bispecific antibody targeting PD-1 and VEGF developed by Akeso. The antibody's Fc was mutated (L234A, L235A) to impair Fc effector functions. In December 2022, Akeso entered into a collaboration and license agreement with Summit Therapeutics. Akeso outlicensed exclusive rights for the development and commercialization of ivonescimab (SMT112) in the US, Canada, Europe, and Japan to Summit Therapeutics. Akeso retains rights to ivonescimab for the rest of the world, including China.

Ivonescimab was granted Breakthrough Therapy designation by NMPA as follows: 1) first-line treatment for NSCLC patients with positive PD-L1 expression, 2) in combination with chemotherapy for the treatment of patients with epidermal growth factor receptor (EGFR)-mutated locally advanced or metastatic NSCLC who have failed to respond to an EGFR TKI, and 3) in combination with docetaxel for the treatment of patients with locally advanced or metastatic NSCLC who failed to respond to a prior PD-(L)1 inhibitor plus platinum-based doublet chemotherapy.[90] An NDA for ivonescimab was granted priority review by NMPA in August 2023.[91]

Akeso is sponsoring two Phase 3 studies evaluating ivonescimab administered IV to NSCLC patients. The Phase 3 AK112–303 study (NCT05499390) is assessing AK112 versus pembrolizumab as first-line treatment for patients with PD-L1 -positive locally advanced or metastatic NSCLC whose tumors have a PD-L1 tumor proportion score ≥1%, while the AK112–306 study (NCT05840016) is evaluating ivonescimab in combination with chemotherapy (carboplatin + paclitaxel) versus

tislelizumab (anti-PD1) and chemotherapy in patients with advanced squamous NSCLC.

In collaboration with Akeso, Summit Therapeutics is sponsoring the Phase 3 HARMONi study (NCT05184712, AK112–301), which is assessing the efficacy and safety of ivonescimab plus pemetrexed and carboplatin vs placebo plus pemetrexed and carboplatin in patients with EGFR-mutant locally advanced or metastatic NSCLC who have progressed on or following growth factor receptor tyrosine kinase inhibitor (EGFR-TKI) treatment. Summit is also sponsoring the Phase 3 HARMONi-3 (NCT05899608, SMT112–3003) of ivonescimab in combination with chemotherapy versus pembrolizumab with chemotherapy in first-line for metastatic squamous NSCLC.

In a Phase 2 trial (NCT04736823), ivonescimab in combination with platinum-doublet chemotherapy showed efficacy signals and a tolerable safety profile in 83 patients across 3 cohorts: 1) patients with untreated advanced NSCLC with no EGFR or anaplastic lymphoma kinase (ALK) gene mutations; 2) patients with EGFR-sensitive mutations who failed previous EGFR-TKI therapy; and 3) patients with advanced NSCLC patients who failed systemic platinum-based chemotherapy and anti-PD1/PDL1 treatment. The confirmed ORR in cohorts 1, 2, and 3 were 53.5% (95% CI, 36.9%–67.1%), 68.4% (95% CI, 43.4%–87.4%), and 40.0% (95% CI, 19.1%–63.9%), respectively.[92]

Socazolimab (Lee's Pharmaceutical Holdings Limited, Sorrento Therapeutics, Inc.)

Socazolimab (首克注利单抗, ZKAB001, STI-A1014) is a human anti-PD-L1 IgG1λ2 antibody discovered by Sorrento Therapeutics, Inc. and licensed to Lee's Pharmaceutical for Greater China territories. In 2021, socazolimab was granted breakthrough designation, and an NDA was accepted by the NMPA for the treatment of recurrent or metastatic cervical cancer patients.[93] Lee's Pharmaceutical is also developing socazolimab as a treatment for small cell lung cancer, as well as other solid tumors.

Results were recently reported for a Phase 1 dose-escalation study (NCT03676959) of patients with recurrent or metastatic cervical cancer.[94] Of 104 patients enrolled, 92 were included in the dose expansion phase and 54 of these had baseline PD-L1-positive tumors. Patients were administered (IV) 5, 10, or 15 mg/kg socazolimab Q2W until disease progression. The primary endpoints of the dose-expansion phase were safety and the ORR of the 5 mg/kg dose. ORR was 15.4% (95% confidence interval (CI), 8.7%–24.5%). The median PFS was 4.44 months (95% CI, 2.37–5.75 months), and the median OS was 14.72 months (95% CI, 9.59-NE months). The ORR of PD-L1-positive patients was 16.7%, and the ORR of PD-L1-negative patients was 17.9%.

Results from a Phase 1 study (NCT04346914) investigating the safety and the efficacy of socazolimab with or without carboplatin plus etoposide for extensive-stage small cell lung cancer (ES-SCLC) patients were recently reported.[95] In this study, 20 patients received socazolimab (5 mg/kg) Q3W until disease progression or physician decision. The primary endpoint was safety measured by the Common Terminology Criteria for Adverse Events. Preliminary data reported confirmed the safety of socazolimab with promising clinical efficacy including an ORR of 70% (95% CI, 45.72%–88.11%) with 14 partial responses. The median PFS was 5.65 months (95% CI: 4.14–6.54), the median duration of response was 4.29 months (95% CI: 2.76–5.85), and the median OS was 14.88 months (95% CI: 10.09–not evaluated). A randomized, placebo-controlled Phase 3 trial (NCT04878016) of socazolimab combined with chemotherapy in the first-line treatment of extensive-stage small-cell lung cancer is ongoing.

Benmelstobart (Sino Biopharmaceutical Limited)

Benmelstobart (CBT-502, TQB2450, 贝莫苏拜单抗) is an anti-PD-L1 humanized IgG1κ with significant sequence divergence in CDRs from anti-PD-L1 benchmark antibodies (atezolizumab, durvalumab, and avelumab) and no Fc activity. The antibody blocks the interaction of PD-L1 with PD1 and CD80 receptors. Benmelstobart is in development by Chia Tai Tianqing Pharmaceutical Group Co, Ltd., a subsidiary of Sino Biopharmaceutical Limited, for commercialization in China. CBT Pharmaceuticals, Inc. retains marketing rights for the rest of the world. In January 2023, the Center for Drug Evaluation of NMPA accepted a marketing application for benmelstobart in combination with anlotinib hydrochloride for first-line treatment of small cell lung cancer.[96]

The safety and efficacy of benmelstobart or placebo combined with anlotinib, etoposide and carboplatin versus etoposide and carboplatin in patients with extensive small cell lung cancer were evaluated in a randomized, double-blind, controlled, Phase 3 study (NCT04234607). Benmelstobart (1200 mg) was IV administered on Day 1 of each 21-d cycle, with other agents administered as per the study protocol. As of September 2023, study results have not been published.

Tagitanlimab (Sichuan Kelun Pharmaceutical Co., Ltd.)

Tagitanlimab (泰特利单抗, A167, KL-A167, HBM9167) is a humanized PD-L1 IgG1κ antibody developed by Sichuan Kelun Pharmaceutical Co., Ltd. Harbour BioMed in-licensed tagitanlimab from Kelun-Biotech for the development and commercialization of this mAb worldwide, excluding Greater China. Tagitanlimab was granted orphan drug designation from the FDA for the treatment of nasopharyngeal carcinoma. In November 2021, NMPA accepted a marketing application for tagitanlimab for nasopharyngeal carcinoma.[97]

The results from the Phase 2 trial (NCT03848286) studying the efficacy and safety of tagitanlimab in previously treated recurrent or metastatic nasopharyngeal carcinoma Chinese patients were released in The Lancet. A total of 153 patients received tagitanlimab (900 mg, IV) every 2 weeks until disease progression, intolerable toxicity, or withdrawal of consent. The data showed that tagitanlimab was well tolerated with promising efficacy with an ORR (primary endpoint) of 26.5% and a disease control rate of 56.8%. Additionally, the authors suggest that low plasma EBV DNA could be a potential predictive biomarker of response to tagitanlimab and that post-

treatment EBV DNA analysis showed a decrease which could be correlated with a better response to tagitanlimab.[98]

A Phase 3 study (NCT05294172) assessed the efficacy and safety of tagitanlimab vs. placebo in the treatment of recurrent or metastatic nasopharyngeal carcinoma in combination with cisplatin and gemcitabine. Patients received 1200 mg tagitanlimab or placebo every 3 weeks, cisplatin 80 mg/m^2 on Day 1 of each 21-d cycle, 4–6 cycles, gemcitabine 1000 mg/m^2, Day 1 and Day 8 of each 21-d cycle, 4–6 cycles. The primary outcome measure is PFS for up to 24 months. The estimated primary completion date for the study is May 2024.

Antibodies to watch in 2024: non-cancer indications

Of the antibody therapeutics in late-stage clinical studies that include patients with any disease other than cancer, companies sponsoring 10 have indicated that they may submit marketing applications to regulatory authorities by the end of 2024 (Table 3). Relevant details for these molecules are summarized below, with the summaries in order according to the approximate timing of possible marketing application submissions, which is as they appear in Table 3. Additional data for these molecules can be found in Supplemental Table S3.

Axatilimab (Syndax Pharmaceuticals, Inc., Incyte Corporation)

Axatilimab (SNDX-6352) is a humanized, hinge-stabilized (S228P) IgG4κ antibody targeting the colony-stimulating factor 1 receptor (CSF-1 R) for the treatment of GvHD. CSF-1 R mediates the pro-inflammatory and pro-fibrotic monocyte and macrophage differentiation and activation, and axatilimab is the first GvHD treatment that targets disease-associated macrophages. Syndax licensed axatilimab from UCB during its preclinical development and subsequently entered into a global partnership and license agreement with Incyte, where Incyte will oversee the international (non-US) commercialization activities for all indications. FDA granted axatilimab Orphan Drug Designation for the treatment of patients with chronic GVHD and idiopathic pulmonary fibrosis. Based on positive results from the pivotal Phase 2 AGAVE-201 study in GvHD, Syndax and Incyte expect to submit a BLA to the FDA by the end of 2023.[99]

The AGAVE-201 study included 241 patients with refractory, late-line chronic GvHD patients of which >70% had prior treatment with ruxolitinib. Patients were randomized 1:1:1 to receive either 0.3 mg/kg Q2W, 1 mg/kg Q2W, or 3 mg/kg Q4W, and all three cohorts met the primary endpoint of ORR at 74%, 67%, and 50%, respectively. Responses were durable at 0.3 mg/kg, with 60% of responders maintaining a response at 12 months. Axatilimab was generally well tolerated at 0.3 mg/kg, with increased frequency of adverse events at 1 mg/kg and 3 mg/kg doses.[100]

AZD3152 (AstraZeneca)

AZD3152 (SARS-CoV-2 LAAB), an anti-SARS-CoV-2 antibody discovered by RQ Biotechnology, was isolated from vaccinated volunteers after an Omicron-BA.1 variant infection. The antibody, which was licensed by AstraZeneca in May 2022, has broad and potent neutralizing activity across all known SARS-CoV-2 variants and is undergoing evaluation for pre-exposure prophylaxis of COVID-19 in patients with conditions causing immune impairment.[101] AstraZeneca anticipates key data readout of the SUPERNOVA study of AZS3152 for prevention of COVID-19 in the second half of 2023.[102] If the study data are positive, AstraZeneca may potentially pursue an EUA from FDA, if an EUA declaration remains in effect, or an approval.

The safety, efficacy, and neutralizing activity of AZD3152 are being evaluated in the Phase 2/3 SUPERNOVA study (NCT05648110). In the Phase 3 portion of the study, patients 12 y of age or older with conditions causing immune impairment are randomized 1:1 to receive AZD3152 300 mg or comparator (600 mg Evusheld or placebo) administered via intramuscular injection in the anterolateral thigh on Day 1; participants will receive a second dose of their original randomized trial intervention 6 months after Visit 1. The primary endpoints of the Phase 3 portion are to evaluate the safety of AZD3152 and Evusheld and/or placebo and to compare the efficacy of AZD3152 to Evusheld and/or placebo in the prevention of symptomatic COVID 19. Initiated in December 2022, the study has an estimated enrollment of 3706 participants and an estimated primary completion date in September 2023.

Table 3. Commercially sponsored investigational monoclonal antibodies in late-stage clinical studies for non-cancer indications, with regulatory submission anticipated during 2023–2024.

INN or drug code	Target(s); format	Indication of relevant* late-stage study (est. submission year#)	Most advanced clinical phase
Axatilimab	CSF-1 R; Humanized IgG4κ	Graft vs. host disease (2023 submission)	Pivotal Phase 2
AZD3152	SARS-CoV-2	Prophylaxis of COVID-19 (2023/4 submission)	Phase 3
Bentracimab	Ticagrelor; Human IgG1l Fab	Reversal of the antiplatelet effects of ticagrelor (2023/4 submission)	Phase 3
CM310	IL-4 Rα; Humanized	Atopic dermatitis (2023 submission)	Phase 3
Rademikibart	IL-4 Rα; Human IgG4κ	Atopic dermatitis (2024 submission)	Pivotal Phase 2
Depemokimab	IL-5; Humanized IgG1κ	Eosinophilic asthma, chronic rhinosinusitis with nasal polyps (2024 submission)	Phase 3
Imsidolimab	IL-36 R; Humanized IgG4κ	Generalized pustular psoriasis (2024 submission)	Phase 3
Anselamimab	Amyloid; Chimeric IgG1κ	Amyloid light chain amyloidosis (2024 submission)	Phase 3
Latozinemab	Sortilin; Human IgG1κ	Frontotemporal dementia (2024 submission)	Phase 3
Apitegromab	Myostatin; Human IgG4λ	Spinal muscular atrophy (2024 submission)	Phase 3

*Indication for which a regulatory submission is anticipated. #First marketing application submission dates are estimates. The table includes information publicly available as of November 1, 2023. Abbreviations: CSF-1 R, colony-stimulating factor-1 receptor; fab, antigen-binding fragment; IL, interleukin; SARS-CoV-2, severe acute respiratory syndrome-coronavirus-2; TF, tissue factor. See supplemental table S3 for more details about each antibody. Additional data for investigational antibody therapeutics in late-stage clinical studies are also available at: https://www.antibodysociety.org/antibodies-in-late-stage-clinical-studies/.

Bentracimab (SFJ Pharmaceuticals, SERB Pharmaceuticals)

Bentracimab (PB2452; formerly MEDI2452) is a human antibody Fab that binds to and neutralizes the platelet inhibitor KADCYLA®/Brilinta® (ticagrelor), which is an oral anticoagulant given to patients undergoing surgery and to patients with specific cardiovascular- and hemostasis-related disorders. Bentracimab binds to ticagrelor with a higher affinity than ticagrelor binds to $P2Y_{12}$ on platelets (K_i: 20 pM vs 2 nM, respectively). Rights to betracimab were licensed to PhaseBio by MedImmune in 2018, and PhaseBio subsequently licensed the rights in the EU and EEA, UK, Russia, Ukraine, and other countries within the Commonwealth of Independent States to Alfasigma S.p.A. In 2020, PhaseBio signed a financing and co-licensing deal for bentracimab with SFJ Pharmaceuticals, and then in December 2022, full rights to bentracimab were transferred to SFJ Pharmaceuticals. Bentracimab has been granted Breakthrough Therapy and PRIME designations from FDA and EMA, respectively. In May 2023, Serb Pharmaceuticals acquired the exclusive US rights to bentracimab, and will work in collaboration with SFJ to submit a BLA in late 2023.[103]

The open-label, prospective single-arm Phase 3 REVERSE-IT study (NCT04286438) is a currently ongoing trial to evaluate the safety and efficacy of bentracimab in patients treated with ticagrelor who required urgent surgery, other invasive procedures, or who have major bleeding. Eligible patients received an initial IV bolus dose of 6 g over 10 min, followed immediately by 4-h IV loading infusion of 6 g, and finally a 6 g IV maintenance infusion over 12 h. Alternatively, patients with the recent concomitant use of moderate or strong CYP3A inhibitors received 36 g of bentracimab over 24 h. Interim analysis of 150 patients, 142 of which required urgent surgery and 8 had major hemorrhage, demonstrated that bentracimab provided a rapid reversal of the antiplatelet effects of ticagrelor within 5–10 min, and this reversal was sustained for more than 48 h, as measured by the VerifyNow $P2Y_{12}$ and vasodilator-stimulated phosphoprotein assays.[104] Adjudicated hemostasis was reached for >90% of patients ($p < 0.001$). This study aims to enroll approximately 200 patients from North America, Europe, and China, and has an estimated completion date of December 2023.

CM310 (Keymed Biosciences Co. Ltd)

CM310 is a recombinant humanized monoclonal antibody targeting interleukin 4 receptor α subunit (IL-4 Rα) developed by Keymed Biosciences for atopic dermatitis and chronic rhinosinusitis with nasal polyps. In June 2022, the company received a Breakthrough Therapy designation from NMPA for CM310 for the treatment of moderate-to-severe atopic dermatitis. Keymed Bio is also working cooperatively with CSPC to develop and commercialize CM310 for the treatment of moderate-to-severe asthma, COPD, and other respiratory diseases in Mainland China. Keymed Bio plans to submit marketing applications to NMPA for CM310 for atopic dermatitis in 2023.[105]

Results of a placebo-controlled, Phase 2b trial (NCT04805411) of CM310 in Chinese adults with moderate-to-severe atopic dermatitis were recently reported.[106] Eligible patients ($n = 120$) were randomized (1:1:1) to receive SC injections of 150 mg (low dose) or 300 mg (high dose) CM310 or placebo Q2W for 16 weeks, followed by an 8-week follow-up period. The primary endpoint was the proportion of patients achieving ≥75% improvement in the Eczema Area and Severity Index (EASI-75) score from baseline at week 16. Compared to the placebo group, at week 16, the proportion of EASI-75 responders from baseline was significantly higher in the CM310 groups (65% (26/40) and 70% (28/40) for low- and high-dose groups, respectively, vs 20% (8/40) for the placebo group). A placebo-controlled Phase 3 study of evaluating SC injections of 300 mg and 600 mg of CM310 Q2W in patients with atopic dermatitis completed enrollment in November 2022.[105]

Rademikibart (Suzhou Connect BioPharma Ltd., Simcere Pharmaceutical Group Ltd.)

Rademikibart (CBP201) is a hinge-stabilized, human IgG4κ monoclonal antibody targeting IL-4 Rα that blocks inflammatory signaling by both IL-4 and IL-13, two important cytokines that drive allergic inflammation.[107] Suzhou Connect Biopharmaceuticals, Ltd., a subsidiary of Connect Biopharma Holdings Limited, is developing rademikibart for a treatment for atopic dermatitis and asthma. Simcere Pharmaceutical Group Ltd., which has been granted exclusive rights to develop, manufacture, and commercialize rademikibart for all indications in Greater China, will be responsible for rademikibart's NDA for AD in China. NDA submission is anticipated by March 31, 2024.[108]

Rademikibart is undergoing evaluation in a pivotal Phase 2 trial (NCT05017480; CN002) in patients with moderate-to-severe atopic dermatitis in China. Stage one of the trial compared a 2-week dosing arm (Q2W) with placebo. Stage 2 includes Q2W and Q4W dosing arms to understand the potential for an extended Q4W dosing regimen, which would substantially differentiate rademikibart from existing treatments that are Q2W. Patients received rademikibart doses via SC administration. The study successfully achieved all primary and key secondary endpoints for the primary analysis population with highly statistically significant results at Week 16,[109] and the clinical response (IGA 0/1 and EASI-75) was maintained through Week 52 with both Q2W and Q4W dosing regimens.[110]

A Phase 2 multi-center, single-arm, open-label clinical study (NCT05905133; CN003) to evaluate the safety and efficacy of rademikibart in Chinese adults with moderate-to-severe atopic dermatitis was started in July 2023. In this study, subjects will receive an SC injection of rademikibart 600 mg (4 mL in total, 2 injections of 2 mL each in different sites) on Day 1, then an SC injection of rademikibart 300 mg (2 mL) from Week 2, and 300 mg (2 mL) every 2 weeks thereafter until Week 10. The study is recruiting an estimated 360 patients and has a primary completion date in June 2024.

Connect Biopharmaceuticals is also conducting a Phase 2 study (NCT04773678) to evaluate efficacy and safety of two dose levels of rademikibart in patients with moderate-to-

severe persistent asthma with Type 2 inflammation that reached primary completion in August 2023 with an estimated study completion of December 2023. The company anticipates reporting top-line results of the study in the second half of 2023.[108]

Depemokimab (GSK)

Depemokimab (GSK3511294) is a humanized IgG1κ anti-IL-5 monoclonal antibody engineered for high affinity and long-acting suppression of IL-5 function in development for the treatment of severe eosinophilic asthma. IL-5 is the major cytokine responsible for the proliferation, activation, and survival of eosinophils, making it a proven treatment target for severe asthma patients with higher levels of eosinophils. GSK is conducting five Phase 3 studies in the eosinophil-driven diseases severe eosinophilic asthma and chronic rhinosinusitis with nasal polyps (CRSwNP) that have primary completion dates in late 2023 or in 2024. The company has indicated that US regulatory submissions may occur in the second half of 2024 for depemokimab in asthma based on the SWIFT-1/2 study and in CRSwNP based on the ANCHOR-1/2 study.[111]

SWIFT-1 (NCT04719832) and SWIFT-2 (NCT04718103) are 52-week, randomized, double-blind, placebo-controlled, parallel-group, multi-center trials of the efficacy and safety of depemokimab adjunctive therapy in adult and adolescent participants with severe uncontrolled asthma with an eosinophilic phenotype. Started in March 2021, the studies each had an estimated enrollment of 375 and are no longer recruiting patients; the primary completion dates for SWIFT-1 and SWIFT-2 are in December 2023 and May 2024, respectively. The Phase 3 NIMBLE (NCT04718389) is recruiting an estimated 1700 participants with severe asthma with an eosinophilic phenotype, who are currently benefitting from mepolizumab or benralizumab treatment, to assess whether they can maintain treatment benefit when switched to depemokimab. The study's primary completion date is in November 2024.

ANCHOR-1 (NCT05274750) and ANCHOR-2 (NCT05281523) are designed to evaluate the efficacy and safety of depemokimab in participants with chronic rhinosinusitis with nasal polyps. The trials started in April 2022 and are actively recruiting participants, with primary completion dates in November 2024.

Imsidolimab (AnaptysBio, Inc.)

Imsidolimab (ANB019) is a humanized IgG4κ carrying the hinge stabilizing S228P mutation developed by AnaptysBio for the treatment of generalized pustular psoriasis (GPP), a rare, chronic, systemic autoinflammatory disease that, if left untreated, is potentially life-threatening. This antibody was designed to inhibit the function of the interleukin-36 receptor (IL-36 R), whose signaling is involved in the pathogenesis of inflammatory diseases, including GPP. FDA granted Orphan Drug Designation to imsidolimab for the treatment of GPP. In October 2023, AnaptysBio announced that imsidolimab met the primary endpoint of the registration-enabling GEMINI-1 study, achieving, after a single dose of 750 mg IV, rapid clearance of pustulation, erythema, and scaling through Week 4. The company anticipates submission of a BLA to FDA by Q3 2024 and plans to out-license the molecule in 2024.[112]

Imsidolimab was evaluated in two Phase 3 studies, the recently completed, registration-enabling, GEMINI-1 (NCT05352893), and the ongoing, long-term extension study, GEMINI-2 (NCT05366855). The Phase 3 GEMINI-1 clinical trial was a four-week, double-blind, placebo-controlled, randomized study evaluating the efficacy and safety of imsidolimab in patients with GPP, irrespective of mutational status. This global study enrolled a total of 45 patients, 15 patients per study arm. Patients were randomized 1:1:1 to receive, at Day 0, a single infusion of 750 mg IV imsidolimab, 300 mg IV imsidolimab, or placebo.

The ongoing GEMINI-2 trial evaluates the efficacy and safety of imsidolimab for the prevention and/or reduction in severity of recurrent GPP flares when administered chronically as a monthly SC dose over a 3-y period. This long-term extension study enrolled patients who were rescued (placebo patients who were worsening or not improved after Day 8) or completed the GEMINI-1 trial. Depending on whether they are responders, partial responders, or non-responders to treatment under GEMINI-1, patients are receiving monthly doses of 200 mg SC imsidolimab or placebo.

Anselamimab (AstraZeneca)

Anselamimab (CAEL-101) is a fibril-reactive IgG1κ antibody for the treatment of amyloid light chain (AL) amyloidosis. AL amyloidosis begins in the bone marrow where abnormal proteins misfold and create free light chains that cannot be broken down. These free light chains bind together to form amyloid fibrils that build up in the extracellular space of organs, affecting the kidneys, heart, liver, spleen, nervous system, and digestive tract, causing significant organ damage and failure that may ultimately be fatal. Anselamimab has been granted Fast Track designation by FDA and Orphan Drug designation by FDA and EMA. AstraZeneca anticipates key Phase 3 data readout from the CAEL101–301 study (NCT04504825) of anselamimab in AL amyloidosis in the second half of 2024.[102] Positive study data may allow marketing application submission(s) in 2024.

Mayo Stage I, Stage II, and Stage IIIa AL amyloidosis patients were enrolled in the Phase 2 multicenter, open-label, sequential cohort, dose-selection study (CAEL101–203; NCT04304144) of anselamimab. The safety and tolerability of CAEL-101, administered in combination with the standard of care (SoC) cyclophosphamide-bortezomib-dexamethasone (CyBorD) chemotherapy, were compared to those of daratumumab in combination with SoC. A total of 25 participants were enrolled in the study, which is scheduled for completion in November 2023.

The Phase 3 double-blind, randomized, multicenter CAEL101–301 study (NCT04504825) of CAEL-101 is recruiting an estimated 124 Mayo Stage IIIb plasma cell dyscrasia (PCD) treatment-naïve AL amyloidosis patients. The safety and efficacy of anselamimab combined with SoC for PCD versus placebo combined with SoC PCD treatment will be evaluated in the study, which has a primary completion date in December 2024. A second Phase 3 study (CAEL101–302;

NCT04512235) with a similar study design is recruiting an estimated 267 Mayo Stage IIIa PCD treatment-naïve AL amyloidosis patients. The primary completion date of the CAEL101–302 study is in March 2025.

Latozinemab (Alector Inc, GSK)

Latozinemab (AL001, GSK4527226) is a human IgG1κ monoclonal antibody being developed by Alector in collaboration with GSK to treat frontotemporal dementia due to progranulin gene mutation (FTD-GRN), a rare early-onset form of dementia. Progranulin (PGRN) levels are severely reduced in the plasma and cerebrospinal fluid of both affected patients and asymptomatic mutation carriers of FTD-GRN. PGRN is a secreted lysosomal chaperone, immune regulator, and neuronal survival factor that is shuttled to the lysosome through multiple receptors, including sortilin. Latozinemab specifically binds sortilin and blocks the sortilin–PGRN interaction and facilitates a decrease in the levels of sortilin. Thus, increasing the levels of PGRN in plasma and cerebrospinal fluid has the potential to slow disease progression in carriers of heterozygous loss-of-function GRN mutations. Latozinemab was generated and affinity-matured through collaboration between Alector and Adimab to optimize in vitro and in vivo activity and manufacturability. The Fc domain of latozinemab was engineered to minimize binding to Fcγ receptors, complement activation, and ADCC.[113] Alector received Orphan Drug designation from the FDA for AL001 for the treatment of frontotemporal dementia.

The Phase 3 double-blind, placebo controlled INFRONT-3 study (NCT04374136) is evaluating the efficacy and safety of AL001 in participants at risk for or with frontotemporal dementia due to heterozygous mutations in the PGRN gene. Designed to include an estimated 180 participants, the study has a primary completion date in October 2023. Alector reported that it, along with GSK, received scientific advice from the FDA and EMA regarding the INFRONT-3 study. Based on feedback from these agencies, the companies performed a sample size re-estimation that is anticipated to support a more focused enrollment of approximately 90–100 symptomatic participants for a treatment duration of 96 weeks. Target enrollment in the INFRONT-3 has been achieved.[114]

Apitegromab (Scholar Rock)

Apitegromab (SRK-015) is a human IgG4λ monoclonal antibody targeting myostatin developed by Scholar Rock for the treatment of spinal muscular atrophy (SMA). SMA is a rare genetic neurological disorder in which the degeneration of motor neurons leads to progressive muscle atrophy and paralysis. Myostatin, a member of the TGFβ superfamily primarily expressed by skeletal muscle cells, is a negative regulator of skeletal muscle growth. Apitegromab was designed to bind both pro- and latent forms of myostatin in the skeletal muscle, thus inhibiting myostatin activation and providing clinically meaningful improvement in motor function in patients with SMA.

Apitegromab has received Fast Track, Orphan Drug, and Rare Pediatric Disease designations from the FDA, as well as Priority Medicines and Orphan Medicinal Product designations from the EMA for the treatment of SMA. Scholar Rock anticipates data readout from the SAPPHIRE Phase 3 study in Q4 2024 and, after approval, launch of apitegromab in 2025.[115]

Following the success of the Phase 2 proof-of-concept study TOPAZ, which assessed the safety and efficacy of apitegromab in later-onset SMA (Type 2 and Type 3) and showed substantial and sustained functional improvements in non-ambulatory Types 2 and 3 SMA patients, Scholar Rock designed two Phase 3 studies, SAPPHIRE (NCT05156320) and ONYX (NCT05626855). SAPPHIRE is a double-blind, placebo-controlled, Phase 3 study evaluating the safety and efficacy of apitegromab in non-ambulatory patients with Types 2 and 3 SMA who are receiving SMN therapy (nusinersen or risdiplam), which has completed the enrollment by September 2023. Patients are randomized 1:1:1 to receive for 12 months either apitegromab 10 mg/kg, apitegromab 20 mg/kg, or placebo by IV infusion every 4 weeks. The primary outcome measure is the change from baseline, up to 12 months, in Hammersmith Functional Motor Scale Expanded (HFMSE) total score. ONYX is an open-label, multicenter, extension study that will evaluate the long-term safety and efficacy of apitegromab in patients with Type 2 and Type 3 SMA who have completed TOPAZ or SAPPHIRE.

Antibodies to watch in 2024: cancer indications

Of the antibody therapeutics in late-stage clinical studies that are being evaluated as treatments for cancer, companies sponsoring 13 of these have indicated that they may submit marketing applications to regulatory authorities by the end of 2024. Notably, three of these molecules are bispecific (linvoseltamab, zenocutuzumab, erfonrilimab) and four are ADCs (tusamitamab ravtansine, patritumab deruxtecan, datopotamab deruxtecan, MRG002). Relevant details for the 13 molecules are summarized below, with the summaries in order according to the approximate timing of possible marketing application submissions, as shown in Table 4. Additional data for these molecules can be found in Supplemental Table S3.

Linvoseltamab (Regeneron)

Linvoseltamab (REGN5458) is a bispecific IgG4κ T-cell engaging antibody targeting BCMA and CD3, derived from Regeneron's proprietary *VelocImmune*® and *Veloci-Bi*® platforms. Linvoseltamab received Fast Track designation from the FDA for MM. Regeneron plans a BLA submission for the fourth quarter of 2023.[116]

Linvoseltamab is under investigation in the ongoing, open-label, multicenter pivotal Phase 1/2 dose-escalation and dose-expansion LINKER-MM1 trial (NCT03761108) in patients with RRMM who have received at least three prior lines of therapy or are triple refractory. The Phase 2 part of the trial evaluated two dosing conditions, 50 mg (*n*

Table 4. Commercially sponsored investigational monoclonal antibodies in late-stage clinical studies for cancer indications, with regulatory submission anticipated during 2023–2024.

INN or drug code	Target(s); format	Indication of relevant* late-stage study (est. submission year#)	Most advanced clinical phase
Linvoseltamab	BCMA, CD3; Human IgG4κ, Bispecific	Multiple myeloma (2023 submission)	Phase 3
Apamistamab-Iodine (131I)	CD45; Murine IgG1κ, Radiolabeled	Ablation of bone marrow prior to transplantation in AML patients (2023 submission)	Phase 3
Tiragolumab	TIGIT; Human IgG1κ	NSCLC (2024 submission)	Phase 3
Tusamitamab ravtansine	CEACAM5; Humanized IgG1κ, ADC	NSCLC (2024 submission)	Phase 3
Patritumab deruxtecan	HER3; Human IgG1κ, ADC	NSCLC (2024 submission)	Phase 3
Datopotamab deruxtecan	TROP-2; Humanized IgG1κ, ADC	HR+/HER2- breast cancer (2024 submission)	Phase 3
MRG002	HER2; Humanized IgG1, ADC	HER2+ breast cancer (2024 submission)	Phase 3
Botensilimab	CTLA-4; Human IgG1κ	Colorectal cancer (2024 submission)	Pivotal Phase 2
Bifikafusp alfa, Onfekafusp alfa	Fibronectin extra-domain B; Human scFv-based immunocytokine, mixture	Melanoma (2024 submission)	Phase 3
Zenocutuzumab	HER2, HER3; Humanized IgG1κ Bispecific	NRG1+ pancreatic ductal adenocarcinoma (2024 submission)	Pivotal Phase 2
Erfonrilimab	PD-L1, CTLA-4; Humanized/chimeric IgG1, Bispecific	Pancreatic ductal adenocarcinoma (2024 submission)	Phase 3
Felzartamab	CD38; Human IgG1λ	Multiple myeloma (2024 submission)	Phase 3
Sabatolimab	TIM-3; Humanized IgG4κ	Myelodysplastic syndrome (2024 submission)	Phase 3

*Indication for which a regulatory submission is anticipated. #First marketing application submission dates are estimates. The table includes information publicly available as of November 1, 2023. Abbreviations: ADC, antibody–drug conjugate; BCMA, B-cell maturation antigen; CEACAM5, carcinoembryonic antigen-related cell adhesion molecule-5; CTLA-4, cytotoxic T lymphocyte antigen-4; HER, human epidermal growth factor receptor; PD-L1, programmed cell death protein ligand 1; TIGIT, T-cell immunoreceptor with ig and ITIM domains; TIM-3, T cell immunoglobulin and mucin-domain containing-3. See supplemental table S3 for more details about each antibody. Additional data for investigational antibody therapeutics in late-stage clinical studies are also available at: https://www.antibodysociety.org/antibodies-in-late-stage-clinical-studies/.

= 104) or 200 mg ($n = 117$), both given Q1W for 3 cycles followed by Q2W dosing onwards. Patients in the 200 mg group who achieved at least a very good partial response reduced dosing to Q4W from cycle 6 onwards. Interim results demonstrate that the 200 mg dosing gave the superior response. Patients treated with 200 mg linvoseltamab had a 71% ORR as measured by the local investigator, with 84% and 79% probability of maintaining a response at 6 and 12 months, respectively.[117] The median PFS was 7.9 months for the 50 mg cohort, whereas it was not yet reached for the 200 mg cohort. The primary endpoint is ORR as assessed by an independent review committee, the data of which will be available in late 2023. Based on the promising interim data, Regeneron has initiated an open-label, randomized Phase 3 LINKER-MM3 trial (NCT05730036) investigating linvoseltamab at 200 mg compared to elotuzumab, pomalidomide, and dexamethasone combination therapy.[118] This study began enrollment in September 2023 and has an estimated completion date in December 2032.

Apamistamab-iodine131 (Actinium Pharmaceuticals, Inc.)

Apamistamab-I131 (Iomab-B) is an anti-CD45 murine IgG1κ antibody radiolabelled with iodine-131. The antibody is designed to deliver targeted myeloablative radioactivity to stem cells and leukemic blasts in the bone marrow as a conditioning therapy to be used prior to an allogeneic bone marrow transplant (BMT) for patients with active, relapsed, or refractory acute myeloid leukemia (AML). Iomab-B has been granted Orphan Drug designations for AML by FDA and EMA. Actinium Pharmaceuticals licensed the European, Middle East, and North African commercial rights of Iomab-B to Immedica Pharma AB in April 2022. BLA submission is expected by the end of 2023, with marketing application submission in Europe expected in 2024.[119]

The marketing applications will be based on positive results from the pivotal Phase 3 SIERRA trial (NCT02665065), which included 153 patients with active RR AML aged 55+ with >5% bone marrow blasts.[120] Patients were randomized 1:1 to receive either individualized doses of Iomab-B or physician's choice of conventional care, with all patients receiving Iomab-B undergoing bone marrow transplant, while only those who achieved complete remission in the conventional care group progressed to bone marrow transplant (14/77). However, 44 of the conventional care patients transferred across to the Iomab-B arm, and 40 of these were able to undergo bone marrow transplant. The primary endpoint of 6-month durable complete remission was met, with 22% of Iomab-B patients achieving this compared to 0% of conventional care patients, which resulted in statistical significance ($p < 0.0001$). In addition, Iomab-B doubled 1-y survival rates and overall survival, and patients administered Iomab-B had fewer adverse events compared to those in the conventional care arm.

Tiragolumab (Genentech, a member of the Roche Group)

Tiragolumab (RG6058, MTIG7192A) is a human IgG1κ mAb targeting T-cell immunoreceptor with Ig and ITIM domains (TIGIT), an inhibitory immune checkpoint expressed on T cells and NK cells. The combination of tiragolumab plus anti-PD-L1 Tecentriq® (atezolizumab) has been extensively evaluated in NSCLC patients, as well as patients with esophageal cancer. Roche anticipates possible submission of marketing applications in 2024 for tiragolumab in first line, PD-L1-high NSCLC based on study read-outs expected in the

first quarter of 2024, and a submission specifically in China for first-line esophageal cancer based on a study read-out anticipated in 2024.[121] Tiragolumab, in combination with atezolizumab, was granted Breakthrough Therapy designation by the FDA, for the first-line treatment of people with metastatic NSCLC whose tumors have high PD-L1 expression with no EGFR mutation or ALK genomic tumor aberrations.

Tiragolumab is being evaluated as a treatment for several types of solid tumors in the SKYSCRAPER program (SKYSCRAPER-01 through -14 studies). SKYSCRAPER-01 (NCT04294810) is a global Phase 3, randomized double-blinded study to evaluate the efficacy and safety of tiragolumab plus atezolizumab compared with placebo plus atezolizumab in participants with previously untreated locally advanced, unresectable, or metastatic PD-L1-selected NSCLC, with no EGFR mutation or ALK translocation. The study was initiated in March 2020 with an estimated enrollment of 660 participants randomized 1:1 to receive either tiragolumab (600 mg administered by IV infusion Q3W on Day 1 of each 21-d cycle) plus Tecentriq (1200 mg administered by IV infusion Q3W on Day 1 of each 21-d cycle) or placebo plus Tecentriq, until disease progression, loss of clinical benefit, or unacceptable toxicity. Roche has reported that SKYSCRAPER-01 did not meet one of its primary endpoints (PFS) as of Q2 2022.[122] Interim results for overall survival were not mature at the time of analysis, with median overall survival estimates of 22.9 months in the tiragolumab plus Tecentriq arm and 16.7 months in the Tecentriq monotherapy arm.[123] SKYSCRAPER-01 study read-outs are expected in the fourth and first quarters of 2023 and 2024, respectively.

SKYSCRAPER-08 (NCT04540211) is a Phase 3 randomized, double-blind study evaluating tiragolumab and atezolizumab in combination with paclitaxel and cisplatin compared with placebo and paclitaxel and cisplatin as first-line treatment in an estimated 540 patients with unresectable locally advanced, unresectable recurrent, or metastatic esophageal carcinoma. Initiated in December 2020, patient recruitment ($n = 461$) was completed in the fourth quarter of 2021; Roche anticipates a readout from the SKYSCRAPER-08 study in 2024.

Tusamitamab ravtansine (Sanofi)

Tusamitamab ravtansine (SAR408701) is a humanized IgG1κ antibody targeting carcinoembryonic antigen-related cell adhesion molecule-5 (CEACAM5) conjugated to DM4, an anti-tubulin maytansinoid agent. The ADC incorporates ImmunoGen's targeted antibody payload technology. Sanofi anticipates marketing application submission(s) for tusamitamab ravtansine in second- and third-line NSCLC in 2024.[124]

A Phase 3 study, as well as two Phase 2 studies, are investigating tusamitamab ravtansine as a single agent and in combination with other therapies in NSCLC patients. The open-label Phase 3 trial (NCT04154956; CARMEN-LC03) is designed to determine whether tusamitamab ravtansine improves PFS and/or OS when compared to docetaxel in participants with metastatic non-squamous NSCLC expressing CEACAM5 greater than or equal to 2+ in intensity in at least 50% of the tumor cell population and previously treated with SoC platinum-based chemotherapy and an immune checkpoint inhibitor. Patients receive either tusamitamab ravtansine 100 mg/m^2 IV Q2W or the SoC treatment docetaxel 75 mg/m^2 IV every 3 weeks. The two primary endpoints, PFS and OS, will be analyzed on randomized participants at the time of the cutoff date for each given analysis. Initiated in February 2020, an estimated 450 participants are being enrolled (with the study actively recruiting participants), and the study has an estimated primary completion date in July 2024. Interim analysis of this study is expected in the second half of 2023.[124]

The CARMEN-LC04 (NCT04394624) is a two-part study, with an estimated enrollment of 43 participants, aiming to evaluate tolerability and to confirm the recommended dose of tusamitamab ravtansine in combination with ramucirumab in the NSQ NSCLC population in part 1. The second part will assess the antitumor activity of tusamitamab ravtansine in combination with ramucirumab in the NSQ NSCLC population. This ongoing study was initiated in August 2020 and has an estimated primary completion date in December 2024.

In the CARMEN-LC05 trial (NCT04524689), an estimated 120 patients with CEACAM positive-expression non-squamous NSCLC will be enrolled with a primary objective to assess the tolerability and to determine the recommended doses of tusamitamab ravtansine in combination with pembrolizumab and tusamitamab ravtansine in combination with pembrolizumab and platinum-based chemotherapy with or without pemetrexed in the NSQ NSCLC population. Secondary objectives include evaluating the safety, antitumor activity, pharmacokinetics, and immunogenicity of each combination. Initiated in October 2020, the study's estimated primary completion date is in May 2024.

Patritumab deruxtecan (Daiichi Sankyo, Merck & Co.)

Patritumab deruxtecan (HER3-DXd, U3–1402) is an ADC consisting of a human IgG1κ monoclonal antibody targeting human epidermal growth factor receptor 3 (HER3) conjugated to DXd/DX-8951, which is a topoisomerase I inhibitor payload, via a stable tetrapeptide (GGFG)-based cleavable linker. Developed by Daiichi Sankyo, Patritumab deruxtecan was granted FDA's Breakthrough Therapy designation by the FDA in December 2021 for the treatment of patients with EGFR-mutated locally advanced or metastatic NSCLC with disease progression on or after treatment with a third-generation tyrosine kinase inhibitor (TKI) and platinum-based therapies. In October 2023, Daiichi Sankyo and Merck & Co., Inc., announced they entered into a global development and commercialization agreement for patritumab deruxtecan, as well as two other Daiichi Sankyo's investigational ADCs. Daiichi Sankyo maintains exclusive rights in Japan and the companies will jointly develop and potentially commercialize these ADC candidates elsewhere. The submission of a BLA for patritumab deruxtecan is planned by the end of March 2024.[125]

The BLA will be based on the results of the Phase 2 HERTHENA-Lung01 study (NCT04619004), which was evaluated HER3-DXd in patients with advanced *EGFR*-mutated NSCLC previously treated with EGFR tyrosine

kinase inhibitor (TKI) therapy and platinum-based chemotherapy (PBC).[126] Patients in the study group 1 (n = 225) received HER3-DXd 5.6 mg/kg (IV) once Q3W. Those in the study group 2 received an up-titration regimen (3.2 → 4.8 → 6.4 mg/kg). The primary end point was confirmed ORR (RECIST 1.1) by blinded independent central review. After a median study duration of 18.9 (range, 14.9–27.5) months, the ORR confirmed by BICR was 29.8% (95% CI, 23.9 to 36.2), while the median duration of response, median PFS, and median OS were 6.4, 5.5, and 11.9 months, respectively. The confirmed CNS ORR by BICR per CNS RECIST was 33.3% (95% CI, 17.3 to 52.8) in patients with nonirradiated brain metastases at baseline (n = 30). The safety profile was manageable and tolerable. The randomized Phase 3 HERTHENA-Lung02 study (NCT05338970) of patritumab deruxtecan vs PBC in *EGFR*-mutated NSCLC after failure of EGFR TKI therapy is ongoing.

Datopotamab deruxtecan (Daiichi Sankyo Co., Ltd., AstraZeneca)

Datopotamab deruxtecan (Dato-DXd) is an ADC composed of a humanized anti-TROP2 IgG1κ antibody attached to a novel topoisomerase I inhibitor payload by a tetrapeptide-based cleavable linker; the drug-to-antibody ratio (DAR) is four. The ADC is being jointly developed by AstraZeneca and Daiichi Sankyo for breast and lung cancer. The companies announced positive topline results for a Phase 3 study of Dato-DXd in HR+/HER2− breast cancer and, as of October 2023, are planning global regulatory submissions.[127]

The Phase 3 TROPION-Breast01 study (NCT05104866) is evaluating the efficacy and safety of Dato-DXd compared with investigator's choice of SoC chemotherapy in patients with inoperable or metastatic HR+/HER2− breast cancer who have received one or two prior lines of systemic chemotherapy in the inoperable or metastatic setting.[128] Patients are randomized 1:1 to Dato-DXd 6 mg/kg IV Q3W or ICC (eribulin, capecitabine, vinorelbine, or gemcitabine) until progression. The dual primary end points are PFS (per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1)), as assessed by blinded independent central review (BICR) and OS. Median PFS was 6.9 months in patients treated with datopotamab deruxtecan vs. 4.9 months in those treated with chemotherapy, while the ORR was 36.4% in patients treated with datopotamab deruxtecan vs. 22.9% in patients treated with chemotherapy. The study is ongoing to assess OS.[127]

The TROPION-Lung01 Phase 3 trial (NCT04656652) TROPION-Lung01 enrolled approximately 600 patients at sites in Asia, Europe, North America, and South America. Patients are randomized 1:1 to Dato-DXd 6 mg/kg IV Q3W or docetaxel. The primary endpoints of TROPION-Lung01 are PFS as assessed by BICR and OS. Median PFS was 5.6 months in patients treated with datopotamab deruxtecan vs. 3.7 months in those treated with docetaxel. The ORR was 31.2% for the datopotamab deruxtecan arm vs 12.8% with docetaxel. The median DoR was 7.7 months in the datopotamab deruxtecan arm vs 5.6 months in the docetaxel arm.[129]

MRG002 (Shanghai Miracogen, Inc., LEPU Biopharma Co., Ltd.)

MRG002, developed by Shanghai Miracogen and Lepu Biopharma, is an ADC targeting HER2. The antibody portion is an IgG1κ with the same amino acid sequence as trastuzumab, but it is hyper-fucosylated to impair ADCC and lower off-target toxicity. The payload is MMAE, conjugated to the interchain cysteines of MAB802 via a cleavable valine-citrulline linker with an average DAR of 3.8.[130] MRG002 was granted Orphan Drug designations for gastric cancer and gastroesophageal junction cancer by the FDA and is currently in late-stage development for HER2-expressing breast cancer and urothelial cancer. The registrational Phase 2/3 study (NCT04924699) of MRG002 versus KADCYLA® (trastuzumab emtansine) for the treatment of patients with HER2-positive unresectable locally advanced or metastatic breast cancer is ongoing. Lepu Biopharma announced completion of the Phase 2 enrollment in China, in January 2023, and plans to submit an NDA for this indication.[131]

The primary objective of the Phase 2 portion of the NCT04924699 study is to evaluate the safety, efficacy, pharmacokinetics, and immunogenicity of MRG002 in patients with HER2-positive, unresectable locally advanced or metastatic breast cancer. Patients receive an IV infusion of 2.6 mg/kg MRG002 once on Day 1 of every 21-d cycle. The primary objective of the Phase 3 portion of the study is to evaluate the efficacy and safety of MRG002 versus KADCYLA® in patients with HER2-positive unresectable locally advanced or metastatic breast cancer, who were previously treated with trastuzumab (or a biosimilar) and an anti-HER2 tyrosine kinase inhibitor and have progressed on or after the most recent therapy. The completion date of the NCT04924699 study is in October 2023.

MRG002 is also being evaluated in an open-label, randomized, multi-center Phase 3 study (NCT05754853) for the treatment of patients with HER2-positive unresectable locally advanced or metastatic urothelial cancer. In this study, MRG002 will be administrated by an IV infusion of 2.2 mg/kg on Day 1 of every 21-d cycle. The study's primary objective is to compare the OS and PFS between MRG002 and investigator selected chemotherapy in patients with HER2-positive unresectable locally advanced or metastatic urothelial cancer, previously treated with platinum-based chemotherapy and PD-1/PD-L1 inhibitors. The primary completion date of the study is in October 2025.

Botensilimab, in combination with Balstilimab (Agenus Inc.)

Botensilimab (AGEN1181), an IgG1κ antibody against cytotoxic T lymphocyte-associated protein 4 (CTLA-4), is in development as monotherapy and in combination with anti-PD-1 balstilimab (AGEN2034) for the treatment of colorectal cancer and melanoma. Botensilimab's Fc is engineered for increased binding to activating Fc receptors (FcgRIIIA), which enhances T cell activation, expansion, and memory. In April 2023, the FDA granted Fast Track Designation for the combination of botensilimab and balstilimab for the treatment of patients with

non-microsatellite instability-high (MSI-H)/deficient mismatch repair (dMMR) metastatic colorectal cancer (CRC) with no active liver involvement. The company plans to submit a BLA to the FDA in mid-2024.[132]

Data from a Phase 1 study (NCT03860272) of the botensilimab and balstilimab combination in CRC patients were presented at the 2023 ESMO World Congress on Gastrointestinal Cancer held in Barcelona, Spain. In 69 evaluable patients with non-MSI-High CRC without active liver metastases treated with botensilimab and balstilimab, the overall response rate was 23% and the median overall survival (mOS) was 20.9 months compared to a 2.8% and 12.9 months with standard care, respectively. In all 87 patients evaluable for efficacy, the overall response rate and OS were 18% and 20.9 months, respectively.[133]

Agenus is sponsoring an open-label, Phase 2 study (NCT05608044) to evaluate the efficacy, safety, tolerability, and pharmacokinetic profiles of botensilimab as monotherapy and in combination with balstilimab or SoC treatments in participants with refractory metastatic colorectal cancer. The study is recruiting an estimated 230 patients and the primary completion date is in January 2024. A global Phase 3 trial in non-MSI-H CRC is being planned.

In addition, a Phase 2 open-label, 2-part, multicenter study (NCT05529316) with an estimated enrollment of 220 participants is evaluating the efficacy, safety, tolerability, and pharmacokinetic profiles of botensilimab as monotherapy and in combination with balstilimab in participants with advanced cutaneous melanoma refractory to checkpoint inhibitor therapy. The study is currently recruiting and has a primary completion date in October 2023.

Bifikafusp alfa, Onfekafusp alfa (Philogen SpA)

Nidlegy™, developed by the Italo-Swiss company Philogen as an intralesional treatment for patients with advanced locoregional melanoma and non-melanoma skin cancers, is a combination of two immunocytokines, L19IL2 and L19TNF. The antibody portion of these molecules is the L19 single-chain variable fragment (scFv) antibody, specific for the extra-domain B (EDB) of fibronectin, which is fused to pro-inflammatory cytokines with anti-tumor activity. In L19IL2 (bifikafusp alfa, Darleukin), the L19 scFv is fused to interleukin 2 (IL2) and assembles in a diabody dimer. In L19TNF (onfekafusp alfa, Fibromun), the L19 scFv is fused to tumor necrosis factor (TNF), and the molecule assembles, via TNF, in a non-covalent trimer. Based on promising results from the Phase 3 PIVOTAL study, Philogen plans to a submit marketing application to the EMA in 2024.[134]

Nidlegy is currently being investigated in two Phase 3 studies (PIVOTAL NCT02938299 in Europe; NeoDREAM NCT03567889 in the US) for the treatment of patients with fully resectable stage IIIB/C melanoma, and two Phase 2 studies for the treatment of non-melanoma skin cancers, including high-risk locally advanced basal cell carcinoma and cutaneous squamous cell carcinoma (NCT04362722, NCT05329792). The PIVOTAL and NeoDREAM Phase 3 trials are open-label, multi-center, randomized, comparator-controlled, studies evaluating the efficacy and safety of intratumoral injections of Nidlegy™ as a neoadjuvant treatment, followed by surgery, versus surgery alone, in stage IIIB/C melanoma patients with locally advanced, fully resectable cutaneous, sub-cutaneous (including satellite/in transit metastases), or nodal metastases accessible to intratumoral injection. In both study arms, patients were allowed to receive approved adjuvant systemic therapies after surgery. Nidlegy™ was injected intralesionally once a week, up to four times, before surgery. In October 2023, Philogen announced that Nidlegy met the primary endpoint of the Phase 3 PIVOTAL study, showing a significant improvement in recurrence-free survival compared to surgery alone, and that treatment-related adverse events observed were benign and manageable.[134]

Zenocutuzumab (Merus N.V.)

Zenocutuzumab (MCLA-128) is a humanized bispecific IgG1 antibody that binds to HER2 and to HER3, blocking the interaction of HER3 with its ligand neuregulin 1 (NRG1) or NRG1-fusion proteins. The antibody was derived from Merus' Biclonics® platform and utilizes their Dock & Block® mechanism. Merus is developing zenocutuzumab as a treatment for NRG1+ cancers. FDA granted Breakthrough Therapy Designation for zenocutuzumab for the treatment of patients with advanced unresectable or metastatic NRG1 fusion (NRG1+) pancreatic cancer following progression with prior systemic therapy or who have no satisfactory alternative treatment options, Fast Track Designation for the treatment of patients with metastatic solid tumors harboring NRG1 gene fusions that have progressed on standard of care therapy, and Orphan Drug Designation for the treatment of patients with pancreatic cancer. Merus expects to have data in the first half of 2024 to support potential BLA submissions for zenocutuzumab in both NRG1+ pancreatic ductal adenocarcinoma (PDAC) and NSCLC.[135]

Merus recently reported interim results of the ongoing pivotal, dose escalation/expansion Phase 1/2 eNRGy trial (NCT02912949), which consists of three cohorts: 1) NRG1+ pancreatic cancer; 2) NRG1+ NSCLC; and 3) NRG1+ cancer, and an early access program (NCT04100694) that allows single patient/named access to zenocutuzumab.[136,137] In the dose expansion period of the eNRGy study, participants receive IV infusions of 750 mg of zenocutuzumab Q2W. The primary endpoint is ORR using RECIST v1.1 per investigator assessment. As of July 31, 2023, data cutoff date, 44 patients with NRG1+ PDAC were treated with zenocutuzumab. Of these, 33 patients, treated with zenocutuzumab more than 24 weeks before the data cutoff date, were included in the primary analysis population. The median duration of exposure was 9.4 months (range, 1–34). The ORR was 42.4% (95% CI, 25.5–60.8), 82% (27/33) experienced tumor reduction, and the clinical benefit rate was 72.7% (95% CI, 54–87). Also, as of July 31, 2023, data cutoff date in the eNRGy trial, 105 patients with NRG1+ NSCLC had been treated with zenocutuzumab. Of these, 78 patients, treated with zenocutuzumab more than 24 weeks before the data cutoff date, were included in the primary analysis population. For these patients, the ORR was 37.2% (29/78; 95% Cl: 26.5–48.9), median DOR was 14.9 months (95% CI, 7.2–20.4), and the clinical benefit rate was 61.5% (95% CI: 49.8–72.3).

Erfonrilimab (Alphamab Oncology)

Erfonrilimab (KN046) is a humanized single-domain bispecific antibody-Fc fusion protein (VH-VH-h-CH2-CH3 dimer) that targets the immune checkpoints PD-L1 and CTLA-4. It is being developed by Jiangsu Alphamab Biopharmaceuticals Co., Ltd., a wholly owned subsidiary of Alphamab Oncology, and has been granted Orphan Drug designations by the FDA for thymic epithelial tumors and in combination with the anti-HER2 bispecific antibody KN026 (anbenitamab) for gastric cancer. Alphamab expects data readout for a Phase 3 study of KN046 in pancreatic ductal adenocarcinoma (PDAC) and intends to initiate pre-BLA activities in the fourth quarter of 2023.[138]

Erfonrilimab is being investigated in the placebo-controlled Phase 3 ENREACH-PDAC-01 study (NCT05149326) as a treatment for advanced PDAC. ENREACH-PDAC-01 was designed to evaluate the efficacy and safety of erfonrilimab in patients with histologically or cytologically confirmed PDAC with no prior systemic therapy. Patients ($n = 408$) were randomized 1:1 to receive 5 mg/kg IV erfonrilimab Q2W combined with chemotherapy (gemcitabine and nab-paclitaxel) or placebo plus chemotherapy. The OS is the primary study endpoint; OS data readout is expected in Q4 2023.[138]

Erfonrilimab is also being evaluated in the Phase 3 ENREACH-LUNG-1 study (NCT04474119) as a treatment for advanced squamous NSCLC. A total of 482 patients with advanced NSCLC who had no previous systemic treatments and no known EGFR mutation were enrolled and subsequently randomized 1:1 to receive either 5 mg/kg IV erfonrilimab Q3W plus chemotherapy (carboplatin and paclitaxel) or placebo plus chemotherapy. In March 2022, the first interim analysis was completed, and the company announced that erfonrilimab had reached the pre-specified progress-free survival endpoint. However, in May 2023, Alphamab Oncology announced that the OS had not yet reached statistically significant difference, and the study is continuing to collect further follow-up OS data until the final OS analysis.[139] This OS data readout is expected in early 2024.

Felzartamab (I-Mab Biopharma, MorphoSys, Human Immunology Biosciences)

Felzartamab (TJ202) is a human IgG1κ antibody directed against CD38, which is highly expressed on the surface of plasma cells. The antibody induces the depletion of such cells via ADCC and ADCP mechanisms. In 2017, MorphoSys entered into an exclusive regional licensing agreement with I-Mab Biopharma to develop and commercialize felzartamab in Greater China (Mainland China, Hong Kong, Macau, and Taiwan). I-Mab is evaluating felzartamab in a Phase 3 study of patients with RRMM. I-Mab Biopharma anticipates a Phase 3 study readout in 2024 may be followed by a marketing application submission for felzartamab for MM.[140]

Felzartamab in combination with lenalidomide and dexamethasone is being evaluated in the randomized, open-label, parallel-controlled Phase 3 study (NCT03952091) as second-line treatment for MM. The study has enrolled a total of 291 patients at multiple sites in China and is no longer recruiting participants. The primary endpoint of the study is PFS, and the estimated primary completion date is in May 2024.

In June 2022, exclusive worldwide rights for felzartamab outside of Greater China were licensed from MorphoSys by HI-Bio, which is evaluating felzartamab for membranous nephropathy and Immunoglobulin A nephropathy in early-stage clinical studies. FDA has granted HI-Bio orphan drug designation for felzartamab for the treatment of membranous nephropathy.[141]

Sabatolimab (Novartis Pharmaceutical Corporation)

Sabatolimab (MBG453) is a hinge-stabilized, humanized anti-T-cell immuno-globulin and mucin-domain domain-containing molecule-3 (TIM-3) IgG4κ antibody in development by Novartis for the treatment of myelodysplastic syndrome (MDS) and AML. Novartis plans regulatory submission(s) in 2024 for sabatolimab in high-risk MDS.[142] Sabatolimab has been granted Fast Track and Orphan Drug designations for MDS by FDA and EMA, respectively.

The efficacy and safety of sabatolimab are being evaluated in two Phase 2 and one Phase 3 clinical studies of patients with MDS, STIMULUS-MDS1 (Phase 2; NCT03946670), STIMULUS-MDS3 (Phase 2; NCT04812548), and STIMULUS-MDS2 (Phase 3; NCT04266301). The placebo-controlled STIMULUS-MDS1 study enrolled 127 participants who were randomized 1:1 to sabatolimab or placebo plus hypomethylating agents (HMA). Patients who received sabatolimab plus HMA had a complete remission rate (CRR) of 21.5% and median PFS of 11.1 months when compared to 17.7% CRR and PFS of 8.48 months for patients taking placebo plus HMA.[143] The open-label STIMULUS-MDS3 study evaluated whether sabatolimab, when given in combination with azacitidine and venetoclax, is safe and has beneficial effects in participants with high or very high-risk MDS. The study, which included a total of 20 participants, was completed in May 2023, but no results are available as of September 2023.

The placebo-controlled Phase 3 STIMULUS-MDS2 is evaluating sabatolimab with or without azacitidine for the treatment of patients with intermediate, high, or very high-risk MDS. Patients enrolled ($n = 530$) receive sabatolimab 800 mg and azacitidine 75 mg/m2 or azacitidine 75 mg/m2 and placebo. Novartis anticipates a readout milestone in 2024.[142]

Outlook for the future

Our data demonstrate the robustness of antibody therapeutics development, as performed by the biopharmaceutical industry over more than two decades. Antibody therapeutics continue to outperform small-molecule drugs in their approval success rates, and nearly 200 have been granted a marketing approval or are currently in regulatory review in at least one country as of November 2023 (www.antibodysociety.org/antibody-therapeutics-product-data). The number of antibody therapeutics in late-stage studies that we include here (138) is identical to than that reported last year, and substantially higher than that reported in Antibodies to Watch in 2010–

2022 (range 26–115; www.tandfonline.com/journals/kmab20/collections/antibodies-to-watch).

Based on our analysis for the early-stage commercial clinical pipeline of antibody therapeutics,[144] we continue to be optimistic about their prospects for development. As of October 2023, company clinical pipelines included over 1100 antibody therapeutics in Phase 1, Phase 1/2, or Phase 2 studies, with nearly 70% of these in development for cancer indications. For both cancer and non-cancer indications, ~60% of the molecules target novel antigens, suggesting the biopharmaceutical industry is engaging in innovative research and development. Of the early-stage antibodies for cancer: 1) the majority are monospecific, but ~33% are multispecific; 2) of the monospecifics, most are naked antibodies with immunomodulatory properties, and ~33% are ADCs; and 3) most of the multispecifics are cell engagers, of which ~33% have immunomodulatory properties. Of the early-stage antibodies for non-cancer indications, most are monospecific, with only 12% that are multispecific, and the majority are for immune mediated/inflammatory disorders (66%), followed by infectious diseases (15%), cardiovascular- or hemostasis-related indications (13%), and neurological disorders (12%).[144] We look forward to documenting the progress of these molecules as they enter late-stage clinical studies and become 'Antibodies to Watch' in the future.

Note added in proof: The following major events occurred around or within two weeks after the December 10, 2023 submission of 'Antibodies to Watch in 2024' for publication: 1) Sanofi announced the company is ending its tusamitamab ravtansine program; 2) BLAs for marstacimab, tarlatamab, and patritumab deruxtecan were submitted in the US; 3) FDA issued a complete response letter for cosibelimab's BLA; 4) marketing applications for CM310 and sacituzumab tirumotecan were submitted in China; 5) socazolimab was approved in China.

Abbreviations

Aβ	amyloid beta
ACR20	American College of Rheumatology 20%
AD	Alzheimer's disease
ADC	antibody-drug conjugate
ADCC	antibody-dependent cell-mediated cytotoxicity
ALK	anaplastic large-cell lymphoma kinase
AMD	age-related macular degeneration
AML	acute myeloid leukemia
Ang-2	angiopoietin-2
ANGPTL3	angiopoietin-like protein 3
ASCO	American Society of Clinical Oncology
BCMA	B cell maturation antigen
BLA	biologics license application
BMT	bone marrow transplant
BTC	biliary tract cancer
CAPOX	capecitabine/oxaliplatin
CAR-T	chimeric antigenic receptor – T cell
CDC	complement-dependent cytotoxicity
CHMP	Committee for Medicinal Products
CI	confidence interval
CLDN18.2	claudin 18.2
CLL	chronic lymphocytic leukemia
CNS	central nervous system
COVID-19	coronavirus disease 2019
CR	complete response
CRSwNP	chronic rhinosinusitis with nasal polyps
cSCC	cutaneous squamous cell carcinoma
CTLA-4	cytotoxic T lymphocyte antigen-4
DLBCL	diffuse large B-cell lymphoma
DM4	N2'-deacetyl-N2'-(4-mercapto-4-methyl-1-oxopentyl) maytansine
dMMR	deficient mismatch repair
EC	European Commission
EGFR	epidermal growth factor receptor
EMA	European Medicines Agency
EpCAM	epithelial cell adhesion molecule
ESCC	esophageal squamous cell carcinoma
ESMO	European Society for Medical Oncology
EU	European Union
EUA	Emergency use authorization
Fab	antigen-binding fragment
Fc	crystallizable fragment
FcγR	receptor for IgG Fc
FcRn	neonatal Fc receptor
FDA	US Food and Drug Administration
FL	follicular lymphoma
FRα	folate receptor alpha
GEA	gastroesophageal adenocarcinoma
GEJ	gastroesophageal junction
GPP	generalized pustular psoriasis
GPRC5D	G Protein-Coupled Receptor Class C Group 5 Member D
GvHD	graft-vs-host disease
HCC	hepatocellular carcinoma
HER2	human epidermal growth factor receptor 2
HLA	human leukocyte antigen
HoFH	homozygous familial hypercholesterolemia
HR	hazard ratio
HSCT	hematopoietic stem cell transplant
iADRS	Integrated AD Rating Scale
IDS	iduronate-2-sulfatase
IFN	interferon
IFNAR1	interferon alpha receptor 1
IGA	Investigator's Global Assessment
IgE	immunoglobulin E
IgG	immunoglobulin G
IL	interleukin
IM	intramuscular
INN	International Nonproprietary Names
IRRC	independent radiology review committee
IV	intravenous
LAG-3	lymphocyte-activation gene 3
LDH	lactate dehydrogenase
LDL	low-density lipoprotein
LM	leptomeningeal metastases
MAA	marketing authorization application
mAb	monoclonal antibody
MASP-2	mannan-binding lectin-associated serine protease-2
MET	mesenchymal epithelial transition factor
MM	multiple myeloma
MMAE	monomethyl auristatin E
MMR	mismatch repair
MSI	microsatellite instability
MTX	methotrexate
NDA	new drug application
NHL	non-Hodgkin's lymphoma
NIH	National Institutes of Health
NK	natural killer
NMPA	National Medical Products Administration
NSCLC	non-small cell lung cancer
OR	overall response
OS	overall survival
PCSK9	proprotein convertase subtilisin/kexin type 9
PD	pharmacodynamics
PD-1	programmed cell death protein 1
PD-L1	programmed cell death protein ligand 1

PD-L2	programmed death ligand 2
PFS	progression-free survival
PNH	paroxysmal nocturnal hemoglobinuria
PK	pharmacokinetics
PR	partial response
PRIME	Priority Medicines
PTCL	peripheral T cell lymphoma
PTI	personalized treatment intervals
RA	rheumatoid arthritis
RECIST	Response Evaluation Criteria in Solid Tumors
RR	relapsed or refractory
RSV	respiratory syncytial virus,
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SC	subcutaneous
scFv	single-chain variable fragment
T1D	type 1 diabetes
TCR	T cell receptor
TIGIT	T-cell Immunoreceptor with Ig and ITIM domains
TIM-3	T-cell immunoglobulin and mucin-domain domain-containing molecule-3
TMAs	thrombotic microangiopathies
TNF	tumor necrosis factor
UK	United Kingdom
US	United States
VEGF	human vascular endothelial growth factor
VHH	variable heavy chain single domain antibodies.

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References

1. Kaplon H, Reichert JM. Antibodies to watch in 2019. MAbs. 2019;11(2):219–238. doi: 10.1080/19420862.2018.1556465.
2. Thomas D, Chancellor D, Micklus A, LaFever S, Hay M, Chaudhuri S, Bowden R, Low AW. Clinical development success rates and contributing factors 2011–2020. Biotechnology Innovation Organization Report; 2021 Feb. [accessed 2023 Sept 12]. https://www.bio.org/clinical-development-success-rates-and-contributing-factors-2011-2020.
3. Thomas D, Burns J, Audette J, Carroll A, Dow-Hygelund C, Hay M Clinical development success rates 2006-2015. Biotechnology Innovation Organization Report; 2016. [accessed 2023 Sept]. https://www.bio.org/sites/default/files/legacy/bioorg/docs/Clinical%20Development%20Success%20Rates%202006-2015%20-%20BIO,%20Biomedtracker,%20Amplion%202016.pdf.
4. Hoy SM. Lecanemab: First Approval. Drugs. 2023;83(4):359–65. doi: 10.1007/s40265-023-01851-2.
5. Eisai. FDA grants traditional approval for LEQEMBI® (lecanemab-irmb) for the treatment of Alzheimer's disease; July 7, 2023, press release. [accessed 2023 Aug 15]. https://www.eisai.com/news/2023/news202349.html.
6. U.S. Food and Drug Administration. RYSTIGGO® (rozanolixizumab-noli) injection, for subcutaneous use. [accessed 2023 Aug 16].
7. Lazaridis K, Tzartos SJ. Autoantibody specificities in myasthenia gravis; implications for improved diagnostics and therapeutics. Front Immunol. 2020;11:212. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761286s000lbl.pdf.
8. Hoy SM. Rozanolixizumab: first approval. Drugs. 2023;83(16):1569. doi: 10.1007/s40265-023-01960-y.
9. Regeneron Pharmaceuticals, Inc. VEOPOZ™ (pozelimab-bbfg) receives FDA approval as the first treatment for children and adults with CHAPLE disease; 2023 Aug 18 press release. [accessed 2023 Oct 7]. https://investor.regeneron.com/news-releases/news-release-details/veopoztm-pozelimab-bbfg-receives-fda-approval-first-treatment.
10. Regeneron Pharmaceuticals, Inc. Regeneron corporate presentation; 2023 Aug. [accessed 2023 Oct 27]. https://investor.regeneron.com/static-files/a73a7d9c-591d-43e4-905f-6851ac1ff04e.
11. Keam SJ. Mirikizumab: first approval. Drugs. 2023;83(11):1045–52. doi: 10.1007/s40265-023-01909-1.
12. Eli Lilly and Company. FDA approves Lilly's Omvoh™ (mirikizumab-mrkz), a first-in-class treatment for adults with moderately to severely active ulcerative colitis; 2023 Oct 26 press release. [accessed 2023 Oct 27]. https://investor.lilly.com/news-releases/news-release-details/fda-approves-lillys-omvohtm-mirikizumab-mrkz-first-class.
13. Dubinsky MC, DB C, Hunter GT, Li X, Vermeire S, Hisamatsu T, SP T. Clinical effect of mirikizumab treatment on bowel urgency in patients with moderately to severely active ulcerative colitis and the clinical relevance of bowel urgency improvement for disease remission. Crohn's & Colitis 360. 2023;5(1). doi: 10.1093/crocol/otac044.
14. Eli Lilly and Company. Lilly's Mirikizumab helped patients with crohn's disease achieve long-term remission in phase 3 trial; 2023 Oct 12 press release. [accessed 2023 Oct 27]. https://investor.lilly.com/news-releases/news-release-details/lillys-mirikizumab-helped-patients-crohns-disease-achieve-long.
15. Janssen Pharmaceutical Companies of Johnson & Johnson. U.S. FDA approves TALVEY™ (talquetamab-tgvs), a first-in-class bispecific therapy for the treatment of patients with heavily pretreated multiple myeloma; 2023 Aug 10 press release. [accessed 2023 Oct 27]. https://www.janssen.com/fda-approves-talveytm-talquetamab-tgvs-first-class-bispecific-therapy-treatment-patients-heavily.
16. Janssen Pharmaceutical Companies of Johnson & Johnson. European Commission approves TALVEY® (talquetamab), Janssen's novel bispecific therapy for the treatment of patients with relapsed and refractory multiple myeloma; 2023 Aug 22 press release. [accessed 2023 Oct 27]. https://www.janssen.com/european-commission-approves-talvey-talquetamab-janssens-novel-bispecific-therapy-treatment.
17. Janssen Pharmaceutical Companies of Johnson & Johnson. Janssen presents longer-term talquetamab follow-up data showing overall response rates of more than 70 percent in heavily pretreated patients with multiple myeloma; 2023 June 3 press release. [accessed 2023 Oct 27]. https://www.janssen.com/emea/sites/www_janssen_com_emea/files/talquetamab_monumental_and_trimm2_asco_2023_press_release_.pdf.

18. Pfizer Inc. Pfizer's ELREXFIO™ receives U.S. FDA accelerated approval for relapsed or refractory multiple myeloma; 2023 Aug 14 press release. [accessed 2023 Oct 27]. https://investors.pfizer.com/Investors/News/news-details/2023/Pfizers-ELREXFIO-Receives-U.S.-FDA-Accelerated-Approval-for-Relapsed-or-Refractory-Multiple-Myeloma/default.aspx.
19. Lesokhin AM, Tomasson MH, Arnulf B, Bahlis NJ, Miles Prince H, Niesvizky R, Rodríguez-Otero P, Martinez-Lopez J, Koehne G, Touzeau C, et al. Elranatamab in relapsed or refractory multiple myeloma: phase 2 MagnetisMM-3 trial results. Nat Med. 2023;29(9):2259–2267. doi: 10.1038/s41591-023-02528-9.
20. Gramer MJ, van den Bremer ET, van Kampen MD, Kundu A, Kopfmann P, Etter E, Stinehelfer D, Long J, Lannom T, Noordergraaf EH, et al. Production of stable bispecific IgG1 by controlled Fab-arm exchange: scalability from bench to large-scale manufacturing by application of standard approaches. MAbs. 2013;5(6):962–73. doi: 10.4161/mabs.26233.
21. AbbVie. EPKINLY™ (epcoritamab-bysp) approved by U.S. FDA as the first and only bispecific antibody to treat adult patients with relapsed or refractory diffuse large B-Cell lymphoma (DLBCL); 2023 May 19 press release. [accessed 2023 Aug 19]. https://news.abbvie.com/news/press-releases/epkinly-epcoritamab-bysp-approved-by-us-fda-as-first-and-only-bispecific-antibody-to-treat-adult-patients-with-relapsed-or-refractory-diffuse-large-b-cell-lymphoma-dlbcl.htm
22. U.S. Food and Drug Administration. FDA grants accelerated approval to epcoritamab-bysp for relapsed or refractory diffuse large B-cell lymphoma and high-grade B-cell lymphoma; 2023 May 19. [accessed 2023 Aug 19]. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-grants-accelerated-approval-epcoritamab-bysp-relapsed-or-refractory-diffuse-large-b-cell.
23. Shirley M. Glofitamab: First Approval. Drugs. 2023;83(10):935–41. doi: 10.1007/s40265-023-01894-5.
24. U.S. Food and Drug Administration. COLUMVI (glofitamab-gxbm) injection, for intravenous use. [accessed 2023 Sep 14]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761309s000lbl.pdf.
25. European Medicines Agency. Columvi. [accessed 2023 Sep 14]. https://www.ema.europa.eu/en/medicines/human/EPAR/columvi
26. U.S. Food and Drug Administration. FDA grants accelerated approval to retifanlimab-dlwr for metastatic or recurrent locally advanced Merkel cell carcinoma; 2023 Mar 22. [accessed 2023 Aug 17]. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-retifanlimab-dlwr-metastatic-or-recurrent-locally-advanced-merkel.
27. Incyte. Incyte announces FDA approval of Zynyz™ (retifanlimab-dlwr) for the treatment of metastatic or recurrent locally advanced Merkel Cell Carcinoma (MCC); 2023 Mar 22 press release. [accessed 2023 Aug 17]. https://investor.incyte.com/news-releases/news-release-details/incyte-announces-fda-approval-zynyztm-retifanlimab-dlwr.
28. Kang C. Retifanlimab: first approval. Drugs. 2023;83(8):731–37. doi: 10.1007/s40265-023-01884-7.
29. Keam SJ. Concizumab: First Approval. Drugs. 2023;83(11):1053–59. doi: 10.1007/s40265-023-01912-6.
30. Biotech F. Novo Nordisk's Hemlibra rival faces another approval setback as FDA raises dosing, manufacturing questions; 2023 May 4 post. [accessed 2023 Oct 27]. https://www.fiercebiotech.com/biotech/novo-nordisks-hemlibra-rival-faces-another-approval-setback-fda-raises-dosing-queries.
31. Almirall SA Almirall receives European Commission approval of EBGLYSS® (lebrikizumab) for moderate-to-severe atopic dermatitis; 2023 Nov 17 press release. [accessed 2023 Nov 17]. https://www.almirall.com/newsroom/news/almirall-receives-european-commission-approval-of-ebglyss-lebrikizumab-for-moderate-to-severe-atopic-dermatitis.
32. Silverberg JI, Guttman-Yassky E, Thaçi D, Irvine AD, Stein Gold L, Blauvelt A, Simpson EL, Chu CY, Liu Z, Gontijo Lima R, et al. Two phase 3 trials of lebrikizumab for moderate-to-severe atopic dermatitis. N Engl J Med. 2023;388(12):1080–1091. doi: 10.1056/NEJMoa2206714.
33. Simpson EL, Gooderham M, Wollenberg A, Weidinger S, Armstrong A, Soung J, Ferrucci S, Lima RG, Witte MM, Xu W, et al. Efficacy and safety of lebrikizumab in combination with topical corticosteroids in adolescents and adults with moderate-to-severe atopic dermatitis: a randomized clinical trial (adhere). JAMA Dermatology. 2023;159(2):182–191. doi: 10.1001/jamadermatol.2022.5534.
34. Innovent Biologics, Inc. The National Medical Products Administration approves anti-PCSK9 monoclonal antibody sintbilo®(tafolecimab injection) for the treatment of adult patients with primary hypercholesterolemia and mixed dyslipidemia. 2023 Aug 16 press release. [accessed 2023 Sept 23]. https://www1.hkexnews.hk/listedco/listconews/sehk/2023/0816/2023081601083.pdf.
35. Huo Y, Li Y, Zhang P, Deng H, Li H, An P, Xue F, Yu Z, Ma Q, Qi L, et al. Efficacy and safety of tafolecimab in Chinese patients with non-familial hypercholesterolemia (CREDIT-1): a 48-week randomized, double-blind, placebo-controlled phase 3 trial. Circulation. 2022;146(Suppl_1):10111. doi:10.1161/circ.146.suppl_1.10111.
36. Chai M, He Y, Zhao W, Han X, Zhao G, Ma X, Qiao P, Shi D, Liu Y, Han W, et al. Efficacy and safety of tafolecimab in Chinese patients with heterozygous familial hypercholesterolemia: a randomized, double-blind, placebo-controlled phase 3 trial (CREDIT-2). BMC Med. 2023;21(1):77. doi: 10.1186/s12916-023-02797-8.
37. Qi L, Liu D, Qu Y, Chen B, Meng H, Zhu L, Li L, Wang S, Liu C, Zheng G, et al. Tafolecimab in Chinese patients with hypercholesterolemia (CREDIT-4). Asia: JACC; 2023. https://www.jacc.org/doi/10.1016/j.jacasi.2023.04.011
38. CSPC Pharmaceutical Group Limited. Biologic license application for narlumosbart for injection (JMT103) approved by the NMPA; 2023 Sept 6 press release. [accessed 2023 Sept 23]. https://doc.irasia.com/listco/hk/cspc/announcement/a230906a.pdf.
39. BioRay Pharmaceutical Co., Ltd. Zuberitamab (Anruixi®), the first domestically developed anti-CD20 antibody as a class I innovative drug from BioRay Pharmaceutical, has been approved for marketing in China; 2023 May 17 press release. [accessed 2023 Oct 27]. https://www.bioraypharm.com/index.php?m=content&a=index&classid=43&id=9.
40. BioRay. 博锐生物淋巴瘤高峰论坛暨安瑞昔®泽贝妥单抗全国上市成功举行. [Chinese]; 2023 July 2 press release. [accessed 2023 Sep 10]. https://www.bioraypharm.com/index.php?m=content&a=index&classid=40&id=100.
41. Jiangsu Hengrui Medicine Co. Ltd. Hengrui Pharmaceutical's PD-L1 inhibitor adebelimab (Arelili®) was approved, and the company has 12 innovative drugs on the market; 2023 Mar 7 press release. [accessed 2023 Sept 23]. https://www.hengrui.com/media/detail-309.html.
42. Wang J, Zhou C, Yao W, Wang Q, Min X, Chen G, Xu X, Li X, Xu F, Fang Y, et al. Adebrelimab or placebo plus carboplatin and etoposide as first-line treatment for extensive-stage small-cell lung cancer (CAPSTONE-1): a multicentre, randomized, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol. 2022;23(6):739–47. doi:10.1016/S1470-2045(22)00224-8.
43. BIOCAD. The Russian Ministry of Health has authorized the first Russian originator for the treatment of multiple sclerosis; 2023 Mar 31, press release. [accessed 2023 Aug 31]. https://biocadglobal.com/posts/the-russian-ministry-of-health-has-authorized-the-first-russian-originator-for-the-treatment-of-multiple-sclerosis.
44. Eli Lilly and Company. U.S. Food and Drug Administration issues complete response letter for accelerated approval of donanemab; 2023 Jan 19 press release. [accessed 2023 Oct 27]. https://investor.lilly.com/news-releases/news-release-details/us-food-and-drug-administration-issues-complete-response-0.
45. Eli Lilly and Company. Results from Lilly's landmark phase 3 trial of donanemab presented at Alzheimer's Association Conference and published in JAMA. 2023 Jul 17 press release. [accessed 2023 Oct 27]. https://investor.lilly.com/news-releases/news-release-

details/results-lillys-landmark-phase-3-trial-donanemab-presented.
46. Sims JR, Zimmer JA, Evans CD, Lu M, Ardayfio P, Sparks J, Wessels AM, Shcherbinin S, Wang H, Monkul Nery ES, et al. Donanemab in early symptomatic Alzheimer disease: the TRAILBLAZER-ALZ 2 randomized clinical trial. JAMA. 2023;330(6):512–527. doi: 10.1001/jama.2023.13239.
47. Eli Lilly and Company. Lilly shares positive donanemab data in first active comparator study in early symptomatic Alzheimer's disease; 2022 Nov 30 press release. [accessed 2023 Oct 27]. http://lilly.mediaroom.com/2022-11-30-Lilly-Shares-Positive-Donanemab-Data-in-First-Active-Comparator-Study-in-Early-Symptomatic-Alzheimers-Disease.
48. Genentech. FDA accepts application for Genentech's crovalimab for the treatment of PNH, a rare life-threatening blood condition; 2023 Sept 4 press release [accessed 2023 Sept 23]. https://www.gene.com/media/press-releases/15000/2023-09-04/fda-accepts-application-for-genentechs-cSept 2023.
49. Liu H, Xia L, Weng J, Zhang F, He C, Gao S, Jia J, Chang AC, Lundberg P, Camelia S, et al. Results from the first phase 3 crovalimab (c5-inhibitor) study (commodore 3): efficacy and safety in complement inhibitor-naive patients with paroxysmal nocturnal hemoglobinuria (PNH). Presentation at: ASH Annual Meeting and Exposition; New Orleans, 2022 Dec 10-13; Abstract #293. doi:10.1182/blood-2022-162452.
50. Scheinberg P, Cle D, Edwards J, Giai V, Hus M, Kim JS, Barrenetxea Lekue C, Nagy Z, Nur E, Panse J, et al. Phase III randomized, multicenter, open-label COMMODORE 1 trial: comparison of crovalimab vs eculizumab in complement inhibitor-experienced patients with paroxysmal nocturnal hemoglobinuria (PNH). Hemasphere. Aug 8, 2023;7(Suppl):e45540d8. doi:10.1097/01.HS9.0000967644.45540.d8.
51. Röth A, He G, Brodsky A, Chai-Adisaksopha CC, Dumagay T, Demichelis R, Höglund M, Kelly R, Lee J-H, Nishimura J-I, et al. The PHASE III, randomized COMMODORE 2 trial: results from a multicenter study of crovalimab vs eculizumab in paroxysmal nocturnal hemoglobinuria (PNH) patients naive to complement inhibitors. Hemasphere. 2023;7(Suppl):e72750f1. doi:10.1097/01.HS9.0000967636.72750.f1.
52. US Food and Drug Administration. FDA authorizes Gohibic (vilobelimab) injection for the treatment of COVID-19. April 4, 2023 press release. [accessed 2023 Oct 27]. https://www.fda.gov/drugs/drug-safety-and-availability/fda-authorizes-gohibic-vilobelimab-injection-treatment-covid-19.
53. Lim EHT, Vlaar APJ, de Bruin S, Rückinger S, Thielert C, Habel M, Guo R, Burnett BP, Dickinson J, Brouwer MC, et al. PANAMO study group. Pharmacokinetic analysis of vilobelimab, anaphylatoxin C5a and antidrug antibodies in PANAMO: a phase 3 study in critically ill, invasively mechanically ventilated COVID-19 patients. Intensive Care Med Exp. 2023;11(1):37. doi:10.1186/s40635-023-00520-8.
54. InflaRx N.V. InflaRx's marketing authorization application (MAA) for vilobelimab for treatment of critically Ill COVID-19 patients under review by European Medicines Agency (EMA); 2023 Aug 30 press release. [accessed 2023 Oct 27]. https://www.inflarx.de/Home/Investors/Press-Releases/08-2023-InflaRx-s-Marketing-Authorization-Application–MAA–for-Vilobelimab-for-Treatment-of-Critically-Ill-COVID-19-Patients-under-Review-by-European-Medicines-Agency–EMA.html.
55. Pfizer, Inc. Pfizer reports second-quarter 2023 results; 2023 Aug 1 press release. [accessed 2023 Sept 27]. https://s28.q4cdn.com/781576035/files/doc_financials/2023/q2/Q2-2023-PFE-Earnings-Release.pdf.
56. European Medicines Agency. Applications for new human medicines under evaluation by the CHMP: November 2023; Published 2023 Nov 7data extracted 2023 Oct 30. [accessed 2023 Nov 7]. https://www.ema.europa.eu/en/medicines/medicines-human-use-under-evaluation.
57. Pfizer, Inc. Pfizer announces positive marstacimab results from pivotal phase 3 hemophilia a and B trial; 2023 May 30 press release. [accessed 2023 Sept 27]. https://www.pfizer.com/news/press-release/press-release-detail/pfizer-announces-positive-marstacimab-results-pivotal-phase.
58. CSL. CSL Limited 2023 Full Year Results; 2023 Aug 15. [accessed 2023 Oct 20]. https://investors.csl.com/pdf/5180b107-7849-4ad4-aeaf-8092e62b4bb6/CSL-Results-Presentation.pdf.
59. Craig TJ, Reshef A, Li HH, Jacobs JS, Bernstein JA, Farkas H, Yang WH, Stroes ESG, Ohsawa I, Tachdjian R, et al. Efficacy and safety of garadacimab, a factor XIIa inhibitor for hereditary angioedema prevention (VANGUARD): a global, multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2023;401(10382):1079–1090. doi:10.1016/S0140-6736(23)00350-1.
60. Omeros Corporation. Omeros announces online publication in advance of ASH annual meeting detailing narsoplimab treatment under compassionate use of 15 patients with hematopoietic stem cell transplant-associated thrombotic microangiopathy; 2023 Nov 3 press release. [accessed 2023 Nov 4]. https://investor.omeros.com/news-releases/news-release-details/omeros-announces-online-publication-advance-ash-annual-meeting.
61. Castelli M, Mico' MC, Grassi A, Algarotti A, Finazzi MC, Rambaldi B, Cristian Meli C, Rizzuto G, Pavoni C, Vendemini F, et al. Clinical safety and efficacy of narsoplimab in pediatric and adult patients with transplant-associated thrombotic microangiopathy: a real-world experience. 65th Annual Meeting of the American Society of Hematology, December 9-12, 2023, San Diego. https://ash.confex.com/ash/2023/webprogram/Paper180917.html.
62. Checkpoint Therapeutics, Inc. Checkpoint therapeutics reports second quarter 2023 financial results and recent corporate highlights; 2023 Aug 14 press release. [accessed 2023 Oct 27]. https://ir.checkpointtx.com/news-events/press-releases/detail/104/checkpoint-therapeutics-reports-second-quarter-2023.
63. Clingan P, Ladwa R, Brungs D, Harris DL, McGrath M, Arnold S, Coward J, Fourie S, Kurochkin A, Malan DR, et al. Efficacy and safety of cosibelimab, an anti-PD-L1 antibody, in metastatic cutaneous squamous cell carcinoma. J Immunother Cancer. 2023;11(10):e007637. doi: 10.1136/jitc-2023-007637.
64. Astellas Pharma Inc. Astellas announces U.S. FDA grants priority review for zolbetuximab biologics license application; 2023 July 6 press release. [accessed 2023 Oct 27]. https://www.astellas.com/en/news/27946.
65. Astellas Pharma Inc. European Medicines Agency accepts Astellas' marketing authorization application for zolbetuximab; 2023 July 13 press release. [accessed 2023 Oct 27]. https://www.astellas.com/en/news/28146.
66. Astellas Pharma Inc. China's National Medical Products Administration accepts Astellas' biologics license application for zolbetuximab; 2023 July 31 press release. [accessed 2023 Oct 27]. https://www.astellas.com/en/news/28211.
67. Shitara K, Lordick F, Bang YJ, Enzinger P, Ilson D, Shah MA, Van Cutsem E, Xu RH, Aprile G, Xu J, et al. Zolbetuximab plus mFOLFOX6 in patients with CLDN18.2-positive, HER2-negative, untreated, locally advanced unresectable or metastatic gastric or gastro-oesophageal junction adenocarcinoma (SPOTLIGHT): a multicentre, randomised, double-blind, phase 3 trial. Lancet. 2023;401(10389):1655–1668. doi:10.1016/S0140-6736(23)00620-7.
68. Shah MA, Shitara K, Ajani JA, Bang YJ, Enzinger P, Ilson D, Lordick F, Van Cutsem E, Gallego Plazas J, Huang J, et al. Zolbetuximab plus CAPOX in CLDN18.2-positive gastric or gastroesophageal junction adenocarcinoma: the randomized, phase 3 GLOW trial. Nat Med. 2023;29(8):2133–2141. doi: 10.1038/s41591-023-02465-7.
69. Bannerji R, Arnason JE, Advani RH, Brown JR, Allan JN, Ansell SM, Barnes JA, O'Brien SM, Chávez JC, Duell J, et al. Odronextamab, a human CD20×CD3 bispecific antibody in patients with CD20-positive B-cell malignancies (ELM-1): results from the relapsed or refractory non-Hodgkin lymphoma cohort in

a single-arm, multicentre, phase 1 trial. Lancet Haematol. 2022;9 (5):e327–e39. doi:10.1016/S2352-3026(22)00072-2.

70. Kim W-S, Kim TM, Cho S-G, Jarque I, Iskierka-Jażdżewska E, Poon ML, Prince HM, Oh SY, Lim F, Carpio C, et al. Odronextamab in patients with relapsed/refractory (R/R) diffuse large b-cell lymphoma (DLBCL): results from a prespecified analysis of the pivotal phase II study ELM-2. Blood. 2022;140 (Supplement 1):1070–71. doi: 10.1182/blood-2022-158406.
71. Byondis BV. U.S. Food and Drug Administration issues complete response letter for Byondis' [Vic-]Trastuzumab Duocarmazine; 2023 May 15 press release. [accessed 2023 Oct 23]. https://www.byondis.com/media/press-releases/us-food-and-drug-administration-issues-complete-response-letter-for-vic-trastuzumab-duocarmazine.
72. Byondis BV Withdrawal of Jivadco (trastuzumab duocarmazine), 80 mg, powder for concentrate for solution for infusion - EMEA/H/C/005654; 2023 Sept 12 letter. [accessed 2023 Oct 18]. https://www.ema.europa.eu/en/documents/withdrawal-letter/withdrawal-letter-jivadco_en.pdf.
73. Byondis BV Byondis announces positive topline results of pivotal phase III TULIP® study in patients with her2-positive unresectable locally advanced or metastatic breast cancer; 2021 June 8 press release. [accessed 2023 Oct 23]. https://www.byondis.com/media/press-releases/byondis-announces-positive-topline-results-of-pivotal-phase-iii-tulip-study.
74. Wong KL, Li Z, Ma F, Wang D, Song N, Chong CH, Luk KK, Leung SO. SM03, an anti-CD22 antibody, Converts Cis-to-Trans Ligand Binding of CD22 against α2,6-linked sialic acid glycans and immunomodulates systemic autoimmune diseases. J Immunol. 2022;208(12):2726–2737. doi: 10.4049/jimmunol.2100820.
75. SinoMab BioScience Limited. BLA accepted by the NMPA for SM03 (suciraslimab) in the treatment of rheumatoid arthritis; 2023 Sept 5 press release. [accessed 2023 Oct 9]. https://manager.wisdomir.com/files/517/2023/0905/20230905121501_30698040_en.pdf.
76. SinoMab BioScience Limited. SinoMab announces that phase III clinical trial of its flagship product SM03 (suciraslimab) achieved the primary endpoint for rheumatoid arthritis; 2023 Apr 26 press release. [accessed 2023 Oct 9]. https://www.sinomab.com/wp-content/uploads/2023/04/Press-Release-SinoMab-3681.HK-Announces-that-Phase-III-Clinical-Trial-of-its-Flagship-Product-SM03-Suciraslimab-Achieved-the-Primary-Endpoint-for-Rheumatoid-Arthritis.pdf.
77. Harbour BioMed. Harbour BioMed announces positive topline results from phase III trial of batoclimab for treatment of generalized myasthenia gravis; 2023 Mar 6 press release. [accessed 2023 Sep 2025]. https://www.prnewswire.com/news-releases/harbour-biomed-announces-positive-topline-results-from-phase-iii-trial-of-batoclimab-for-treatment-of-generalized-myasthenia-gravis-301763029.html.
78. Akeso Inc. Akeso announced NDA acceptance of IL-12/lL-23 monoclonal antibody ebdarokimab for moderate-to-severe plaque psoriasis by China NMPA; 2023 Aug 24 press release. [accessed 2023 Oct 7]. https://www.akesobio.com/en/media/akeso-news/230824/.
79. Medicine Cube. The first domestically produced one! Zhixiang Jintai's anti-IL-17A monoclonal antibody has been submitted for marketing; 2023 Mar 25 post. [accessed 2023 Oct 17]. https://www.pharmcube.com/index/news/article/13097.
80. Jiangsu Hengrui Pharmaceuticals Co., Ltd. R&D pipeline by Mar. 31, 2023. [accessed 2023 Oct 8]. https://www.hengrui.com/en/pipeline.html.
81. Xu J, Yan K, Han L, Zhang Z, Li F, Bi X, Li Y, Zhang L, Wang X, Li L, et al. Efficacy and safety of vunakizumab in moderate-to-severe chronic plaque psoriasis: a randomized, double-blind, placebo-controlled phase 3 trial. European Academy Of Dermatology And Venereology Congress, Abstract, 11–14 October, 2023, Berlin. https://s3.eu-central-1.amazonaws.com/m-anage.com.storage.eadv/abstracts_congress2023/32842.pdf
82. Akeso Inc. NMPA accepted Akeso's ebronucimab (PCSK9) marketing application in two indications. 2023 June 2 press release. [accessed 2023 Sept 25]. https://www.akesobio.com/en/media/akeso-news/230602/.
83. Jiangsu Hengrui Pharmaceuticals Co., Ltd. 2023 ESC annual meeting: a phase III study of Hengrui Pharmaceuticals' innovative lipid-lowering drug recarcizumab was presented as an oral report; 2023 Aug 29 press release. [accessed 2023 Oct 8]. https://www.hengrui.com/media/detail-393.html.
84. Junshi Biosciences. Junshi Biosciences announces ongericimab (anti-PCSK9 mAb) met primary endpoints in two phase 3 clinical studies; 2023 Feb 28 press release. [accessed 2023 Sept 25]. https://www.biospace.com/article/releases/junshi-biosciences-announces-ongericimab-anti-pcsk9-mab-met-primary-endpoints-in-two-phase-3-clinical-studies/.
85. Sichuan Kelun-Biotech Biopharmaceutical Co Ltd. 2023 Interim Report. [accessed 2023 Oct 16]. https://ir-upload.realxen.net/iis/6990/uploads/iis/2023/10901518-0.PDF.
86. CSPC Pharmaceuticals. NMPA acceptance of application for marketing approval of enlonstobart for injection; 2023 Mar 13 press release. [accessed 2023 Oct 16]. https://en.e-cspc.com/news/nmpa-acceptance-of-application-for-marketing-approval-of-enlonstobart-for-injection.html.
87. Medicine Cube. Qilu Pharmaceutical's PD-1 antibody "ipalolizumab" applies for marketing; 2023 Sept 17 post. [accessed 2023 Oct 16]. https://bydrug.pharmcube.com/news/detail/bc171f6b537a767dfbc996adbdfc5c85.
88. Liu J, Fang C, Zhou Q, He L, Yu J, Li Y, Feng M, Pan M, Zhao L, Tang D, et al. A phase II, open-label, single-arm study of QL1604 plus paclitaxel-cisplatin/carboplatin as first-line treatment in patients with recurrent or metastatic cervical cancer. Ann Oncol. 2022;33(suppl_9):S1503–S14. doi:10.1016/annonc/annonc1126.
89. Zhao Y, Ma Y, Zang A, Cheng Y, Zhang Y, Wang X, Chen Z, Qu S, He J, Chen C, et al. First-in-human phase I/Ib study of QL1706 (PSB205), a bifunctional PD1/CTLA4 dual blocker, in patients with advanced solid tumors. J Hematol Oncol. 2023;16(1):50. doi: 10.1186/s13045-023-01445-1.
90. Akeso B. Akeso's ivonescimab (PD-1/VEGF bispecific antibody, AK112) granted breakthrough therapy designation for I-O resistance NSCLC patients in China; 2022 Nov 13 press release. [accessed 2023 Oct 7]. https://prn.to/3tx62MK.
91. Akeso Inc. Akeso announced that ivonescimab granted priority review of NDA by China NMPA; 2023 Aug 25 press release. [accessed 2023 Oct 7]. https://www.prnewswire.com/news-releases/akeso-announced-that-ivonescimab-granted-priority-review-of-nda-by-china-nmpa-301910028.html
92. Zhao Y, Chen G, Chen J, Zhuang L, Du Y, Yu Q, Zhuang W, Zhao Y, Zhou M, Zhang W, et al. AK112, a novel PD-1/VEGF bispecific antibody, in combination with chemotherapy in patients with advanced non-small cell lung cancer (NSCLC): an open-label, multicenter, phase II trial. EClinicalMedicine. 2023;62:102106. doi:10.1016/j.eclinm.2023.102106. 102106.
93. Sorrento Therapeutics, Inc. Corporate presentation; 2023 Jan. [accessed 2023 Sept 25]. https://investors.sorrentotherapeutics.com/static-files/ded13448-aa64-4405-a2d9-de644cfe9dfc.
94. An J, Tang J, Li BX, Xiong H, Qiu H, Luo L, Wang L, Wang D, Zhou Q, Xu Q, et al. Efficacy and safety of the anti-PD-L1 mAb socazolimab for recurrent or metastatic cervical cancer: a phase I dose-escalation and expansion study. Clin Cancer Res. 2022;28 (23):5098–106. doi:10.1158/1078-0432.CCR-22-1280.
95. Lu S, Chen Z, Cui J, Guo R, Li Z, Xiaoyi B, Day X. Efficacy and safety of anti–programmed death-ligand 1 monoclonal antibody socazolimab with carboplatin and Etoposide for extensive-stage SCLC: results from the phase 1b clinical trial. JTO Clin Res Reports. 2023;4(4):4. doi: 10.1016/j.jtocrr.2023.100478.
96. Sino Pharmaceutical Limited. Application for marketing of category 1 innovative drug TQB2450 injection in combination with anlotinib hydrochloride capsules for the indication of first-line treatment of small cell lung cancer accepted; 2023 Jan 13 press

release. [accessed 2023 Oct 7]. https://www1.hkexnews.hk/listedco/listconews/sehk/2023/0113/2023011300357.pdf.
97. Sichuan Kelun Pharmaceutical Co., Ltd. Announcement on the acceptance of the marketing application for the new PD-L1 drug tetelimab injection by NMPA [Chinese]; 2021 Nov 19 press release. [accessed 2023 Sept 25]. http://static.cninfo.com.cn/finalpage/2021-11-20/1211637118.PDF.
98. Shi Y, Qin X, Peng X, Zeng A, Li J, Chen C, Qiu S, Pan S, Zheng Y, Cai J, et al. Efficacy and safety of KL-A167 in previously treated recurrent or metastatic nasopharyngeal carcinoma: a multicenter, single-arm, phase 2 study. Lancet Reg Health West Pac. 2022;31:100617. doi:10.1016/j.lanwpc.2022.100617. PMID: 36879786.
99. Syndax Pharmaceuticals, Inc. SNDX third quarter 2023 results; 2023 Nov 2 presentation. [accessed 2023 Nov 4]. https://ir.syndax.com/static-files/b92ab47e-8e26-46bf-af5b-d5f135f54f10.
100. Syndax Pharmaceuticals, Inc. Corporate presentation; 2023 Aug. [accessed 2023 Oct 16]. https://ir.syndax.com/static-files/1c3a5493-5046-4d16-a9da-0bfda68ec4d9.
101. RQ Biotechnology Limited. Innovative antibody discovered by RQ BIO enters clinic as part of antibody combination within 12 months of discovery; 2022 Dec 21 press release. [accessed 2023 Sept 25]. https://www.rqbiotechnology.com/media/innovative-antibody-discovered-by-rq-bio-enters-clinic-as-part-of-antibody-combination-within-12-months-of-discovery.
102. AstraZeneca. Clinical trials appendix, 9M and Q3 2023 results update; 2023 Nov 9. [accessed 2023 Nov 10]. https://www.astrazeneca.com/content/dam/az/PDF/2023/q3/9M_and_Q3_2023_results_clinical_trials_appendix.pdf.
103. SERB Pharmaceuticals. SERB Pharmaceuticals and SFJ Pharmaceuticals announce a U.S. partnership for bentracimab, a ticagrelor reversal agent; 2023 May 11 press release. [accessed 2023 Oct 16]. https://serb.com/news/serb-pharmaceuticals-and-sfj-pharmaceuticals-announce-a-u-s-partnership-for-bentracimab-a-ticagrelor-reversal-agent/.
104. Bhatt DL, Pollack CV Jr., Mazer CD, Angiolillo DJ, Steg G, James SK, Weitz JI, Ramnath R, Arnold SE, Mays MC, et al. Bentracimab for ticagrelor reversal in patients undergoing urgent surgery. NEJM Evid. 2022;1(3). doi: 10.1056/EVIDoa2100047.
105. Keymed Biosciences. 2022 Annual results and latest updates; 2023 Mar presentation. [accessed 2023 Sept 25]. https://en.keymedbio.com/uploadfile/2023/0317/20230317080809187.pdf
106. Zhao Y, Zhang J, Yang B, Li J, Ding Y, Wu L, Zhang L, Wang J, Zhu X, Zhang F, et al. Efficacy and safety of CM310 in moderate-to-severe atopic dermatitis: a multicenter, randomized, double-blind, placebo-controlled phase 2b trial. Chin Med J (Engl). 2023. doi:10.1097/CM9.0000000000002747.
107. Zhang L, Ding Y, Wang Q, Pan W, Wei Z, Smith PA, Yang X. Preclinical immunological characterization of rademikibart (CBP-201), a next-generation human monoclonal antibody targeting IL-4Rα, for the treatment of Th2 inflammatory diseases. Sci Rep. 2023;13:12411. doi: 10.1038/s41598-023-39311-2.
108. Connect Biopharma Holdings Limited. Connect biopharma and simcere announce exclusive licensing and collaboration agreement in Greater China; 2023 Nov 21 press release. [accessed 2023 Nov 21]. https://investors.connectbiopharm.com/news-releases/news-release-details/connect-biopharma-and-simcere-announce-exclusive-licensing-and.
109. Suzhou Connect Biopharmaceuticals, Ltd. Connect biopharma, top line results: CBP-201 pivotal trial in China (CN002); 2022 Oct. [accessed 2023 Sept 25]. https://investors.connectbiopharm.com/static-files/e98617f2-b84a-4aa9-9123-8cb766cd17ad.
110. Connect Biopharma Holdings Limited. Connect biopharma announces positive long-term data from the China pivotal trial of rademikibart in patients with moderate-to-severe atopic dermatitis; 2023 Nov 21 press release. [accessed 2023 Nov 21]. https://investors.connectbiopharm.com/news-releases/news-release-details/connect-biopharma-announces-positive-long-term-data-china.
111. GSK. Third quarter 2023 results; 2023 Nov 1 presentation. [accessed 2023 Nov 4]. https://www.gsk.com/media/10668/q3-2023-results-slides.pdf.
112. AnaptysBio, Inc. Anaptys announces positive top-line phase 3 clinical trial results of imsidolimab (IL-36R) in generalized pustular psoriasis (GPP); 2023 Oct 9 press release. [accessed 2023 Oct 25]. https://ir.anaptysbio.com/news-releases/news-release-details/anaptys-announces-positive-top-line-phase-3-clinical-trial.
113. Kurnellas M, Mitra A, Schwabe T, Paul R, Arrant AE, Roberson ED, Ward M, Yeh F, Long H, Rosenthal A. Latozinemab, a novel progranulin-elevating therapy for frontotemporal dementia. J Transl Med. 2023;21(1):387. doi: 10.1186/s12967-023-04251-y.
114. Alector, Inc. Alector announces achievement of target enrollment in the pivotal INFRONT-3 phase 3 clinical trial of latozinemab in individuals with frontotemporal dementia due to a progranulin gene mutation (FTD-GRN); 2023 Oct 27 press release. [accessed 2023 Nov 4]. https://investors.alector.com/news-releases/news-release-details/alector-announces-achievement-target-enrollment-pivotal-infront.
115. Scholar Rock. Deep insights advancing impactful medicines; 2023 Oct corporate presentation. [accessed 2023Oct 25]. https://investors.scholarrock.com/static-files/3645e0f2-3012-4c8f-8b2f-6e1c57bd68fe.
116. Regeneron. Regeneron corporate presentation; 2023 Nov. [accessed 2023 Nov 4]. https://investor.regeneron.com/static-files/27bf1467-a410-414b-9bec-916fa90e7748.
117. Regeneron. Updated linvoseltamab (BCMAxCD3) data from pivotal trial demonstrates early, deep and durable responses in patients with heavily pre-treated multiple myeloma; 2023 May 25 press release. [accessed 2023 Oct 20]. https://investor.regeneron.com/news-releases/news-release-details/updated-linvoseltamab-bcmaxcd3-data-pivotal-trial-demonstrates.
118. Weisel K, Hungria V, Quach H, Yoon S-S, Rodríguez-Otero P, Kroog G, Sinha A, Boyapati A, Lyon C, Lorenc KR, et al. PB2133: trial in progress: LINKER-MM3, a phase 3, open-label, randomized study of linvoseltamab versus elotuzumab, pomalidomide, and dexamethasone (EPD) in relapsed/refractory multiple myeloma (RRMM). Hemasphere. 2023;7(Suppl):e465366a. doi:10.1097/01.HS9.0000975296.46536.6a.
119. Actinium Pharmaceuticals, Inc. Investor presentation: targeted radiotherapies for patients with unmet needs; 2023 Sept. [accessed 2023 Oct 20]. https://d1io3yog0oux5.cloudfront.net/_e867432f4d7e6dd09397644109efb94f/actiniumpharma/db/206/1137/pdf/Actinium+Investor+Presentation±+September+2023+FINAL.pdf.
120. Actinium Pharmaceuticals, Inc. Iomab-B SIERRA trial: Phase 3 results; 2023 Feb 18. [accessed 2023 Oct 20]. https://d1io3yog0oux5.cloudfront.net/_e867432f4d7e6dd09397644109efb94f/actiniumpharma/db/206/1110/pdf/Actinium_SIERRA_Data_Webcast_vFINAL_02.18.2023.pptx+for+webinar.pdf.
121. Roche. YTD September 2023 performance. [accessed 2023 Oct 20]. https://assets.roche.com/f/176343/x/84b57800eb/irp231019.pdf.
122. Roche. HY 2023 results; 2023 July 27. [accessed 2023 Sept 25]. https://assets.cwp.roche.com/f/176343/x/418a8c95c6/irp230727.pdf.
123. Genentech provides update on phase III skyscraper-01 study in PD-L1-high metastatic non-small cell lung cancer; 2023 Aug. [accessed 2023Sept 25] https://www.gene.com/media/press-releases/14998/2023-08-22/genentech-provides-update-on-phase-iii-s.
124. Sanofi. Q3 2023 results; 2023 Oct 27. [accessed 2023 Nov 4]. https://www.sanofi.com/assets/dotcom/content-app/events/quaterly-results/2023/2023-q3-2023-results/q3-2023-presentation-en.pdf.
125. Daiichi Sankyo. Daiichi Sankyo and Merck & Co., Inc., Rahway, N. J., USA announce global development and commercialization collaboration for three Daiichi Sankyo DXd ADCs; 2023 Oct 20 press release. [accessed 2023 Oct 20]. https://www.daiichisankyo.com/files/news/pressrelease/pdf/202310/20231020_E.pdf.

126. Yu HA, Goto Y, Hayashi H, Felip E, Chih-Hsin Yang J, Reck M, Yoh K, Lee SH, Paz-Ares L, Besse B, et al. HERTHENA-Lung01, a phase II trial of patritumab deruxtecan (HER3-DXd) in epidermal growth factor receptor-mutated non-small-cell lung cancer after epidermal growth factor receptor tyrosine kinase inhibitor therapy and platinum-based chemotherapy. J Clin Oncol. 2023; JCO2301476. doi:10.1200/JCO.23.01476.
127. Daiichi Sankyo Co., Ltd. Datopotamab deruxtecan significantly extended progression-free survival versus chemotherapy in patients with HR positive, HER2 low or negative breast cancer in TROPION-Breast01 phase 3 trial; 2023 Oct 23 press release. [accessed 2023 Oct 20]. https://www.daiichisankyo.com/files/news/pressrelease/pdf/202310/20231023_E2.pdf.
128. Bardia A, Jhaveri K, Kalinsky K, Pernas S, Tsurutani J, Xu B, Hamilton E, Im SA, Nowecki Z, Sohn J, et al. TROPION-Breast01: datopotamab deruxtecan vs chemotherapy in pretreated inoperable or metastatic HR+/HER2– breast cancer. Future Oncol. 2023. doi:10.2217/fon-2023-0188.
129. Daiichi Sankyo Co., Ltd. Datopotamab deruxtecan improved progression-free survival versus chemotherapy in patients with previously treated non-small cell lung cancer in TROPION-Lung01 phase 3 trial; 2023 Oct 23 press release. [accessed 2023 Oct 24]. https://www.daiichisankyo.com/files/news/pressrelease/pdf/202310/20231023_E3.pdf.
130. Li H, Zhang X, Xu Z, Li L, Liu W, Dai Z, Zhao Z, Xiao L, Li H, Hu C. Preclinical evaluation of MRG002, a novel HER2-targeting antibody-drug conjugate with potent antitumor activity against HER2-positive solid tumors. Antib Ther. 2021;4(3):175–84. doi:10.1093/abt/tbab017.
131. Biopharma L. 2023 Interim Report. September 2023 [accessed 2023 Oct 24]. https://en.lepubiopharma.com/upload/listedco/listconews/sehk/2023/0922/2023092200478.pdf.
132. Agenus, Inc. Agenus reports third quarter 2023 results; 2023 Nov 7 press release. [accessed 2023 Nov 10] https://investor.agenusbio.com/news/news-details/2023/Agenus-Reports-Third-Quarter-2023-Results/default.aspx.
133. Bullock AJ, Fakih MG, Gordon MS, Tsimberidou A, El-Khoueiry A, Wilky B, Pimentel A, Margolin K, Mahadevan D, Balmanoukian A, et al. Results from an expanded phase 1 trial of botensilimab, a multifunctional anti-CTLA-4, plus balstilimab (anti-PD-1) for metastatic heavily pretreated microsatellite stable colorectal cancer. Annals Of Oncology. 2023;34(suppl 1):S178–S79. doi:10.1016/j.annonc.2023.04.014.
134. Philogen. Nidlegy™ Phase III PIVOTAL trial meets the study's primary objective demonstrating statistically significant and clinically meaningful improvement in recurrence-free survival for patients with locally advanced fully resectable melanoma; 2023 Oct 16 press release. [accessed 2023 Oct 24]. https://www.philogen.com/philogen/wp-content/uploads/2023/10/Press_release_PIVOTAL.pdf.
135. Merus N.V. Merus' Zeno interim data continues to demonstrate robust and durable responses in NRG1+ cancer; 2023 Oct 23 press release. [accessed 2023 Oct 24]. https://ir.merus.nl/news-releases/news-release-details/merus-zeno-interim-data-continues-demonstrate-robust-and-durable.
136. Schram AM, Goto K, Kim D-W, Hollebecque A, Rha SY, Nishino K, Duruisseaux M, Umemoto K, Park JO, Leighl N, et al. Durable efficacy of zenocutuzumab, a HER2 x HER3 bispecific antibody, in advanced NRG1 fusion-positive (NRG1+) non-small cell lung cancer (NSCLC). Oral Presentation At The European Society For Medical Oncology (ESMO) Congress; 2023 Oct 20-24, Madrid, Spain. https://merus.nl/wp-content/uploads/2023/10/ESMO%202023%20NSCLC%20Mini%20Oral%20Pres%20(MOZ-75963)_vFinal_19Oct2023.pdf.
137. Schram AM, Macarulla T, Cleary JM, Neuzillet C, Arnold D, Reiss KA, Bekaii-Saab T, Rodon J, Goto K, Rha SY, et al. Durable efficacy of zenocutuzumab, a HER2 × HER3 bispecific antibody, in advanced NRG1 fusion–positive (NRG1+) pancreatic ductal adenocarcinoma (PDAC). Poster presented at the European Society for Medical Oncology (ESMO) Congress 2023, 20-24 Oct 2023, Madrid, Spain. https://merus.nl/wp-content/uploads/2023/10/ESMO2023NRG1+PDAC.pdf.
138. Alphamab Oncology. 2023 interim results presentation. [accessed 2023 Oct 24]. https://www.alphamabonc.com/en/uploads/2023/08/169286574293454.pdf.
139. Alphamab Oncology. Updates in relation to a phase III clinical trial of KN046 for the treatment of advanced SQ NSCLC; 2023 May 19 press release. [accessed 2023 Oct 24]. https://www.alphamabonc.com/en/uploads/2023/05/168445306222985.pdf.
140. I-Mab. I-Mab provides mid-year 2023 financial results, business and corporate updates; 2023 Aug 17 press release. [accessed 2023 Sept 25]. https://ir.i-mabbiopharma.com/news-releases/news-release-details/i-mab-provides-mid-year-2023-financial-results-business-and.
141. Human Immunology Biosciences. HI-Bio receives FDA orphan drug designation for felzartamab for the treatment of membranous nephropathy; 2023 May 25 press release. [accessed 2023 Sept 25]. https://hibio.com/news/hi-bio-receives-fda-orphan-drug-designation-for-felzartamab-for-the-treatment-of-membranous-nephropathy.
142. Novartis Pharmaceutical Corporation. Q3 2023 results investor presentation; 2023 Oct. [accessed 2023 Nov 4]. https://www.novartis.com/sites/novartiscom/files/q3-2023-investor-presentation.pdf.
143. Zeidan AM, Ando K, Rauzy O, Turgut M, Wang M-C, Cairoli R, Hou H-A, Kwong Y-L, Sangerman MA, Meers S, et al. Primary results of stimulus-MDS1: a randomized, double-blind, placebo-controlled phase II study of TIM-3 inhibition with sabatolimab added to hypomethylating agents (HMAs) in adult patients with higher-risk myelodysplastic syndromes (MDS). Blood. 2022;140(Supplement 1):2063–65. doi:10.1182/blood-2022-158612.
144. Crescioli S, Reichert JM. Trends in the commercial development of antibody therapeutics: the early stage clinical pipeline; 2023 Oct 24 online presentation. [accessed 2023 Nov 11]. https://www.youtu.be/Z0SvGPbpk7s.