Journey of therapeutic antibodies: from discovery to future

Abhay H. Pande[†*] ⓘ, Sandeep[†] ⓘ, J. Anakha ⓘ

Department of Biotechnology, National Institute of Pharmaceutical Education and Research (NIPER), Mohali 160062, Punjab, India

[†]These authors contributed equally to this work.

*Correspondence: Abhay H. Pande, Department of Biotechnology, National Institute of Pharmaceutical Education and Research (NIPER), Sector 67, S.A.S. Nagar, Mohali 160062, Punjab, India. apande@niper.ac.in; abbupande@yahoo.co.in

Abstract

Antibodies currently represent a leading segment of the biopharmaceutical market and are expected to maintain a significant presence in the therapeutic landscape. Development of therapeutic antibodies represents one of the most transformative advances in the modern medicine field, with hundreds of successful products on the market that have changed the lives of millions and the history of mankind by revolutionizing medical treatment. In its broadest context, antibody-based products consist of full-length antibodies, antibody fragments, polyvalent and polyspecific antibodies, and their conjugates (for targeted delivery of other therapeutic drugs/agents). High target specificity, tailored mechanisms of action, and broad applicability have made antibodies indispensable in a variety of diseases. With advancements in protein engineering as well as growing integration of computational biology, the field of antibody development continues to push boundaries and is expected to drive the next era of breakthroughs. This article charts the journey of therapeutic antibodies from their conceptual roots to their central role in current medicine, and offers a forward-looking perspective on what lies ahead in this dynamic field.

Keywords

Introduction

Biopharmaceuticals, the largest segment of the healthcare market, are medicinal products derived from biological sources and/or designed to mimic biological molecules. Based on their biological characteristics, the biopharmaceutical segment can be categorized into seven verticals [1], and antibody-based products constitute the largest vertical, dominating the biopharmaceutical segment [2, 3]. Although antibodies emerged later in the therapeutic landscape, their unparalleled success has allowed them to surpass all other biologic categories in terms of both clinical utility and commercial impact. Since the approval of the first antibody (muromonab in 1986) [4], the field has experienced remarkable growth, underscoring the pivotal role antibodies now play in modern therapeutics. Their high safety, bioavailability, and precise and high-
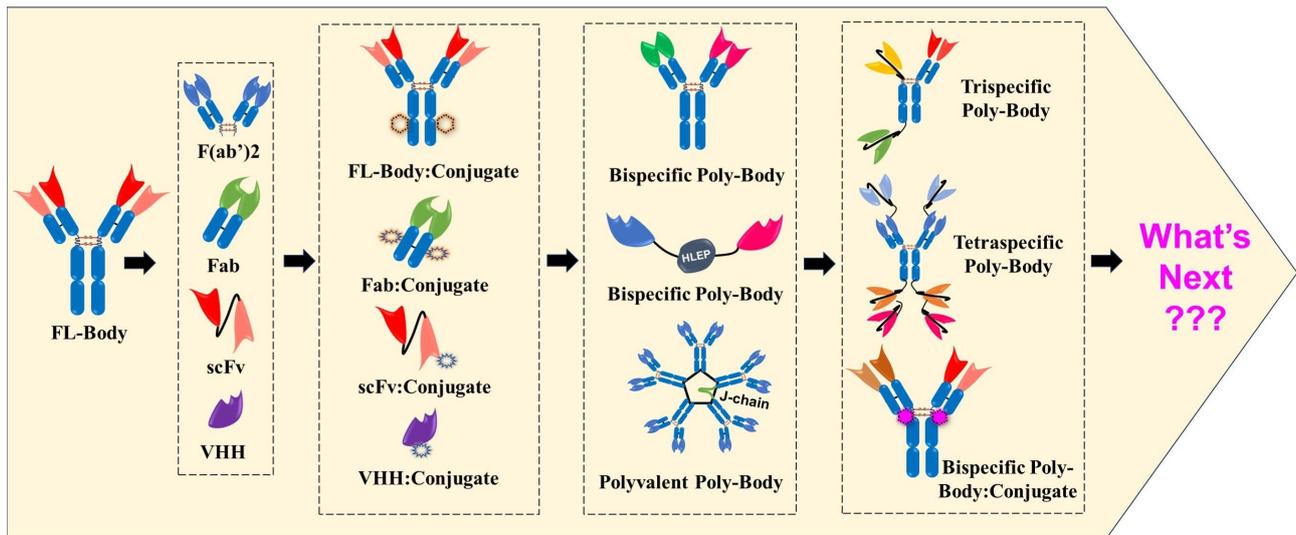
Graphical abstract. Journey of therapeutic antibodies. Antibody journey started with the discovery of full-length antibody (FL-Body), the invention of antibody fragment (Frag-Body), and FL-Body conjugates, which progressed to include Frag-Body conjugates and Poly-Body (including polyspecific and polyvalent) in the present. The future will highlight the rise of advanced Poly-Body and Poly-Body conjugates.

affinity binding to disease-specific targets have made antibody-based products essential in modern therapies, leading to significant improvements in quality of life and life expectancy [5]. By selectively neutralizing or modulating the biological function of their targets, antibodies have become powerful therapeutic agents in the development of innovative treatments across a broad spectrum of diseases [3]. To date, over 200 antibodies and antibody-conjugated products have been approved and are currently in use for the treatment of a wide range of disease conditions, spanning from infectious diseases to cancers [6, 7]. Beyond their therapeutic applications, antibodies and their conjugates are also widely employed in diagnostics, owing to their exceptional target specificity [8–11]. In this article, we explore the evolution of therapeutic antibodies, examining their past and present advancements, while also anticipating future developments in this rapidly advancing field.

Antibody past (1986–2000)

The history of antibodies began with the discovery of anti-sera in the 1890s by Emil von Behring and Kitasato [12], which were used as a defensive therapy for invading pathogens and therapeutics for several infections such as diphtheria, influenza, polio, scarlet fever, measles, tetanus, etc. These natural antibodies were polyclonal in nature, i.e., a mixture of antibodies produced from multiple B-cell clones, and were capable of binding to specific and non-specific targets (antigens), resulting in generating undesirable effects. Despite their limitations, these early developments laid the conceptual groundwork for what would become one of the most transformative fields in modern medicine. Later in 1975, with the invention of hybridoma technology, monoclonal antibodies (MAbs) were developed. These full-length antibodies (FL-Bodies) are Y-shaped immunoglobulins, each having two Fab regions joined to an Fc region via a flexible hinge region. The two Fab regions bind to identical epitopes on a single target antigen, making these conventional antibodies bivalent and monospecific in nature [13]. These conventional antibodies transformed the immunotherapy field and were considered as 'magic bullets' due to their precise target binding with high specificity. Subsequently, Köhler and Milstein [14] were awarded the Nobel Prize in 1984 for their invention of hybridoma technology and monoclonal monospecific antibodies [15]. This was not merely a scientific breakthrough, but a turning point in the philosophy of medicine, one that shifted the focus from broadly acting treatments to precision-guided therapies rooted in molecular recognition. MAbs generated with hybridoma technology were of murine origin (generated in a mouse), and thus were immunogenic to use as therapeutics for humans. This limitation was addressed by chimeric antibodies, in which murine variable regions were grafted onto constant domains of human origin antibodies. Infliximab

antibody is an example of a chimeric antibody. Chimeric antibodies still have a major portion of mice origin, so this was further reduced by CDRs grafting to the human framework, resulting in humanized antibodies. Later on, complete humanized antibodies originated either by producing from transgenic animals or by producing antibodies by phage-display library, which are 100% human in nature. These fully human FL-Bodies become the gold standard with favourable tolerance, optimal pharmacokinetics in humans [7]. The therapeutic success of FL-Bodies led to more targeted and effective therapeutics and a new era of specialized medicine, where target-specific antibodies are used as a therapeutic for a variety of diseases, offering renewed hope and better patient outcomes. Muromonab (which targets the CD3 receptor on T-lymphocytes and blocks their function) became the first antibody to get approval in 1986, and was used as an immunosuppressive therapy in organ transplants [16]. Muromonab was a murine MAb, and thus it was associated with several side effects, such as cytokine release syndrome (CRS) and neurological issues, and thus it was discontinued in 2010–2011. However, the clinical therapeutic efficacy of muromonab laid the foundation for the era of antibody therapeutics. Later on, the surge in the development of new MAbs and their approval for multiple diseases promoted intense research in the antibody field [17]. This rapid progress underscored antibodies' unmatched versatility and therapeutic relevance across a wide spectrum of clinical conditions. As of today, more than 130 different FL-Bodies have been approved by regulatory agencies in the world for various diseases ranging from infectious diseases to cancer [6]. Frag-Bodies (antibody fragments) are the truncated versions of FL-Bodies (or heavy chain antibodies which are found in Camelidae and Shark families) that retain the capacity to bind to antigen and include F(ab')2 (~110 kDa), Fab (~50 kDa), scFv (~25 kDa), and VHH or Nanobody (~12 kDa) [7]. Frag-Bodies are also being developed for therapeutic use. For example, Licartin, a F(ab')2-based Frag-Body is an immunoradioconjugate that targets the hepatocellular cancer-associated antigen (HAb18G/CD147) and was approved in 2006 by the NMPA (China) [18]. Similarly, Certolizumab-pegol, a Fab-based Frag-Body, blocks the binding of TNF-alpha to its receptor and is used as an anti-inflammatory therapy [19]. Brolucizumab, a scFv-based Frag-Body, binds to VEGF-A and inhibits neovascularization in macular degeneration disease [20]. Similarly, Caplacizumab is an anti-vWF nanobody approved for the treatment of acquired thrombotic thrombocytopenic purpura [21]. As of today, more than 40 Frag-Bodies products have been approved for various diseases. Their smaller size, improved tissue penetration, and potential for engineering multifunctional formats make Frag-Bodies a highly promising subclass in the expanding antibody landscape.

Thus, the period from the first antibody approval in 1986 to 2000 represents the 'past era' of therapeutic antibodies, characterized by the emergence of both FL-Bodies and Frag-Bodies, which laid the foundation for the present-day antibody-based products (Figure 1; 1986–2000). This era of antibody development also witnessed the initiation of a new field: development of FL-Body:Conjugates, a new class of antibody-based products in which FL-Body is conjugated to non-antibody drugs, viz., small chemical drugs, radioisotopes, bacterial toxins, etc., for their targeted (site-specific) delivery. A notable milestone was the approval of Gemtuzumab ozogamicin in 2000, the first FL-Body:Conjugate where an anti-CD33 IgG4 is conjugated to cytotoxic *N*-acetyl gamma calicheamicin drug, for the treatment of acute myeloid leukemia [22]. Collectively, this foundational era represents not only technical innovation but also marks a paradigm shift in therapeutic science, establishing the core principles of specificity and modularity that now define the era of precision medicine.

Antibody present (2001–2026)

The success of antibodies as therapeutic agents has made them a dominant force in the biopharmaceutical field in the current world. Their market share now represents one of the fastest-growing segments in pharma, underscoring the economic and clinical indispensability of antibodies [23, 24]. However, treatment regimens using antibodies are challenged by the realization that not only one but many pathways are involved in the pathogenesis of diseases, and there is a need to inhibit/target multiple pathways (antigens) to provide better therapeutic outcomes [25]. This prompted the development of antibodies that can bind to multiple antigens simultaneously [26], i.e., Poly-Bodies, and initiated the present era of therapeutic antibody development. Poly-Bodies are engineered antibodies that can bind to two or more different
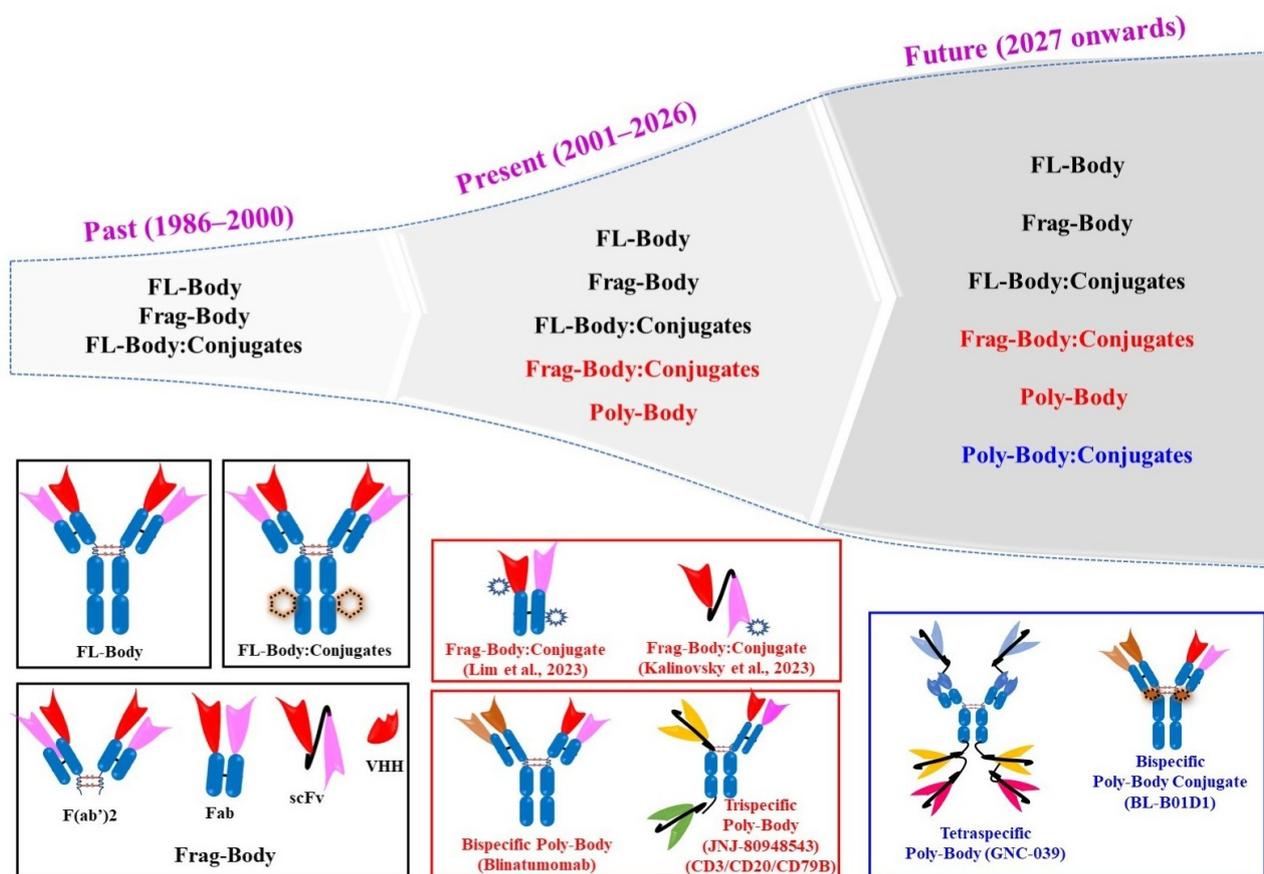
Figure 1. Past, present, and future of therapeutic antibodies [34, 35]. FL-Body: full-length antibody; Frag-Body: antibody fragment; Poly-Body: polyspecific and polyvalent antibody.

antigens simultaneously. Thus, Poly-Bodies can be bispecific, trispecific, tetraspecific, and so on. Similarly, Poly-Bodies can be polyvalent, i.e., they can have more than two binding sites for the same epitope (trivalent, tetravalent, and so on). This innovation reflects a deeper shift in therapeutic strategy from one drug-one target to a multifaceted approach that acknowledges the complexity of human diseases. Poly-Bodies have high efficacy due to high affinity and high avidity and are considered superior therapeutic options to conventional antibodies [27]. Thus, Blinatumomab (anti-CD19/CD3) became the first FDA-approved Poly-Body (polyspecific and polyvalent antibody; in 2014) [28]. Similarly, JNJ-80948543 (anti-CD3/CD79b/CD20) is a trispecific Poly-Body developed for the treatment of non-Hodgkin lymphoma patients and is currently in phase I clinical trials (NCT05424822, NCT06139406, NCT06660563) [29]. Since the approval of the first bispecific Poly-Body in 2014, an additional 14 different Poly-Bodies have been granted approval in different countries by March 2025 [7, 27]. In the last couple of years itself (2023–2024), nine different polyspecific Poly-Bodies got approval for the treatment of a variety of diseases and conditions; Glofitamab (anti-CD20/CD3), Epcoritamab (anti-CD20/CD3), Elranatamab (anti-BCMA/CD3), Talquetamab (anti-GPCR5D/CD3), Tarlatamab (anti-DLL3/CD3), Zanidatamab (anti-HER2 epitope 1/HER2 epitope 2), Zenocutuzumab (anti-HER2/HER3), Odronextamab (anti-CD20/CD3), Ivonesclmab (anti-PD-1/VEGF-A) [3, 7, 30]. Thus, the number of Poly-Bodies entering clinical trials and obtaining approval has been increasing at an exponential rate, demonstrating not only scientific advancement but a deepening of antibody utility in treating previously untreatable or refractory diseases.

The present era of antibody development (Figure 1; 2001–2026) has also witnessed the development and approval of numerous other FL-Bodies and Frag-Bodies. The era has also seen a surge in the exploration of new categories of conjugating drugs (nucleic acids, photosensitizers, cytokines, etc.), resulting in the development of newer FL-Body:Conjugates and Frag-Body:Conjugates. For example, in 2020, a photosensitizer-conjugated antibody, Cetuximab Saratolacan (anti-EGFR antibody conjugated to IRDye 700DX), was approved for the treatment of Unresectable Locally Advanced and Recurrent Head &

Neck Cancer in Japan [31]. FL-Bodies offer extended half-life and Fc-mediated effector functions but suffer from poor tissue penetration. In contrast, Frag-Bodies provide superior tumor access and rapid clearance, though they lack stability and Fc-mediated immunological responses. Considering the advantages of Frag-Bodies, such as their small size, ease of design and production, and improved tissue penetration, they have become a preferred choice for conjugation. FL-Bodies typically have a half-life of 2–3 weeks, whereas Frag-Bodies, including Fab, scFv, and VHH formats, exhibit half-lives ranging from minutes to hours. This rapid clearance makes Frag-Bodies and their conjugates particularly well-suited for diagnostic applications [32, 33]. Recently, Lim et al. [34] developed a Frag-Body:Conjugate in which an anti-cMET Fab Frag-Body is conjugated to Duo5 cytotoxic drug as a potential treatment for solid tumors. Similarly, Kalinovsky et al. [35] developed anti-GD2 scFv Frag-Body:Conjugate in which anti-GD2 scFv Frag-Body is conjugated to monomethyl auristatin E for the treatment of GD2-positive solid tumors. As of today, more than 15 Frag-Body:Conjugates are in clinical trials, which will be in market in the coming years. This trend highlights not only the therapeutic flexibility of Frag-Bodies but also their increasing value in combination modalities. In contrast to FL-Bodies and Frag-Bodies, Poly-Bodies are multi-targeting, high-avidity, and have superior therapeutic efficacy. However, Poly-Bodies have a challenge of complex manufacturing and potential immunogenicity. Most approved Poly-Bodies are anti-cancer, involving T-cell engager bispecific antibodies, which have a challenge of CRS [36].

The present era of antibodies marks success for conjugated antibodies, especially in diagnostic and therapeutic treatment of cancer and suggests an exciting era of targeted, highly effective, and safer cancer treatment that promises to substitute conventional chemotherapies across various cancers [37]. Building on this progress, advances in computer-based biology, high-throughput screening technologies, and artificial intelligence have greatly accelerated the pace of antibody discovery and development, firmly establishing antibodies as a vital element of precision medicine. It is notable that, despite these remarkable advances, antibody development still faces several critical obstacles that can limit therapeutic potential. Immunogenicity remains a primary concern, as anti-drug antibody (ADA) responses can reduce therapeutic efficacy, alter pharmacokinetic properties, and, in some cases, trigger severe adverse immune reactions. The challenge is compounded by the fact that ADA development varies among patients, influenced not only by individual factors but also by geographical and racial differences. However, the major reason for ADA development is the non-human nature of antibodies for murine, chimeric, and humanized antibodies. This results in poor pharmacokinetics (fast clearance) and immunogenicity, and thus limits clinical efficacy. These interpatient variations highlight a complex obstacle in antibody therapy that still needs to be effectively addressed [38, 39]. Beyond immunogenicity and pharmacokinetic concerns, antibody therapeutics face major challenges in large-scale production, cost management, and supply sustainability. Despite their clinical success, high manufacturing costs continue to restrict accessibility, particularly in low- and middle-income countries. A substantial share of these costs arises from drug substance (DS) manufacturing, including both upstream and downstream processes. Meeting the growing and diversifying demand for antibodies also requires adequate and flexible biomanufacturing capacity. Most MAbs are produced in mammalian systems, mainly Chinese hamster ovary (CHO) cells, using large-scale bioreactors. While global capacity has expanded, imbalances persist, with some firms facing shortages and others excess capacity and financial strain. To address this, the industry increasingly relies on contract manufacturing organizations (CMOs) and single-use bioreactor technologies, which provide flexibility, rapid scalability, and lower capital investment. Moreover, emerging DS manufacturing technologies and formats are being explored to reduce costs, increase supply flexibility, and enhance development efficiency. Incorporating process economic analysis from the preclinical stage through late-stage development is also critical to evaluate feasibility, optimize manufacturing strategies, and select the most suitable production approach for each antibody program [40].

Antibody future (2027 onwards)

The clinical success of antibodies initiated a competitive environment among pharma companies and research groups. This positive competition is driving innovations in making highly efficacious and precision antibody-based products. The development of Poly-Bodies and conjugated antibodies is an example of such

innovations (Figure 1; 2027 onwards). Hundreds of these next-generation products are in advanced stages of clinical trials which are going to be marketed in the coming years [41, 42]. The clinical success of Poly-Bodies and conjugated antibodies is expanding the boundaries of therapy, especially in complex diseases such as cancer and multifaceted inflammatory disorders. As clinical approvals for antibody-based products increase each year, the field is expected to grow further, providing more opportunities for diverse clinical uses.

Specificity is a crucial deciding factor for the therapeutic efficacy in the case of antibodies. The future of antibody-based products looks incredibly promising with the ongoing development of trispecific, tetraspecific, and pentaspecific antibodies. Sonelokimab (anti-interleukin (IL)-17A/IL-17F/albumin) is a trispecific antibody for hidradenitis suppurativa disease that is currently in phase 3 clinical trial (NCT07007637) and is expected to be approved in the near future [43]. Umizortamig (GNC039, anti-CD3/4-1BB/EGFRVIII/PD-L1) is a tetraspecific Poly-Body for glioma and solid tumor and is currently in a phase I clinical study (CN110831973A) [44]. Researchers are also pushing boundaries in engineering multivalent antibodies or Poly-Bodies with 10, 20, or even more binding sites which were once thought impossible. Thanks to accelerating technological advances, these ultra-multivalent antibodies may soon become a reality. The development of Poly-Body:Conjugates is also significantly advancing the antibody-based product pipeline. BL-B01D1 is a first-in-class Poly-Body:Conjugate in which an anti-EGFR/HER3 bispecific Poly-Body is conjugated to topoisomerase I inhibitor (Ed-04) and is currently in phase 3 clinical trial (NCT06118333) for recurrent or metastatic nasopharyngeal carcinoma [45]. Thus, in the future, we will see more Poly-Bodies and their immunoconjugates in the market.

Drug payload in antibody:conjugates is a crucial factor for deciding their efficacy. Rapid progress in conjugation chemistry, therapeutic payload engineering, and nanotechnology is expanding the spectrum of payloads that can be effectively conjugated to antibodies. In the future, there will be a variety of payloads such as carbon-dots [46], nanorobots [47], PROTACs (proteolysis targeting chimeras) [48], etc. This could offer new mechanisms, improved efficacy with a multi-payload strategy that further enhances the versatility and clinical potential of antibody conjugates. Moreover, the future of antibodies is being transformed by advances in genetic and protein engineering technologies [49] that enable the precise design of Poly-Bodies, their optimization with enhanced affinity and specificity, stability, pharmacokinetics, and especially the design of complex Poly-Body formats and their conjugates. With every engineering milestone, the vision of truly personalized treatments is coming closer to reality, inspiring optimism across the scientific community. Along with that, artificial intelligence and machine learning (AI/ML) are also accelerating antibody development, helping in predictive analytics, high-throughput screening of lead candidates, and ultimately shortening the antibody development timeline and enhancing the success rate [50]. AI's role in the design of de novo antibodies and predicting their molecular behavior will reshape antibody development [51, 52]. This convergence of biology and computation is already producing candidates that would have taken years to generate by traditional means. A notable example is AU-007, a human IgG1 MAb designed using AI to bind IL-2 at its CD25 binding epitope. Developed by Aulos Bioscience, AU-007 has advanced to the Phase 2 portion of a Phase 1/2 clinical trial evaluating its efficacy in treating solid tumors. Interim results presented at the 2024 ASCO Annual Meeting demonstrated AU-007's ability to harness IL-2 to reduce solid tumors, supporting ongoing and planned Phase 2 expansion cohorts in combination with low-dose aldesleukin in melanoma, renal cell carcinoma, and non-small cell lung cancer [53] (Aulos https://aulosbio.com/). While specific wet-lab validation hit rates for AU-007 are not publicly disclosed, the development of AI-designed antibodies like AU-007 exemplifies the potential of AI/ML to enhance the efficiency and success rates of antibody discovery, offering a promising alternative to traditional methods such as hybridoma technology and phage display. While AI/ML approaches have significantly accelerated antibody discovery and optimization, their application still faces important limitations. Current models rely heavily on the availability and quality of training data, which are often biased toward well-studied targets and antibody formats. As a result, predictions may not generalize reliably to novel antigens or complex multispecific architectures [54, 55]. In addition, AI-based designs frequently require extensive experimental validation, as in silico predictions do not fully capture protein

folding, developability issues, immunogenicity, or in vivo behavior. Limited interpretability of some models and integration with downstream manufacturing and regulatory requirements further constrain widespread adoption [56]. Addressing these challenges will be essential for realizing the full potential of AI/ML in antibody design. The approved therapeutic antibodies, along with their format, target, clinical indication, and approval status, are summarized in Table 1.

Table 1. List of approved therapeutic antibodies.

Name	Format	Target	Indication	Approval
Muromonab*	FL-Body	CD3	Organ transplant rejection (heart, liver, kidney)	FDA (1986); EMA (1986); CECMED (1989); NMPA (1999)
IOR-T3	FL-Body	CD3	Organ transplant rejection	CECMED (1989); NMPA (1999)
Nebacumab*	Poly-Body	CD3	Gram-negative sepsis	EMA (1991)
(99m Tc) Fanolesomab	Poly-Body:Conjugate	CD15	Scintigraphic imaging of patients with equivocal signs and symptoms of appendicitis	FDA (2004)
Edrecolomab*	FL-Body	EpCAM	Colorectal cancer	EMA (1995)
Abciximab	Frag-Body	GPIIb/IIIa	Blood clotting	FDA (1994); EMA (1995)
Daclizumab*	FL-Body	IL-2R (CD25)	Organ transplant rejection, multiple sclerosis	FDA (1997); EMA (1999)
Rituximab	FL-Body	CD20	Rheumatoid arthritis, lymphocytic leukemia, follicular lymphoma, non-Hodgkin's lymphoma, systemic scleroderma	FDA (1997); EMA (1998); PMDA (2001); NMPA (2000); CDSCO (2002)
Infliximab	FL-Body	TNF-alpha	Crohn's disease, psoriatic arthritis, ankylosing spondylitis, rheumatoid arthritis, Behcet's disease, ulcerative colitis (UC), plaque psoriasis, Kawasaki disease	FDA (1998); EMA (1998); NMPA(2006); PMDA (2002); CDSCO (2013)
Trastuzumab	FL-Body	HER2	Breast and gastric cancer	FDA (1998); EMA (1998); CDSCO (2012)
Palivizumab	FL-Body	RSV-F	Prevention of respiratory syncytial viral infection	FDA (1998); EMA (1999)
Basiliximab	FL-Body	IL-2R (CD25)	Organ (kidney, liver) transplant rejection	FDA (1998); EMA (1998); PMDA (2002); NMPA (2004); CDSCO (1999)
Etanercept	Frag-Body	TNF-alpha	Psoriasis, psoriatic arthritis, ankylosing spondylitis, rheumatoid arthritis, plaque psoriasis	FDA (1998); EMA (2000); PMDA (2005); NMPA (2010); CDSCO (2012)
(99m Tc) Arcitumomab	Frag-Body:Conjugate	Carcinoembryonic antigen (CEA)	Diagnosis of CEA expression in cancer	FDA (1999)

Table 1. List of approved therapeutic antibodies. (*continued*)

Name	Format	Target	Indication	Approval
Gemtuzumab ozogamicin	FL-Body:Conjugate	CD33	Acute myelogenous leukemia	FDA (2017); PMDA (2005); EMA (2018);
Wut3	FL-Body	CD3	Organ transplant rejection	NMPA (2010)
Alemtuzumab	FL-Body	CD52	Lymphocytic leukemia, multiple sclerosis	FDA (2001); EMA (2001); PMDA (2014)
Adalimumab	FL-Body	TNF-alpha	Ankylosing spondylitis, rheumatoid arthritis, psoriatic arthritis, IBD	FDA (2002); EMA (2003); PMDA (2008); NMPA (2010); CDSCO (2014)
Ibritumomab tiuxetan	FL-Body:Conjugate	CD20	Non-Hodgkin's lymphoma, relapsed or refractory, low-grade or follicular NHL	FDA (2002); EMA (2004); CDSCO (2017)
Tositumomab-I131*	FL-Body:Conjugate	CD20	Non-Hodgkin lymphoma	FDA (2003)
Omalizumab	FL-Body	IgE	Allergic asthma, urticaria	FDA (2003); EMA (2005); PMDA (2006); CDSCO (2015); NMPA (2017)
Efalizumab*	FL-Body	Integrin subunit alpha L (ITGAL) or CD11a	Psoriasis	FDA (2003); EMA (2004)
Anti-IL-8 monoclonal antibody (ENBOKE)	FL-Body	IL-8	Atopic dermatitis, pustular psoriasis	NMPA (2003)
Alefacept*	Frag-Body	CD2	Psoriasis	FDA (2003)
Cetuximab	FL-Body	EGFR	Colorectal, head and neck cancer	FDA (2004); EMA (2004); PMDA (2008); NMPA (2020); CDSCO (2006)
Bevacizumab	FL-Body	VEGF-A	Colorectal, breast, cervical, liver, ovarian, renal cancer	FDA (2004); EMA (2005); CDSCO (2005); PMDA (2007); NMPA (2010)
Natalizumab	FL-Body	Integrin subunit alpha 4 (ITGA4)	Multiple sclerosis, Crohn's disease	FDA (2004); EMA (2006); PMDA (2014); CDSCO (2018)
Tocilizumab	FL-Body	IL-6R	Rheumatoid arthritis, Castleman's disease, vasculitis, drug hypersensitivity, SARS-CoV-2, scleroderma	FDA (2010); EMA (2009); PMDA (2005); CDSCO (2009); NMPA (2013)
Abatacept	Frag-Body	CD80, CD86	Psoriatic arthritis, rheumatoid arthritis, graft versus host disease	FDA (2005); EMA (2007); PMDA (2010); NMPA (2020)

Table 1. List of approved therapeutic antibodies. (*continued*)

Name	Format	Target	Indication	Approval
Panitumumab	FL-Body	EGFR	Colorectal cancer	FDA (2006); EMA (2007); PMDA (2010); CDSCO (2017)
I131 derlotuximab biotin	FL-Body:Conjugate	DNA/Histone H1	Lung cancer	NMPA (2006)
I131 metuximab	Frag-Body:Conjugate	CD147	Liver cancer	NMPA (2006)
Nimotuzumab	FL-Body	EGFR	Head & neck cancer, anaplastic astrocytoma, brain & esophageal cancer, glioma	CECMED (2006); CDSCO (2006); NMPA (2012)
Ranibizumab	Frag-Body	VEGF-A	Macular degeneration, choroidal neovascularization, diabetic macular edema, diabetic retinopathy	FDA (2006); EMA (2007); PMDA (2009); NMPA (2010); CDSCO (2007)
Eculizumab	FL-Body	C5	Paroxysmal nocturnal hemoglobinuria, myasthenia gravis, neuromyelitis optica, hemolytic uremic syndrome	FDA (2007); EMA (2007); PMDA (2010); NMPA (2018)
Rilonacept	Frag-Body	IL-1	Cryopyrin-associated periodic syndrome, an inborn genetic disorder, pericarditis	FDA (2008)
Certolizumab pegol	Frag-Body:Conjugate	TNF-alpha	Psoriatic arthritis, rheumatoid arthritis, Crohn's disease, and ankylosing spondylitis	FDA (2008); EMA (2009); PMDA (2012); NMPA (2019)
Romiplostim	Frag-Body	Thrombopoietin receptor (TPOR)	Aplastic anemia, acute radiation syndrome, idiopathic thrombocytopenic purpura	FDA (2008); EMA (2009); PMDA (2011); NMPA (2022)
Canakinumab	FL-Body	IL-1β	Muckle-wells syndrome, adult-onset still's disease, gouty arthritis, rheumatoid arthritis	FDA (2009); EMA (2009); PMDA (2011); CDSCO (2011)
Catumaxomab*	Poly-Body	CD3/EpCAM	Malignant ascites	EMA (2009)
Ustekinumab	FL-Body	IL-12/23	Psoriatic, IBD	FDA (2009); EMA (2009); PMDA (2011); NMPA (2017)
Ofatumumab	FL-Body	CD20	Chronic lymphocytic leukemia, multiple sclerosis	FDA (2009); EMA (2010); PMDA (2013); NMPA (2021); CDSCO (2016)
Golimumab	FL-Body	TNF-alpha	Rheumatoid and psoriatic arthritis, ankylosing spondylitis, UC, axial spondyloarthritis	FDA (2009); EMA (2009); PMDA (2011); CDSCO (2014); NMPA (2017)

Table 1. List of approved therapeutic antibodies. (*continued*)

Name	Format	Target	Indication	Approval
Denosumab	FL-Body	RANKL	Bone loss, rheumatoid arthritis, bone metastases, bone cancer, malignant hypercalcaemia, osteoporosis	FDA (2010); EMA (2010); PMDA (2012); CDSCO (2017); NMPA (2019)
Brentuximab vedotin	FL-Body:Conjugate	CD30	Hodgkin lymphoma, large T-cell lymphoma, Sezary syndrome, Mycosis fungoides,	FDA (2011); EMA (2012); PMDA (2014); NMPA (2020)
Belatacept	Frag-Body	CD80, CD86	Renal transplant rejection	FDA (2011); EMA (2011); CDSCO (2012)
Aflibercept	Frag-Body	VEGF	Colorectal cancer, retinal vein occlusion, diabetic macular edema, diabetic retinopathy, macular edema	FDA (2011); EMA (2012); PMDA (2012); NMPA (2018)
Belimumab	FL-Body	BAFF	Systemic lupus erythematosus, lupus nephritis	FDA (2011); EMA (2011); PMDA (2017); NMPA (2022)
Ipilimumab	FL-Body	CTLA-4	Metastatic melanoma, liver cancer, renal cell carcinoma, mesothelioma, non-small cell lung cancer	FDA (2011); EMA (2011); PMDA (2015); NMPA (2021)
Pertuzumab	FL-Body	HER2	Breast cancer	FDA (2012); EMA (2013); PMDA (2013); NMPA (2018)
Raxibacumab	FL-Body	*Bacillus anthracis* protective antigen	Anthrax infection	FDA (2012)
Mogamulizumab	FL-Body	CCR4	Mycosis fungoides, T-cell lymphoma	FDA (2018); PMDA (2012); EMA (2018)
Trastuzumab emtansine	FL-Body:Conjugate	HER2	Breast cancer	FDA (2013); EMA (2013); NMPA (2020); PMDA (2013)
Obinutuzumab	FL-Body	CD20	Chronic lymphocytic leukemia, follicular lymphoma, non-Hodgkin's lymphoma	FDA (2013); EMA (2014); PMDA (2018); NMPA (2021)
Conbercept	Frag-Body	VEGF	Macular degeneration	NMPA (2013)
Itolizumab	FL-Body	CD6	CRS (cytokine release syndrome), plaque psoriasis, SARS-CoV 2	CDSCO (2013)
Blinatumomab	Poly-Body	CD19/CD3	Acute lymphoblastic leukemia	FDA (2014); EMA (2015); PMDA (2018); NMPA (2020)

Table 1. List of approved therapeutic antibodies. (*continued*)

Name	Format	Target	Indication	Approval
Pembrolizumab	FL-Body	PD-1	Breast, cervical, colorectal, esophageal, gastric, liver, head & neck, lung, pancreatic, urogenital, cancer, and B-cell lymphoma, Hodgkin's lymphoma, malignant lymphoma	FDA (2014); EMA (2015); PMDA (2016); CDSCO (2016); NMPA (2018)
Eftrenonacog alfa	Frag-Body	Factor IX	Hemophilia B	FDA (2014); PMDA (2014); EMA (2016); NMPA (2021)
Vedolizumab	FL-Body	α4β7 integrin	Inflammatory bowel disease	FDA (2014); EMA (2014); CDSCO (2016); PMDA (2018)
Secukinumab	FL-Body	IL-17A	Psoriasis, psoriatic arthritis, ankylosing spondylitis, plaque psoriasis	FDA (2015); EMA (2015); PMDA (2014); CDSCO (2015); NMPA (2019)
Ramucirumab	FL-Body	VEGFR-2	Liver, gastric, colorectal, and non-small cell lung cancer	FDA (2014); EMA (2014); PMDA (2015); CDSCO (2016); NMPA (2022)
Efmoroctocog alfa	Frag-Body	Factor VIII (FVIII)	Hemophilia A	FDA (2014); EMA (2015); PMDA (2014)
Siltuximab	FL-Body	IL-6	Multicentric Castleman's disease	FDA (2014); EMA (2014); NMPA (2021); CDSCO (2016)
Nivolumab	FL-Body	PD-1	Melanoma, non-small cell lung cancer, colorectal cancer, esophageal cancer, gastric cancer, Hodgkin's lymphoma, renal carcinoma, head and neck cancer, mesothelioma	FDA (2014); EMA (2015); PMDA (2014); CDSCO (2016); NMPA (2019)
Elotuzumab	FL-Body	SLAMF7 (SLAM family member 7)	Multiple myeloma	FDA (2015); EMA (2016); PMDA (2016)
Alirocumab	FL-Body	PCSK9 (Proprotein convertase subtilisin/kexin type 9)	High cholesterol, hyperlipoproteinemia type IIa	FDA (2015); EMA (2015); PMDA (2016)
Axicabtagene ciloleucel	Frag-Body	CD19	Large B-cell lymphoma (LBCL)	FDA (2022); EMA (2015)
Mepolizumab	FL-Body	IL-5	Asthma	FDA (2015); EMA (2015); PMDA (2016); CDSCO (2018); NMPA (2021)

Table 1. List of approved therapeutic antibodies. (*continued*)

Name	Format	Target	Indication	Approval
Necitumumab	FL-Body	EGFR	Non-small cell lung cancer	FDA (2015); EMA (2016); PMDA (2019)
Idarucizumab	Frag-Body	Dabigatran	Reversal of dabigatran-induced anticoagulation	FDA (2015); EMA (2015); PMDA (2016); NMPA (2018); CDSCO (2017)
Dinutuximab	Frag-Body	GD2	Neuroblastoma	FDA (2015); EMA (2015); PMDA (2021); NMPA (2021)
Daratumumab	FL-Body	CD38	Multiple myeloma	FDA (2015); EMA (2016); PMDA (2017); CDSCO (2017); NMPA (2019)
Evolocumab	FL-Body	PCSK9	Hypercholesterolemia, hyperlipoproteinemia, coronary artery disease, stroke	FDA (2015); EMA (2015); PMDA (2016); CDSCO (2017); NMPA (2018)
Atezolizumab	FL-Body	PD-L1	Bladder, liver, lung, urogenital cancer	FDA (2016); EMA (2017); CDSCO (2017); PMDA (2018); NMPA (2020)
Olaratumab*	FL-Body	PDGFRA	Soft tissue sarcoma	FDA (2016); EMA (2016)
Bezlotoxumab	FL-Body	*Clostridium difficile* Toxin B	Prevention of *C. difficile* infection recurrence	FDA (2016); EMA (2017); PMDA (2017)
Ixekizumab	FL-Body	IL-17A	Plaque psoriasis, psoriatic arthritis, pustular psoriasis, non-radiographic axial spondyloarthritis	FDA (2016); EMA (2016); PMDA (2016); NMPA (2019)
Brodalumab	FL-Body	IL-17R	Plaque psoriasis, psoriatic arthritis, pustular psoriasis, axial spondylarthritis, erythrodermic psoriasis	FDA (2017); EMA (2017); PMDA (2016); NMPA (2020)
SII rmab	FL-Body	Rabies virus GP	Post-exposure prophylaxis of rabies	CDSCO (2016)
Reslizumab	FL-Body	IL-5	Asthma	FDA (2016); EMA (2016)
Obiltoxaximab	FL-Body	*B. anthracis* PA	Anthrax infection	FDA (2016); EMA (2020)
Inotuzumab ozogamicin	FL-Body:Conjugate	CD22	Hematological malignancy	FDA (2017); EMA (2017);

Table 1. List of approved therapeutic antibodies. (*continued*)

Name	Format	Target	Indication	Approval
				PMDA (2018);
				CDSCO (2018);
				NMPA (2021)
Sarilumab	FL-Body	IL-6R	Rheumatoid arthritis	FDA (2017);
				EMA (2017);
				PMDA (2017);
				HC (2017)
Dupilumab	FL-Body	IL-4R alpha	Atopic dermatitis, eosinophilic esophagitis, asthma, nasal polyps	FDA (2017);
				EMA (2017);
				PMDA (2018);
				NMPA (2020)
Durvalumab	FL-Body	PD-L1	Bladder cancer, lung cancer	FDA (2017);
				EMA (2018);
				PMDA (2018);
				NMPA (2019)
Idecabtagene vicleucel	Frag-Body	BCMA	Refractory multiple myeloma	FDA (2021)
Avelumab	FL-Body	PD-L1	Merkel cell carcinoma, renal cell carcinoma, urogenital cancer	FDA (2017);
				EMA (2017);
				PMDA (2017)
Emicizumab	Poly-Body	Factor IXa/X	Hemophilia A	FDA (2017);
				CDSCO (2018);
				EMA (2018);
				PMDA (2018);
				NMPA (2018)
Benralizumab	FL-Body	IL-5R alpha subunit	Asthma	FDA (2017);
				EMA (2018);
				PMDA (2018)
Ocrelizumab	FL-Body	CD20	Multiple sclerosis	FDA (2017);
				EMA (2018)
Guselkumab	FL-Body	IL-23p19 subunit	Plaque psoriasis, psoriatic arthritis, palmoplantar pustulosis, erythrodermic psoriasis, generalized pustular psoriasis	FDA (2017);
				EMA (2017);
				PMDA (2018);
				NMPA (2019)
Erenumab	FL-Body	CGRP-R (Calcitonin gene-related peptide receptor)	Migraine prevention	FDA (2018);
				EMA (2018);
				PMDA (2021)
Ravulizumab	FL-Body	C5	Paroxysmal nocturnal hemoglobinuria, myasthenia gravis, haemolytic	FDA (2018);
				EMA (2019);
				PMDA (2019)
Moxetumomab pasudotox*	FL-Body:Conjugate	CD22	Hairy cell leukemia	FDA (2018);
				EMA (2021)
Fremanezumab	FL-Body	CGRP	Migraine prevention	FDA (2018);
				EMA (2019);
				PMDA (2021)
Sintilimab	FL-Body	PD-1	Non-small cell lung cancer, liver cancer, gastric cancer, esophageal cancer, Hodgkin's lymphoma	NMPA (2018)

Table 1. List of approved therapeutic antibodies. (*continued*)

Name	Format	Target	Indication	Approval
Ibalizumab	FL-Body	CD4	HIV infection	FDA (2018); EMA (2019)
Galcanezumab	FL-Body	CGRP	Migraine prevention, cluster headache	FDA (2018); EMA (2018); PMDA (2021)
Tildrakizumab	FL-Body	IL-23p19	Plaque psoriasis	FDA (2018); EMA (2018); PMDA (2020)
Emapalumab	FL-Body	IFN-γ	Primary hemophagocytic lymphohistocytosis	FDA (2018); NMPA (2022)
Cemiplimab	FL-Body	PD-1	Cutaneous squamous cell carcinoma, basal cell carcinoma, and non-small cell lung cancer	FDA (2018); EMA (2019)
Toripalimab	FL-Body	PD-1	Nasopharyngeal carcinoma, esophageal squamous cell carcinoma, urogenital cancer, malignant melanoma	NMPA (2018); FDA (2023); EMA (2024)
Caplacizumab	Frag-Body	vWF (von Willebrand Factor)	Thrombotic thrombocytopenic purpura	FDA (2019); EMA (2018)
Lanadelumab	FL-Body	Plasma kallikrein	Hereditary angioedema attacks	FDA (2018); EMA (2018); PMDA (2022); NMPA (2020)
Burosumab	FL-Body	FGF23	X-linked hypophosphatemia, osteomalacia	FDA (2018); EMA (2018); PMDA (2019); NMPA (2021)
Tislelizumab	FL-Body	PD-1	Esophageal squamous cell carcinoma, liver cancer, urogenital cancer, non-small cell lung cancer, Hodgkin's lymphoma	FDA (2024); EMA (2023); NMPA (2019)
Risankizumab	FL-Body	IL-23p19	Plaque psoriasis, psoriatic arthritis, Crohn's disease	FDA (2019); EMA (2019); PMDA (2019)
Trastuzumab deruxtecan	FL-Body:Conjugate	HER2	Breast and gastric cancer	FDA (2019); EMA (2021); PMDA (2020)
Brolucizumab	Frag-Body	VEGF-A	Macular degeneration	FDA (2019); EMA (2020); PMDA (2020)
Crizanlizumab	FL-Body	P-selectin	Vaso-occlusive crisis	FDA (2019)
Enfortumab vedotin (PADCEV)	FL-Body:Conjugate	Nectin-4	Urogenital cancer	FDA (2019); EMA (2022); PMDA (2021)
Romosozumab	FL-Body	Sclerostin	Osteoporosis in postmenopausal women at risk of fracture, male osteoporosis	FDA (2019); EMA (2019); PMDA (2019)
Efgartigimod alfa	Frag-Body	FcRn	Myasthenia gravis	FDA (2021); EMA (2022); PMDA (2022)

Table 1. List of approved therapeutic antibodies. (*continued*)

Name	Format	Target	Indication	Approval
Camrelizumab	FL-Body	PD-1	Advanced renal cell carcinoma, esophageal cancer, liver cancer, nasopharyngeal cancer, non-small cell lung cancer	NMPA (2019)
Polatuzumab vedotin	FL-Body:Conjugate	CD79b	Diffuse large B-cell lymphoma	FDA (2019); EMA (2020); PMDA (2021)
Luspatercept	Frag-Body	TGF-β	Beta-thalassemia, myelodysplastic syndrome	FDA (2019); EMA (2020); NMPA (2022)
Rabimabs	Poly-Body	Rabies virus GP (glycoprotein)	Rabies virus infection	CDSCO (2019)
Netakimab	FL-Body	IL-17A	Plaque psoriasis, psoriatic arthritis, and ankylosing spondylitis	MoH RF (2019)
Racotumomab	FL-Body	NeuGcGM3	Recurrent or advanced non-small cell lung cancer	CECMED (2013); ANMAT (2013)
Pabinafusp alfa	FL-Body:Conjugate	Transferrin receptor	Mucopolysaccharidosis II	PMDA (2021)
Inebilizumab	FL-Body	CD19	Neuromyelitis optica and neuromyelitis optica spectrum disorders	FDA (2020); NMPA (2022); PMDA (2021)
Teprotumumab	FL-Body	IGF-1R (insulin-like growth factor-1 receptor)	Thyroid eye disease (Graves' orbitopathy)	FDA (2020)
Sacituzumab govitecan	FL-Body:Conjugate	TROP-2	Urogenital and breast cancer	FDA (2020); EMA (2021); NMPA (2022)
Atoltivimab + Odesivimab + Maftivimab (INMAZEB)	Poly-Body	Ebola virus glycoprotein	Ebola virus infection	FDA (2020)
Cetuximab sarotalocan	FL-Body:Conjugate	EGFR	Head and neck cancer	PMDA (2020)
Isatuximab	FL-Body	CD38	Multiple myeloma	FDA (2020); EMA (2020); PMDA (2020)
Belantamab mafodotin	FL-Body:Conjugate	BCMA	Multiple myeloma	FDA (2025); EMA (2025)
Levilimab	FL-Body	IL-6R	COVID-19, rheumatoid arthritis	Russia (2020)
Margetuximab	FL-Body	HER2	Breast cancer	FDA (2020)
Satralizumab	FL-Body	IL-6R	Neuromyelitis optica and neuromyelitis optica spectrum disorders	FDA (2020); EMA (2021); PMDA (2020); HC (2020); NMPA (2021)
Tafasitamab	FL-Body	CD19	Diffuse large B-cell lymphoma	FDA (2020); EMA (2021)
Naxitamab	FL-Body	GD2	High-risk neuroblastoma and refractory osteomedullary disease	FDA (2020)
Ansuvimab	FL-Body	Ebola virus glycoprotein	Ebola infection	FDA (2020)
Eptinezumab	FL-Body	CGRP	Migraine prevention	FDA (2020); EMA (2022)

Table 1. List of approved therapeutic antibodies. (*continued*)

Name	Format	Target	Indication	Approval
Prolgolimab	FL-Body	PD-1	Melanoma	Russia (2020)
Olokizumab	FL-Body	IL-6	Rheumatoid arthritis, COVID-19	Russia (2020)
Penpulimab	FL-Body	PD-1	Metastatic nasopharyngeal carcinoma, non-small cell lung cancer, Hodgkin's lymphoma	FDA (2025); NMPA (2021)
Dostarlimab	FL-Body	PD-1	Endometrial cancer is a solid cancer	FDA (2021); EMA (2021)
Evinacumab	FL-Body	ANGPTL3	Homozygous familial hypercholesterolemia	FDA (2021); EMA (2021)
Sugemalimab	FL-Body	PD-L1	Non-small cell lung cancer	NMPA (2021)
Envafolimab	Frag-Body	PD-L1	Solid tumors	NMPA (2021)
Telitacicept	Frag-Body	BAFF	Systemic lupus erythematosus	NMPA (2021)
Regdanvimab*	FL-Body	SARS-CoV-2	COVID-19 infection	EMA (2021); ANVISA (2021)
Amubarvimab + Romlusevimab	Poly-Body	SARS-CoV-2	COVID-19 infection	NMPA (2021)
Brexucabtagene autoleucel	Frag-Body	CD19	Relapsed or refractory mantle cell lymphoma, acute lymphoblastic leukaemia	FDA (2020); EMA (2020)
Amivantamab	Poly-Body	EGFR/c-Met	Non-small cell lung cancer	FDA (2021); EMA (2021)
Zimberelimab	FL-Body	PD-1	Hodgkin's lymphoma	NMPA (2021)
Bimekizumab	FL-Body	IL-17A/IL-17F	Plaque psoriasis, pustular psoriasis, erythrodermic psoriasis	FDA (2023); EMA (2021); PMDA (2022)
Loncastuximab tesirine	FL-Body:Conjugate	CD19	Diffuse large B-cell lymphoma	FDA (2021); EMA (2022)
Tisotumab vedotin	FL-Body:Conjugate	TF (tissue factor)	Cervical cancer	FDA (2021)
Tralokinumab	FL-Body	IL-13	Atopic dermatitis	FDA (2021); EMA (2021)
Tezepelumab	FL-Body	TSLP (thymic stromal lymphopoietin)	Severe asthma	FDA (2021); EMA (2022)
Aducanumab	FL-Body	Amyloid beta	Alzheimer's disease	FDA (2021)
Disitamab vedotin	FL-Body:Conjugate	HER2	Gastric and urothelial cancer	NMPA (2021)
Sotrovimab*	FL-Body	SARS-CoV-2	COVID-19 infection	EMA (2021); PMDA (2021)
Casirivimab + Imdevimab*	Poly-Body	SARS-CoV-2	COVID-19 infection	EMA (2021)
Anifrolumab	FL-Body	IFNAR-1 (Interferon alpha receptor-1)	Systemic lupus erythematosus	FDA (2021); EMA (2022); PMDA (2021)
Faricimab	Poly-Body	VEGF-A/ANG-2	Diabetic macular edema and wet age-related macular degeneration	FDA (2022); EMA (2022); PMDA (2022)
Teplizumab	FL-Body	CD3	Delayed onset of type 1 diabetes	FDA (2022); EMA (2026)
Cadonilimab	Poly-Body	CTLA-4/PD-1	Cervical cancer	NMPA (2022)
Ublituximab	FL-Body	CD20	Multiple sclerosis	FDA (2022); EMA (in review)

Table 1. List of approved therapeutic antibodies. (*continued*)

Name	Format	Target	Indication	Approval
Ormutivimab	FL-Body	Rabies virus GP (glycoprotein)	Rabies virus prophylaxis	NMPA (2022)
Tisagenlecleucel (KYMRIAH)	Frag-Body	CD19	Relapsed or refractory follicular lymphoma, ALL, DLBCL, FL	FDA (2022); EMA (2018)
Tremelimumab	FL-Body	CTLA-4	Liver cancer	FDA (2022); EMA (2023); PMDA (2022)
Lisocabtagene maraleucel	Frag-Body	CD19	DLBCL, PMBCL, FL3B	FDA (2021); EMA (2022)
Mirvetuximab soravtansine	FL-Body:Conjugate	Folate receptor alpha	Ovarian cancer	FDA (2022)
Spesolimab	FL-Body	IL-36R	Generalized pustular psoriasis	FDA (2022); EMA (2022)
Sutimlimab	FL-Body	C1s	Cold agglutinin disease and autoimmune hemolytic anemia	FDA (2022); EMA (2022)
Mosunetuzumab-axgb	Poly-Body	CD20/CD3	Follicular lymphoma	FDA (2022); EMA (2022)
Nirsevimab	FL-Body	RSV	RSV infection	FDA (2023); EMA (2022)
Nemolizumab	FL-Body	IL-31RA	Atopic dermatitis	PMDA (2022); FDA (2024); EMA (2025)
Relatlimab + Nivolumab	Poly-Body	LAG-3/PD-1	Melanoma	FDA (2022); EMA (2022)
Tixagevimab + Cilgavimab*	FL-Body	SARS-CoV-2 spike protein	Covid infection	EMA (2022)
Serplulimab	FL-Body	PD-1	Solid cancer, lung cancer	NMPA (2022)
Teclistamab	Poly-Body	BCMA/CD3	Multiple myeloma	FDA (2022); EMA (2022)
Ozoralizumab	Poly-Body	TNF-alpha/albumin	Rheumatoid arthritis	FDA (in review); PMDA (2022)
Tebentafusp	Poly-Body	CD3 and GP100	Metastatic uveal melanoma	FDA (2022); EMA (2022)
Retifanlimab	FL-Body	PD-1	Metastatic or recurrent locally advanced Merkel cell carcinoma	FDA (2023)
Lecanemab	FL-Body	Amyloid beta protofibrils	Alzheimer's disease	FDA (2023); EMA (in review)
Mirikizumab	FL-Body	IL-23p19	Inflammatory bowel disease	PMDA (2023)
Rozanolixizumab	FL-Body	FcRn	Myasthenia gravis	FDA (2023); EMA (2024); PMDA (2023)
Talquetamab	Poly-Body	GPCR- 5D and CD3	Multiple myeloma	FDA (2023); EMA (2023)
Epcoritamab	Poly-Body	CD20 and CD3	B-cell lymphoma	FDA (2023); EMA (2023)
Lebrikizumab	FL-Body	IL-13	Atopic dermatitis	FDA (2024); EMA (2023)
Glofitamab	Poly-Body	CD20 and CD3	B-cell lymphoma	FDA (2023); EMA (2023)

Table 1. List of approved therapeutic antibodies. (*continued*)

Name	Format	Target	Indication	Approval
Elranatamab	Poly-Body	BCMA and CD3	Multiple myeloma	FDA (2023); EMA (2023)
Pozelimab	FL-Body	C5	CD55-deficient protein-losing enteropathy (CHAPLE) disease	FDA (2023)
Narsoplimab	FL-Body	MASP-2	Hematopoietic stem cell transplant-associated thrombotic microangiopathy (TA-TMA)	FDA (2025)
Donanemab	FL-Body	Amyloid beta	Alzheimer's disease	FDA (2024); EMA (2025)
Cosibelimab	FL-Body	PD-L1	Squamous cell carcinoma	FDA (2024)
Concizumab	FL-Body	Tissue factor pathway inhibitor (TFPI)	Hemophilia A or B	FDA (2024); EMA (2024); PMDA (2023)
Crovalimab	FL-Body	C5	Paroxysmal nocturnal hemoglobinuria	FDA (2024); EMA (2024)
Odronextamab	Poly-Body	CD20, CD3	Follicular lymphoma	EMA (2024)
Zolbetuximab	FL-Body	Claudin 18.2	Gastroesophageal junction adenocarcinoma	FDA (2024); EMA (2024)
Vilobelimab	FL-Body	C5a	SARS-CoV-2-induced septic acute respiratory distress syndrome	FDA (2025)
Garadacimab	FL-Body	Factor XIIa	Hereditary angioedema	FDA (2025); EMA (2025)
Marstacimab	FL-Body	TFPI	Hemophilia	FDA (2024); EMA (2024)
Tarlatamab	Poly-Body	DLL3 and CD3	Small-cell lung cancer	FDA (2025)
Axatilimab	FL-Body	CSF-1R	Graft-versus-host disease	FDA (2024)
Linvoseltamab	Poly-Body	BCMA and CD3	Multiple myeloma	FDA (2025); EMA (2025)
Zanidatamab	Poly-Body	HER2	Biliary tract cancers	FDA (2024); EMA (2025)
Zenocutuzumab	Poly-Body	HER2 and HER3	NRG1+ non-small cell lung and pancreatic cancer	FDA (2024)
Datopotamab deruxtecan	FL-Body:Conjugate	TROP-2	Breast cancer	FDA (2025); EMA (2025)
Nipocalimab	FL-Body	FcRn	Generalized myasthenia gravis	FDA (2025); EMA (2025)
Clesrovimab	FL-Body	RSV	RSV infection	FDA (2025)
Sibeprenlimab	FL-Body	APRIL	Nephropathy proteinuria	FDA (2025)
Telisotuzumab vedotin	FL-Body:Conjugate	cMET	Non-small cell lung cancer	FDA (2025)
Depemokimab	FL-Body	IL-5	Asthma with type 2 inflammation and chronic rhinosinusitis with nasal polyps	FDA (2025)

* Indicates antibodies withdrawn from the market due to one or more reasons such as clinical failure, loss of efficacy, severe side effects, or commercial reasons. FDA: Food and Drug Administration; EMA: European Medicines Agency; PMDA: Pharmaceuticals and Medical Devices Agency; NMPA: National Medical Products Administration; CDSCO: Central Drugs Standard Control Organization; CECMED: Centro para el Control Estatal de Medicamentos, Equipos y Dispositivos Médicos; HC: Health Canada; MoH RF: Ministry of Health of the Russian Federation; ANMAT: National Administration of Drugs, Food and Medical Devices. FL-Bodies: full-length antibodies; Frag-Bodies: antibody fragments; Poly-Body: polyspecific and polyvalent antibody; ALL: acute lymphoblastic leukemia; DLBCL: diffuse large B-cell lymphoma; FL: follicular lymphoma; FL3B: follicular lymphoma grade 3B; NHL: non-Hodgkin lymphoma; PMBCL: primary mediastinal large B-cell lymphoma.

Conceptual outlook

Currently, antibody production primarily relies on mammalian cell culture platforms, particularly CHO cells, which remain the industry standard for achieving proper folding and post-translational modifications

[57, 58]. However, considering the rapid progress in biotechnology, materials science, and biofabrication, we hypothesize that bioprinting may, in the distant future, emerge as an alternative approach for antibody production. Although no experimental evidence currently supports this concept, protein-based 3D printing materials have already demonstrated success in creating complex biological structures, providing a conceptual foundation for such a possibility [59]. If such technological convergence were achieved, it might allow decentralized, on-demand antibody manufacturing, where hospitals or clinical facilities could potentially fabricate personalized antibodies at the point of care, thereby reducing logistical and supply-chain challenges. Building on this perspective, we also propose the theoretical concept of 'reversible antibodies' or 'RoboBodies', a highly speculative idea in which engineered antibodies could transiently bind one target and then sequentially interact with others with precise control. While there is currently no experimental evidence to support this idea, advances in protein engineering, nanotechnology, and synthetic biology may eventually make such innovations scientifically conceivable.

It is important to note that the implementation of such next-generation antibody therapies would face considerable regulatory, ethical, and economic challenges. Regulatory approval processes would need to adapt to account for AI-designed molecules and on-demand bioprinted therapeutics, ensuring safety and efficacy. Ethical considerations, including equitable access and potential misuse, would require careful evaluation. Additionally, the economic feasibility of decentralized antibody production and advanced AI-driven design platforms remains uncertain and would likely influence the pace of adoption. At present, these ideas remain our theoretical hypothesis, proposed to highlight the long-term potential of merging advanced manufacturing technologies with antibody therapeutics. Rigorous experimental exploration and technological validation will be required before this concept can move toward practical application. Rapid technological progress is bringing these innovations closer to practical application, as demonstrated by the successful development of Poly-Bodies, which were previously considered a significant engineering challenge. The future of the field holds substantial promise, and antibodies are expected to remain a central component of therapeutic strategies, with ongoing research focused on improving their efficacy and broadening their clinical applications.

Conclusions

Antibody-based therapeutics have established themselves as an important player in modern medicine, with proven effectiveness in infectious diseases and a rapidly expanding role in oncology, autoimmune, cardiovascular, and neurodegenerative disorders. Their strong clinical performance, combined with sustained commercial success, continues to drive intensive research and development efforts, resulting in the emergence of next-generation antibody formats such as multispecific Poly-Bodies, antibody–drug conjugates, and innovative delivery platforms. Moreover, advances in manufacturing technologies, including optimized mammalian and alternative expression systems, single-use bioprocessing, and emerging production strategies, are expected to improve scalability, flexibility, and cost efficiency. At the same time, progress in genetic and protein engineering, conjugation chemistry, and computational approaches like AI-driven discovery and optimization is accelerating antibody design, enhancing specificity, potency, and multi-pathway targeting capabilities.

Despite these advances, several challenges remain, including immunogenicity, manufacturing complexity, supply sustainability, and global accessibility. Addressing these limitations will require continued innovation across discovery, development, and regulatory frameworks. Thus, antibody therapeutics are expected to remain a central component of future treatment strategies, playing a critical role in advancing precision and personalized medicine and improving patient outcomes across a wide range of diseases.

Abbreviations

ADA: anti-drug antibody

AI/ML: artificial intelligence and machine learning

CHO: Chinese hamster ovary

CRS: cytokine release syndrome

DS: drug substance

FL-Bodies: full-length antibodies

Frag-Bodies: antibody fragments

IL: interleukin

MAbs: monoclonal antibodies

Poly-Body: polyspecific and polyvalent antibody

Declarations

Author contributions

AHP: Writing—original draft, Data curation, Writing—review & editing, Funding acquisition. Sandeep: Writing—original draft, Data curation, Writing—review & editing, Funding acquisition. JA: Writing—original draft, Writing—review & editing. All authors read and approved the submitted version.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical approval

Not applicable.

Consent to participate

Not applicable.

Consent to publication

Not applicable.

Availability of data and materials

Not applicable.

Publisher's note

Open Exploration maintains a neutral stance on jurisdictional claims in published institutional affiliations and maps. All opinions expressed in this article are the personal views of the author(s) and do not represent the stance of the editorial team or the publisher.

References

1. Pande AH, Prasad YR, Anakha J. What are biopharmaceuticals? Explor Drug Sci. 2025;3:100880. [DOI]
2. Martin KP, Grimaldi C, Grempler R, Hansel S, Kumar S. Trends in industrialization of biotherapeutics: a survey of product characteristics of 89 antibody-based biotherapeutics. MAbs. 2023;15:2191301. [DOI] [PubMed] [PMC]
3. Crescioli S, Kaplon H, Wang L, Visweswaraiah J, Kapoor V, Reichert JM. Antibodies to watch in 2025. MAbs. 2025;17:2443538. [DOI] [PubMed]
4. Smith SL. Ten years of Orthoclone OKT3 (muromonab-CD3): a review. J Transpl Coord. 1996;6: 109–21. [DOI] [PubMed]
5. Kesik-Brodacka M. Progress in biopharmaceutical development. Biotechnol Appl Biochem. 2018;65: 306–22. [DOI] [PubMed] [PMC]
6. Sandeep, Shinde SH, Ahmed S, Sharma SS, Pande AH. Engineered polyspecific antibodies: A new frontier in the field of immunotherapeutics. Immunology. 2024;171:464–96. [DOI] [PubMed]
7. Chan AC, Martyn GD, Carter PJ. Fifty years of monoclonals: the past, present and future of antibody therapeutics. Nat Rev Immunol. 2025;25:745–65. [DOI] [PubMed]
8. Gao Y, Huang X, Zhu Y, Lv Z. A brief review of monoclonal antibody technology and its representative applications in immunoassays. J Immunoassay Immunochem. 2018;39:351–64. [DOI] [PubMed]
9. Khristunova Y, Korotkova E, Kratochvil B, Barek J, Dorozhko E, Vyskocil V, et al. Preparation and Investigation of Silver Nanoparticle‾Antibody Bioconjugates for Electrochemical Immunoassay of Tick-Borne Encephalitis. Sensors (Basel). 2019;19:2103. [DOI] [PubMed] [PMC]
10. Khristunova E, Barek J, Kratochvil B, Korotkova E, Dorozhko E, Vyskocil V. Electrochemical immunoassay for the detection of antibodies to tick-borne encephalitis virus by using various types of bioconjugates based on silver nanoparticles. Bioelectrochemistry. 2020;135:107576. [DOI] [PubMed]
11. Dorozhko EV, Solomonenko AN, Erkovich AV, Koltsova AV, Korotkova EI, Kolobova EN, et al. Copper-enhanced electrochemical immunosensor based on gold nanoparticles for the quality control of hepatitis A virus vaccines. Talanta. 2026;297:128579. [DOI] [PubMed]
12. Behring, Kitasato. On the development of immunity to diphtheria and tetanus in animals. Dtsch Med Wochenschr. 1965;90:2183. German. [PubMed]
13. Chiu ML, Goulet DR, Teplyakov A, Gilliland GL. Antibody Structure and Function: The Basis for Engineering Therapeutics. Antibodies (Basel). 2019;8:55. [DOI] [PubMed] [PMC]
14. Köhler G, Milstein C. Continuous cultures of fused cells secreting antibody of predefined specificity. Nature. 1975;256:495–7. [DOI] [PubMed]
15. Freysd'ottir J. Production of monoclonal antibodies. Methods Mol Med. 2000;40:267–79. [DOI] [PubMed]
16. Wilde MI, Goa KL. Muromonab CD3: a reappraisal of its pharmacology and use as prophylaxis of solid organ transplant rejection. Drugs. 1996;51:865–94. [DOI] [PubMed]
17. Leavy O. Therapeutic antibodies: past, present and future. Nat Rev Immunol. 2010;10:297. [DOI] [PubMed]
18. Zhu H, Yang B, Yang X, Wang L, Xu J, Liao C, et al. A novel antibody fragment targeting HAb18G/CD147 with cytotoxicity and decreased immunogenicity. Cancer Biol Ther. 2009;8:1035–44. [DOI] [PubMed]
19. Goel N, Stephens S. Certolizumab pegol. MAbs. 2010;2:137–47. [DOI] [PubMed] [PMC]
20. Sharma A, Kumar N, Parachuri N, Sharma R, Bandello F, Kuppermann BD, et al. Brolucizumab and fluid in neovascular age-related macular degeneration (n-AMD). Eye (Lond). 2020;34:1310–2. [DOI] [PubMed] [PMC]
21. Duggan S. Caplacizumab: First Global Approval. Drugs. 2018;78:1639–42. [DOI] [PubMed] [PMC]
22. Giles F, Estey E, O'Brien S. Gemtuzumab ozogamicin in the treatment of acute myeloid leukemia. Cancer. 2003;98:2095–104. [DOI] [PubMed]

23. Lu R, Hwang Y, Liu I, Lee C, Tsai H, Li H, et al. Development of therapeutic antibodies for the treatment of diseases. J Biomed Sci. 2020;27:1. [DOI] [PubMed] [PMC]

24. Bhushan A, Misra P. Economics of Antibody Drug Conjugates (ADCs): Innovation, Investment and Market Dynamics. Curr Oncol Rep. 2024;26:1224–35. [DOI] [PubMed]

25. Fitzgerald J, Lugovskoy A. Rational engineering of antibody therapeutics targeting multiple oncogene pathways. MAbs. 2011;3:299–309. [DOI] [PubMed] [PMC]

26. Gu J, Ghayur T. Rationale and development of multispecific antibody drugs. Expert Rev Clin Pharmacol. 2010;3:491–508. [DOI] [PubMed]

27. Pande AH, Sandeep, Shinde SH. Polybodies: Next-generation clinical antibodies. Drug Discov Today. 2024;29:104198. [DOI] [PubMed]

28. Burt R, Warcel D, Fielding AK. Blinatumomab, a bispecific B-cell and T-cell engaging antibody, in the treatment of B-cell malignancies. Hum Vaccin Immunother. 2019;15:594–602. [DOI] [PubMed] [PMC]

29. Tapia-Galisteo A, Álvarez-Vallina L, Sanz L. Bi- and trispecific immune cell engagers for immunotherapy of hematological malignancies. J Hematol Oncol. 2023;16:83. [DOI] [PubMed] [PMC]

30. Crescioli S, Kaplon H, Chenoweth A, Wang L, Visweswaraiah J, Reichert JM. Antibodies to watch in 2024. MAbs. 2024;16:2297450. [DOI] [PubMed] [PMC]

31. Nguyen A, Bhandari C, Keown M, Malkoochi A, Quaye M, Mahmoud D, et al. Increasing the Dye Payload of Cetuximab-IRDye800CW Enables Photodynamic Therapy. Mol Pharm. 2024;21:3296–309. [DOI] [PubMed] [PMC]

32. Xenaki KT, Oliveira S, van Bergen en Henegouwen PMP. Antibody or Antibody Fragments: Implications for Molecular Imaging and Targeted Therapy of Solid Tumors. Front Immunol. 2017;8: 1287. [DOI] [PubMed] [PMC]

33. Adams R, Griffin L, Compson JE, Jairaj M, Baker T, Ceska T, et al. Extending the half-life of a fab fragment through generation of a humanized anti-human serum albumin Fv domain: An investigation into the correlation between affinity and serum half-life. MAbs. 2016;8:1336–46. [DOI] [PubMed] [PMC]

34. Lim RK, Buschman M, Khasanov A, Ledesma A, Chen J, Nguyen T, et al. Discovery of novel cMET-targeting antibody Fab drug conjugates as potential treatment for solid tumors with highly expressed cMET. Expert Opin Biol Ther. 2023;23:1137–49. [DOI] [PubMed]

35. Kalinovsky DV, Kholodenko IV, Kibardin AV, Doronin II, Svirshchevskaya EV, Ryazantsev DY, et al. Minibody-Based and scFv-Based Antibody Fragment-Drug Conjugates Selectively Eliminate GD2-Positive Tumor Cells. Int J Mol Sci. 2023;24:1239. [DOI] [PubMed] [PMC]

36. Radtke KK, Bender BC, Li Z, Turner DC, Roy S, Belousov A, et al. Clinical Pharmacology of Cytokine Release Syndrome with T-Cell-Engaging Bispecific Antibodies: Current Insights and Drug Development Strategies. Clin Cancer Res. 2025;31:245–57. [DOI] [PubMed] [PMC]

37. Pérez VMM, Baselga M, Schuhmacher AJ. Single-Domain Antibodies as Antibody-Drug Conjugates: From Promise to Practice-A Systematic Review. Cancers (Basel). 2024;16:2681. [DOI] [PubMed] [PMC]

38. Vaisman-Mentesh A, Gutierrez-Gonzalez M, DeKosky BJ, Wine Y. The Molecular Mechanisms That Underlie the Immune Biology of Anti-drug Antibody Formation Following Treatment With Monoclonal Antibodies. Front Immunol. 2020;11:1951. [DOI] [PubMed] [PMC]

39. Mosch R, Guchelaar H. Immunogenicity of Monoclonal Antibodies and the Potential Use of HLA Haplotypes to Predict Vulnerable Patients. Front Immunol. 2022;13:885672. [DOI] [PubMed] [PMC]

40. Chen C, Garcia Z, Chen D, Liu H, Trelstad P. Cost and supply considerations for antibody therapeutics. MAbs. 2025;17:2451789. [DOI] [PubMed]

41. Pashov A, Murali R, Makhoul I, Karbassi B, Kieber-Emmons T. Harnessing Antibody Polyspecificity for Cancer Immunotherapy. Monoclon Antib Immunodiagn Immunother. 2022;41:290–300. [DOI] [PubMed]

42. Wei J, Yang Y, Wang G, Liu M. Current landscape and future directions of bispecific antibodies in cancer immunotherapy. Front Immunol. 2022;13:1035276. [DOI] [PubMed] [PMC]

43. Papp KA, Weinberg MA, Morris A, Reich K. IL17A/F nanobody sonelokimab in patients with plaque psoriasis: a multicentre, randomised, placebo-controlled, phase 2b study. Lancet. 2021;397:1564–75. [DOI] [PubMed]

44. Jin S, Sun Y, Liang X, Gu X, Ning J, Xu Y, et al. Emerging new therapeutic antibody derivatives for cancer treatment. Signal Transduct Target Ther. 2022;7:39. [DOI] [PubMed] [PMC]

45. Ma Y, Huang Y, Zhao Y, Zhao S, Xue J, Yang Y, et al. BL-B01D1, a first-in-class EGFR-HER3 bispecific antibody-drug conjugate, in patients with locally advanced or metastatic solid tumours: a first-in-human, open-label, multicentre, phase 1 study. Lancet Oncol. 2024;25:901–11. [DOI] [PubMed]

46. Disha, Kumari P, Patel MK, Kumar P, Nayak MK. Carbon Dots Conjugated Antibody as an Effective FRET-Based Biosensor for Progesterone Hormone Screening. Biosensors (Basel). 2022;12:993. [DOI] [PubMed] [PMC]

47. Soto F, Wang J, Ahmed R, Demirci U. Medical Micro/Nanorobots in Precision Medicine. Adv Sci (Weinh). 2020;7:2002203. [DOI] [PubMed] [PMC]

48. Chan K, Sathyamurthi PS, Queisser MA, Mullin M, Shrives H, Coe DM, et al. Antibody-Proteolysis Targeting Chimera Conjugate Enables Selective Degradation of Receptor-Interacting Serine/Threonine-Protein Kinase 2 in HER2+ Cell Lines. Bioconjug Chem. 2023;34:2049–54. [DOI] [PubMed] [PMC]

49. Saeed AFUH, Wang R, Ling S, Wang S. Antibody Engineering for Pursuing a Healthier Future. Front Microbiol. 2017;8:495. [DOI] [PubMed] [PMC]

50. Mullin M, McClory J, Haynes W, Grace J, Robertson N, van Heeke G. Applications and challenges in designing VHH-based bispecific antibodies: leveraging machine learning solutions. MAbs. 2024;16:2341443. [DOI] [PubMed] [PMC]

51. Kim J, McFee M, Fang Q, Abdin O, Kim PM. Computational and artificial intelligence-based methods for antibody development. Trends Pharmacol Sci. 2023;44:175–89. [DOI] [PubMed]

52. Zheng J, Wang Y, Liang Q, Cui L, Wang L. The Application of Machine Learning on Antibody Discovery and Optimization. Molecules. 2024;29:5923. [DOI] [PubMed] [PMC]

53. Amit I, Levin I, Wyant T, Levitin N, Barak R, Ben-Mayor M, et al. 704 The computationally designed human antibody, AU-007, mediates human immune activation by endogenous IL-2, while uniquely breaking the IL-2 auto-inhibitory loop and preventing Treg expansion. J Immunother Cancer. 2021;9:A732–4. [DOI]

54. Vecchietti LF, Wijaya BN, Armanuly A, Hangeldiyev B, Jung H, Lee S, et al. Artificial intelligence-driven computational methods for antibody design and optimization. MAbs. 2025;17:2528902. [DOI] [PubMed] [PMC]

55. Cheng J, Liang T, Xie X, Feng Z, Meng L. A new era of antibody discovery: an in-depth review of AI-driven approaches. Drug Discov Today. 2024;29:103984. [DOI] [PubMed]

56. Dewaker V, Morya VK, Kim YH, Park ST, Kim HS, Koh YH. Revolutionizing oncology: the role of Artificial Intelligence (AI) as an antibody design, and optimization tools. Biomark Res. 2025;13:52. [DOI] [PubMed] [PMC]

57. Kunert R, Reinhart D. Advances in recombinant antibody manufacturing. Appl Microbiol Biotechnol. 2016;100:3451–61. [DOI] [PubMed] [PMC]

58. Rives D, Richbourg T, Gurtler S, Martone J, Blenner MA. Recent Advances in Engineering the Unfolded Protein Response in Recombinant Chinese Hamster Ovary Cell Lines. Int J Mol Sci. 2025;26:7189. [DOI] [PubMed] [PMC]

59. Mirzaei M, Okoro OV, Nie L, Petri DFS, Shavandi A. Protein-Based 3D Biofabrication of Biomaterials. Bioengineering (Basel). 2021;8:48. [DOI] [PubMed] [PMC]