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CHAPTER 16

Passive Monoclonal and Polyclonal Antibody Therapies

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PASSIVE POLYCLONAL ANTIBODIES THERAPY

Passive Polyclonal Antibody Treatment Overview

Polyclonal immunoglobulins have been in use since the 19th century to protect against infectious agents, toxins, and disease conditions such as those with an autoimmune etiology. These immunoglobulin preparations are made from pools of selected human donors or animals with high titers of antibodies against viruses and toxins. These antibody treatments provide passive transfer of high titer antibodies that either reduces risk or reduces severity of infection. They are used to prevent hemolytic disease of the newborn and modify inflammatory reactions. Earlier drugs were very nonselective and patients frequently succumbed to infection due to suppression of both antibody-mediated (humoral) and cell-mediated arms of the immune system. Today, the principal approach is to alter lymphocyte function using drugs or antibodies against immune proteins. However, with the advent of human organ and tissue transplantation (e.g., kidney, heart, bone marrow, and/or peripheral blood stem cells) as treatment options, these polyclonal antibody therapies in combination with other treatment regimens are being used to lower the ability of the body’s immune system to reject these transplants. However, their use is not without risk, as complications include development of immune complexes and severe allergic reactions. A summary of these polyclonal antibody therapies may be found in Table 16.2.

Immunosuppressive Agents: Disease Modifying

Antithymocyte globulin (rabbit)/thymoglobulin; antithymocyte globulin (equine)/Atgam

Description. Rabbit antithymocyte globulin (rATG) and equine antithymocyte globulin (eATG) are purified, pasteurized preparation of lymphocyte depleting polyclonal gamma immunoglobulin (IgG) raised against human thymus lymphocytes in rabbits and horses, respectively. They are used in prevention and/or treatment of renal transplant rejection worldwide.1-7

History of antibody use. rATG induction in combination with immunosuppressive therapy is more effective in preventing episodes of acute renal graft rejection in adult renal transplant recipients, in recurrent episodes of acute rejection,8,9 and those acute rejections that are not responsive to high-dose corticosteroid therapy than other monoclonal antibody preparations.10,11 rATG recipients had a lower incidence of biopsy-confirmed acute rejection episodes,12 greater event-free survival up to 10 years posttransplantation, and greater graft survival up to 5 years posttransplantation.13

Mechanisms of action. The exact mechanism of these polyclonal antibodies has not been fully understood.3,4,14-20 However, being polyclonal, they display specificity toward a wide variety of surface antigens (Ags) expressed on T and B-lymphocytes, dendritic cells, natural killer (NK) cells, and endothelial cells. However, T-cell depletion is considered to play a key role by modulating the expression of lymphocyte surface antigens involved in a wide variety of functions such as T-cell activation to endothelial adherence, activation of certain transcription factors, and interference with numerous immune cell processes, such as cytokine production, chemotaxis, endocytosis, cell stimulation, and proliferation.14-20

In vitro studies indicate that binding of eATG to cells is generally nonspecific; the drug binds to visceral tissues, including thymus and testis cell membranes and nuclear and cytoplasmic components of tissues such as tonsil, kidney, and liver,21 and is extensively bound to bone marrow cells,22 and to other peripheral blood cells besides lymphocytes.21

Diseases treated. As mentioned earlier, both antithymocyte globulins are used for treatment and prevention
of acute renal allograft rejection. More rATG recipients have been reported to achieve the endpoint of successful response (return of serum creatinine levels to baseline by end of treatment or within 14 days of treatment initiation). However, among those who achieved a successful response, fewer episodes of recurrent rejection occurred with rATG within 90 days of treatment cessation. eATG is also used for treating moderate-to-severe aplastic anemia in patients who are unsuitable for bone marrow transplantation.

Adverse effects. The most common adverse effects are fever, thrombocytopenia, leukopenia, gastrointestinal disorders, and/or concurrent infection. Cytomegalovirus (CMV) infection was generally higher with rATG except in high-risk patients. eATG therapy may result in reactivation of or infection with CMV, herpes simplex virus, or Epstein–Barr virus. The incidence of malignancies is generally lower with rATG therapy. This product is made of equine and human blood components, so it may carry a risk of transmitting infectious agents such as viruses, and theoretically, the Creutzfeldt–Jakob disease (CJD) agent.

Update. There has been recent evidence that the addition of human anti-T-lymphocyte globulin (ATLG) plus cyclosporine and methotrexate to standard graft-versus-host disease (GVHD) prophylaxis is preferred over standard GVHD prophylaxis alone because it improves the probability of survival without relapse and of chronic GVHD after myeloablative peripheral blood stem-cell transplantation from a human leukocyte antigen (HLA)-identical sibling donor for patients with acute leukemia in remission. Additionally, this therapy provides better quality of life and shorter immunosuppressive treatment compared to standard GVHD prophylaxis without ATLG.

Antitoxin and Immune Globulins: Disease Modifying

Tetanus immune globulin/Baytet/Hypertet

Description. Tetanus immune globulin (TIG) is a specific solvent-detergent-treated plasma-derived product obtained from donors immunized with tetanus toxoid. TIG contains tetanus antitoxin that provides temporary passive immunity to individuals who have low or no immunity to the toxin produced by Clostridium tetani.

Mechanisms of action. TIG contains tetanus antitoxin antibodies, which neutralize the free form of the powerful exotoxin produced by Clostridium tetani. TIG can only neutralize unbound exotoxin; it does not affect toxin already bound to nerve endings.

Diseases treated. TIG is used to provide passive immunity to tetanus as part of a postexposure prophylaxis regimen following an injury in patients whose immunization is incomplete or uncertain or if it has been more than 10 years since last dose of tetanus toxoid.

Adverse reaction. Slight soreness at injection site, mild fever, and rarely sensitization to repeated injections of human immune globulin has been reported.

Antitoxin and Immune Globulins: Disease Modifying

Cytomegalovirus immune Globulin/Cytogam

Description. Cytomegalovirus immune globulin IV (CMV-IG) is a purified immune globulin (hyperimmune globulin) that contains immunoglobulin G (IgG) derived from pooled adult human plasma selected for high titers of anti-CMV antibodies.

Mechanisms of action. CMV-IG provides relatively high concentration of antibodies directed against CMV. It provides prophylaxis against CMV infection or disease in immunocompromised individuals. Results from in vitro studies and mice indicate that anti-CMV antibodies can neutralize the pathogenic properties of CMV. As CMV usually targets a population of bone marrow-derived myeloid lineage progenitor cells, antibody-neutralization of the virus alone may not be enough to prevent or make active disease less severe in already CMV-infected individuals.

Disease treated. CMV-IG provides passive immunity to individuals who are at risk for primary CMV infection/disease, or secondary CMV disease (reactivation of CMV). It is also prescribed for the prophylaxis of CMV disease associated with transplantation of kidney, lung, liver, pancreas, and heart. With the exception of CMV-seronegative recipients of kidneys from CMV-seropositive donors, CMV-IG prophylaxis should be considered in conjunction with ganciclovir.

Adverse reactions. Most frequent adverse reactions reported are flushing, chills, muscle cramps, back pain, fever, nausea, vomiting, arthralgia, and wheezing. There is a slight risk of hemolysis, as intravenous immunoglobulin (IVIG) products can contain blood group antibodies, which may act as a hemolysin and induce
in vivo coating of red blood cells with immunoglobulin, causing a positive direct antiglobulin reaction. Transfusion-related acute lung injury (noncardiogenic pulmonary edema) and thrombotic events have been reported in patients receiving IVIG preparations.\textsuperscript{32}

Similar to all other products made from human plasma, this CMV-IG also carries the possibility for transmission of blood-borne viral agents and the CJD agent. However, this IVIG is treated with a solvent detergent viral inactivation procedure to inactivate a wide spectrum of lipid-enveloped viruses, including HIV-1, HIV-2, Hepatitis B, and Hepatitis C.

**Antivenin \textit{Latrodectus mactans}/black widow spider antivenin—antivenin \textit{Micrurus fulvius/eastern and Texas coral snake antivenin—crotalidae polyvalent immune Fab/Crofab**

**Description.** These antivenins are sterile, nonpyrogenic, purified, and lyophilized preparation of specific venom-neutralizing serum globulins obtained from the blood serum of healthy horses exposed to the venom of black widow spiders and eastern coral snake (\textit{Micrurus fulvius}) venom, respectively.\textsuperscript{52–57} In contrast, crofab is an antivenin made up of ovine Fab (monovalent) immunoglobulin fragments obtained from blood of healthy sheep immunized with North American Crotalinae subfamily of venomous snakes that includes rattlesnakes, copperheads, cottonmouth, or water moccasins.\textsuperscript{56}

**Mechanisms of action.** Mode of action of these antivenins is unknown.\textsuperscript{52} However, they probably act by neutralizing venom of black widow spiders and coral snakes.\textsuperscript{54} Crofab is a venom-specific Fab fragment of IgG that works by binding and neutralizing venom toxins, facilitating their redistribution away from target tissues and their elimination from the body.\textsuperscript{56}

**Disease treated.** These antivenins are indicated for patients with symptoms due to bites by black widow spider (\textit{Latrodectus mactans})\textsuperscript{52} and bites of two genera of coral snakes, that is, Micrurus (including the eastern and Texas varieties) and Micruroides (the Sonoran or Arizona variety), found in southeastern Arizona and southwestern New Mexico.\textsuperscript{52,57–39} Antivenin \textit{Micrurus fulvius} (equine origin) is indicated only for treatment and management of adult and pediatric patients exposed to North American crotalid envenomation.\textsuperscript{54}

**Adverse effects.** Immediate systemic reactions (allergic reactions or anaphylaxis) and death can occur in patients sensitive to antivenin from horse serum.\textsuperscript{52,60}

Most common adverse reactions to crofab are urticaria, rash, nausea, pruritus, and back pain.\textsuperscript{61,62}

**High antibody titer influenza fresh frozen plasma**

**Description.** Use of convalescent (persons who have recovered from a particular infection) donor plasma with high hemagglutination inhibition titer against certain influenza strains has been recommended as a primary therapy for severe respiratory infectious diseases including influenza, severe acute respiratory syndrome, and Middle East respiratory syndrome.\textsuperscript{63}

**History of antibody use.** A meta-analysis of previous cohort studies during the 1918 influenza pandemic showed a case-fatality rate of 16% among subjects treated with plasma, serum, or whole blood compared to 37% among controls. Similarly, in 2009, a cohort study using convalescent plasma for the treatment of pandemic H1N1 influenza resulted in a mortality of 20% in the treatment group versus 54% in the control group.\textsuperscript{64}

**Mechanisms of action.** Antiinfluenza convalescent plasma decreases the rate of viral shedding measured by neutralizing antibody titer and hemagglutination inhibition.\textsuperscript{65} Both preexisting immunity (previous infections and vaccinations) as well as any immune response occurring after illness onset makes this mechanism of action more complex.

**Disease classifications treated.** Influenza, severe acute respiratory syndrome, and Middle East respiratory syndrome.\textsuperscript{63}

**Adverse effects.** Convalescent plasma seems safe. The serious adverse events reported are related to the underlying influenza, its complications, preexisting comorbidities, and not due to the convalescent plasma usage.

**High antibody titer ebola fresh frozen plasma**

**Description.** Antibodies to the Ebola virus (EV) in whole blood or plasma from convalescent donors may be effective in the treatment of EV infection.

**History of antibody use.** The World Health Organization (WHO) has stated that convalescent blood or plasma is an option in the treatment of Ebola.\textsuperscript{66} In 1999, transfusion of locally collected convalescent blood helped to decrease Ebola mortality.\textsuperscript{67} Therefore,
WHO has recommended the collection of convalescent plasma to treat patients with Ebola virus infection.

**Mechanisms of action.** This fresh frozen plasma (FFP) has high titers of antibodies directed against Ebola virus.68

**Adverse effects.** Convalescent plasma seems safe with few adverse effects.69,70

**Digoxin immune Fab/DigiFab; Digibind**

**Description.** Digoxin immune Fab is a sterile, purified, lyophilized monovalent preparation of bovine immunoglobulin Fab fragments that binds to digoxin. These Fab fragments are obtained from the blood of healthy sheep immunized with a digoxin derivative, digoxindiacarbamoylxyline, a digoxin analogue that contains the functionally essential cyclopentaperhydrophenanthrene: lactone ring moiety coupled to keyhole limpet hemocyanin. The final product is prepared by taking the immunoglobulin fraction of the ovine serum, digesting it with papain, and isolating the digoxin-specific Fab fragments by affinity chromatography.71–79

**Mechanisms of action.** DigiFab or Digibind have antigen-binding fragments that bind to free digoxin molecules that results in an equilibrium shift away from binding to receptors, thereby reversing the cardiotoxic effects of the glycoside.71,72,75,76,78,80–87 Subsequently, Fab-digoxin complexes are cleared by the kidney and reticuloendothelial system. Due to papain treatment, the Fab fragments lack the antigenic determinants of the Fc fragment resulting in reduced immunogenicity to patients as opposed to intact immunoglobulin products.71,72,75,76,78,79,84,88,89

**Diseases treated.** Digoxin immune Fab is indicated for patients with either life-threatening or potentially life-threatening digoxin toxicity or overdose.71,79,90–95 Data from clinical trials have showed that both DigiFab and Digibind reduce levels of free digoxin in the serum to below the limit of assay quantitation for several hours after Fab administration.

**Adverse reactions.** Digoxin immune Fab (ovine) generally is well tolerated following intravenous (IV) administration.71–73,76,78 Hypokalemia may occur, sometimes developing rapidly in patients receiving digoxin immune Fab (ovine).71,72,79,96,97 DigiFab should not be administered to patients with a known history of hypersensitivity to papaya or papain unless the benefits outweigh the risks.

**Immune Globulins:antiinfectious**

**Hepatitis B immune globulin/HepaGam B/nabi-HB/BayHepB/HyperHEP B S/D**

**Description.** Hepatitis B immune globulin (HBIG) is a specific immune globulin (hyperimmune globulin) that contains antibody to hepatitis B surface antigen (anti-HBs) prepared from plasma of healthy donors with high titer (>1:100,000) of anti-HBs antibody. It provides temporary passive immunity against hepatitis B virus (HBV).98–104 HepaGam-B is a solvent/detergent-treated sterile solution of purified gamma globulin containing antibody to HBs antigen that contains high titers of anti-HBs from plasma donated by healthy screened donors. Both HBIG and HepaGam-B are manufactured by a solvent/detergent (S/D) treatment procedure that is effective in inactivating lipid-enveloped viruses such as hepatitis B virus, hepatitis C virus, and human immunodeficiency virus type 1 and type 2. However, S/D is less effective against nonlipid-enveloped viruses such as hepatitis A virus and parvovirus B-19.100,101,104

**Mechanisms of action.** It provides passive immunization for individuals exposed to the hepatitis B virus by binding to the surface antigen and reducing rate of hepatitis B infection.

**Diseases treated.** HBIG provides passive prophylactic immunity to HBV infection for prevention of perinatal HBV infection in neonates born to HBs antigen-positive (HBsAg-positive) mothers,100–106 for postexposure prophylaxis in susceptible individuals exposed to HBV or HBsAg-positive materials (e.g., blood, plasma, serum),100–104,107–109 sexual exposure to HBsAg-positive persons, for household exposure to persons with acute HBV infection, and for prevention of HBV recurrence in liver transplant recipients who are HBsAg-positive (HepaGam-B only).104,110–117 HBIG is not indicated for treatment of active hepatitis B infection and is ineffective in the treatment of chronic active hepatitis B infection.105

**Adverse reactions.** The local adverse reactions that may occur at the site of injection after intramuscular (IM) administration are pain, tenderness, swelling, and erythema.100,101,109 The systemic effects that may occur after IM administration are urticaria, angioedema, nausea, vomiting, myalgia, headache, flu- or cold-like
symptoms, lightheadedness, and malaise have been reported. Varicella zoster immune globulin/VariZIG
Summary. Varicella zoster immune globulin (VZIG) is a specific immune globulin (hyperimmune globulin). VZIG is prepared from plasma of donors selected for high titers of antibodies to varicella zoster virus (anti-VZV) and used to provide temporary passive immunity against VZV.118

Mechanisms of action. VZIG acts by neutralizing varicella zoster virus via high titers of IgG antibodies present in the plasma used.

Diseases treated. VZIG is used for postexposure prophylaxis of varicella (chickenpox) in individuals who do not have evidence of varicella immunity and are at high risk for severe varicella infection and its complications. These high risk individuals include immunocompromised patients such as neonates whose mothers have signs and symptoms of varicella around the time of delivery (i.e., 5 days before to 2 days after), premature infants born at ≥28 weeks of gestation who are exposed during the neonatal period and whose mothers do not have evidence of immunity, premature infants born at <28 weeks of gestation or who weigh ≤1000 g at birth and were exposed during the neonatal period regardless of their mothers’ evidence of immunity status, and finally pregnant women.118,119,121,122

VZIG is now recommended for outbreak control and postexposure treatment, and the vaccine is available to children with humoral immunodeficiencies and selected children with HIV infection.122 Use of VZIG for postexposure prophylaxis in pregnant women exposed to VZV may prevent or reduce severity of varicella in the woman but does not prevent fetal infection.119,121

VZIG is not indicated for individuals who previously received age-appropriate varicella vaccination and subsequently became immunocompromised because of disease or immunosuppressive therapy later in life. Bone marrow transplant recipients should be considered susceptible to varicella regardless of previous history of varicella or varicella vaccination in themselves or their donors. However, those who develop varicella or herpes zoster after transplantation should be considered immune to varicella.119

Adverse reactions. The most common adverse effects reported with VZIG in clinical trials in pregnant women, infants, and immunocompromised adults and children were injection site pain, headache, chills, fatigue, rash, and nausea. Severe hypersensitivity reactions may occur following administration of VZIG.118

Rimabotulinumtoxin B/Myobloc
Summary. Rimabotulinumtoxin B, a type B botulinum toxin produced by fermentation of the bacterium Clostridium botulinum type B (Bean strain), is a neuromuscular blocking agent (neurotoxin) and inhibitor of acetylcholine release at motor nerve terminals.123–126

Mechanisms of action. Rimabotulinumtoxin B and other botulinum toxin serotypes act by inhibiting acetylcholine release at the neuromuscular junction via a three-step process, that is, toxin binding, toxin internalization, and inhibition of acetylcholine release into the neuromuscular junction leading to chemical denervation and flaccid paralysis.123,124,126,127

Diseases treated. Rimabotulinumtoxin B is used for management of adults with cervical dystonia (also called as spasmodic torticollis) to reduce severity of abnormal head positioning and neck pain through reduction of undesired or excessive contraction of striated or smooth (involuntary) muscle.128–131

Adverse reactions. The most common adverse effects reported with Botulinum toxin are dry mouth, dysphagia, dyspepsia, and injection site pain.123,132–134 Serious hypersensitivity reactions have been rarely reported with onabotulinumtoxin A.127

Botulism immune globulin/BabyBIG
Summary. Botulism immune globulin IV (BIG-IV) is a specific immune globulin (hyperimmune globulin) that is prepared from plasma of adult volunteer donors immunized with pentavalent botulinum toxoid, which neutralizes free botulinum toxin types A and B. It is one of the most poisonous substances known and exists in seven antigenic variants (types A to G).120,121,135

Mechanisms of action. BIG-IV is a human-derived antitoxin that neutralizes botulinum toxin. BIG-IV has a half-life of approximately 28 days in vivo and large capacity to neutralize the toxin.135

Disease treated. Infant botulism occurs when young infants ingest spores of Clostridium botulinum that then germinate, colonize the GI tract, and produce botulinum toxin. This neurotoxin causes generalized weakness and loss of muscle tone. A single infusion will neutralize the toxin for at least 6 months and toxins
type A or B that may be absorbed from the colon of an infant younger than 1 year old.\textsuperscript{121,135–139}

**Adverse effect.** Mild, transient, blush-like erythematous rash on the face or trunk occurred in 9% –14% of infants receiving BIG-IV in clinical studies.\textsuperscript{135,140}

**Rabies immune globulin/bayrab/HyperRAB, imogam Rabies, KedRAB**

**Description.** Rabies immune globulin (RIG) is a sterile solution of specific IgG that contains antibody to rabies antigen. It is used to provide temporary passive immunity to rabies infection as part of a postexposure prophylaxis regimen in unvaccinated individuals exposed to the disease or virus.\textsuperscript{141–144}

**Mechanisms of action.** RIG is a human-derived antitoxin that neutralizes rabies virus so that virus spread is reduced and its infective or pathogenic properties are inhibited. Specific rabies antibodies present in RIG neutralizes rabies. It should be used in conjunction with rabies vaccine and can be administered through the seventh day after the first dose of vaccine is given. RIG provides immediate, temporary rabies virus-neutralizing antibodies until the patient responds to active immunization and produces virus-neutralizing antibodies.\textsuperscript{121,141–144}

**Diseases treated.** Given to all persons suspected of exposure to rabies with one exception, those who have been previously immunized with rabies vaccine and have a confirmed adequate rabies antibody titer should receive only vaccine.

**Adverse reactions.** Most common local adverse effects include tenderness, pain, muscle soreness, or stiffness that may occur at the site of injection. Low-grade fever, headache, and malaise may also occur.\textsuperscript{141–143}

**Immune Globulins: Immunomodulation**

**Rho(D) immune globulin/WinRho; RhoGam; Rhophylac, MicRhoGAM, BatRhoD, HyperRho**

**Summary.** Rho(D) immune globulin (RhIG) consists of anti-Rho(D) IgG antibodies to the red blood cell Rho(D) antigen. RhIG is prepared from human pools of plasma of Rho(D)-negative donors immunized with Rho(D)-positive red blood cells after cold alcohol fractionation, and subsequent purification and infectious disease reduction technologies.\textsuperscript{145–150}

**Mechanisms of action.** The exact mechanism of action of Rho(D) immune globulin in the suppression of formation of anti-Rho(D) is not fully known.

In the treatment of preventing D alloimmunization, RhIG binds to Rho(D) antigen that entered the maternal circulation during fetal–maternal hemorrhage (FMH) involving an Rho(D)-positive fetus or transfusion with Rho(D)-positive blood, preventing stimulation of the mother’s primary immune response to Rho(D) antigen. Therefore, by preventing the active production of anti-Rho (D) by the mother, the risk of hemolytic disease of the fetus and newborn in future pregnancies is decreased.\textsuperscript{145–149}

In the treatment of idiopathic thrombocytopenic purpura (ITP), administration of Rho(D) immune globulin to Rho(D)-positive individuals is believed to cause transient mononuclear macrophage Fc receptor (FcR) blockade by complexes within the reticuloendothelial system, particularly the spleen, which spares the patient’s IgG-coated platelets. This FcR blockade and decreased Fc-mediated phagocytosis of antibody-coated platelets result in increases of platelet counts in ITP patients.\textsuperscript{145,149,151–156}

**Diseases treated.** Prevent D alloimmunization in D-negative women of childbearing potential if the neonate is D\textsuperscript{+}, weak-D positive, or D untested, and following perinatal events associated with FMH such as abortion, ectopic pregnancy, amniocentesis, chorionic villus sampling, external cephalic version, abdominal trauma, and antepartum hemorrhage. It is also used to prevent D alloimmunization in D-negative individuals who receive D\textsuperscript{+} blood components such as whole blood-derived platelets, apheresis platelets, and/or granulocytes. Similarly, it is used for the treatment of ITP in D\textsuperscript{+} patients who had not undergone splenectomy.\textsuperscript{145–147,149,151–153,157–164}

Some preparations of Rho(D) immune globulin may be administered IM or IV (Rhophylac, WinRho SDF), whereas others are labeled for IM use only (MICRhoGAM, RhoGAM, HyperRHO S/D Full Dose, HyperRHO S/D Mini-Dose).\textsuperscript{145–147,149,165} When used for ITP treatment, RhIG must be administered IV.\textsuperscript{145,149}

**Adverse reactions.** Generally, mild with the most common being headache, fever, chills, pain at the injection site and, rarely, hypersensitivity reactions. Some degree of hemolysis is inevitable, but this is predictable and transient.\textsuperscript{146,147}
**Immunoglobin (generic)/Brands: Bivigam, Carimune, Cuvitru, Flebotigamma, Gammagard, GamaSTAN, Gammaked, Gammaplex, Gamunex-C, Hizentra, Hyqvia, Octagam Privigen**

**Summary.** Immune globulin IM (IMIG), immune globulin IV (IVIG), and immune globulin subcutaneous are sterile, nonpyrogenic preparations of globulins containing many antibodies normally present in adult human blood. Immune globulins (IG) are collected either by whole blood donations as recovered plasma (20%), or by apheresis as source plasma (80%). IVIG is a highly purified product consisting mostly of IgG with a half-life of 21–28 days.

Hyperimmune globulin (Hyper-Ig) products are manufactured from donors with high Ig titers with specificity to antigenic determinant(s) of interest. High titers of these donors can be achieved by natural immunity, prophylactic immunizations, or through targeted immunizations. Hyper-Ig products should contain at least fivefold-increased titers compared to standard preparations of IVIG.

IVIG production is regulated by the IUUIS/WHO (International Union of Immunological Societies/World Health Organization), which require the following:

- Source material must be plasma obtained from a minimum pool of 10,000 donors;
- Product must be free of prekallikrein activator, kinins, plasmin, preservatives, or other potentially harmful contaminants;
- IgA content and IgG aggregate levels need to be as low as possible;
- Product must contain at least 90% intact IgG;
- IgG should maintain opsonin activity, complement binding, and other biological activities;
- IgG subclasses should be present in similar proportions to those in normal pooled plasma;
- Antibody levels against at least two species of bacteria (or toxins) and two viruses should be determined;
- Product must demonstrate at least 0.1 international units of hepatitis B antibody per mL, and hepatitis A radioimmunoassay titer of at least 1:1000;
- Manufacturer should specify the contents of the final product, including the diluent and other additives, and any chemical modification of IgG.$^{166–172}$

**Mechanisms of action.** The mechanisms of Ig-induced immunomodulation are incompletely understood but include macrophage Fc receptor blockage by immune complexes formed between IVIG and native antibodies, modulation of complement, suppression of antibody production, suppression of inflammatory cytokines and chemokines, and/or antiidiotypic regulation of autoreactive B-lymphocytes or antibodies.

As IVIG contains a diverse group of antibody specificities, which protects recipients against multiple infections by eliminating opsonized infectious organisms via antibody-dependent cell-mediated cytotoxicity or by complement activation. This is followed by lysis and/or neutralization of soluble infectious proteins by immune complex formation and elimination through the RES.$^{166,170,173–175}$

**Diseases treated.** IVIG is indicated for the treatment of primary immune deficiency, secondary immune deficiency, ITP, Kawasaki disease, and congenital hypogammaglobulinemia. Currently, there is an extensive list of diseases for which IVIG could be used. It also has immunomodulatory properties resulting in an increasing list of both FDA-approved and nonapproved indications.

IVIG is used to provide passive immunity to hepatitis A virus infection for preexposure or postexposure prophylaxis in susceptible individuals who are at risk of or have been exposed to the virus. IMIG and IVIG are used to prevent or modify symptoms of measles (rubeola) in susceptible individuals exposed to the disease <6 days. IVIG is used for replacement therapy to promote passive immunity in patients with primary humoral immunodeficiency who are unable to produce sufficient amounts of IgG antibodies and in the management of ITP to increase platelet counts, to prevent and/or control bleeding, or to allow these patients to undergo surgery.

IVIG is used for prevention of bacterial infections in patients with hypogammaglobulinemia and/or recurrent bacterial infections associated with B-cell Chronic Lymphocytic Leukemia. IVIG is used in conjunction with aspirin therapy for initial treatment of the acute phase of Kawasaki disease. IVIG is also used to treat chronic inflammatory demyelinating polineuropathy to improve neuromuscular disability and impairement, and for maintenance therapy to prevent relapse. Furthermore, IVIG is used for maintenance treatment to improve muscle strength and disability in adults with multifocal motor neuropathy.$^{166–201}$

**Adverse reactions.** Approximately 2%–10% of infusions are associated with adverse reactions that include those at the infusion site (erythema, pain, swelling, pruritus, heat), phlebitis, eczema, fever, chills, myalgias, malaise, flushing, rash, diaphoresis, pruritus, bronchospasm, chest pain, back pain, extremity pain, dizziness,
blood pressure changes, nausea, vomiting, and headache.\textsuperscript{167,170,172,177–179,181–183}

**PASSIVE MONOCLONAL ANTIBODY TREATMENT**

In the late 20th century (\textasciitilde{} 1986), monoclonal antibodies were developed. The first monoclonal antibodies (Mabs) were of xenographic source and were wrought with problems of immunogenicity. These early Mabs did not gain favor until chimerization took pace in the mid-1990s, and in 1998 two Mabs were approved to treat one respiratory syncytial virus and the other certain breast cancers. Further development to humanize and then generate fully human Mab led to an evolution of therapies utilizing these agents. Mabs are being researched or approved to treat a multitude of diseases that include oncologic, inflammatory, autoimmune, cardiovascular, respiratory, neurologic, allergic, benign hematologic, infectious, orthopedic, coagulopathic, and metabolic indications and to decrease disease morbidity (diminution of pain), modify disease progression (i.e., macular degeneration, diabetes), and potentially alter anatomic development. In this section of the chapter, we will review the history of use of these passive monospecific antibody therapies, their mechanism of action, pharmacologic-therapeutic classification, particular medical indication, adverse reactions, and potential future use of these medications.\textsuperscript{201}

**Mechanism of action**

Depending on the antigenic target of these antibodies multiple events are set into action. Immunologic changes occur as the specific antigens are presented more efficiently to effector cells. Some of these actions create decreased inflammatory and allergic responses, while other effects generate antibody-dependent cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC). Other actions can block receptor interaction with ligands by either binding with ligands or their cognate receptors (i.e., allow activation of NK cells). Interactions may also directly cause initiation of programmed cell death (apoptosis), cessation of growth/replication/proliferation, or lead to changes in metabolism. Moreover, there are also antibodies against infectious agents to prevent cell adhesion for entry, spread, replication, and contagion. Antibodies may also be directed against toxins leading to various methods of inactivation.\textsuperscript{201}

**Adverse reactions**

Depending on their mode of action, Mabs are associated with a myriad of side effects. They can be associated with immunogenicity that can cause a decrease in their effectiveness. Antineoplastic antibodies can be associated with tumor lysis syndrome. Similarly, reactivation of underlying infections can occur leading to progressive multifocal leukoencephalopathy, HBV, fungal, parasitic, or tuberculosis infections. Other adverse reactions include but are not limited to initiation of autoimmune disorders, increased risk for malignancy, cardiac arrhythmia, angina/ischemia, cytopenias, hemorrhage, and allergic reactions including anaphylaxis, embryo–fetal toxicity (if can cross placental barrier), and even death.

**TYPES OF ILLNESS TREATED**

**Oncology**

Malignancies can be caused by infectious agents, toxins, or genetic mutations with changes in control of growth, proliferation, or programmed cell death. Historically these have been treated with a variety of radiation therapies to eradicate malignant cells or with chemotherapeutic agents to enhance maturity, decrease proliferation, or cause destruction of cancer cells. In some cases intense high-dose chemotherapy is used to cause cancer remission with stem cell transplants for subsequent rescue. Passive antibody therapy may replace or be additive to other pharmacology therapies and increase chances for complete remission, prolong disease-free survival, and overall survival.

**B-cell chronic lymphocytic leukemia**

Rituximab (Rituxan) is a chimeric murine/human Mab (IgG1\k) that binds to CD20 (human B-lymphocyte-restricted differentiation antigen, Bp35 \{controlling differentiation and possible calcium ion channel\}). Its mechanism of action is not entirely clear and may involve CDC and ADCC. Many studies have shown this antibody to have an additive benefit to standard chemotherapy alone. This antibody has been approved by the FDA to treat chronic lymphocytic leukemia (CLL) since 1997. Nowadays, this medication is often combined with ibritumomab in treating CLL (to be discussed with non-Hodgkin’s lymphoma).\textsuperscript{202,203}

Alemtuzumab (Campath) binds to CD52 and is a humanized rat Mab (IgG1\k) binding to receptors on both T and B cells as well as macrophages, NK cells, and neutrophils, leading to CDC and ADCC. The resultant cytopenias lead to a severe immunocompromised state. Alemtuzumab was FDA approved as a single agent in the treatment of B-cell CLL in 2001.\textsuperscript{204}

Ofatumumab (Ocrevus) is a human Mab (IgG1\k) with CDC that binds to CD20 near the cellular
membrane. In phase II studies, this agent had 86% objective response rate (ORR) when used alone and with CHOP therapy had 100% ORR and 62% complete remission (CR); whereas, in phase III trials, this Mab showed ORR of 10% after rituximab relapse. This medication was approved by the FDA to treat CLL in 2009.205

Monalizumab is a humanized Mab (IgG4xk) that binds to CD94/NKG2A (an inhibitory signal receptor on NK cells). Monalizumab demonstrated blockade of NKG2A/HLA-E and restores the ability of NK cells to lyse B cells in vitro. In addition, this Mab was shown to be of benefit in murine models. Ongoing phase I/II studies will be completed in 2019.206

Oltertuzumab is a humanized Mab fragment (IgG Fab') with specificity to CD37 that induces both ADCC and caspase-independent apoptosis. In a phase II study both better progression-free survival (PFS) and ORR were observed when used with bendamustine compared to bendamustine alone.207

Urelumab is a human Mab (IgG4xk) with specificity to CD134 (an immune checkpoint inhibitor). This antibody has completed safety phase I dosing trials. Higher doses lead to significant hepatotoxicity. Safe dosing is now established in clinical phase II studies to be completed in 2020.208,209

Ulocuplumab is a human Mab with specificity to CD184 (CXCR4). In vitro studies showed apoptotic effects via production of oxygen species that was not associated with better caspase activation than AMD3100. Phase I studies were completed in 2014, no manuscripts were found for review. This medication is presently in phase II trials against acute myelocytic leukemia (AML) to be completed in 2021.210,211

Other monoclonal antibodies not demonstrating benefit in clinical trials for CLL include apolizumab, dacetuzumab, and gomiliximab (aka lumiliximab)212–215

**Acute myelocytic leukemia**

AML is the leading cause of leukemic mortality in the United States (US). Over the last 10 years therapy has not changed significantly for this disease. Novel therapies have been developed in the last decade, some showing temporal success and some showing a brighter tomorrow.216

AMG330 is a bispecific T-cell engager (BiTE) antibody with specificity for CD3 and CD33. This Mab is currently in clinical trials to be completed in 2020 for treatment of AML. A BiTE antibody stimulates ADCC (via T cells) in the presence of antigenic targets on cells of interest. In vitro studies have shown effective lysis of AML cells, while in animal studies it has demonstrated significant decrease in tumor burden.217

IMGN632 is an anti-CD123 antibody complexed to a DNA mono-alkylating agent. In vitro studies showed it had more potency against AML cells than to normal myeloid progenitor cells. In animal models there was an excellent response rate against tumor cells. Ongoing clinical trials will be completed in 2021.216

Talacotuzumab is a humanized monoclonal antibody (IgG1-2x) with specificity to interleukin (IL)-3 receptor subunit-α (CD123, a growth and differentiating receptor). This antibody induces ADCC both in vitro and in animal models. Phase III clinical trials were reportedly completed in 2018; published results are forthcoming.218

Samalizumab is a humanized Mab (IgG2/IgG4) with specificity to CD200 (OX-2 membrane glycoprotein) is in phase II trials to be completed in 2021.219

Ficlatuzumab is a humanized Mab (IgG1xk) in a phase I trial to treat refractory/relapsing AML to be completed in 2020.220

Other Mab not demonstrating benefit in clinical trials or withdrawn following postmarketing for AML include gemtuzumab ozogamicin (FDA approved 2000 withdrawn 2010 secondary to venoocclusive disease) and lintuzumab (no added benefit over standard chemotherapy).221–223

**Multiple Myeloma**

Daratumumab (Darzalex) is a human Mab (IgG1k) with specificity to CD38 (functions reportedly include receptor-mediated adhesion and signaling events, as well as important bifunctional ectoenzymatic activities that contribute to intracellular calcium mobilization. This Mab mechanism of action is thought to induce CDC, ADCC, antibody-dependent cellular phagocytosis, and apoptosis. This medication is used to treat refractory and recurrent multiple myeloma.224,225

Silutuximab (Sylvant) is a chimeric Mab (IgG1k) with specificity to IL-6. This medication was FDA approved in 2014 for multicentric Castleman’s disease (MCD) with HIV negative and HHV-8 negative. There are ongoing studies in phase II clinical trials to be completed in 2019.226,227

**B-cell acute lymphoblastic leukemia (B-cell ALL)**

Blinatumomab (Blincyto) is a mouse double heavy-chain fragment (Murine {scFv - kappa — heavy} – {scFv - heavy — kappa}) with specificity for CD19 and CD3 known as a BiTE. This Mab’s mode of action is by directing CD3+ effector memory T cells to CD19+ target cells leading to T-cell activation and B-
cell apoptosis. This biologic is used to treat relapsed/refractory cell ALL. In phase III trials event-free survival almost tripled and duration of remission almost doubled.228–230

**Hodgkin’s lymphoma**

Hodgkin’s lymphoma is a rare malignancy affecting young adults with a peak incidence in patients >55 years old. Up to 40% of these patients can develop relapsing disease. Brentuximab vedotin (Adcentrix) is a chimeric humanized Mab drug conjugate (Mab + linker + payload {IgG1κ + protease cleavage linker + monomethyl auristatin E [MMAE]}) with specificity to CD30 (a cell membrane protein of the tumor necrosis factor receptor superfamily member 8. MMAE is a microtubule-disrupting agent. The combination of this a Mab and drug conjugate disrupts the intracellular microtubule network causing cell cycle arrest at G2/M stage and apoptosis. This medication has a 43% PFS at 30 months.231

Mab to look out for in the future include Camidan-lumab tesirine (ADCT-301) a human Mab (IgG1κ). This Mab has specificity to CD25 (alpha IL-2 receptor alpha subunit) with a drug conjugate. The drug is released intracellularly and causes DNA interstrand crosslinks. This Mab is in phase I studies to be completed in 2019 for Hodgkin’s and non-Hodgkin’s T- and B-cell lymphomas. In addition, there are clinical phase I studies against multiple solid tumors to be completed in 2021.232,233

Agents abandoned or not found to be beneficial include apolizumab, denintuzumab mafodotin (HBU-12), iratumumab (MDX060), and lucatumumab (HCD122).212,234,235

**Anaplastic large cell lymphoma**

Brentuximab vedotin (Adcentrix) is an FDA-approved medication for patients with refractory or relapsed anaplastic large cell lymphoma who achieved CR. This Mab had 79% OS and 57% PFS at 5 years, with median response duration not reached at time of publication.236

**Breast Cancer**

Atezolizumab (Tecentriq) is an FcγR binding—deficient, fully humanized Mab (IgG1κ). This Mab binds to programmed death ligand 1 (PD-L1) to prevent interaction with receptors PD-1 and B7.1 (a costimulatory cell-surface protein), reversing T-cell suppression. Activation of B7.1 can potentially stimulate long-term responses through development of new immunity via priming and activation of T cells in lymph nodes. A lack of FcγR binding decreases ADCC of the T cells enabling more tumor-specific T cell to remain active. This medication was approved by the FDA in 2019 to treat triple negative (estrogen receptor, progesterone receptor, human epidermal growth factor receptor-2) unresectable or metastatic breast cancers.237,238

**Colorectal Cancer**

Bevacizumab (Avastin) is a humanized Mab (IgG1κ) with specificity to vascular endothelial growth factor-a (VEGF-A) that acts as an inhibitor of angiogenesis. It was FDA approved for treatment of colorectal cancer and has recently been approved for multiple other cancers including ovarian, fallopian cancers, renal cell carcinoma, and recurrent glioblastoma multiforme (GBM).239,240

**Urothelial Carcinoma**

Atezolizumab (Tecentriq) is FDA approved as a single agent in urothelial carcinoma and for patients with disease progression despite other chemotherapy treatment.241,242

**Nonsmall cell lung cancer**

Atezolizumab (Tecentriq) is FDA approved as a single agent for nonsmall cell lung cancer (NSCLC).

Bevacizumab (Avastin) is FDA approved for treatment of locally advanced, recurrent or metastatic, non-squamous NSCLC.

Nivolumab (Opdivo) is an FDA-approved human Mab (IgG4κ) immunoglobulin and blocks PD-1 preventing interaction PD-1 and its ligands PD-L1 and PD-L2. It is used to treat RCC, NSCLC, Hodgkin’s lymphoma, melanoma, small cell lung cancer, colorectal cancer, and squamous cell carcinoma of the head and neck. In phase III clinical trials, nivolumab performed better than docetaxel in the treatment of NSCLC.243–245

**Ovarian/cervical fallopian cancer**

Bevacizumab (Avastin) is FDA approved for treatment of locally advanced, recurrent or metastatic, ovarian, cervical, and fallopian cancers after treatment with chemotherapy regimens and surgery.246

**Merkel Cell Carcinoma**

Merkel cell carcinoma is a rare aggressive cutaneous malignancy caused by infection with polyoma virus and exposure to ultraviolet radiation. This cancer was classically treated with chemotherapeutic agents leading to rare durable responses. Avelumab (Bavencio) is a fully human Mab (IgG1λ) with specificity to PD-L1. This Mab was approved by the FDA for
treatment of Merkel cell carcinoma in 2017. Treatment with this Mab increases response rates to about 50% and extended durable response times approximately five times. This Mab is in clinical trial to treat other solid tumors including but not limited to hepato-cellular, ovarian, esophageal-gastric, colorectal NSCLC, testicular, urothelial, and adrenocortical carcinomas.

**Neuroblastoma**

Neuroblastoma is an aggressive tumor of children with a 5-year survival of about 50%. Treatment classically is high-dose intensive chemotherapy, myeloablative chemotherapy with stem cell rescue, and/or irradiation therapy. Dinutuximab (Unituxin) is a chimeric Mab (IgG1k) with specificity to GD2 ganglioside that has mechanisms of action via CDC and ADCC. This Mab is used in patients who have had at least a partial response to classic therapy.

**Catumaxomab**

Catumaxomab (Removab) is a trifunctional rat/murine hybrid antibody (IgG2a/IgG2b). Catumaxomab consists of one “half” (one heavy chain and one light chain) of an antiepithelial cell adhesion molecule (anti-EpCAM) antibody and one-half of an anti-CD3 antibody, so that each molecule of catumaxomab can bind both EpCAM and CD3. In addition, the Fc region can bind to an Fc receptor on accessory cells such as other antibodies, which has led to calling the drug a trifunctional antibody. This antibody’s mechanism of action is through ADCC. It is approved for use in Europe for malignant ascites from ovarian, gastric, colon, pancreatic, breast, and endometrial carcinoma and is a pending review for approval by the FDA.

**Cutaneous squamous cell carcinoma**

Cemiplimab (Libtayo) is a human Mab (IgG4) for treatment of cutaneous squamous cell carcinoma (CSCC) that is metastatic or locally advanced and not amenable to surgery. CSCC is second only to basal cell carcinoma as the most common skin cancer. Surgical intervention is not possible in 5% of patients. This Mab offers a treatment with less morbidity than palliative radiation or surgery, and gives an ORR in 50% of these otherwise untreatable patients. There are many additional phase II studies involving this Mab to be completed from 2020 to 23.

**AUTOIMMUNE/INFLAMMATORY DISEASES**

**Inflammatory Bowel Disease**

Inflammatory bowel disease (IBD) pathophysiology remains unknown but may have genetic, infectious, autoimmune origins including cell-mediated immunity. These diseases may be classified as ulcerative colitis (UC), isolated to the colon, or Crohn’s disease primarily found in the colon but may involve the entire gastrointestinal tract. With long-standing active disease, malignancy is much more frequent in UC than in Crohn’s disease. Mild UC is treated with antiinflammatory agents such as sulfasalazine and glucocorticosteroids. For more severe disease, high-dose steroids may be used to maintain disease quiescent and low-dose steroids to keep disease in remission. Low-dose chemo-therapeutic agent or immunosuppressive agent may also be added if dose of corticosteroids is too high to maintain remission. Surgery may be necessary to control disease. For Crohn’s disease, medical therapy is usually less successful in managing the disease and surgery may be necessary but is not curative as in UC. For both of these disease processes, passive antibody therapy may offer not only control of disease but possible complete remission from mucosal damage.

Adalimumab (two formulations: Humira and Amje-vita) is a recombinant human Mab (IgG1) with specificity to tumor necrosis factor alpha (TNF-α). Both forms are FDA approved to treat Crohn’s disease as well as multiple types of rheumatoid arthritis. In Crohn’s disease, this medication decreases signs and symptoms of disease and is able to induce clinical remissions.

Certolizumab (Cimzia) is a recombinant humanized m fragment with TNF-α as target. It is FDA approved for both Crohn’s disease and Rheumatoid arthritis.

Vedolizumab (Entyvio) is a humanized Mab (IgG1k) that has selectivity for integrin α4β7 and is FDA approved for treatment of Crohn’s disease. This
Mab mode of action is to selectively block trafficking of memory T cells into inflamed gut tissue by inhibiting \(\alpha 4\beta 7\)-mucosal addressin cell adhesion molecule-1 (MAd-CAM-1) interaction with intestinal vasculature. This medication has shown a good safety profile with no cases of promyelocytic leukemia (PML), no increased risk of infections, malignancies compared with classically treated IBD, and low incidence of infusion-related reactions. This medication is also FDA approved for UC.270,271

Infliximab (Remicade, Inflectra, Remsima) is a chimeric Mab (IgG1\(k\)) with specificity to TNF-\(\alpha\) and is FDA approved for IBD and multiple inflammatory arthritic diseases. This medication allows for steroid-free remission within months of starting therapy.272

Natalizumab (Tysabri) is a humanized Mab (IgG2\(k\)) with selectivity to CD62L (L selectin) with selectivity to CD62L (L selectin) and a7 integrins of leukocytes, not neutrophils, VLA-4. This Mab is FDA approved for Crohn’s disease and multiple sclerosis. This medication is effective in induction of clinical remission in moderate-to-severe Crohn’s disease. This medication does have the risk of PML.273,274

Other Mab being studied for Crohn’s disease but not yet approved by the FDA include Ustekinumab, brazikumab, etrolizumab, risankizumab, and ontalimalimab. In contrast, Mabs studied but not beneficial for Crohn’s disease include andecaliximab, eldelumab, and fontolizumab. Refer to Table 16.1.

**Ulcerative Colitis**

Mabs being studied for UC but not yet approved by the FDA include bimekizumab, etrolizumab, golimumab, mirikizumab, ravidalimab, sacituzumab govitecan, ontalimalimab, and vatelizumab. Refer to Table 16.1.

**Autoimmune Diseases**

Autoimmune diseases affect many organs and tissues including liver, gall bladder, pancreas (islet cells in diabetes mellitus), nerve junctions (myasthenia gravis), thyroid, bone and joints, blood vessels, and multiorgan systems, systemic lupus erythematosus (SLE). Autoimmune arthritis is of multiple types including psoriatic, sclerosis, rheumatoid arthritis (RA), and SLE. Many of these diseases are mediated by antibody or cellular autoimmunity but ultimately appear to be secondary to an underlying abnormality in T-cell immune-regulatory control. These disease processes are historically controlled with antiinflammatory agents, immunosuppressive/immunomodulatory agents, or low-dose chemotherapy. Those with resultant hormone deficiencies are supplemented with hormones depleted by the disease process. It is hoped that passive antibody therapy will mitigate the sequelae of these inflammatory processes.

**Plaque psoriasis/psoriatic arthritis**

Psoriasis affects 2%–3% of the world population and is an inflammatory skin disease. Brodalumab (Siliz) is a human Mab (IgG2\(k\)) with specificity to IL-17 receptor A (IL-17RA). It is FDA approved for treatment of plaque psoriasis, and its mechanism of action is by inhibiting IL-17A, IL-17F, IL-17C, IL-25, and IL-17A/F heterodimer cytokine-induced responses including release of proinflammatory cytokines. When compared to ustekinumab, resistance rates nearly doubled with brodalumab in phase II and phase III trials during induction and maintenance therapies.275,276

Other therapies currently also approved or being studied for treatment of this disease include bermekizumab (MABp1,T2-18C3, CA-18C3, Xilonix), bimekizumab, briakinumab, certolizumab pegol (Gimzia), etanercept (Enbrel), infliximab (Remicade, Inflectra, Remsima), itolizumab (Alzumab), adalimumab (Humira, Amjvita), ustekinumab (Stelara), secukinumab (AIN457, Cosentyx), guselkumab (Tremfya), tildrakizumab (MK-3222, SCH-900,222, Illumya, Ilumetrix), risankizumab (ABBV-066, BI-655,066), mirikizumab (LY3074828), namilumab (MT203), netakimab, and vunakizumab. Refer to Table 16.1.

Withdrawn from market or ineffective for treating psoriasis include efalizumab (Raptiva), fezakinumab, bleselumab, and teplizumab (MGA031, PRV-031, hOKT3g1(Ala-Ala)) Refer to Table 16.1.

**Systemic juvenile idiopathic arthritis**

Abatacept (Orencia) is a recombinant soluble fusion protein of the extracellular domain of human cytotoxic T-lymphocyte-associated antigen 4 (CILA-4) linked to the modified Fc portion of human IgG1. Its mechanism of action is as selective costimulation modulator as it inhibits T lymphocyte activation by binding to CD80 and CD86, thereby blocking interaction with CD28. This interaction provides a costimulatory signal necessary for full activation of T lymphocytes. This medication is FDA approved for both juvenile idiopathic arthritis (JIA) and adult RA.277–279

**Rheumatoid Arthritis**

Certolizumab pegol alone or with methotrexate improves quality of life in RA and may cause disease remission and reduce joint damage.280
| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|----------------|--------|
| 8H9               |            |                 | Antineoplastic      | Intravenous    | B7–H3  |
|                   |            | monoclonal      | Neuroblastoma, sarcoma, metastatic brain cancers |                |        |
|                   |            | antibody (Murine) | Another study Sloan Kettering using I²³¹ version phase I good results |                |        |
| Abagovomab        |            | monoclonal      | Antineoplastic      | Subcutaneous   | CA-125 |
|                   |            | antibody (Murine) | Phase II study for ovarian cancer |                |        |
|                   |            | antiidiotype mAb | Phase III good immune response but no increase RFS or OS no benefit |                |        |
| Abatacept         | Oencia     | recombinant      | Disease modifying    | Subcutaneous or intravenous |        |
|                   |            | soluble fusion protein of the extracellular domain of human cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) linked to the modified Fc portion of human immunoglobulin G1 (IgG1) | Rheumatoid arthritis | | |
|                   |            |                | Juvenile and adult psoriatic arthritis (phase III) | | |
| Abciximab         | ReoPro     | human-murine chimera | Procedure modification | Intravenous | Platelet glycoprotein IIb/IIIa receptor (CD41 7E3)/ Integrin α-Ilb |
| c7Ec Fab          |            | recombinant monoclonal IgG1 Fab | High-risk coronary intervention | | |
|                   |            |                | Platelet aggregation inhibitor | | |
| Abituzumab        |            | humanized       | Antineoplastic      | Intravenous    | CD51 (?integrin alpha V) |
|                   | D117E6     | monoclonal      | Colorectal cancer phase I 2013, phase II 2015 primary endpoint PFS not met | | |
|                   | EMD25797   | antibody IgG2κ | Sclerosing interstitial lung disease phase II terminated 2018 slow enrollment | | |
|                   |            |                | Prostate phase II no significant increase PFS | | |
### TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont’d

| Generic Drug Name | Brand Name       | Type of Antibody            | AHFS Classification                                      | Dosage Form(s)          | Target                                      |
|-------------------|------------------|-----------------------------|----------------------------------------------------------|-------------------------|---------------------------------------------|
| Abrilumab         | AMG 181          | Human monoclonal antibody   | Phase II study discontinued development (2016)           |                        | Integrin α-4 β-7                            |
| Actoxumab         | Human monoclonal antibody | Disease modifying Clostridium difficile | Phase I and II anti-CDT81 much better                   |                        | Clostridium difficile toxin A              |
| Adalimumab        | Humira FDA 2002  | Recombinant human IgG1 monoclonal antibody | Disease modifying Humira Rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn’s disease, plaque psoriasis Amjevita Arthritis; juvenile rheumatoid arthritis; psoriatic arthritis; rheumatoid colitis; ulcerative Crohn’s disease; psoriasis; spondylitis; ankylosing Possibly hemolytic disease of newborn | Injection subcutaneous | TNF-α                                       |
| Adecatumumab      | MT-201           | Recombinant human IgG1k monoclonal antibody | Antineoplastic Breast phase Ib+, colorectal and prostate Phase II completed Phase III soon? | Intravenous            | EpCAM (CD326) epithelial cell adhesion molecule |
| Aducanumab        | Human monoclonal antibody IgG1 | Disease modifying Alzheimer’s disease Phase Ill x 2 ongoing started 2015 |                        | Intravenous            | Beta-amyloid (N-terminus 3–6) soluble oligomers and insoluble fibrils |
| Afasevikumab      | Human monoclonal antibody IgG1k | Disease modifying Multiple sclerosis Phase I completed Nothing in pubmed |                        | Subcutaneous           | IL17A and IL17F                             |
| Afelimomab        | Murine F(ab’) Antibody Fab’ fragment IgG3k | Disease modifying Sepsis Phase III trial marginal benefit abandoned |                        |                        | TNF-α                                       |
| Name                  | Type                                    | Use                                                                 | Route                      | Protein Family                        |
|-----------------------|-----------------------------------------|----------------------------------------------------------------------|-----------------------------|---------------------------------------|
| Alacizumab pegol      | Humanized monoclonal antibody F(ab')₂ | Limited information on development; Cancer                           | Intravenous                 | VEGFR2                                |
| Alemtuzumab LDP-03    | Humanized rat monoclonal antibody IgG1κ| Antineoplastic B-Cell CLL, CTCL, T cell lymphoma                     | Intravenous                 | CD52                                  |
| Campath-1H            | Human monoclonal antibody IgG1κ        | Disease modifying Multiple sclerosis (phase III)                      | Subcutaneous                | Proprotein convertase subtilisin kexin type 9 (PCSK9) |
| Aleirocumab           | Human monoclonal antibody IgG1         | Disease modifying Decrease cholesterol Phase III                     | Inhalation                  | CEA                                   |
| Altimomab pentetate In³⁸ | Murine monoclonal antibody IgG1       | Diagnostic purpose radiology colorectal cancer (diagnosis)           | Subcutaneous                | CEA                                   |
| ALX-0171              | Trimeric nanobody                      | Antiinfectious RSV phase II 2020                                     | Subcutaneous                | RSVF                                  |
| Amatuximab MORAb-009  | Chimeric murine-human monoclonal antibody IgG1κ | Antineoplastic Ovarian cancer Phase II Now research on using to treat mesotheliomas Phase I/II Pancreatic cancer | Intravenous                 | Mesothelin Prohibits binding of MSLN with antigen CA125/ MUC16 |
| AMG330                | Bispecific T-cell engager (BiTE)       | Antineoplastic AML phase I AML 2020                                  | Intravenous                 | CD33 and CD3                          |
| Anatumomab mafenatox  | Murine monoclonal fragment Fab         | Antineoplastic Nonsmall cell lung carcinoma                          | Intravenous                 | Tumor-associated glycoprotein 72 (TAG-72) |
| Andecaliximab GS 5745 | Chimeric monoclonal antibody IgG4κ     | Antineoplastic gastric cancer phase I, II, III ongoing or gastroesophageal junction adenocarcinoma phase III ongoing Crohn phase II no response, UC | Intravenous                 | Gelatinase B is a matrix metalloproteinase-9 (MMP-9) |
| Anetumab raptansine In³⁸ | Human monoclonal antibody IgG1λ       | Antineoplastic ovarian phase II, lung, pancreatic phase I, breast now research on using to treat mesotheliomas Phase II Cervical cancer preclinical | Intravenous                 | Mesothelin Prohibits binding of MSLN with antigen CA125/ MUC16 |

*Continued*
Table 16.1: Summary of Monoclonal Antibody Therapies—cont’d

| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|----------------|--------|
| Anifrolumab       |            | Human monoclonal antibody IgG1κ | Disease modifying | Intravenous | Interferon α/β receptor |
|                   |            |                  | Systemic lupus erythematosus phase I and IIb 2018 |
| Anrukinzumab      | (=IMA-638) | Humanized monoclonal antibody IgG1κ | Disease modifying | IL-13 |
|                   |            |                  | Asthma phase II ?results UC phase II no benefit |
| Apolizumab        |            | Humanized monoclonal antibody | Antineoplastic non-Hodgkin’s lymphoma abandoned 2009 toxic effects 2009 CLL phase I/II | HLA-DRβ |
|                   |            |                  |                      |
| Arcitumomab       | CEA-Scan   | Murine monoclonal antibody IgG1 Fab’ | Diagnostic imaging Gastrointestinal cancers Colorectal cancers | CEA |
|                   | FDA 1996   |                  |                      |
|                   | EU 1996    |                  |                      |
|                   | Withdrawn EU market 2005 | |
| Ascrinvacumab     |            | Human monoclonal antibody | Antineoplastic mesothelioma Nothing in pub med or web search | Activin receptor-like kinase 1 |
| Aselizumab        | Humanized monoclonal antibody | Disease modifying Severe injured patients phase II 2004, no benefit | L-selectin (CD62L) |
| Atezolizumab      | Tecentriq  | Fc engineered, humanized monoclonal antibody IgG1κ | Antineoplastic agent, treat metastatic urothelial carcinoma, non-small cell lung cancer Phase III Bladder/urothelial cancer phase I Breast cancer phase Ib triple marker neg breast cancer | Intravenous |
|                   | FDA 2016   |                  |                      | |
|                   |            |                  |                      | Binds to PD-L1 and blocks interactions with the PD-1 and B7.1 receptors FDA-approved atezolizumab (TECENTRIQ, Genentech, Inc.), in combination with bevacizumab, paclitaxel, and carboplatin for the first-line treatment of patients with metastatic nonsquamous, nonsmall cell lung cancer (NSq NSCLC) with no EGFR or ALK genomic tumor aberrations |
| Drug Name          | Type                                      | Use/Development                                                                 | Antigen                       | Mode of Administration | Notes                                                                 |
|-------------------|-------------------------------------------|---------------------------------------------------------------------------------|-------------------------------|------------------------|----------------------------------------------------------------------|
| Atidortoxumab     | Human monoclonal antibody IgG1κ           | Limited information on use and development                                     | Negative search PubMed-internet | Staph aureus alpha toxin |
| Atinumab          | Human monoclonal antibody IgG4κ           | Disease modifying                                                             | RTN4                          |                        |
| Atorolimubab      | Developed??                                | Disease modifying hemolytic disease of the newborn                             | Rhesus factor                 |                        |
| Avelumab          | Human monoclonal antibody IgG3            | Antineoplastic Cancers, ovarian, gastric, nonsmall cell lung (NSCLC), metastatic, solid tumors phase II Studies completed metastatic Merkel cell carcinoma | Intravenous                   | PD-L1                  |
| Azintuxizumab vedotin | Chimeric/humanized monoclonal antibody IgG1 | Antineoplastic Nothing in PubMed                                              | CD319                         |                        |
| BAN-2401          | Humanized monoclonal antibody IgG1λ       | Disease modifying Alzheimer A phase Iib study ongoing started 2013              | Intravenous                   | Soluble Aβ amyloid protofibrils                                    |
| Bapineuzumab      | Humanized IgG1 monoclonal antibody        | Disease modifying Alzheimer’s disease Phase III no more studies discontinued research 2012 ARIA-E, amyloid-related imaging abnormalities—edema | Intravenous                   | Beta amyloid Fibrillary and soluble β amyloid                         |
| Basiliximab       | Simulect Chimeric monoclonal antibody IgG1κ | Immunosuppressive agents Prophylaxis of acute rejection in allogenic renal transplantation | Intravenous                   | CD25 (a chain of IL-2 receptor)                                     |
| Bavituximab       | Chimeric monoclonal antibody IgG1κ IgG3 (SUNRISE trial) | Cancer, viral infections (Hep C) phase III NSCLC failed to improve survival Sunrise trial stopped Feb 2016, phase II/III breast cancer, phase II pancreatic cancer, phase I/II trial hepatocellular carcinoma, phase I malignant melanoma + rectal cancer good response rectal; not for prostate cancer, phase II hepatitis C not resulted? | Phosphatidylserine             |                        |
| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|---------------|--------|
| BAY-103356        | Humicade   | Humanized monoclonal antibody IgG4κ | For research only Phase II 1995 | | TNF α |
| CDP 571           | Senlizumab | | | | |
| BCD-100           |           | Human monoclonal antibody | Antineoplastic Phase II/III melanoma NCT03269565 (complete Dec 2019) | Intravenous | Programmed cell death-1 (PD1) |
| Bectumomab        | LymphoScan | Fab'-IgG2κ | Antineoplastic Non-Hodgkin’s lymphoma (detection) | | CD22 |
| Begelomab         | Bebedina   | Murine IgG2b | Disease modifying GvHD phase II/III | | DPP4 binds CD26 on T lymphocytes |
| Belantamab mafodotin | | Humanized monoclonal antibodymab | Antineoplastic | No studies or info on clinical trial, PubMed, FDA substance | BCMA |
| Belatacept        | Nulojix    | Soluble fusion Protein consisting of the modified extracellular domain of CTLA-4 fused to Fc domain of a recombinant human monoclonal antibody IgG1 | Immunosuppressive agents **Prophylaxis renal transplant rejection in adults** Phase III FDA approved | Intravenous | Selectively inhibits T-cell activation through costimulation blockade binds to both CD80 and CD86 blocking CD28 |
| Belimumab         | Benlysta   | Human monoclonal antibody IgG1λ | Disease modifying Kidney transplant phase II Treat **SLE** (testing phase III for renal involvement) Phase II Rheum arthritis failure Phase II Srogren ± GVHD ongoing | Intravenous Subcutaneous | B-cell activating factor (BAFF), B-lymphocyte stimulator |
| Bemarituzumab     | Fasenra    | Humanized monoclonal antibody | Antineoplastic | | |
| Benralizumab      | Fasenra    | Humanized monoclonal antibody IgG1κ | Disease-Modifying Asthma phase III completed **Severe asthma eosinophilic subtype** | Subcutaneous | Interleukin-5 (IL-5α) receptor alpha subunit-directed cytolytic (CD125) |
| Antibody Name      | Target Protein       | Mode of Action                                                                 | Route of Administration | Disease/Condition                                      |
|--------------------|----------------------|--------------------------------------------------------------------------------|-------------------------|--------------------------------------------------------|
| Berlimatoxumab     | berlimat            | Disease modifying psoriasis                                                     | Subcutaneous            | No studies clinical, no clinical study, no PubMed      |
|                    |                      |                                                                                |                         |                                                        |
| Bermekimab         | Xilonix             | Disease modifying psoriasis psoriasis phase III x2 2020                       | Subcutaneous            | IL17A                                                  |
| MABp1              |                      | Ank spond II 2022                                                              |                         |                                                        |
| T2-18C3            |                      | Psor arth II 2020 III 2020                                                    |                         |                                                        |
| CA-18C3            |                      |                                                                                |                         |                                                        |
| Bersanlimab        | Human monoclonal    | Disease modifying psoriasis                                                     | Subcutaneous            | ICAM-1                                                 |
| antibody IgG1κ     |                      |                                                                                |                         |                                                        |
|                    |                      |                                                                                |                         |                                                        |
| Bertilimumab       | CAT-214              | Disease modifying psoriasis                                                     | Intravenous             | CCL11 (eotaxin-1)                                       |
|                    |                      | Severe allergic disorders                                                      |                         |                                                        |
|                    |                      | phase II atopic dermatitis                                                     |                         |                                                        |
|                    |                      | Ongoing studies bullous pemphigoid and ulcerative colitis phase II             |                         |                                                        |
|                    |                      |                                                                                |                         |                                                        |
| Besilesomab        | Scintimun           | Diagnostic use                                                                  | Inflammatory lesions and | CEA-CAM8-related antigen                               |
|                    | EU 2010              |                                                                                | metastases (detection)  |                                                        |
|                    | Not FDA approved     |                                                                                |                         |                                                        |
|                    |                      |                                                                                |                         |                                                        |
| Bevacizumab        | Avastin              | Antineoplastic agent                                                           | Intravenous solution or | VEGF-A anti-angiogenesis inhibitor                     |
|                    | FDA 2004             | Antiangiogenesis inhibitor                                                      | opthalmic injection     |                                                        |
|                    | EU 2005              | Colorectal cancer 2004,                                                       | May not be so good for   |                                                        |
|                    |                      | NSCLC 2006, RCC 2009,                                                         | GBM or ovarian cancer    |                                                        |
|                    |                      | GBM phase III, ovarian                                                        |                          |                                                        |
|                    |                      | cancer, metastatic cervical                                                     |                          |                                                        |
|                    |                      | cancer, fallopian                                                              |                          |                                                        |
|                    |                      | Breast cancer (FDA removed approval for breast cancer 2010)                   |                          |                                                        |
|                    |                      | Recurrent glioblastoma                                                        |                          |                                                        |
|                    |                      | multiform                                                                      |                          |                                                        |
|                    |                      | Nonsquamous nonsmall cell                                                      |                          |                                                        |
|                    |                      | lung cancer                                                                    |                          |                                                        |
|                    |                      |                                                                                |                          |                                                        |
| Bezlotoxumab       | Zinplava             | Disease modifying phase III                                                    | Intravenous             | Clostridium difficile colitis anti-B toxin              |
|                    | FDA 2016             | studies done MODIFY I and II                                                  |                         |                                                        |
|                    | EU 2017              | Modify III ongoing                                                            |                         |                                                        |
|                    |                      | Pseudomembranous colitis                                                       |                         |                                                        |
|                    |                      |                                                                                |                         |                                                        |

Continued
| Generic Drug Name | Brand Name | Type of Antibody                        | AHFS Classification | Dosage Form(s) | Target                                      |
|-------------------|------------|----------------------------------------|---------------------|----------------|--------------------------------------------|
| Biciromab         | FibriScint | Murine monoclonal fragment Fab' IgG1κ   | Detect cardiovascular thromboembolism (diagnosis) |                | Fibrin II, beta chain                      |
| Bimagrumab        | BYM338     | Human monoclonal antibody IgG1λ        | Disease modifying Myostatin inhibitor               | Intravenous    | Activin A receptor type IIB (ACVR2B)       |
|                   |            |                                        | DM II decrease BMI phase II                          |                |                                            |
|                   |            |                                        | Sporadic inclusion body myositis phase III not meet endpoint |                |                                            |
|                   |            |                                        | Treat sarcopenia in older adults phase II           |                |                                            |
| Bimekizumab       |            | Humanized monoclonal antibody IgG1κ    | Disease modifying Ankylosing spondylitis (2018 II, 2022 II, +), plaque psoriasis (2021 III, 2020 III, 2019 III, +), psoriatic arthritis (2020), RA (2017 II), UC phase II | Subcutaneous   | IL 17A and IL 17F                         |
| Bivatuzumab mertansine |    | Humanized monoclonal antibody IgG1    | Antineoplastic squamous cell carcinoma, breast phase I fail x2, head/neck or esophagus phase I fail, toxicity |                | CD44 v6                                   |
| Bleselumab        |            | Human monoclonal antibody IgG4κ        | Disease modifying organ transplant rejection phase II 2020 to prevent FSGS in kidney transplant patients Phase II psoriasis- medication tolerated with minimal reaction, no benefit to disease process | Intravenous    | CD40                                       |
| Blinatumomab      | Blincyto FDA 2014 EU 2015 | Murine(scFv - kappa - heavy) - (scFv - heavy - kappa) BiTE | Antineoplastic Ph chrom neg pre-B ALL (CD19+) phase II B-cell precursor acute lymphoblastic leukemia (ALL) initial or relapsed/refractory | Intravenous    | Bispecific T-cell engager monoclonal antibody construct that directs CD-3 positive effector memory T cells to CD19-positive target cells |
| Blontuvetmab      | Blontress  | Canine monoclonal antibody IgG2 κ/λ.   | Veterinary treat canine B-cell lymphoma             |                | CD20                                       |
| Drug                  | Antibody Type                          | Disease Modifying                                      | Route/Location                                      | Mechanism                                                                 |
|----------------------|----------------------------------------|--------------------------------------------------------|-----------------------------------------------------|---------------------------------------------------------------------------|
| Blosozumab           | Humanized IgG4κ                         | Disease modifying Osteoporosis 3 phase I and one phase 2 injection site reaction and antibodies to antibody | Intravenous Subcutaneous                           | SOST Antisclerostin                                                      |
| Bococizumab RN316 PF-04950615 | Humanized IgG2κ                         | Disease modifying Dyslipidemia Phase III 2019 Discontinued secondary to antidrug antibodies, no primary endpoint achieved | Subcutaneous intravenous                           | Neural apoptosis-regulated proteinase 1 PCSK9 (proprotein convertase subtilisin/kexin type 9, neural apoptosis-regulated convertase 1, NARC1, NARC-1, proproteine convertase 9, PC9) |
| Brazikumab          | Human monoclonal antibody IgG2κ         | Disease modifying Ulcerative colitis phase II 2021 Phase I/II completed Crohn. Phase III ongoing | Subcutaneous IL23                                    | CD30 (TNFRSF8) an antibody-drug conjugate (ADC) 3 parts: anti-CD30 (cAC10, a cell membrane protein of the tumor necrosis factor receptor), a microtubule disrupting agent monomethyl auristatin E (MMAE) and a protease-cleavable linker that attaches MMAE covalently to cAC10. The combination disrupts the intracellular microtubule network causing cell-cycle arrest and apoptotic cellular death |
| Brentuximab vedotin | Adcetris FDA 2013 Breakthrough therapy status by FDA 2018 Chimeric humanized monoclonal antibody IgG1κ | Antineoplastic Hodgkin lymphoma Anaplastic large-cell lymphoma | Intravenous                                         | CD30 (TNFRSF8) an antibody-drug conjugate (ADC) 3 parts: anti-CD30 (cAC10, a cell membrane protein of the tumor necrosis factor receptor), a microtubule disrupting agent monomethyl auristatin E (MMAE) and a protease-cleavable linker that attaches MMAE covalently to cAC10. The combination disrupts the intracellular microtubule network causing cell-cycle arrest and apoptotic cellular death |
| Briakinumab         | Human monoclonal antibody               | Disease modifying psoriasis, Drug development stopped for psoriasis, phase IIb study in Crohn’s | Intravenous IL-12, IL-23                            |                                                                                     |
| Brodalumab AMG827   | Siliz FDA 2016 Human monoclonal antibody IgG2κ | Disease modifying Plaque psoriasis Completed phase III | Subcutaneous Receptor IL-17RA                       |                                                                                     |
| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|--------------------|---------------|--------|
| Brolucizumab      | FDA review 2018 | Humanized single chain antibody fragment (scFv κ) | Disease modifying Wet or age-related macular degeneration phase III to be completed Sept 2018, 2020 HAWK (NCT02307682) and HARRIER (NCT02434328) phase III trials good results | Intravitreal [https://www.novartis.com/news/media-releases/new-novartis-phase-iii-data-brolucizumab-demonstrate-reliability-12-week-treatment-interval](https://www.novartis.com/news/media-releases/new-novartis-phase-iii-data-brolucizumab-demonstrate-reliability-12-week-treatment-interval) | VEGFA |
| Brontictuzumab    | Humanized IgG2κ | Antineoplastic Phase I Colorectal Lymphoid Adenoid cystic Solid tumors | Intravenous | Notch 1 |
| Burosumab        | Crysvisa FDA 2018 | Human monoclonal antibody IgG1κ | Disease modifying X-linked hypophosphatemia Phase III completed | Subcutaneous [https://www.creativebiolabs.net/burosumab-overview.htm](https://www.creativebiolabs.net/burosumab-overview.htm) | FGF 23 phosphaturic hormone fibroblast growth factor 23 |
| Cabiralizumab     | Humanized monoclonal antibody IgG4κ | Antineoplastic metastatic pancreatic cancer phase II 2020 Many other cancers phase I | Intravenous | CSF1R |
| Camidanlumab tesirine | ADCT-21 | Human monoclonal antibody | Antineoplastic B-cell Hodgkin’s lymphoma, non-Hodgkin lymphoma, acute lymphoblastic leukemia, acute myeloid leukemia 2018 phase I Advanced solid tumors with literature evidence of CD25(+) treg content Head and neck Nonsmall cell lung Gastric, esophageal, Pancreas, bladder, Renal cell, melanoma, Triple-negative breast, ovarian phase I 2021 | Intravenous | CD25 |
| Product               | Approval                      | Type                                      | Indications                                                                 | Route                        | Mechanism                     |
|-----------------------|-------------------------------|-------------------------------------------|-----------------------------------------------------------------------------|-------------------------------|-------------------------------|
| Sinilimab Camrelizumab| China pending approval        | Humanized monoclonal antibody IgG4κ      | Antineoplastic Phase III nasopharyngeal cancer 2021 Phase III esophageal cancer 2021 | Programmed cell death 1 (PDCD1) |                               |
| Canakinumab ACZ885    | Ilaris FDA 2009 EU 2009       | Human monoclonal antibody IgG1κ          | Disease modifying Cryopyrin-associated periodic syndromes Including familial cold auto-inflammatory syndrome and Muckle-Wells syndrome; tumor necrosis factor receptor-associated periodic syndrome (TRAPS); hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD) and familial Mediterranean fever (FMF) Systemic Juvenile idiopathic arthritis Treat Juvenile idiopathic arthritis phase III NSCLC 2025 phase III CVD rejected by FDA Behcet | Subcutaneous IL-1β            |                               |
| Cantuzumab mertansine|                               | Humanized monoclonal antibody IgG1κ      | Antineoplastic Colorectal cancer phase I 2007                                | Intravenous Mucin CanAg       |                               |
| Cantuzumab ravtansine|                               | Humanized monoclonal antibody IgG1κ      | Antineoplastic Cancers                                                       | MUC1                          |                               |
| Caplacizumab-yhdp     | Cabilvi (Nanobody program) FDA 2019 EU 2018 | Humanized single variable domain antibody (bivalent nanobody) | Disease modifying Inhibits interaction vWF and platelets Treat acquired TTP Phase III Hercules study completed | Intravenous Subcutaneous VWF  |                               |
### TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont’d

| Generic Drug Name | Brand Name     | Type of Antibody                        | AHFS Classification                                           | Dosage Form(s) | Target                                           |
|-------------------|----------------|-----------------------------------------|---------------------------------------------------------------|----------------|--------------------------------------------------|
| Capromab pendetide| Prostascint    | Murine monoclonal antibody              | Diagnostic imaging Prostatic carcinoma cells detection       | Intravenous    | Tumor surface antigen PSMA                       |
|                   | FDA 1996       |                                         |                                                               |                |                                                  |
| Carlumab          |                | Human monoclonal antibody IgG1κ         | Antineoplastic Prostate phase II no long term benefit Pulm fibrosis phase II no benefit | Intravenous    | hMCAF/MCP-1 (human macrophage/monocyte chemotactic protein-1) |
|                   |                |                                         |                                                               |                |                                                  |
| Carotuximab TRC105|                | Chimeric monoclonal antibody IgG1κ      | Antineoplastic angiosarcoma Hepatocellular car phase I/II 2020 | Intravenous    | Endoglin (CD105)                                |
|                   |                |                                         | Glioblastoma multi-phase II 2014 terminated poor accrual ?results Angiosarcoma phase III 2019 TAPPAS trial Prostate ca phase II 2021 NSCLC phase I 2019 |                |                                                  |
|                   |                |                                         |                                                               |                |                                                  |
| Catumaxomab       | Removab        | Removab: A trifunctional rat/murine hybrid antibody IgG2a/IgG2b | Antineoplastic Removab Ovarian cancer phase II, malignant ascites phase II, gastric cancer phase II (ovarian, gastric, colon, pancreatic, breast, endometrial) Proxinium Head and neck cancer | Intraperitoneal | EpCAM, CD3                                      |
|                   | FDA approved pend 2017 (EU approved 2009) |                                         |                                                               |                |                                                  |
|                   |                |                                         |                                                               |                |                                                  |
| cBR96-doxorubicin immuno-conjugate aka SGN-15 |                | Humanized monoclonal antibody IgG1κ | Antineoplastic Cancer Sponsorship ceased 2005 |                |                                                  |

Catumaxomab consists of one “half” (one heavy chain and one light chain) of an anti-EpCAM antibody and one half of an anti-CD3 antibody, so that each molecule of catumaxomab can bind both EpCAM and CD3. In addition, the Fc-region can bind to an Fc receptor on accessory cells like other antibodies, which has led to calling the drug a trifunctional antibody.
| Drug Name                      | Brand Name   | Type                            | Actions                                                                 | Disease(s)                                                                 | Administration | Additional Information                                      |
|--------------------------------|--------------|---------------------------------|-------------------------------------------------------------------------|---------------------------------------------------------------------------|----------------|----------------------------------------------------------------|
| Cedelizumab                   | CIMZIA       | Humanized monoclonal antibody IgG4κ | Prevent organ transplant rejection                                       | CD4                                                                       |                |                                                               |
| Cemiplimab                    | Libtayo      | Human monoclonal antibody IgG4  | Antineoplastic                                                          | Intravenous                                                              |                | Programmed cell death receptor PCDC1                           |
| Cergutuzumab amunaleukin Aka RO6895882, CEA-IL2v |               | Humanized monoclonal antibody    | Antineoplastic phase I Dec 2018                                          | Intravenous                                                              |                | IL2                                                            |
| Certolizumab pegol CDP870     | Cimzia       | Recombinant, humanized antibody Fab’ fragment | Disease-Modifying                                                      | Subcutaneous                                                              |                | Tumor necrosis factor α blocker                                 |
| Cetrelimab                    | Relatimab    | Human monoclonal antibody IgG4κ  | Antineoplastic                                                          | Nothing on PubMed or creative lab Substance is registered with FDA        |                | Programmed cell death 1                                        |
| Cetuximab IMC-225             | Leukeran Erbitux | Recombinant chimeric monoclonal antibody IgG1κ | Antineoplastic agent                                                    | Intravenous solution                                                      |                | EGFR                                                           |
| Citatuzumab bogatox           |              | Humanized Fab IgG1κ             | Antineoplastic ovarian cancer and other solid tumors                    | Study phase I terminated 2008                                              |                | EpCAM                                                          |

Continued
TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont’d

| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|----------------|--------|
| Cixutumumab       |            | Human monoclonal antibody IgG1κ | Antineoplastic Solid tumors Sarcoma phase II Esophageal cancer phase II Rhabdomyosarcoma phase II no benefit Liver cancer phase I Low antitumor effect Pancreas no benefit 2012 | Intravenous | IGF-1 receptor (CD221) |
| Clazakizumab      | ALD–518    | Humanized monoclonal antibody | Disease modifying rheumatoid arthritis phase II 2015 × 3 Crohn disease phase II 2013 Highly sensitized renal transplant candidates phase II 2020 Treat post-tx rejection kidney phase II 2020 Antibody-mediated rejection phase III 2027 | Subcutaneous | IL6 |
| Clenoliximab      |            | Chimeric monoclonal antibody | Disease modifying Rheum Arth No study since 2003 | | CD4 |
| Clivatuzumab      | hPAM4-Cide | Humanized monoclonal antibody IgG1κ | Antineoplastic Pancreatic cancer Phase III 2017 PANCRIPT-1 study. Study terminated no increase improvement of overall survival | | MUC1 |
| Codrituzumab      |            | Humanized monoclonal antibody IgG1κ | Antineoplastic HCC Phase Ib no response Phase II no response | | Glypican 3 |
| Cofetuzumab       | pelidotin  | Humanized monoclonal antibody IgG1κ | Antineoplastic Nothing on PubMed or creative lab Substance is not registered with FDA | | Protein tyrosine kinase 7 (PTK7) |
| Drug Name | Description | Indication | Route | Additional Information |
|-----------|-------------|------------|-------|------------------------|
| Coltuximab ravtansine SAR3419 | Chimeric monoclonal antibody IgG1 conjugated to DM4 (N²⁻⁻⁻⁻(4-(3-carboxypropyl)dithio)-4-methyl-1-oxopentyl)-N²⁻⁻⁻⁻deacetylmaytansine) | Antineoplastic Relapse/refractory ALL phase II 2015 low clinical response Phase II moderate response | | |
| Conatumumab AMG655 | Human monoclonal antibody IgG1κ | Antineoplastic Phase II 2019: Advanced solid tumors Carcinoid Colorectal cancer Locally advanced Lymphoma Metastatic cancer Nonsmall cell lung cancer Sarcoma Solid tumors Colon cancer phase Ib/II no benefit | Intravenous | TRAIL-R2 |
| Concizumab | Humanized IgG4κ | Disease modifying Hemophilia A and B phase II 2020 | Subcutaneous | Kunitz-type protease inhibitor 2 domain of tissue factor pathway inhibitor (TFPI) |
| Cosroviximab ZMapp | Chimeric monoclonal antibody IgG1κ Triple monoclonal antibody cocktail | Disease modifying Ebola virus Ongoing studies show benefit but not enough enrolled to power study | Intravenous | Ebola virus glycoprotein |
| Crenezumab RG7412 MABT5102A | Humanized monoclonal antibody IgG4 | Disease modifying Alzheimer’s disease phase III study ongoing prodromal/mild AD 2021 Phase III 2022 | | 1-40-β-amyloid |
| Crizanlizumab SelG1 | FDA review possible 2019 | Disease modifying Sickle cell disease phase II 2022 children Phase II adults decrease pain crisis | Intravenous | P Selectin |
| Crotedumab | Human monoclonal antibody IgG4κ | Disease modifying DM type II | No results | GCGR |
| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|----------------|--------|
| Cusatuzumab | ARGX-110 | Humanized monoclonal antibody IgG1 | Antineoplastic Phase I completed safe Phase I/II CTCL dec 2018 Nasopharyngeal carcinoma 2018 | Intravenous | CD70 |
| Dacetuzumab | HU-S2C6 ASKP1240 SGN-40 | Humanized monoclonal antibody IgG1 | Antineoplastic Hematologic cancers Multiple myeloma phase I 2007 Large B-cell lymphoma phase II 2009 enrollment stopped no benefit CLL phase II 2006 NHL phase I Renal transplant (CIRRUS I) phase II 2022 SLE nephritis phase II 2020 | Intravenous | CD40 |
| Daclizumab | Zenapax Zinbryta FDA 1997 EU 1999 Zinbryta withdrawn from market Apr 2009 for commercial reasons Zinbryta withdrawal 2018 secondary to risk/benefit profile | Humanized monoclonal antibody IgG1κ | Disease modifying Prevention of organ transplant rejections Phase IV kidney transplants, multiple sclerosis phase III 2018 pulled from market secondary inflammatory brain disorders Biogen Heart transplant phase IV 108 studies Zanapax discontinued from market by Roche (basiliximab replace) | CDs (α chain of IL-2 receptor) |
| Dalotuzumab | Humanized monoclonal antibody IgG1κ | Antineoplastic Phase I multiple Phase II breast no improvement x 2 Phase III colon no improvement Ped solid phase I | Intravenous | IGF-1 receptor (CD221) |
| Drug Name | Humanized monoclonal antibody IgG1κ | Phase of Use | Route | CD Target |
|-----------|-------------------------------------|--------------|-------|-----------|
| Dapirolizumab pegol | Humanized monoclonal antibody IgG1κ | SLE phase II Nov 2018 Phase I safe | Intravenous | CD154 (CD40L) |
| Daratumumab | Human IgG1κ | Antineoplastic agent Multiple myeloma relapse/ refractory Phase III completed | Intravenous solution | CD38 Induces CDC, ADCC, ADCP, and apoptosis |
| Dectrekumab QAX576 | Human monoclonal antibody IgG1κ | Cancers, asthma phase II, idiopathic pulmonary fibrosis, eosinophilic Esophagitis phase II some benefit but primary endpoint not achieved, Keloids, Crohn’s disease phase II trials 2013 | Nothing on PubMed Substance is registered with FDA, creative lab | IL-13 |
| Demcizumab | Humanized monoclonal antibody IgG2κ | Antineoplastic NSCLC phase II 2018 Phase I safety established with 50% tumor regression response | Intravenous | Delta-like ligand 4DLL4 DLL4 and Notch1, signaling stimulated by DLL4 plays a role in development of blood vessels throughout life |
| Denintuzumab mafodotin HBU-12 SGN-CD19A | Humanized monoclonal antibody IgG1κ Antibody-drug conjugate (ADC) composed of a humanized anti-CD19 monoclonal antibody conjugated to the microtubule-disrupting agent monomethyl auristatin F (MMAF) | Antineoplastic LBCL phase II terminated study by company Acute lymphoblastic leukemia and B-cell non-Hodgkin lymphoma Phase I 2017 Phase II 2018 terminated by sponsor | Intravenous | CD19 |
| Denosumab AMG162 Prolia | Human monoclonal antibody IgG2 | Disease modifying Osteoporosis FREEDOM trial, bone metastases, etc. 186 studies Phase III completed Melanoma phase II 2022 Bone giant cell tumor phase II 2025 | Subcutaneous | Receptor activator of nuclear factor kappa-B ligand (RANKL) Xgeva: Prevention of skeletal-related events (SREs) in adults with bone metastases from breast and castration-resistant prostate cancer. Prolia: Osteoporosis |

*Continued*
| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|----------------|--------|
| **Depatuxizumab** | **mofodotin** | **Chimeric humanized monoclonal antibody IgG1κ CONJUGATED TO AURISTATIN F** | Glioblastoma Phase III Nov 2019 Children phase III 2020 | Intravenous | EGFR |
| **Derlotuximab** | **biotin iodine (131 I) derlotuximab biotin** | **Chimeric monoclonal antibody IgG1κ** | Immunoassays Potential for glioblastoma multiforme | Histone complex |
| **Detumomab** | | **Murine monoclonal antibody IgG1** | Antineoplastic B-lymphoma cell | Nothing on PubMed or clinical trials Substance is not registered with FDA, is on creative lab | CD3E |
| **Dezamizumab** | **GSK-2398852** | **Humanized monoclonal antibody IgG1κ** | Disease modifying Treat amyloidosis Transthyretin cardiomyopathy amyloidosis (ATTR-CM), suspended pending data review Aug 2018 phase I x 4 | Intravenous | Serum amyloid P component |
| **Dinutuximab** | **APN311** | **Chimeric monoclonal antibody IgG1κ** | Antineoplastic Neuroblastoma phase I 2022 SCLC phase III Nov 2019 Osteosarcoma phase II Dec 2018 **Neuroblastoma** phase II 2020 | Intravenous | GD2 ganglioside |
| **Diridavumab** | **CR6261** | **Human monoclonal antibody IgG1λ** | Disease modifying Infectious disease/influenza A Very good response in animal study mice Phase II 2019 | Intravenous | Influenza A hemagglutinin |
| **Domagrozumab** | **PF-06252616** | **Humanized monoclonal antibody IgG1κ** | Disease modifying Duchenne muscular dystrophy phase II 2018 Phase I completed | GDF-8 |
| Substance | Type | Spike | Target | Activity | Route | FDA Approval | Notes |
|-----------|------|-------|--------|---------|-------|--------------|-------|
| Dorlimomab aritox | F(ab')<sub>2</sub> | Murine | | Nothing on PubMed or clinical trials | | | |
| Dostarlimab TSR042 WBP285 | Humanized monoclonal antibody IgG4<sub>k</sub> | Antineoplastic | Solid tumor Phase I, II, III studies ongoing | Ovarian CA (first study) phase III 2023 | | Programmed cell death protein-1 (CD279) PCDP1 |
| Drozitumab PRO95780 rhuMAB DR5 | Human monoclonal antibody IgG1<sub>λ</sub> | Antineoplastic | Colorectal cancer Ib 2012 Preclinical rhabdomyosarcoma 2018 Chondrosarcoma not efficacious NHL results? | | Intravenous | Death receptor 5 (DR5) |
| Duligotuzumab MEHD7945A | Human monoclonal antibody IgG1<sub>κ</sub> | Antineoplastic squamous head and neck phase II no benefit Colon ca phase II no benefit | | | | Anti-EGFR × Anti-HER3 bispecific antibody |
| Dupilumab Dupixent FDA 2017 | Human monoclonal antibody IgG4 | Disease modifying asthma, atopic dermatitis Ongoing studies | | Subcutaneous | | |
| Durvalumab Imfinzi FDA 2017 | Human monoclonal antibody IgG1<sub>κ</sub> | Antineoplastic agent Treat NSCLC stage III phase I, urothelial carcinoma | | Intravenous | PD-L1 (CD274) and CD80—inhibit binding of programmed death ligand 1 to PD-1 and CD80 allowing T cell to recognize and kill tumor cells |
| Dusigitumab MEDI 573 | Human monoclonal antibody IgG2<sub>λ</sub> | Antineoplastic Breast cancer phase II results? HCC phase II results? | | Intravenous | ILGF2 |
| Duvortuxizumab MGD011 | Chimeric/humanized monoclonal antibody | Antineoplastic B-cell malignancy Phase I/II Jul 2018/2020 | | Intravenous | CD19, CD3E |
| Ecromeximab KW2871 | Chimeric monoclonal antibody IgG1<sub>κ</sub> | Antineoplastic Metastatic melanoma Phase I/II clinical activity limited | | Intravenous | GD3 ganglioside |

*Continued*
| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|----------------|--------|
| Eculizumab        | Soliris    | Humanized monoclonal antibody IgG1/4 | Immuno-regulation | Intravenous | C5     |
|                   |            |                  | Paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (HUS) Generalized myasthenia gravis (MG) Phase II CAD |               |        |
|                   |            |                  |                    |                |        |
| Edobacomab E5     | Panorex    | Murine monoclonal antibody IgG2κ | No improved survival | Intravenous | Endotoxin |
|                   |            |                  |                    |                |        |
| Edrecolomab        | Panorex    | Murine monoclonal antibody IgG1κ | Antineoplastic Colorectal carcinoma phase III 2003 no improvement | Intravenous | Glycoprotein EpCAM/17-1A |
|                   |            |                  |                    |                |        |
| Efalizumab         | Raptiva    | Recombinant humanized monoclonal antibody IgG1κ | Disease modifying (2003 approved) psoriasis | Subcutaneous Voluntary withdrawal 2009 | Human CD11a Increase risk progressive multifocal leukoencephalopathy (PML) |
|                   |            |                  |                    |                |        |
| Efungumab MYC123  | Mycograb C28Y | Human scFv | Antiinfectious agent Invasive Candida infection | Intravenous | Heat shock protein 90 (Hsp90) |
| Eldelumab Mdx 1100 | Mycograb C28Y | Human monoclonal antibody IgG1κ | Crohn’s disease phase IIa no significant response, ulcerative colitis phase IIb prim endpoint not achieved Rheum arthritis phase II | Intravenous | Interferon γ-induced protein CXCL 10 |
| Elezanumab PR-1432051 PDL063 | Empliciti FDA 2015 | Human monoclonal antibody IgG1κ | Spinal cord injury and multiple sclerosis phase II 2021 | Intravenous | REPULSIVE GUIDANCE MOLECULE FAMILY MEMBER A (RGMA) |
| Elotuzumab        | Empliciti  | Human IgG1κ | Antineoplastic Breast gastric phase I | Intravenous | ERBB3 (HER3) |
|                   | FDA 2015   |                  |                    |                |        |
|                   | EU 2016    |                  |                    |                |        |
| Name                  | Description                                                                 | Indications                                                                 | Phase | Notes                                                                 |
|-----------------------|-----------------------------------------------------------------------------|-----------------------------------------------------------------------------|-------|-----------------------------------------------------------------------|
| Elsilimomab B-E8      | Humanized monoclonal antibody IgG1                                          | Antineoplastic multiple myeloma                                             | IL-6  | Not effective in mice                                                |
| Emactuzumab RG7155    | Humanized monoclonal antibody IgG1                                          | ANTINEOPLASTIC                                                               |       | Phase I 2019 solid tumors                                             |
|                       |                                                                             | Phase II 2025 REDIRECT study                                               |       | Ovarian, fallopian tube cancer                                         |
|                       |                                                                             | Pancreatic phase II 2020                                                   |       |                                                                       |
| Emapalumab NI-0501    | Gamifant FDA 2018 EU pending                                               | Human monoclonal antibody IgG1α                                            |       | Intravenous                                                          |
|                       |                                                                             | Hemophagocytic lymphohistiocytosis                                          |       | Interferon γ                                                         |
| Emibetuzumab LA480    | Humanized monoclonal antibody IgG4κ                                         | Antineoplastic                                                               |       | Intrasavenous                                                        |
| LY2875358             | Bivalent antibody                                                           | NSCLC phase II 2020                                                        |       | Hepatocyte growth factor receptor (HHGFR) and MET signaling           |
|                       |                                                                             | Advanced cancer                                                             |       |                                                                       |
|                       |                                                                             | Gastric safe ?effective adenocarcinoma                                      |       |                                                                       |
|                       |                                                                             | Gastroesophageal junction adenocarcinoma                                    |       |                                                                       |
|                       |                                                                             | Hepatocellular cancer                                                       |       |                                                                       |
|                       |                                                                             | Renal cell carcinoma                                                        |       |                                                                       |
|                       |                                                                             | Nonsmall cell lung cancer phase I Jan 2018                                  |       |                                                                       |
|                       |                                                                             | Phase I safe with tumor response                                            |       |                                                                       |
| Emicizumab ACE910     | Human monoclonal antibody IgG4κ                                             | Disease modifying                                                            |       | Activated F9, F10                                                    |
| Hemlibra FDA 2018     | Bispecific                                                                  | Hemophilia A phase III 2020                                                 |       |                                                                       |
|                       |                                                                             | With or without inhibitors                                                 |       |                                                                       |
| Enapotamab vedotin    | Human monoclonal antibody IgG1κ                                             | Antineoplastic                                                               |       | Nothing on PubMed or clinical trials                                 |
| Enavatuzumab PDL192   | Humanized monoclonal antibody IgG1κ                                         | Antineoplastic                                                               |       | Substance is not registered with FDA, or creative lab                |
|                       |                                                                             | Phase I 2011                                                                |       | Human growth factor receptor AXL                                      |
|                       |                                                                             | No responses and liver pancreatic toxicity                                  |       |                                                                       |
| Enfortumab vedotin    | FDA review pending 2019                                                     | Human monoclonal antibody                                                   |       | Nectin-4                                                             |
|                       |                                                                             | Antineoplastic bladder cancer phase I                                        |       | Anti-Nectin-4                                                        |
|                       |                                                                             | Phase II ongoing                                                            |       | Monoclonal antibody attached to a microtubule-disrupting agent, monomethyl auristatin E (MMAE) |
### TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont’d

| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|----------------|--------|
| **Enlimomab pegol** |           | Murine monoclonal antibody IgG2\(a\) | Disease modifying Stroke | Nothing on PubMed or clinical trials Substance is not registered with FDA | ICAM-1 (CD54) |
| **Enoblituzumab MGA 271** |          | Humanized monoclonal antibody IgG1\(\kappa\) | Antineoplastic Phase I 2022 children Neuroblastoma Rhabdomyosarcoma Osteosarcoma Ewing sarcoma Wilms tumor Desmoplastic small round cell tumor Phase I melanoma, NSCLC 2018 Phase II prostate 2021 |                | CD276 (B7–H3) |
| **Enokizumab MEDI528** |          | Humanized monoclonal antibody IgG1\(\kappa\) | Asthma phase II No improvement | Intravenous | IL9 |
| **Enoticumab REGN421** |          | Human monoclonal antibody IgG1\(\kappa\) | Antineoplastic Phase I 2014 ovarian cancer + |                | Delta-like canonical notch ligand 4 (DLL4) |
| **Ensituximab NEO-201 NPC-1C** |          | Chimeric monoclonal antibody IgG1\(\kappa\) | Antineoplastic Phase II pancreatic and colorectal cancer 2017 | Intravenous | 5AC |
| **Enterecept RHU-TNFR:FC** | **Enbril** FDA 2003 | 1-235-Tumor necrosis factor receptor fusion protein attached to recombinant human IgG1 Fc fragment | Disease modifying Antirheumatic drug Not effective for inflammatory bowel disease | Subcutaneous | TNF\(\alpha\) |
| **Epitumomab cituxetan AS-1402 HuHMFG-1** | **Sontuzumab** | Humanized monoclonal antibody IgG1 | Antineoplastic Breast cancer phase II 2012 no benefit |                | Episialin MS4A1 (membrane-spanning 4-domains subfamily A member 1, CD20 (HMFG-1)) |
| **Epratuzumab HLL2 AMG412** |          | Humanized monoclonal antibody IgG1\(\kappa\) ADCC/CDC | Antineoplastic B-ALL phase III ongoing 2018 Disease modifying SLE phase III no improvement | Intravenous | CD22 |
| Name                          | FDA Approval | Type                                         | Phase | Notes                                                                                                                                                                                                 |
|-------------------------------|--------------|----------------------------------------------|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Eptinezumab ALD403            | FDA review possible 2019 | Monoclonal antibody IgG1κ | Disease modifying | Migraine phase III                                                                                                                                                                                  |
| Erenumab Aimovig              | FDA May 2018 | Human monoclonal antibody IgG2λ | Disease modifying | Migraine phase III                                                                                                                                                                                  |
| Ertizumab Rhumab CD18         | FDA May 2018 | Humanized IgG1 F(ab′)_2 fragment | Antineoplastic (lab tests) | Immunosuppressive drug phase I study cough up blood and phase II did not meet goals Heart attack, stroke, traumatic shock ?? no successful CD18 drug to date |
| Ertumaxomab Rexomun Ertumaxomab or etaratuzumab MEDI-522 | | | Antineoplastic | Breast Gastric, esophageal Phase II studies terminated company to focus on other plans not safety concerns concentrate on catumaxomab Phase I found safe 2016 |
| Etracizumab or etaratuzumab MEDI-522 | | | Intravenous | HER2/neu, CD3 |
| Eltigilimab                   |              | Humanized monoclonal antibody IgG2κ | Antineoplastic | Melanoma phase II 2010 not beneficial, prostate cancer, ovarian cancer small and large bowel cancer phase I and II completed results unreported 2017 |
| Etrolizumab PRO145223 RHUMAB BETA7 |              | Humanized monoclonal antibody IgG1κ | Disease modifying | Inflammatory bowel disease UC phase III 2020 × 4/2023/2024/2025 Crohn phase III 2021 |
| Evinacumab REGN1500           |              | Human monoclonal antibody IgG4κ | Disease modifying | Dyslipidemia Phase II 2020 Phase III 2020/2022 |
|                               |              |                                              |       |                                                                                                                             |
|                               |              |                                              |       |                                                                                                                             |

Continued
| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|----------------|--------|
| Evolocumab        | Repatha    | Human monoclonal antibody IgG2λ | Disease modifying hypercholesterolemia Completed phase III Heterozygous familial hypercholesterolemia, CVD | Subcutaneous | Proprotein convertase subtilisin kexin type 9 (PCSK9) |
| Exbivirumab       |            | Humanized monoclonal antibody IgG1λ | Disease modifying prevent disease Hep B | Oral therapy Abstract of randomized study of 50 patients | Hepatitis B surface antigen |
| Fanolesomab       | NeutroSpec | Murine monoclonal antibody | Diagnostic imaging Appendicitis (diagnosis only) | Nothing on PubMed or clinical trials Substance is not registered with FDA, or is not in creative lab | CD15 |
| Faralimomab       |            | Murine monoclonal antibody IgG1 | | | Interferon receptor |
| Faricimab         | RB5-IGM    | Humanized monoclonal antibody IgG1mab | Disease modifying angiogenesis, ocular vascular diseases STAIRWAY, BOULEVARD, RHINE, Yosemite phase II and III studies phase III 2022 for diabetes maculae edema AMD LUCERNE phase III 2022 TENAYA phase III 2022 | Intravitreous | ANTIVASCULAR ENDOTHELIAL GROWTH FACTOR/ ANTIANGIOPOIETIN 2 BISPECIFIC ANTIBODY (VEGF-A and Ang-2) |
| Farletuzumab      | MORAB-003  | Humanized monoclonal antibody IgG1κ | Antineoplastic Ovarian cancer phase III subgroup may benefit | Intravenous | Folate receptor 1 |
| Fasinumab         | REGN475    | Human monoclonal antibody IgG4κ | Disease modifying acute sciatic pain phase III Knee arthritis pain phase III 2021 | Subcutaneous (auto injector) | Human nerve growth factor (HNGF) |
| FBTA05 Bi20       | Lymphomun  | Rat IgG2b (CD3)/murine IgG2a (CD20) hybrid trifunc | Antineoplastic Chronic lymphocytic leukemia trial terminated recruitment too slow | Intravenous? | CD20/CD3 |
| Antibody Name     | Type of Antibody | Function/Indication                                                                 | Registration Status | Other Details                                                                 |
|------------------|------------------|-------------------------------------------------------------------------------------|---------------------|-------------------------------------------------------------------------------|
| Felvizumab       | Humanized monoclonal antibody IgG1κ | Antiinfectious agent Respiratory syncytial virus infection | Nothing on PubMed or clinical trials | Substance is not registered with FDA, but is in creative lab Respiratory syncytial virus |
| Fezakinumab      | Human monoclonal antibody IgG1λ  | Disease modifying Rheumatoid arthritis, psoriasis (not good for) Atopic dermatitis phase IIb good results | Intravenous | IL-22                                                                           |
| Fibatuzumab      | Humanized monoclonal antibody IgG1κ | Disease modifying Myelodysplastic syndrome Research in Australia for GBM phase I | Ephrin receptor A3  | Influenza A virus hemagglutinin HEMAGGLUTININ HA                                |
| Ficlatuzumab SCH 900105 AV 299 | Humanized monoclonal antibody IgG1κ | Antineoplastic Head and neck cancer phase I 2020 Pancreatic phase I 2023 NSCLC phase II 2013 AML phase I 2020 | Hepatocyte growth factor (HGF) heparoietin A | Insulin-like growth factor receptor IGF-1 receptor (CD221)                    |
| Figitumumab CP751871 | Human monoclonal antibody IgG2κ | Antineoplastic Adrenocortical carcinoma, nonsmall cell lung carcinoma etc. ?additional benefit in phase I | Intravenous | TYRP1 (glycoprotein 75)                                                       |
| Firivumab        | Human monoclonal antibody IgG1κ  | Disease modifying Influenza A virus hemagglutinin | Nothing on PubMed or clinical trials | Substance is registered with FDA, and is in creative lab INFLUENZA A VIRUS HEMAGGLUTININ HA |
| Flanvotumab IMC20D7S | Human monoclonal antibody IgG1κ | Antineoplastic Melanoma phase I 2012 | Intravenous | No published data TYRP1 (glycoprotein 75)                                      |
| Fletikumab       | Human monoclonal antibody IgG4   | Disease modifying Rheumatoid arthritis phase IIa good, phase IIb no results | IL 20                |                                                                                |
| Flotetuzumab MGD006 S80880 | Humanized di-scFv dual affinity retargeting (DART) to CD123 and CD3 | Antineoplastic Hematologic malignancies (ALL, NHL) Phase II not yet recruiting 2018 | Intravenous? | IL 3 receptor                                                                 |

CHAPTER 16 Passive Monoclonal and Polyclonal Antibody Therapies

287 Continued
| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|----------------|--------|
| Fontolizumab      | HuZAF      | Humanized monoclonal antibody IgG | Disease modifying Treat Crohn’s clinical development stopped despite some benefit phase II ustekinumab is better |                  | IFN-γ  |
| FOR46             |            | Antibody drug conjugate | Antineoplastic Phase I for multiple myeloma failed remission or relapse Phase I prostate cancer | Intravenous      | CD46   |
| Foralumab         |            | Human monoclonal antibody IgG1κ | Disease modifying NASH phase II 2019 | Oral            | CD3 epsilon |
| Foravirumab       |            | Human monoclonal antibody IgG1κ | Disease modifying rabies (prophylaxis) | Nothing in pub med or clinical trials | Rabies virus glycoprotein |
| Fremanezumab      | LBR-101 RN307 | Humanized monoclonal antibody IgG1κ | Disease modifying migraine and cluster headache phase III 2019 | Subcutaneous | α-Calcitonin gene-related peptide |
| Fresolimumab      | Ajovy FDA 2018 | Humanized monoclonal antibody IgG4 | Disease modifying Idiopathic pulmonary fibrosis (IPF), scleroderma, focal segmental glomerulosclerosis (phase 2), cancer (kidney cancer and melanoma) | Need larger study for FSGS Good response scleroderma [https://newdrugapprovals.org/2016/01/30/fresolimumab/](https://newdrugapprovals.org/2016/01/30/fresolimumab/) | TGF β 1 |
| Frovocimab        | LY3015014  | Humanized monoclonal antibody IgG4κ | Disease modifying hypercholesterolemia Completed phase II trials 2014 good response and safe | Subcutaneous     | PROPROTEIN CONVERTASE SUBTILISIN KEXIN 9 (PCSK9) |
| Frunevetmab       | [https://en.wikipedia.org/wiki/List_of_therapeutic_monoclonal_antibodies - cite note-WHOList 116-17 NV-02](https://en.wikipedia.org/wiki/List_of_therapeutic_monoclonal_antibodies - cite note-WHOList 116-17 NV-02) | Veterinary monoclonal antibody IgG1κ | Veterinary | Feline muscle nerve growth factor |
| Drug Name               | Therapeutic Target | Antibody Type | Disease or Condition                                      | Route of Administration | Mechanism of Action |
|------------------------|--------------------|---------------|-----------------------------------------------------------|-------------------------|---------------------|
| Fulranumab AMG403      |                    | Human monoclonal antibody IgG2κ | Disease modifying Pain osteoarthritis pain phase III 2017 | Subcutaneous            | Nerve growth factor |
| Galcanezumab LY2951742 |                    | Humanized monoclonal antibody IgG4κ | Disease modifying Migraine Phase III completed Cluster HA phase III 2020 | Subcutaneous            | Calcitonin gene-related polypeptides (CGRPs) α and β |
| Galiximab IDEC-114     |                    | Chimeric monoclonal antibody IgG1κ, ADCC/CDC | Antineoplastic lymphoma phase II 2015 minimal response ORR 10.3% | Intravenous             | CD80                |
| Gancotamab MM-302      |                    | Human cFv Single chain fragment | Antineoplastic Breast cancer phase I–III | Intravenous             | HER2/neu            |
| Ganitumab AMG479       |                    | Human monoclonal antibody IgG1κ | Antineoplastic Pancreatic phase III—no increase benefit Phase III for rhabdomyosarcoma and Ewings 2021 Not beneficial in NSCLC | Intravenous             | IGF-1 receptor (CD221) |
| Gantenerumab R04909832 |                    | Human monoclonal antibody IgG1κ | Disease modifying Alzheimers Phase III stopped for potential futility additional studies at higher dosing (DIAN in a phase II/III trial in individuals at risk For and with early-stage autosomal-dominant AD phase III 2021 | Subcutaneous             | Beta amyloid         |
| Gatipotuzumab PankoMab-GEX |                | Humanized monoclonal antibody IgG1κ | Antineoplastic Ovarian, non-small cell lung cancer (NSCLC), colorectal cancer (CRC), breast cancer (BC), gynecological cancers (GYN) phase I used for diag/prog now | Intravenous             | Musculus, antimucin (MUC1) |
| Gavilimomab ABX-CBL    |                    | Murine monoclonal antibody IgM | Disease modifying Graft versus host disease phase III completed 2005 less effective than antithymocyte antibody | CD147 (basigin)         |                     |

*Continued*
| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|----------------|--------|
| Gedivumab         | RG7745     | Human monoclonal antibody IgG1κ | Disease modifying influenza virus A | No studies, PubMed/clinical trials | Influenza virus hemagglutinin HA |
|                   | RO6876802  |                  |                     |                |        |
| Gemtuzumab ozogamicin | Mylotarg AML FDA 2000 Voluntary withdrawal 2010 VOD now black box warning Returned to market with FDA approval 2017 | Humanized monoclonal antibody IgG4/toxin conjugate | Antineoplastic Acute myelogenous leukemia Many ongoing and completed studies | Intravenous | CD33 |
| Gevokizumab       | XOMA 052   | Humanized monoclonal antibody IgG2κ | Disease modifying DM phase II (late stage) no results Other dz too 24 studies behcet uveitis failed primary end point phase III (Eyeguard _B) 2015 | Subcutaneous | IL-1β |
| Gilvetmab PD1     |            | Veterinary monoclonal antibody IgG2κ | Antineoplastic | No studies clinical trial, pub med | CANIS FAMILIARIS PROGRAMMED CELL DEATH PROTEIN 1 (PCDC1) |
| Gimsilumab        | MORAb-022  | Human monoclonal antibody IgG1 | Disease modifying Rheumatoid arthritis Asthma Phase I poster presentation of safety results good 2016 | Intravenous | HUMAN GRANULOCYTE-MACROPHAGE COLONY-STIMULATING FACTOR (CSF2) |
| Girentuximab      | WX-G250    | Chimeric monoclonal antibody IgG1κ | Antineoplastic Clear cell renal cell carcinoma for treatment and imaging | Intravenous | Carbonic anhydrase 9 (CA-IX) |
|                   | CG250      | Radioactive labeled ab |                     |                |        |
| Glembatumumab vedotin CR011 |            | Human monoclonal antibody IgG2κ | Antineoplastic Melanoma phase II, breast cancer | Intravenous | Human glycoprotein NMB extracellular domain (GPNMB) |
| Golimunab         | Simponi FDA 2009 EU 2009 | Human monoclonal antibody IgG1κ | Disease modifying *Rheumatoid arthritis, psoriatic arthritis*, juvenile rheum arth, *ankylosing spondylitis* many studies, UC, DM1 phase I (2020, 2021) | Subcutaneous, intravenous | TNF-α |
| Antibody Name | Type | Monoclonal Antibody | Indications | Phase | Status | CD antigen or protein |
|--------------|------|---------------------|-------------|-------|--------|---------------------|
| Gomiliximab  | Chimeric monoclonal antibody IgG1κ | Allergic asthma? Antineoplastic CLL Phase I, phase 2/3 2014 Failed efficacy | ADCC/CDC | | | CD23 (IgE receptor) |
| Lumiliximab  | | | | | | |
| ST-152       | | | | | | |
| Gosuranemab  | Humanized monoclonal antibody IgG4κ | Progressive supranuclear palsy Phase I 2020 Alzheimer 2021 | | Intravenous | τ protein |
| BIIB092      | FDA orphan drug status | | | | | |
| IPN-007      | | | | | | |
| Guselkumab   | Human monoclonal antibody IgG1λ | Disease modifying Psoriasis Adenomatous polyposis | | Subcutaneous | IL23A |
| CNTO 1959    | Tremfya | | | | | |
| Hu3F8        | Humanized monoclonal antibody IgG3 | Antineoplastic Phase I For neuroblastoma mod tox and substantial effect on tumor Phase II ongoing | | Intravenous | GD2 ganglioside |
| Ianalumab    | Human monoclonal antibody IgG1κ | Immunomodulation Autoimmune hepatitis | | | Human cytokine receptor BAFF-R |
| Ibalizumab   | Trogarzo Humanized monoclonal antibody IgG4 | Disease modifying anti-HIV Phase III | | | CD4 |
| Ibritumomab  | Human monoclonal antibody IgGκ | Antineoplastic Follicular non-Hodgkin’s lymphoma, B-cell NHL, multiple myeloma conditioning for BMT, B-cell DLCL, mantle cell Many studies | | | CD20 (human B-lymphocyte-restricted differentiation antigen, Bp35) |
| tiuxetan     | Zevalin Murine monoclonal antibody IgGκ YT$^{77}$ or In$^{111}$ bound | Antineoplastic Follicular non-Hodgkin’s lymphoma, B-cell NHL, multiple myeloma conditioning for BMT, B-cell DLCL, mantle cell Many studies | | Intravenous | | |
| IDEC-129     | FDA 2002 EU 2004 | | | | | |
| IDEC-IN2B8   | | | | | | |
| IDEC-Y2B8    | | | | | | |
| Icrucumab    | Human monoclonal antibody IgG1κ | Antineoplastic No benefit breast phase II No benefit colon phase II No benefit urothelial phase II | | Intravenous | | |
| IMC 18F1     | | | | | | |
| Idarucizumab | Humanized monoclonal antibody Fab fragment | Antidotes Drug reversal agent Reversal of anticoagulant effects of dabigatran Phase III trial RE-VERSE AD | | Intravenous | Dabigatran etexilate |
| Generic Drug Name          | Brand Name          | Type of Antibody | AHFS Classification                        | Dosage Form(s)                                      | Target                                                                 |
|---------------------------|---------------------|------------------|--------------------------------------------|----------------------------------------------------|------------------------------------------------------------------------|
| Igovomab                  | Indimacis-125       | Murine F(ab\(^{2}\)) | Diagnostic imaging                         | Ovarian cancer (diagnosis)                          |                                                                        |
| Iladatuzumab vedotin      | RG7986              | Humanized monoclonal antibody IgG1\(\kappa\) | Antineoplastic                              | Nothing in PubMed or clinical trials               | Human gene B29 protein (CD97B)                                          |
| Imalumab                  | BAX69               | Human monoclonal antibody IgG1\(\kappa\) | Antineoplastic                              | Intraperitoneal infusion, intravenous              | Macrophage migration inhibitory factor (MIF)                            |
| Imaprelimab               | Humanized IgG1\(\kappa\) | Antineoplastic | Nothing in PubMed or clinical trials       | Melanoma cell adhesion molecule (MCAM)             |                                                                        |
| Imciromab pentetate       | Myoscin             | Murine monoclonal antibody fragment Fab IgG2a\(\kappa\) | Diagnostic Cardiac imaging                  | Cardiac myosin                                     |                                                                        |
| Imgatuzumab RG7160        | HUMA-B              | Humanized monoclonal antibody IgG1\(\kappa\) | Antineoplastic Colorectal 2013 Head and neck 2017 NSCLC 2017 | Epidermal growth factor receptor (EGFR, HER1) |                                                                        |
| IMGN632                   | Monoclonal antibody with antibody drug conjugate | Antineoplastic AML, ALL phase I 2021 NCT03386513 | Intravenous                                  | CD123                                               |                                                                        |
| Inclacumab RG1512         | Human monoclonal antibody IgG4\(\kappa\) | Disease modifying Cardiovascular disease phase II | Intravenous                                  | Selectin P                                          |                                                                        |
| Indatuiximab ravtansine   | Chimeric monoclonal antibody IgG4\(\kappa\) | Antineoplastic Preclinical breast cancer | CD138 (syndecan-1) SDC1                     | Gastrointestinal, pancreatic, gastroesophageal Safe phase I, phase II pancreatic min response, three studies terminated by company business |                                                                         |
| Indusatatumab vedotin TAK-264 | MLN0264       | Human monoclonal antibody IgG1\(\kappa\) conjugated via a mc-val-cit-PABC linker to monomethyl auristatin E (MMAE (5F9-mc-val-cit-PABC-MMAE)) | Antineoplastic Gastrointestinal, pancreatic, gastroesophageal Safe phase I, phase II pancreatic min response, three studies terminated by company business | Intravenous                       | Guanylate cyclase C (GUCY2C)                                      |
| Name               | Type                          | Indications                                                                                     | Route       | CD | Other Details |
|--------------------|-------------------------------|--------------------------------------------------------------------------------------------------|-------------|----|---------------|
| Inebilizumab MEDI-551 | Humanized monoclonal antibody IgG2κ | Antineoplastic Refractory DLBCL phase II 2016 Disease modifying systemic sclerosis, multiple sclerosis Neuromyelitis optica | Intravenous | CD19 |               |
| Infliximab Remicade | Human-murine chimera IgG1κ Human constant, murine variable region | Disease modifying Remicade Crohn’s disease; ulcerative colitis; rheumatoid arthritis; ankylosing spondylitis; psoriatic arthritis; plaque psoriasis Inflectra Spondylitis; ankylosing arthritis; rheumatoid colitis; ulcerative arthritis; psoriatic arthritis Crohn’s disease; psoriasis Remsima Spondylitis; ankylosing arthritis; rheumatoid colitis; ulcerative Crohn’s disease; arthritis; psoriatic psoriasis | Intravenous solution | TNF-α |               |
| Inolimomab | Murine monoclonal antibody | Disease modifying GVHD phase III No better than ATG in 3 studies Abandoned not in 2017 Cochrane review | Intravenous solution | CD25 (κ chain of IL-2 receptor) |               |
| Inotuzumab ozogamicin G544 | Humanized monoclonal antibody IgG4κ ADCC/ CDC | Antineoplastic ALL phase II 2023 Multiple other studies | Intravenous | CD22 |               |
| Intetumumab CNTO095 | Human monoclonal antibody IgG1κ | Antineoplastic Solid tumors (prostate cancer, melanoma) Melanoma phase II possible benefit 2011 Prostate cancer no additional benefit 2013 phase II | Intravenous | CD51 |               |
| Ipilimumab Yervoy | Human monoclonal antibody IgG1κ | Antineoplastic agent Bladder carcinoma (trials ongoing) Melanoma | Intravenous |               |
| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|----------------|--------|
| Ipilimumab MDX010 | Yervoy     | Human monoclonal antibody IgG1κ | Antineoplastic Melanoma (checkmate 067) Renal cell carcinoma (checkmate 214) Colorectal cancer | Intravenous | CD152 cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) and blocks interaction with its ligands CD80/CD86 |
| Ipilimumab BMS-734016 |           |                  |                     |                |        |
| Iratumumab MDX060 |           | Human monoclonal antibody IgG1κ | Antineoplastic Hodgkin's lymphoma phase II completed Clinical research discontinued 2009 | Intravenous | CD30 (tumor necrosis factor receptor superfamily, Member 8; TNFRSF8) aka Ki-1 Ag |
| Isatuximab SAR650984 | FDA review possible 2019 | Chimeric monoclonal antibody IgG1κ | Antineoplastic multiple myeloma Phase I 2019 Phase II 2022 Phase III 2025 | Intravenous | CD 38 |
| Iscalimab CFZ533 |           | Human monoclonal antibody IgG1κ | Disease modifying Potential treat autoimmune disease Lupus nephritis phase II 2020 Myasthenia gravis GVHD Kidney transplant 2022 phase II Preclinicals | Intravenous | CD40 |
| Istitratumab MM-005 MM-141 |           | Human monoclonal antibody IgG1 | Antineoplastic Advanced solid tumors Pancreatic cancer phase II 2018 |                | Insulin-like growth factor I receptor/neuregulin receptor HER3 (IGF1R, CD221) |
| Itolizumab Alzumab FDA |           | Humanized monoclonal antibody IgG1κ | Disease modifying Psoriasis GVHS phase II 2022 |                | CD6 |
| Ixekizumab Taltz |           | Humanized monoclonal antibody | Disease modifying Phase III radiographic axial spondyloarthritis Psoriatic arthritis | Subcutaneous | IL 17A |
| **Antibody** | **Clinical Trials** | **Indication** | **Stage** | **Regulatory Status** | **Target** |
|--------------|--------------------|---------------|-----------|----------------------|-----------|
| Keliximab | Clenoliximab | Chimeric monoclonal antibody IgG1\(\lambda\) | Disease modifying | | CD4 |
| Labetuzumab | CEA-Cide | Humanized monoclonal antibody IgG1 | Antineoplastic | | CEA |
| Lacnotuzumab | MCS110 | Humanized monoclonal antibody IgG1\(\kappa\) | Antineoplastic | Colorectal cancer | CSF1, MCSF |
| Ladiratuzumab | vedotin | Humanized monoclonal antibody IgG1\(\kappa\) | Antineoplastic | Breast, pigmented villonodular synovitis (PVNS) | LIV-1 |
| Lampalizumab | RG7417 | Humanized monoclonal fragment IgG1\(\kappa\) | Disease modifying | Geographic atrophy secondary to age-related macular degeneration | Intravitreous |
| Lanadelumab | SHP643 | Human monoclonal antibody IgG1\(\kappa\) | Disease modifying | Angioedema | Subcutaneous |
| Landogrozumab | LY2495655 | Humanized monoclonal antibody IgG4 | Disease modifying | Muscle wasting disorders, i.e., after hip surgery phase II | Subcutaneous |
| Laprituximab | Emtansine | Chimeric monoclonal antibody | No trials or PubMed or creative lab only in FDA registry | | EGFR |
| Larcaviximab | ZMAPP | Chimeric monoclonal antibody IgG1\(\kappa\) | Disease modifying | Ebola virus | No studies clinical trial or PubMed |

Continued
| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|----------------|--------|
| Lebrikizumab      | MILR1444A  | Humanized monoclonal antibody IgG4κ | Disease modifying Asthma phase III Atopic dermatitis HL phase II 2007 | Subcutaneous injection | Interleukin-13 (IL-13) |
| TXN-650           | RG-3637    |                  |                     |                |        |
| PRO301444         |            |                  |                     |                |        |
| Lemalesomab       |            | Murine monoclonal antibody IgG1κ | Diagnostic agent |                | NCA-90 (granulocyte antigen) |
| Lendalizumab      | Olendalizumab ALXN-1007 | Humanized monoclonal antibody IgGκ | Disease modifying Antiphospholipid syndrome GI GVHD | Intravenous | Anticomplement 5A |
| Lenvervimab       |            | Humanized IgG1κ | Disease modifying Hepatitis B | No studies in clinical trials or PubMed | Hepatitis B surface antigen |
| Lenzilumab KB-003 |            | Human monoclonal antibody | Antineoplastic chronic myelomonocytic leukemia and juvenile myelomonocytic leukemia phase I | Intravenous | GRANULOCYTEMACROPHAGE COLONY-STIMULATING FACTOR (GM-CSF) |
| Lerdelimumab CAT-152 | Trabio | Human monoclonal antibody IgG4 | Disease modifying Phase I studies ?Cancer and fibrosis Trials stopped for fibrosis after glaucoma surgery | | Transforming growth factor β 2 |
| Leronlimab        | FDA review 2018 | Humanized IgG4κ | Disease modifying HIV phase III ongoing no results published good results phase II | Subcutaneous | Chemokine receptor 5 (CCR5) |
| PRO-140           |            |                  |                     |                |        |
| Lesofavumab RG70026 |            | Human monoclonal antibody IgG1κ | Disease modifying Influenza A | No studies clinical trials or PubMed | Hemagglutinin HA |
| Letolizumab       |            | Humanized synthetic light chain variable region (scFv) | Disease modifying inflammatory diseases | No studies clinical trials or PubMed or creative labs | TRAP |
| Lexatumumab HGS1018 | HGS-ETR2 | Human monoclonal antibody IgG1λ | Antineoplastic Breast Pancreatic | Intravenous | Tumor necrosis factor receptor superfamily member 10B/death receptor 5 (TRAIL-R2) |
| Drug Name                  | Antibody Type                  | Application                          | Route  | Indications                                                                 |
|---------------------------|--------------------------------|--------------------------------------|--------|-----------------------------------------------------------------------------|
| Libivirumab               | Humanized monoclonal antibody IgG1κ | Antiinfectious                        | Oral   | Prevent disease Hep B                                                        |
|                           |                                |                                      |        | Abstract of randomized study of 50 patients                                 |
|                           |                                |                                      |        | Hepatitis B surface antigen                                                 |
| Lifastuzumab vedotin      | Humanized monoclonal antibody  | Antineoplastic                        | Intravenous | Ovarian cancer Phase 2                                                       |
| DBNIB0600A                |                                |                                      |        | Phosphate-sodium cotransporter                                              |
| Ligelizumab QGE031        | Humanized monoclonal antibody IgG1κ | Disease modifying                      | Subcutaneous | Severe asthma and chronic spontaneous urticaria phase II and III ongoing trial 2021 |
|                           |                                |                                      |        | Immunoglobulin E (IGHE)                                                     |
| Lilotomab satetraxetan    | Betalutin                        | Antineoplastic                        |        | CD37                                                                        |
|                           | Murine monoclonal antibody IgG1 | NHL 2020/phase II 2025 Diffuse Ig B-cell lymphoma 2019 |
|                           |                                |                                      |        | CD33                                                                        |
|                           |                                |                                      |        | CD37                                                                        |
|                           |                                |                                      |        | CD37                                                                        |
|                           |                                |                                      |        | CD37                                                                        |
|                           |                                |                                      |        | CD37                                                                        |
|                           |                                |                                      |        | CD37                                                                        |
|                           |                                |                                      |        | CD37                                                                        |
| Lirilumab IPH2102         | Human monoclonal antibody IgG4 | Antineoplastic                        | Intravenous | Solid and hematological cancers No good aml, squam cell head neck no good, bladder cancer ongoing? May benefit MDS |
|                           |                                |                                      |        | Kill cell immunoglobulin like (KIR2D) Block the interaction between KIR2DL-1,-2,-3 inhibitory receptors and their ligands |
| Lodelizumab LFU720        | Humanized monoclonal antibody IgG1κ | Disease modifying                      | Unknown studies in clinical trials and PubMed | Proprotein convertase subtilisin/kexin type 9 (PCSK9) |
|                           |                                |                                      |        | Canis lupus familiaris IL31                                                  |
| Lokivetmab                | Cytopoint FDA approved for dogs only | Canis monoclonal antibody IgG2κ        | Disease modifying Veterinary Clinical signs of atopic dermatitis in dogs | |
| Loncastuximab tesirine    | Chimeric monoclonal antibody IgG1κ | Antineoplastic                        | Intravenous | Diffuse large B-cell lymphoma phase II 2020                                  |
| ADCT-402                  |                                |                                      |        | CD19                                                                        |
| Lorvotuzumab mertansine   | Humanized monoclonal antibody IgG1κ | Antineoplastic                        | Intravenous | SCLC Ovarian AML phase II Wilm, rhabdomyosarcoma, Neuroblast, MPNST, Synovial sarcoma 2018 phase II |
| BB-10901 IMGN901          |                                |                                      |        | CD56                                                                        |

Continued
| Generic Drug Name            | Brand Name                                      | Type of Antibody                                      | AHFS Classification          | Dosage Form(s)  | Target                                                                 |
|------------------------------|-------------------------------------------------|-------------------------------------------------------|------------------------------|-----------------|-------------------------------------------------------------------------|
| Losatuxizumab vedotin        | ABBV-221                                         | Chimeric/humanized monoclonal antibody IgG1           | Antineoplastic               |                 | Epidermal growth factor (EGRF, ERBB1 HER1)                              |
| Lucatumumab HCD122           | Discontinued development by Novartis 2013       | Human monoclonal antibody IgG1κ                         | Antineoplastic               | Intravenous     | CD40                                                                     |
| Lulizumab pegol              |                                                  | Human monoclonal antibody                              | Disease modifying SLE         | Intravenous     | CD28                                                                     |
| Lumretuzumab RG7116 RO5479599|                                                  | Human monoclonal antibody IgG1κ                         | Antineoplastic               | Intravenous     | CD28; receptor for tyrosine-protein kinase(erbB-3, HER3)                |
| Lupartumab amadotin BAY-1129980|                                              | Human monoclonal antibody IgG                          | Phase I terminated Why?      | Intravenous     | GPI- anchored cell surface-associated protein C4.4A (LYPD3)            |
| Lutikizumab ABT981           |                                                  | Human monoclonal antibody                              | Disease modifying Osteoarthritis | Subcutaneous    | Interleukin 1 alpha/interleukin 1 beta                                  |
| Mapatumumab HGS1012          |                                                  | Human monoclonal antibody IgG4λ                         | Antineoplastic Hepatocellular no benefit Multiple myeloma Cervical cancer NSCLC no benefit NHL Bladder cancer may be beneficial |                 | Tumor necrosis factor receptor superfamily member 10A; cytokine receptor DR4 (death receptor 4 tumor necrosis receptor apoptosis-induced ligand (TRAIL-R1) |
| Margetuximab MGAH22          |                                                  | Chimeric/Humanized monoclonal antibody IgG1κ           | Antineoplastic Breast cancer Gastric cancer/GEC phase Ib/II trial | Intravenous     | erbB2/HER2                                                               |
| Marstacimab PF-06741086      |                                                  | Human monoclonal antibody IgG1λ                         | Disease modifying Bleeding with hemophilia phase II 2020 | Subcutaneous    | Tissue pathway factor inhibitor (TFPI)                                  |
| Antibody          | Type                  | Function                      | Target                                        | Route         | Notes                                                                 |
|-------------------|-----------------------|-------------------------------|-----------------------------------------------|---------------|-----------------------------------------------------------------------|
| Maslimomab        | Murine monoclonal     | Immunosuppressive             | Unknown no studies and not listed in creative lab or FDA | T-cell receptor | T-cell receptor                                                      |
| Matuzumab         | Humanized monoclonal  | Antineoplastic                | Colorectal, lung and stomach cancer weakly beneficial | Intravenous   | Epidermal growth factor receptor (EGFR)                              |
| EMD 72000         | antibody IgG1κ        |                               |                                               |               |                                                                       |
| Mavrilimumab      | Human monoclonal      | Disease modifying rheumatoid  | Arthritis phase IIb good                      | Subcutaneous  | GMCSF receptor α-chain                                                |
| CAM3001           | antibody IgG4κ        |                               |                                               |               |                                                                       |
| MEDI565           | Fab IgG1 BiTE         | Antineoplastic                | Gastrointestinal adenocarcinoma phase I 2018  | Intravenous   | CD3 and CEA                                                           |
| MT111 AMG211      |                       |                               |                                               |               |                                                                       |
| Mepolizumab       | Human monoclonal IgG1κ| Disease modifying             | No benefit in eosinophilic esophagitis        | Subcutaneous  | Interleukin-5 (IL-5) antagonist                                       |
| SB-240563         |                       |                               | Beneficial allergic severe asthma            |               |                                                                       |
| Metelimumab       | Humanized monoclonal  | Disease modifying             | Scleroderma                                   | Dropped from further development | TGF β 1                                                               |
| CAT 192           | antibody IgG4         |                               |                                               |               |                                                                       |
| Milatuzumab       | Humanized monoclonal  | Antineoplastic                | Multiple myeloma                              | Intravenous   | CD74                                                                  |
| HLL1 IMMU-115     | antibody IgG1κ        |                               | Lupus Leukemia                                |               |                                                                       |
| Minretumomab      | Murine monoclonal     | Diagnostic                    | Tumor detection/diagnostic/prognostic         | Tumor-associated glycoprotein 72 (TAG-72) |                                                                       |
| MOAB CC49         | antibody IgG1         |                               | Failed phase I clinical trials               |               |                                                                       |
| Mirikizumab       | Humanized monoclonal  | Disease modifying             | Psoriasis phase III 2020                      | Intravenous   | IL23A                                                                |
| LY3074828         | antibody              |                               | UC phase III 2023                            |               |                                                                       |
| Mirvetuximab      | Chimeric monoclonal   | Antineoplastic                | Ovarian phase III 2019                        | Intravenous   | Folate receptor alpha                                                 |
| soravtansine      | antibody IgG1         |                               | Breast ca phase II 2020                       |               |                                                                       |
| M9346A            |                       |                               |                                               |               |                                                                       |
| IMGN853           |                       |                               |                                               |               |                                                                       |
| Mitomomab         | Murine monoclonal     | Antineoplastic                | SCLC phase III no benefit 2005                | GD3 ganglioside|                                                                       |
| BEC-2             | antibody              |                               |                                               |               |                                                                       |
| Modotuximab       | Chimeric monoclonal   | Antineoplastic                | Colorectal                                    | Subcutaneous  | EGFR extracellular domain III/HER1                                    |
| 1024 DS Zatuximab | antibody IgG1κ        |                               | Colorectal Phase 2019                         |               |                                                                       |
| Futuximab SYM004  |                       |                               | Phase 2019 Phase III 2025                     |               |                                                                       |
| Minretumomab      |                       |                               |                                               |               |                                                                       |
| Generic Drug Name | Brand Name          | Type of Antibody                        | AHFS Classification                                                                 | Dosage Form(s) | Target                                                                 |
|------------------|---------------------|-----------------------------------------|--------------------------------------------------------------------------------------|----------------|-------------------------------------------------------------------------|
| Mogamulizumab    | Poteligeo           | Humanized monoclonal antibody IgG1κ     | Antineoplastic                                                                       | Intravenous    | CC chemokine receptor CCR4                                              |
| AMG761           | FDA 2018            |                                         | Adult T-cell leukemia/lymphoma                                                        |                |                                                                         |
| KM8761           |                     |                                         | Solid tumors                                                                         |                |                                                                         |
|                  |                     |                                         | Many studies ongoing                                                                 |                |                                                                         |
| MOR202           | MOR03087            | Human monoclonal antibody IgG1          | Antineoplastic multiple myeloma phase I 2018                                          | Intravenous    | CD38                                                                    |
| NN8765           |                     |                                         |                                                                                      |                |                                                                         |
| IPH2201          |                     |                                         |                                                                                      |                |                                                                         |
| Monalizumab      |                     | Humanized monoclonal antibody IgG4κ     | Disease modifying                                                                     | Intravenous    | Killer cell lectin-like receptor subfamily C member1 (NKG2A, CD159A, CD94) that recognize nonclassical HLA (i.e., HLA-E) |
| NN8765           |                     |                                         | Rheumatoid arthritis, antineoplastic gynecologic malignancies, and other cancers phase II 2021 |
|                   |                     |                                         | NSCLC phase II 2022                                                                  |                |                                                                         |
|                   |                     |                                         | s/p stem cell transplant phase I 2020                                                |                |                                                                         |
|                   |                     |                                         | CLL phase II 2019                                                                    |                |                                                                         |
| Morolimumab      |                     | Human monoclonal antibody IgG1          | ?Diagnostic                                                                           | No studies in pub med, creative lab or FDA substance | Rhesus factor |
| Mosunetuzumab    |                     | Humanized monoclonal antibody IgG1κ bispecific | Antineoplastic                                                                       | Intravenous    | CD3E, MS4A1, CD20                                                     |
| RG7828           |                     |                                         | NHL phase II 2023                                                                    |                |                                                                         |
| BTCT4465A        |                     |                                         | DLBCL phase II 2023                                                                  |                |                                                                         |
| Motavizumab      | Numax               | Humanized monoclonal antibody IgG1κ     | Disease modifying                                                                     | Intramuscular   | Respiratory syncytial virus glycoprotein F                              |
| MEDI-524         | FDA not approved 2010 |                                         | Respiratory syncytial virus phase III completed                                       |                |                                                                         |
|                  |                     |                                         | Safety concerns hives and allergic reactions                                          |                |                                                                         |
| Moxetumomab      | Lumoxiti            | Recombinant immunotoxin comprised of a variable fragment (Fv) of a Murine IgG4 anti-CD22 monoclonal antibody genetically Fused to a truncated fragment of Pseudomonas exotoxin A | Antineoplastic Hairy cell leukemia Phase I ALL peds | Intravenous    | CD22                                                                    |
| **Muromonab-CD3** | **Orthoclone OKT3** | **Humanized monoclonal antibody IgG2κ** | **Disease modifying** | **Intravenous** | **CD3** |
|-------------------|-------------------|--------------------------------------|----------------------|---------------|---------|
| **Muromab**       | **FDA 1986**      | **Prevention of kidney transplant rejection** | **Oral**            |               |         |
| **Aka teplizimab**| **EU 1986**       | **Many trials GVHD, NASH and T2DM, giant cell myocarditis AbATE** |               |               |         |
| **MGA031**        | (country specific approval) | | | | |

| **Nacolomab tafenatox** | **Murine monoclonal fragment Fab** | **Antineoplastic** | **No studies in clinical trial or PubMed** | **C242 antigen** |
|------------------------|----------------------------------|-------------------|------------------------------------------|-----------------|
| **MT203**              |                                   |                   |                                          |                 |

| **Namilumab MT203** | **Human monoclonal antibody IgG1κ** | **Disease modifying** | **Subcutaneous** | **Colony-stimulating factor 2 (CSF2)** |
|---------------------|------------------------------------|----------------------|-----------------|----------------------------------------|
| **C242 antigen**    |                                    |                      |                 |                                        |

| **Naptumomab estafenatox** | **Murine monoclonal antibody fragment Fab** | **Antineoplastic** | **Intravenous** | **Tumor-associated antigen 5T4** |
|---------------------------|-----------------------------------------------|-------------------|---------------|-------------------------------|
| **TTS-CD3**               | **Non-small cell lung carcinoma, renal cell carcinoma phase III completed primary endpoint not achieved** | | | |
| **ANYARA**                | **ABR-217620**                                |                   |               |                               |

| **Naratuximab emtansine IMGN529** | **Chimeric monoclonal antibody IgG1κ** | **Antineoplastic** | **Intravenous** | **Tetraspanin-26 (CD37)** |
|-----------------------------------|----------------------------------------|-------------------|---------------|--------------------------|
| **IMGN529**                       | **B-Cell lymphoma NHL**                |                   |               |                           |

| **Narmatumab IMC-RON-8 Ron8** | **Human monoclonal antibody IgG1κ** | **Antineoplastic** | **Intravenous** | **Human cell surface receptor RON (CD 135) macrophage-stimulating 1 receptor** |
|---------------------------------|-------------------------------------|-------------------|---------------|--------------------------------------------------------------------------------|
| **Ron8**                        |                                    |                   |               |                                                                               |

| **Natalizumab Antegran Antegren** | **Humanized monoclonal antibody IgG4κ** | **Disease modifying** | **Intravenous** | **C4 selectin (CD62L) α4-subunit of α4β1 and α4β7 integrins of leukocytes (except neutrophils) (VLA-4)** |
|-----------------------------------|----------------------------------------|----------------------|---------------|--------------------------------------------------------------------------------|
| **Tysabri FDA 2004 EU 2006**      | **Relapsing multiple sclerosis, Crohn's disease** | | | | |

| **Navicixizumab OMP 305B83** | **Humanized/chimeric monoclonal antibody IgG2κ** | **Antineoplastic** | **Intravenous** | **Delta-like 4 (DLL4) Vascular endothelial growth factor A (VEGF-A)** |
|---------------------------|---------------------------------------|------------------|---------------|-----------------------------|
| **CT-P27**                | **Phase I study colorectal gyn tumors** |                   |               |                             |

| **Navivumab CT-P27** | **Human monoclonal antibody IgG1κ** | **Disease modifying** | **No studies PubMed** | **Influenza A virus hemagglutinin HA** |
|---------------------|-----------------------------------|----------------------|-----------------------|---------------------------------------|

| **Naxitamab HU3F8** | **Humanized monoclonal antibody IgG3** | **Antineoplastic** | **?Intravenous** | **c-Met Ganglioside anti-GD2** |
|---------------------|----------------------------------------|-------------------|-----------------|-------------------------------|
|                      | **High-risk neuroblastoma and refractory osteomedullary disease study 2023** | | | |

| **Nebacumab** | **Humanized monoclonal antibody IgM** | | **Withdrawn for safety, Efficacy and commercial reasons** | **Endotoxin** |
|---------------|--------------------------------------|-----------------|------------------------------------------------|--------------|

*Continued*
| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target                  |
|-------------------|------------|------------------|---------------------|----------------|-------------------------|
| Necitumumab IMC-11F8 | Portrazza FDA 2015 EU 2016 | Human monoclonal antibody IgG1κ | Antineoplastic Non small cell lung carcinoma | Intravenous | EGFR                    |
| Nemolizumab CIM331 CD14152 | | Humanized monoclonal antibody IgG2κ | Disease modifying Eczema phase I and II | Subcutaneous | Interleukin-31 receptor A (IL31RA) |
| NEOD001 Birtamimab ELT1-01 HU2A4 | | Humanized monoclonal antibody IgG1κ | Disease modifying Primary systemic amyloidosis lack clinical benefit | Intravenous | Amyloid A protein/ amyloid light chain |
| Nesvacumab REGN910 SAR307746 | | Human monoclonal antibody IgG1κ | Antineoplastic Solid tumors not as beneficial as other agents in breast cancer Disease modifying Macular degeneration | Intravenous | Angiopoietin 2 |
| Netakimab | | Chimeric monoclonal antibody | Disease modifying Psoriasis PLANETa study (Russia, future EU and China) Disease modifying Macular degeneration | | Interleukin 17A |
| Nimotuzumab Theracim Teraloc | | Humanized monoclonal antibody IgG1κ | Antineoplastic Squamous cell carcinoma, head and neck cancer, nasopharyngeal cancer, glioma | Intravenous | EGFR |
| Nirsevimab MEDI8897 | | Human monoclonal antibody IgG1κ | Disease modifying Respiratory syncytial virus phase II 2018 | Intramuscular | Respiratory syncytial virus fusion protein (RSVFR) |
| Antibody | Trade Name | FDA Approval | Type | Target | Function |
|----------|------------|--------------|------|--------|----------|
| Nivolumab | Opdivo | FDA 2015 EU 2015 | Human monoclonal antibody IgG4 immunoglobulin | Antineoplastic agent Programmed death receptor-1 (PD-1) blocking antibody | NSCLC, bladder cancer, renal cell cancer phase III 2021 Hodgkin lymphoma Melanoma Small cell lung cancer Squamous carcinoma head and neck Colorectal cancer GBM no added benefit 2017 |
| Nofetumomab merpentan | Verluma | FDA 1996 No longer marketed in USA | Murine monoclonal fragment IgG2κ Fab | Cancer diagnostic imaging SCLC | |
| Obiltoxaximab ETI-204 | Anthim | FDA 2016 | Chimeric monoclonal antibody IgG1κ | Disease modifying Bacillus anthracis anthrax phase IV 2021 | Intravenous Intra muscular Bacillus anthracis spores PA component of B. anthracis toxin |
| Obinutuzumab GA101HUMAB RG7159 RO5072759 Afutuzumab | Gazyvaro | FDA 2013 | Humanized monoclonal antibody IgG1κ | Antineoplastic lymphoma phase II (MCL, DLBCL) Chronic lymphocytic leukemia Phase II 2021 | Intravenous | CD20 Induces B-cell apoptosis |
| Ocaratuzumab LY2469298 AME-133V | Ocrevus | FDA 2017 | Humanized monoclonal antibody IgG1κ | Antineoplastic NHL Pemphigus phase III | Intravenous | CD20 |
| Ocrelizumab | | | Humanized monoclonal antibody IgG1κ | Disease modifying Multiple sclerosis | Intravenous | CD20 |
| Odulimomab | | | Murine monoclonal antibody | Disease modifying Transplant rejection Only studied in mice | | Lymphocyte function-associated antigen-1 (LFA-1 (CD11a)) |
| Ofatumumab | Arzerra | FDA 2009 EU 2010 | Human monoclonal antibody IgG1κ Complement-dependent cytotoxicity (CDC) | Antineoplastic CLL Phase III 10% ORR after ritux Phase II as first line 86% ORR With CHOP 100% ORR with 62% CR | Intravenous | CD20 |
| Olaratumab IMC3G3 | Lartruvo | FDA 2016 EU 2016 | Human monoclonal antibody IgG1κ | Antineoplastic Sarcoma phase II 2023 Ovarian not beneficial | Intravenous | Platelet derived growth factor receptor alpha (PDGF-Rα) |

Continued
| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|----------------|--------|
| Oleclumab MEDI9447 |            | Human monoclonal antibody IgG1λ | Antineoplastic pancreatic phase II 2021 Colorectal cancer Bladder cancer phase I 2020 Breast cancer phase II 2022 NSCLC phase II 2022 | Intravenous? | 5′-nucleotidase CD73 |
| Olokizumab | Xolair | Humanized monoclonal antibody IgG4κ | Disease modifying rheumatoid arthritis Phase I 2014 phase IIb modified results IL6 | Subcutaneous | IgE Fc region |
| Omalizumab | Xolair | Humanized monoclonal antibody IgG1κ | Disease modifying allergic asthma Urticaria | Subcutaneous | IgE Fc region |
| Omburtamab |            | Murine monoclonal antibody IgG1κ | Antineoplastic Neuroblastoma Phase III 2022 Intracerebroventricular treatment | CD276 | |
| OMS721 |            | Human monoclonal antibody | Disease modifying Atypical hemolytic uremic syndrome phase III 2020 Lupus nephritis phase II 2018 | Intravenous | Mannan-binding lectin-associated serine protease-2 (MASP-2) |
| Onartuzumab PRO143966 RO5490258 METMAB |            | Humanized monoclonal antibody IgG | Antineoplastic | Intravenous | Human scatter factor receptor kinase |
| Ontuxizumab MORAB-004 |            | Chimeric/humanized monoclonal antibody | Antineoplastic No clinical response | Intravenous | Endosialin tumor endothelial marker-1 (TEM1) |
| Onvatilimab |            | Human monoclonal antibody IgG1κ | Disease modifying multiple sclerosis Phase II 2020 | Nothing in PubMed | Vista (V-domain immunoglobulin suppression of T activation (VSIR)) |
| Opicinumab BIIB033 |            | Human monoclonal antibody IgG1 | Disease modifying multiple sclerosis Phase II 2020 | Intravenous | Leucine-rich repeat and immunoglobulin domain containing neurite outgrowth inhibitor receptor interacting protein-1 (LINGO-1) LINGO-1 |
| Drug Name | Other Names | Type | Target | Application |
|-----------|-------------|------|--------|-------------|
| Oportuzumab | Vicinium Proxinium | Humanized monoclonal antibody fragment scFv | Antineoplastic | Intravesical |
| | VB4-845 | Bladder phase III | Head and neck cancer | | Epithelial cell adhesion molecule (EPCAM) and tumor-associated calcium signal transducer 1 (TACSTD1) and pseudomonas exotoxin A immunotoxin fusion protein (anti-EPCAM antibody fragment-Pseudomonas exotoxin fusion protein) |
| Oregovomab | OvaRex | Murine monoclonal antibody IgG1κ | Antineoplastic | Subcutaneous |
| | MAB-B43.13 | Antiidiopathic antibody to ovarian antigen CA-125 | Ovarian cancer | Intravenous |
| | | Not effective in achieving increase RFS or OS | Ovarian phase I 2021 Phase II 2019 | CA-125 |
| Orticumab | Human monoclonal antibody fragment Fab | Disease modifying | Antinflammatory | Oxidized low-density lipoprotein oxLDL |
| | RG7418 | | | |
| Otelixizumab | Chimeric humanized monoclonal antibody IgG1 | Disease modifying | Diabetes mellitus type 1 | Subcutaneous |
| | | | TTedd phase II | CD3 |
| | | | DEFEND-1 phase III failed | |
| | | | DEFEND-2 phase III- no real benefit | |
| Ottilimab | Human monoclonal antibody IgG1λ | Disease modifying | Osteoarthritis, rheumatoid arthritis phase II 2012 Multiple sclerosis phase II 2014 | Intravenous |
| | MOR103 GSK3196165 | | | Granulocyte-macrophage colony-stimulating factor (GMCSF) |
| Otlertuzumab | Humanized monoclonal antibody IgG fragment | Antineoplastic | CLL phase I and II 2014 and 2019 | Intravenous |
| | TRU-016 | | | CD37 |
| Oxelumab | Human monoclonal antibody IgG1κ | Disease modifying | Asthma mainly preclinical mice Many clinical studies ongoing leukemia and asthma | Intravenous |
| | OX40L R4930 HUMAB OX40L | | OX-40 (CD252) | |
| Ozanezumab | Humanized IgG1 | Disease modifying | ALS phase II 2015 ALS no good | Intravenous |
| | GSK1223249 | | | Neurite outgrowth inhibitor (NOGO-A) |
### TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont’d

| Generic Drug Name | Brand Name                  | Type of Antibody          | AHFS Classification | Dosage Form(s) | Target                                      |
|-------------------|-----------------------------|----------------------------|---------------------|----------------|---------------------------------------------|
| Ozoralizumab      | ATN 103                     | Humanized monoclonal antibody | Disease modifying  | Subcutaneous   | TNF-α                                       |
|                   |                             |                            | Rheumatoid arthritis phase II 2012 |
| Pagibaximab       |                             | Chimeric monoclonal antibody | Disease modifying  | Intravenous    | Lipoteichoic acid                           |
|                   |                             |                            | Staph sepsis low birth weight infants Phase II/III studies 2010 |
| Palivizumab       | Synagis, Abbosynagis FDA 1998 EU 1999 | Humanized monoclonal antibody IgG1κ | Disease modifying  | Intramuscular | F protein of respiratory syncytial virus |
|                   |                             |                            | RSV many phase III studies |
| Pamrevlumab FG-3019|                             | Human monoclonal antibody IgG1κ | Disease modifying  | Connective tissue growth factor (CTGF) |
|                   |                             |                            | Idiopathic pulmonary fibrosis (IPF), Antineoplastic |
|                   |                             |                            | Pancreatic cancer |
|                   |                             |                            | Muscular dystrophy phase II 2021 |
|                   |                             |                            | Diabetes nephropathy |
| Panitumumab       | Vectibix FDA 2006 EU 2007   | Human monoclonal antibody IgG2κ | Antineoplastic  | Intravenous | EGFR/erbB-1/HER1 |
|                   |                             |                            | Metastatic colorectal cancer |
| PankoMab-GEX Gatifotuzumab | Humanized monoclonal antibody IgG1κ | Antineoplastic | Intravenous | Tumor-specific glycosylation of MUC1 |
| Panobacumab 11 AR-101 KBPA-101 | Human monoclonal antibody | Antimicrobial Pseudomonas aeruginosa infection | Intravenous | Pseudomonas aeruginosa serotype O11 |
| MAb/MAb | Description | Therapy | Notes |
|---------|-------------|---------|-------|
| **Parsatuzumab**<br>MEGF0444A<br>RG-7414 | Human monoclonal antibody IgG1κ | Antineoplastic | Epidermal growth factor-like domain 7 (EGFL7) |
| **Pascolizumab**<br>Pascolizumab<br>RG7415<br>PRO283698<br>MLTA3698A | Humanized monoclonal antibody | Disease modifying | IL-4 |
| **Pasotuxizumab**<br>Pasotuxizumab | Chimeric/humanized monoclonal antibody fragment | Antineoplastic | No studies | Folate hydrolase/prostate-specific membrane antigen (PSMA) |
| **Pateclizumab**<br>RG7415<br>PRO283698<br>MLTA3698A | Humanized monoclonal antibody IgG1κ | Disease modifying rheumatoid arthritis<br>Phase II not as efficacious as adalimumab but had response | Subcutaneous | Lymphotoxin-α |
| **Patritumab**<br>AMG888<br>U3-1287 | Human monoclonal antibody IgG1κ | Antineoplastic | ErbB3 (HER3) |
| **Spartalizumab**<br>PDR001 | FDA review possible 2019<br>Humanized monoclonal antibody | Antineoplastic | Intravenous | PD1, PDCD1, CD279 |
| **Pembrolizumab**<br>MK-3475 | Keytruda<br>FDA 2014<br>EU 2015<br>FDA 2018 for metastatic Merkel cell carcinoma, HCC, NSCLC<br>Humanized monoclonal antibody IgG4κ<br>Humanized monoclonal antibody | Antineoplastic<br>Squamous carcinoma trachea, NSCLC, urothelial (HCC phase II)<br>Melanoma chL, LgB cell lymph<br>Gastric cancer<br>Cervical cancer<br>Hepatocellular carcinoma<br>Intravenous<br>Trials for multiple myeloma discontinued by FDA | PD-1 |
| **Pemtumomab**<br>HMFG1 antibody labeled with 90Yttrium | Murine monoclonal antibody<br>Theragyn | Antineoplastic<br>Phase III Europe 2009/US 2013 no benefit after 3.5 years follow-up | MUC1/human milk fat globule antigen 1 (HMFG1) |
| **Perakizumab** | Humanized monoclonal antibody IgG1κ | Disease modifying psoriatic arthritis<br>Phase I discontinued | IL 17A |

*Continued*
| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|----------------|--------|
| Pertuzumab | Perjeta |
| FDA2012 | EU 2013 |
| Odmitarg | Humanized monoclonal antibody IgG1 |
| | | Antineoplastic agent |
| | Breast cancer |
| | HER2-positive metastatic breast cancer |
| | Gastric/breast cancer |
| | Phase III gastric |
| | | Intravenous |
| | Extracellular dimerization domain (subdomain II) of the human epidermal growth factor receptor 2 protein (HER2/neu) |
| Pexelizumab | Humanized scFv |
| | Disease modifying acute myocardial infarctions |
| | APEX-AMI trial negative results |
| | PRIMO-CABG I and II trials no significant benefit |
| | C5 |
| Pidilizumab | CT-011 |
| | Humanized monoclonal antibody IgG1κ |
| | Antineoplastic |
| | Mult myeloma |
| | DLBCL |
| | Pontine glioma |
| | Pancreas |
| | Melenaoma |
| | HCC |
| | Antineoplastic |
| | | Intravenous |
| | PD-1 |
| Pinatuzumab vedotin | Humanized monoclonal antibody ADC consisting of the microtubule-disrupting agent, monomethyl auristatin E (MMAE), conjugated to an anti-CD22 mAb via the protease-cleavable peptide linker maleimidocaproylvaline-citrulline(vc)-p-aminobenzoyloxy carbonyl |
| | Antineoplastic B-cell NHL |
| | Phase I study good response |
| | Phase II completion 2019 |
| | Intravenous |
| | CD22 |
| Pintumomab | Murine monoclonal antibody |
| | Not therapeutic |
| | Diagnostic imaging |
| | Adenocarcinoma antigen |
| Placulumab | Human monoclonal antibody V-kappa2 FC |
| | Disease modifying pain and inflammatory diseases |
| | Development discontinued |
| | 2012 |
| | Human TNF |
| Plozalizumab | Withdrawn by company | Humanized monoclonal antibody IgG1κ | Disease modifying | Intravenous | CC chemokine receptor 2 (CCR2) |
| MLN1202 HU1D9 | | | Diabetic nephropathy and arteriovenous graft patency | RA no benefit |

| Pogalizumab | MOXR0916 R07021608 Vonlerolizumab | Humanized monoclonal antibody IgG1κ | Antineoplastic | Intravenous | Tumor necrosis factor receptor superfamily member 4 (ACT35, OX40, CD134) |
| | | | Solid tumors phase I 2019 may be safe but may not be effective | No formal manuscripts yet |

| Polatuzumab vedotin | FDA review 2018 | Humanized monoclonal antibody IgG1κ | Antineoplastic | Intravenous | CD79B |
| FCU2711 RO5541077-000 | | | NHL phase II 2019 DLBCL phase III 2023 |

| Ponezumab RN1219 PF-04360365 | Humanized monoclonal antibody IgG2 | Disease modifying Alzheimer’s disease | Intravenous | Human beta-40-amyloid Aβ40 |
| | | Safe but no clinical efficacy 2013 |

| Porgaviximab C2G4 | Chimeric monoclonal IgG1κ | Antinfectious | No known ongoing studies | Zaire ebolavirus glycoprotein |
| | | Ebola virus disease |

| Prasinezumab PRX002 RG7935 RO7046015 | Humanized monoclonal antibody IgG1κ | Disease modifying Parkinson’s disease Phase II 2021 | Intravenous | Anti-alpha-synuclein (NACP) |
| | | |

| Prezalizumab AMG-557 MEDI5872 | Humanized monoclonal antibody IgG2 | Disease modifying SLE phase II 2018 Sjogren’s | Subcutaneous | B7-related protein inducible T-cell costimulator ligand (ICOSL) |

| Priliximab cMT 412 CEN 000029 | Chimeric monoclonal antibody | Disease modifying Crohn’s disease, multiple sclerosis | IN FDA no known studies | CD4 |

| Pritoxaximab | Chimeric monoclonal antibody IgG1κ | Antiinfectious | | E. coli shiga toxin type-1 |

| Pritumumab | Human monoclonal antibody IgG1κ | Antineoplastic | Brain cancer Phase II studies in Japan, could not find literature reportedly increase survivability 10 fold | Vimentin |

*Continued*
| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|----------------|--------|
| Quilizumab        | MEMP1972A  | Humanized monoclonal antibody IgG1κ | Disease modifying Asthma phase II 2014 no great benefit Urticaria phase II 2014 no great benefit Allergic rhinitis | Subcutaneous Intravenous | M1 prime segment of membrane bound IgE (IGHE) |
| Racotumomab       | Vaxira     | Murine monoclonal antibody IgG1κ | Antineoplastic Nonsmall cell lung cancer phase III 2016 cimavax better (recombinant EGF injection) 2 more months survival over placebo Neuroblastoma phase II 2020 | Intradermal Subcutaneous | N-glycolyneuraminic acid gangliosides (NGNA ganglioside) |
| Radretumab        | F16SIP     | Human monoclonal antibody Imaging study PET | Antineoplastic Lymphoma brain mets 2012 phae I Stage III NSclC |  | Fibronectin extra domain-B |
| Rafivirumab       | CR57       | Human monoclonal antibody IgG1λ Used in cocktail and with vaccination Antiinfectious Rabies (prophylaxis) | No known studies | Rabies virus glycoprotein |
| Ralpancizumab     | RN317      | Humanized monoclonal antibody IgG2α | Disease modifying Dyslipidemia phase I 2017 |  | PCSK9 (proprotein convertase subtilisin/ kexin type 9, neural apoptosis-regulated convertase 1, NARC1, NARC-1, proprotein convertase 9, PC9) |
| Ramucirumab       | Cyramza    | Human monoclonal antibody IgG1κ | Antineoplastic Urothelial phase III done Adenocarcinoma stomach and GE junction phase II 2023 Colorectal cancer NSCLC HCC phase III 2017 no additional benefit | Intravenous | VEGF2 |
| **Target** | **Monoclonal Antibody** | **Disease/Condition** | **Route** | **Clinical Trials** | **Additional Information** |
|------------|-------------------------|-----------------------|-----------|---------------------|--------------------------|
| Nerve growth factor-β (NGF-β) | Veterinary monoclonal antibody IgG1κ canine | Disease modifying | Intravitreal | | |
| Vascular endothelial growth factor A (VEGF-A) | Humanized monoclonal fragment IgG1κ Fab | Disease modifying Macular degeneration (wet form) post market studies phase II | Intravenous | | |
| CD40 | Humanized monoclonal antibody IgG1κ | Disease modifying UC phase II 2023 | Subcutaneous | | |
| Complement C5 (C5) | Humanized monoclonal antibody IgG2/ IgG4κ | Disease modifying Paroxysmal nocturnal hemoglobinuria (PNH) Phase III 2021 similar to eculizumab, atypical hemolytic uremic syndrome phase III 2021 | Intravenous | | |
| Bacillus anthracis protective antigen | Human monoclonal antibody IgG1κ | Antiinfectious Treat inhalation anthrax | Intravenous | | |
| Myelin-associated glycoprotein | Humanized monoclonal antibody IgG1κ | Disease modifying recovery of motor function after stroke Phase II completed 2011 no benefit | Intravenous | | |
| Cytomegalovirus infection | Human monoclonal antibody | Antiinfectious Cytomegalovirus glycoprotein B ONLY STUDIES IN RATS 1994 | | | |
| Lymphocyte activation gene 3 (LAG3) CD223 | Human monoclonal antibody IgG4κ | Antineoplastic Melanoma phase II 2022 Colon cancer phase II 2022 Chordoma phase II 2020 Cannot find manuscripts but company website phase II good results Glioblastoma phase I 2020 | Intravenous | | |
| Interleukin 17 alpha, TNF-α | Human monoclonal antibody | Disease modifying RA Phase II 2016 no increased benefit over adalimumab | Subcutaneous | | |

**CHAPTER 16** Passive Monoclonal and Polyclonal Antibody Therapies

**References**

1. Tan, M., & Zhang, S. (2023). Passive Monoclonal and Polyclonal Antibody Therapies. In J. Smith (Ed.), Advanced Therapies: Delivering a Better Future. Academic Press. pp. 311-320.
| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|----------------|--------|
| Reslizumab DCP 835 | Cincair FDA 2016 EU 2016 | Humanized monoclonal antibody IgG4κ | Disease modifying Inflammations of the airways asthma completed and ongoing, skin and gastrointestinal tract, polyarteritis stage II 2018 Rhino sinusitis 2020 | Intravenous Subcutaneous | IL-5 |
| Rilotumumab AMG-102 | | Human monoclonal antibody IgG2κ | Antineoplastic Gastric completed phase III 2015 not effective NSCLC phase II 2014 no benefit Glioma phase II no response | Intravenous | Hepatocyte growth factor (HGF) |
| Rinucumab REGN2176 | | Human monoclonal antibody IgG4κ | Disease modifying neovascular age-related macular degeneration phase II 2014 | Intravitreal | Platelet-derived growth factor receptor beta |
| Risankizumab ABBV-066 BI-655066 | FDA/EU pending approval | Humanized monoclonal antibody IgG1κ | Disease modifying Crohn’s disease phase II good, phase III ongoing psoriasis phase II response better than ustekinumab, psoriatic arthritis, and asthma | Subcutaneous | IL23A |
| Rituximab GP2013 IDEC-102 RG-105 | MabThera, Rituxan FDA 1997 EU 1998 | Chimeric monoclonal antibody IgG1κ | Antineoplastic Non-Hodgkin lymphomas, chronic lymphocytic leukemias, some autoimmune disorders, i.e., rheumatoid arthritis, >2K studies ongoing | Subcutaneous | CD20 |
| Rivabazumab pegol | | Humanized monoclonal antibody fragment Fab’ IgG1κ | Antiinfectious | No studies found | Pseudomonas aeruginosa type III secretion system |
| Rmab | Rabishield Made in India | Human monoclonal antibody | Antiinfectious Postexposure prophylaxis of rabies | | Rabies virus G glycoprotein |
| Name                      | Type                                      | Phase | Tumor Type | Route | Target/Pathway                          |
|---------------------------|-------------------------------------------|-------|------------|-------|----------------------------------------|
| Robatumumab               | Human monoclonal antibody IgG1κ           |       | Antineoplastic | Intravenous | Colorectal phase II 2009 little benefit Ewings no response 2016 |
| Roledumab                 | Human monoclonal antibody IgG1κ           |       | Immunomodulation | Intravenous | RHD                                    |
| Romilkimab                | Humanized chimeric monoclonal antibody IgG4 bispecific |       | Disease modifying | Subcutaneous | Interleukin 13 and IL4                  |
| Romosozumab               | Humanized monoclonal antibody IgG2κ       |       | Disease modifying | Intravenous | Sclerostin/scleroscin SOST              |
| Rontalizumab rhuMAb IFNalpha | Humanized monoclonal antibody             |       | Disease modifying | Subcutaneous | IFN-α                                  |
| Rosman-tuzumab OMP-131R10 | Humanized monoclonal antibody IgG1κ       |       | Antineoplastic | Intravenous | Root plate-specific spondin r-spondin-3 WNT? (wingless/ integrated) |
| Rovalpituzumab tesirine SC0002 SC16LD6.5 ABBV-181 | Humanized monoclonal antibody IgG1κ |       | Antineoplastic | Intravenous | Delta-like ligand-3 (DLL3)            |
| Rovelizumab Hu23F2G LeukArrest | Humanized monoclonal antibody IgG1κ |       | Disease modifying | CD11, CD18 | Hemorrhagic shock, MI stroke phase III goals not met 2000 |
| Rozanolixizumab UCB7665    | Chimeric/humanized monoclonal antibody IgG4κ |       | Thrombocytopenia ITP phase II 2019 Myasthenia gravis phase II 2018 | Subcutaneous | Neonatal Fc receptor (FCGRT) |
| Generic Drug Name | Brand Name          | Type of Antibody                  | AHFS Classification                                                                 | Dosage Form(s)                                           | Target                                                                 |
|-------------------|---------------------|-----------------------------------|--------------------------------------------------------------------------------------|----------------------------------------------------------|----------------------------------------------------------------------|
| Ruplizumab        | Antova              | Humanized monoclonal antibody     | Disease modifying lupus and lupus nephritis not effective Life-threatening thromboembolism | BioDrugs. 2004; 18(2): 95–102. Costimulation blockade in the treatment of rheumatic diseases | CD154 (CD40L)                                                        |
| Sacituzumab       | FDA/EU pending approval | Humanized monoclonal antibody IgG1κ | Antineoplastic agent Prostate cancer phase II 2021                                   | Intravenous                                              | Tumor-associated calcium signal transducer 2 (TROP-2) inhibits topoisomerase I |
| Samalizumab       | ALXN6000            | Humanized monoclonal antibody IgG2/G4κ | Antineoplastic CLL MM phase I 2010 (terminated by sponsor) AML phase II 2021         | Intravenous                                              | OX-2 membrane glycoprotein (CD200)                                   |
| Samrotamab        | vedotin             | Chimeric/humanized monoclonal antibody IgG1κ | Antineoplastic no studies found                                                      | No studies found                                         | Leucine-rich repeat-containing protein 15 (LRRRC15)                    |
| Sarilumab         | Kevzara             | Human monoclonal antibody IgG1κ   | Disease modifying rheumatoid arthritis phase III 2015/2020/2027(preg exposure); ankylosing spondylitis Juvenile idiopathic arthritis phase II 2022 | Subcutaneous                                             | IL6                                                                 |
| Satralizumab      | SA237               | Humanized monoclonal antibody IgG2κ | Disease modifying Neuromyelitis optica phase III 2019/2020                           | Subcutaneous?                                            | IL6 receptor                                                          |
| Satumomab         | CR103               | Murine monoclonal antibody IgGk fragment Fab' | Diagnostic imaging Detection colorectal and ovarian cancer                           | Intravenous                                              | Tumor-associated glycoprotein (TAG-72)                                 |
| Secukinumab       | Cosentyx            | Human monoclonal antibody IgG1κ   | Disease modifying Uveitis, rheumatoid arthritis psoriasis phase II 2019 over 100 other studies arthritis; psoriatic psoriasis; spondylitis; ankylosing   | Subcutaneous                                             | IL 17A                                                               |
| Drug Name             | Type of Antibody | Use                                      | Route     | Other Information                                                                 |
|----------------------|------------------|------------------------------------------|-----------|-----------------------------------------------------------------------------------|
| Selicrelumab         | Human monoclonal antibody IgG2\(\kappa\) | Antineoplastic Solid tumors phase I 2020 Pancreatic cancer phase II 2020 Colon cancer phase II 2020 Mesothelioma phase I b 2015 | Subcutaneous Intravenous | Tumor necrosis factor receptor superfamily member 5 (CD40) |
| Seribantumab         | Human monoclonal antibody IgG2\(\lambda\) | Antineoplastic Breast phase II 2020 Ovarian phase I 2014 | Intravenous | Receptor tyrosine-protein kinase erbB-3 (HER3) |
| Setoxaximab          | Chimeric monoclonal antibody IgG1\(\kappa\) | Antinfectious E. coli | No known studies or clinical use | E. coli shiga toxin type-2 |
| Setrusumab           | Human monoclonal antibody IgG2 | Disease modifying Osteogenesis imperfecta phase II 2020 | Intravenous | Sclerostin (SOST) |
| Sevirumab            | Human monoclonal antibody IgG2 | Antiinfectious CMV retinitis early termination trial secondary to safety Phase II 2003 | | Cytomegalovirus infection |
| SHP647 Ontamalimab   | Human monoclonal antibody IgG2\(\kappa\) | Disease modifying Crohn’s/UC phase III 2020—2025 \(\times\) 7 Phase II study 2007 better response in UC than in Crohn (?more time needed to evaluate clinical significance | Subcutaneous | Mucosal addressin cell adhesion molecule (MADCAM) |
| Sibrotuzumab         | Humanized monoclonal antibody IgG1\(\kappa\) | Antineoplastic Colorectal cancer phase II 2003 failed Lung cancer 2001 | Intravenous | FAP |
| Sifalimumab          | Humanized monoclonal antibody IgG1\(\kappa\) | Disease modifying SLE phase II 2015 Dermatomyositis, polymyositis | Intravenous | IFN-\(\alpha\) |
| Siltuximab            | Chimeric monoclonal antibody IgG1\(\kappa\) | Antineoplastic Multiple myeloma phase II 2019 DM type I phase I 2017 Schizophrenia adjunct 2020 phase II Multicentric Castleman’s disease (MCD) with HIV negative and HHV-8 negative | Intravenous | IL-6 |
| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|---------------|--------|
| Simtuzumab        | AB0024     | Humanized monoclonal antibody IgG4κ | Disease modifying Hepatic fibrosis Phase II 2016 no benefit Pulm fibroses phase II 2017 no benefit Myelo fibr 2017 phase II | Subcutaneous | Lysyl oxidase homolog 2 (LOXL2) |
|                   | GS-6624    |                  |                     | Intravenous   |        |
| Sipilizumab       | MEDI-507   | Humanized monoclonal antibody IgG1κ | Antineoplastic | CD2 T Or NK cells |        |
| Sirtratumab       | vedotin    | Human monoclonal antibody | Antineoplastic | Nothing in PubMed or clinical trials | SLITRK6 |
| Sirukumab         | vedotin    | Human monoclonal antibody IgG1κ | Disease modifying Rheumatoid arthritis Phase III done good results | Subcutaneous | IL-6 |
| Sofituzumab       | vedotin    | Humanized monoclonal antibody | Antineoplastic Ovarian pancreatic Phase I (2014) | CA-125 |        |
| Solanezumab       | LY2062430  | Humanized monoclonal antibody IgG1 | Disease modifying Alzheimer’s Phase III study discontinued no effect In preclinical trial for secondary prevention 2022 Hereditary AD phase III 2021 | Intravenous | Beta amyloid |
| Solitomab         | MT110-011  | Murine monoclonal antibody bispecific T-cell engager (BiTE) | Antineoplastic Gastrointestinal, lung, and other cancers Phase I 2015 | Intravenous | Epithelial cell adhesion molecule (EpCAM) CD3 |
|                   | AMG1110    |                  |                     |              |        |
| Sonepcizumab      | iSONEP    | Humanized monoclonal antibody | Disease modifying Choroidal and retinal neovascularization phase II 2015 not so good Antineoplastic phase II renal cancer 2017 potential | Intravenous | Sphingosine-1-phosphate (S1P) |
|                   | LT1009     |                  |                     | Intravitreous |        |
| Stamulumab        |           | Humanized monoclonal antibody | Disease modifying muscular dystrophy Animal studies, minimal efficacy Phase I/II studies ongoing (no improvement) | Intravenous | Myostatin |
| Name               | Code                        | Type                                      | Field                                      | Status                                      |
|--------------------|-----------------------------|-------------------------------------------|--------------------------------------------|---------------------------------------------|
| Sulesomab          | IMMU-MN3 LeukoScan EU 1997  | Murine monoclonal IgG1 fragment Fab’     | Diagnostic Osteomyelitis (imaging)        | NCA-90 (granulocyte antigen)                |
| Suptavumab         | REGN2222 SAR438584          | Human monoclonal antibody IgG1κ          | Antiinfectious Medically attended lower respiratory disease phase III 2017 not meet primary endpoint Another study no data yet at 30 mg/kg dose | Intramuscular Resp sync virus fusion protein (RSVFR) |
| Sutimlimab         | BIVV009                     | Chimeric/humanized monoclonal antibody IgG4κ | Disease modifying cold agglutinin disease phase III 2020 | Intravenous Complement C1s (C1s) |
| Suvizumab          | KD-247                      | Humanized monoclonal antibody IgG1κ      | Antiinfectious HIV Phase I KD-247 2007    | Intravenous Human immunodeficiency virus glycoprotein 120 third variable loop |
| Suvratoxumab       | MEDI4893                    | Human monoclonal antibody IgG1κ          | Disease modifying Nosocomial pneumonia phase II 2018 | Intravenous Staphylococcus aureus alpha toxin |
| Tabalumab          | LY2127399                   | Human monoclonal antibody IgG4κ          | Antineoplastic Rheum arthr phase III 2013 no signif response SLE phase III 2015 endpoints not met Mult myelo phase I 2014 may not treat but be prognostic | Subcutaneous Cytokine B-cell activating factor (BAFF) |
| Tacatuzumab        | tetraxetan HAFP-31          | Humanized monoclonal antibody yttrium⁷⁷   | Antineoplastic                             | No studies in clinical trial or PubMed Alpha-fetoprotein |
| Tadocizumab        | C4G1 YM337                  | Humanized monoclonal antibody fragment IgG1κ Fab’ | Disease modifying Percutaneous coronary intervention phase I 1999 ?not further developed | Integrin αIIbβ3 |
| Talacotuzumab      | CSL362 JNJ-56022473         | Humanized monoclonal antibody IgG1-2κ    | Antineoplastic AML phase III 2018 MDS phase II 2019 SLE 2019 phase I | Intravenous Interleukin 3 receptor subunit-α (IL3Rα, CD123) |
| Talizumab          | C21/AL-90 TNX-901           | Humanized monoclonal antibody IgG1κ      | Disease modifying Peanut allergy Allergic reaction Phase II 2003 good results legal issues shelved the drug | Subcutaneous IgE |
| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|----------------|--------|
| Tamtuvetmab AT-005 | Tactress   | Canine monoclonal antibody IgG2α | Disease modifying Pain Osteoarthritis Back pain Metastatic cancer pain Phase II ~2008 | CD52 |
| Tanezumab RN624 PF-4383119 | FDA review possible 2019 | Humanized monoclonal antibody IgG2 | Disease modifying Antineoplastic Phase I glioblastoma 2020 Breast cancer phase I 2020 AMD murine no human studies found | Nerve growth factor (NGF) |
| Tanibirumab Olinvacimab TTAC-0001 | Human monoclonal antibody IgG1 | Disease modifying Antineoplastic Phase II trial NSCLC no benefit 2017 Pancreatic phase II 2017 | Intravenous | VEFR-2 |
| Taplitumomab paptox | Murine monoclonal antibody IgG1κ | Antineoplastic | No studies pub med or clinical trials | CD19 |
| Tarextumab OMP-59R5 | Human monoclonal antibody IgG2 | Antineoplastic | Intravenous | Notch2/3, Notch receptor |
| Tavolimab MEDI0562 | Chimeric/humanized monoclonal antibody IgG1κ | Antineoplastic Head and neck phase I 2024 Ovarian cancer phase II 2023 | Intravenous | Tumor necrosis factor receptor superfamily member 4 (TNFRS4) OX40L receptor (CD134) |
| Technetium (99 mTc) acritumomab | Rabbit monoclonal IgG | Not for use in humans- research purpose only | | CEA |
| Technicium (99 mTc) Fanolesomab NeutroSpec FDA2004 | Murine monoclonal IgM radiolabeled | Disease modifying osteomyelitis Sales and marketing suspended (2005) **Diagnostic scans for acute appendicitis** | Intravenous | CD15 |
| Tefibazumab INH—H2002 | Humanized monoclonal antibody IgG1κ | Antiinfectious *Staphylococcus aureus* infection Phase II 2006 | Intravenous | Clumping factor A |
| Name                      | Description                                                                 | Indication                                      | Status                                      | Target |
|---------------------------|------------------------------------------------------------------------------|-------------------------------------------------|---------------------------------------------|--------|
| Telimomab aritox (TAB-885)| Recombinant murine monoclonal antibody Fab with ricin                       | Antineoplastic T Cell lymphoma/leukemia          | No studies in pub med or clinical trials    | CD5    |
| Telisotuzumab vedotin ABT-700 | Humanized monoclonal antibody IgG1κ                                      | Antineoplastic Phase I 2017 SCLC phase II 2022 NSCLC phase II 2021 | Intravenous                               | Hepatocyte growth factor receptor HGFR |
| Tenatumomab               | Murine monoclonal antibody IgG2b                                         | Antineoplastic Phase I 2017 Phase II brain tumors 2010 | Intravenous                               | P24821, tenascin C |
| Teneliximab               | Chimeric monoclonal antibody IgG1                                        | Not in clinical trials 2009                      | CD40 (TNF receptor superfamily member 5)    |        |
| Teplizumab MGA031 PRV-031 hOKT3g1(Ala-Ala) | Humanized monoclonal antibody IgG1κ                                 | Disease modifying type I DM phase II completion AbATE trial 2019 Psoriasis phase I and II completed 2010 study stopped secondary to injection reaction severe allergy | Intravenous Subcutaneous | CD3    |
| Tepoditamab               | Human monoclonal antibody IgG1κ bispecific                                 | Antineoplastic                                  | No studies on PubMed or clinical trials    |        |
| Teprotumumab RV001 R-1507 RO4858696 HZN-001 | Human monoclonal antibody                                               | Disease modifying Thyroid eye disease phase II 2017 Graves phase III 2020 | Intravenous                               |        |
| Tesidolumab LFG316 NOV-4  | Human monoclonal antibody                                                 | Phase I 2017 PNH phase II 2020 AMD phase II 2015 not beneficial | Intravenous Intravitreous                  | C5     |
| Tetulomab tetraxetan LU-177 | Humanized monoclonal antibody                                             | Antineoplastic Animal studies 2013               | CD37                                        |        |
| Tezepelumab MEDI9929 AMG-157 | Human monoclonal antibody IgG2λ                                      | Disease modifying Asthma, atopic dermatitis Phase II 2017 | Subcutaneous                               |        |

Continued
| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|----------------|--------|
| Theralizumab      |            | Humanized monoclonal antibody | Antineoplastic Solid tumors phase I 2020 Disease modifying Rheum arth, SLE phase II | Intravenous | CD28 History of cytokine storm at higher doses 2006 |
| Tibulizumab       |            | Humanized monoclonal antibody bispecific tetravalent | Disease modifying Autoimmune disorder Phase I 2020 | Subcutaneous Intravenous | Human B-cell activating factor of the tumor necrosis factor family interleukin 17 (BAFF) |
| Tigatuzumab       | CS-1008    | Humanized monoclonal antibody IgG1κ | Antineoplastic Colon phase II 2011 no added benefit Colon phase I 2013 NSCLC phase II 2011 no benefit Pancreatic phase II 2008 benefit TN breast canc 2015 phase II no added benefit | Subcutaneous Intravenous | Cytokine receptor DR5 (death receptor 5) TRAIL-R2 |
| Tildrakizumab     | MK-3222    | Humanized monoclonal antibody IgG1κ | Immunologically mediated inflammatory disorders Mod/Severe psoriasis phase III 2018-20 | Subcutaneous | IL23 |
| Timigutuzumab     |            | Humanized monoclonal antibody IgG1κ | Antineoplastic | No studies in clinical trial or PubMed | erbB2/HER2 |
| Timolumab         | BTT-1023   | Human monoclonal antibody | Disease modifying Scler cholang phase II 2019 | Intravenous | AOC3 |
| Tiragotumab       | MTIG-7192A | Human monoclonal antibody IgG1κ | Antineoplastic Phase I 2020 NSCLC phase II 2021 HL phase II 2019 | Intravenous | T-cell IG and immune-receptor tyrosine-based inhibitory motif (TIGIT) |
| Tislelizumab       | China pending approval | Humanized monoclonal antibody | Antineoplastic NSCLC phase III 2020 Gastric phase III 2022 Esophageal cancer phase I 2021 NHL phase II 2020 | Intravenous | PCDC1, CD279 |
| **Agent**                   | **Type**                  | **Indications**                                                                 | **Route**   | **Target**                      |
|----------------------------|---------------------------|-------------------------------------------------------------------------------|-------------|---------------------------------|
| Tisotumab vedotin          | Human monoclonal antibody IgG1κ | Antineoplastic                                                                 | Intravenous | Coagulation factor III          |
|                            |                           | Ovary cancer                                                                   |             |                                 |
|                            |                           | Cervix cancer                                                                  |             |                                 |
|                            |                           | Endometrium cancer                                                             |             |                                 |
|                            |                           | Bladder cancer                                                                 |             |                                 |
|                            |                           | Prostate cancer                                                                |             |                                 |
|                            |                           | Esophagus cancer                                                               |             |                                 |
|                            |                           | Lung cancer, NSCLC                                                             |             |                                 |
|                            |                           | Squamous cell carcinoma of the head and neck                                   |             |                                 |
|                            |                           | Pancreatic phase II 2022/3                                                     |             |                                 |
| Tocilizumab                | Humanized monoclonal antibody IgG1κ | Disease modifying rheumatoid arthritis                                              | Intravenous | IL-6 receptor                   |
| MRA R-1569 RG-1569 RHPM-1  |                           | >100 studies                                                                   |             |                                 |
| R-4877533 Atlizumab        |                           | Behcet syndrome                                                               |             |                                 |
| Tomuzotuximab E-6040       | Humanized monoclonal antibody IgG1κ | Antineoplastic Phase I 2019                                                     | Subcutaneous |                                 |
| IDEC-131                   |                           | Disease modifying rheumatoid arthritis, lupus nephritis etc.                   |             | EGFR, HER1                      |
| Toralizumab                | Humanized monoclonal antibody IgG1κ | Phase II trials failed with TE                                                  |             |                                 |
| Tosatoxumab               | Human monoclonal antibody IgG1λ | Antiinfectious                                                                 | No studies PubMed or Clin trials | Staphylococcus aureus α-hemolysin |
| Tositumomab and iodine 131 | Murine monoclonal antibody IgG2αλ | Antineoplastic Follicular lymphoma (NHL) >100 studies                          | Intravenous | CD20                            |
| Tositumomab                |                           | Phase I/II 2012 Glialoblastoma limited clin activity                            |             |                                 |
| Tovetumab MEDI-575         | Human monoclonal antibody IgG2κ | Antineoplastic                                                                  | Intravenous | Platelet-derived growth factor receptor α (CD140a) |
| Tralokinumab CAT-354       | Human monoclonal antibody IgG4 | Disease modifying asthma phase IIb +/-, atopic dermatitis phase II 2016         | Intravenous | IL-13                           |
|                           |                           |                                                                                | Subcutaneous |                                 |

*Continued*
| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|----------------|--------|
| Trastuzumab 4D5v8 R-597 SYD977 | Herceptin FDA 1998 EU 2000 Herceptin Hylecta FDA 2019 — trastuzumab/hyaluronidase Herzuma 2018 | Humanized monoclonal antibody IgG1κ | Antineoplastic Breast cancer Gastric and gastro-esophageal junction cancer HER2-positive phase III | Subcutaneous Intravenous | HER2/neu |
| Trastuzumab Deruxtecan DS-8201 | Hercion FDA breakthrough therapy | Antibody drug conjugate humanized antibody IgG1κ with topoisomerase I inhibitor (DXd) | Antineoplastic breast cancer phase I study breast, gastric, colorectal, salivary, and nonsmall cell lung cancer participated in part 2 2020 phase II DESTINY-Breast01 | | HER2 |
| Trastuzumab emtansine RG-3502 PRO132365 | Kadcyla FDA2013 EU 2013 | Humanized monoclonal antibody IgG1κ as ADC | Antineoplastic Breast cancer | Intravenous | HER2/neu |
|TRBS07 | Ektomab | 3funct | Antineoplastic Melanoma | GD2 ganglioside | Tribbles-related protein (TRB) family members are the mammalian orthologs of Drosophila tribbles. Tribbles was originally identified as a cell cycle regulator during Drosophila development. Tribbles genes are evolutionary conserved, and three TRB genes (TRB1, TRB2 and TRB3) have been identified in mammals. TRBs are considered pseudokinases because they lack an ATP binding site or one of the... |
conserved catalytic motifs essential for kinase activity. Instead, TRBs play important roles in various cellular processes as scaffolds or adaptors to promote the degradation of target proteins and to regulate several key signaling pathways. Recent research has focused on the role of TRBs in tumorigenesis and neoplastic progression. In this review, we focus on the physiological roles of TRB family members in tumorigenesis through the regulation of the ubiquitin-proteasome system and discuss TRBs as biomarkers or potential therapeutic targets in cancer.

| Antibody | Type | Disease | Phase | Drug Target |
|----------|------|---------|-------|-------------|
| Tregalizumab  
BT-061 | Humanized monoclonal antibody IgG1κ | Disease modifying | Subcutaneous | | CD4 |
| Tremelimumab  
*CP-675,206  
(aka ticilimumab) | Human monoclonal antibody IgG2 | Antineoplastic agent | CTLA4 (cytotoxic T lymphocyte-associated antigen 4, CD152) |
| Trevogrumab  
REGN1033  
SAR391786 | Human monoclonal antibody IgG4κ | Disease modifying | | Myostatin, growth differentiation factor 8 (GDF8) |
| TRL3d3  
3D3 | IgG | Studies only in mice to this point | | Ati-G protein antibody (RSVG) |
| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|---------------|--------|
| Tucotuzumab       |            | Humanized monoclonal antibody IgG1 | Antineoplastic Ovarian phase II 2008 Lung, kidney, bladder phase I 2000 no benefit | Intravenous | Interleukin2 (EpCAM) |
| Tuvirumab         |            | Humanized monoclonal antibody     | Antiinfectious     | Intravenous   | Hepatitis B virus surface antigen |
| Ublituximab       | FDA review pending 2019 | Chimeric monoclonal antibody IgG1κ | Antineoplastic Chronic lymphocytic leukemia, follicular cell lymphoma phase II 2020 Disease modifying Multiple sclerosis phase II 2019, phase III 2021 Awaiting result looks good prelim | Intravenous | CD20 MS4A1 |
| Ulocuplumab       |            | Human monoclonal antibody IgG4    | Antineoplastic CLL phase I 2014 Phase I/II Waldenstrom macroglobulinemia 2025 Phase I/II AML 2021 | Intravenous | CXCR4 (CD184) |
| Urelumab          |            | Human monoclonal antibody IgG4κ   | Antineoplastic CLL phase II 2020 Solid tumors phase II 2023 | Intravenous | Human receptor 4-1BB (CD137) |
| Urtoxazumab       |            | Humanized monoclonal antibody IgG1κ | Disease modifying EHEC animal studies | Subcutaneous | Escherichia coli (EHEC) shiga toxin 2 |
| Ustekinumab       | Stelara FDA 2009 EU 2009 | Human monoclonal antibody IgG1κ | Disease modifying Crohn disease Plaque psoriasis Psoriatic arthritis | Intravenous | p40 subunit of interleukin 12 (IL-12p40), IL-23 |
| Utomilumab        |            | Human monoclonal antibody IgG2    | Antineoplastic Diffuse large B-cell lymphoma Phase I 2021 phase II 2020 Breast phase II 2025 | Intravenous | 4-1BB (CD137) |
| Drug Name                  | Monoclonal or Polyclonal Antibody | Biological Target | Clinical Indication                                      | Route of Administration | Effect \(k\) |
|---------------------------|----------------------------------|-------------------|----------------------------------------------------------|--------------------------|--------------|
| Vadastuximab              | Chimeric monoclonal antibody IgG1\(k\) | Antineoplastic    | Acute myeloid leukemia phase II 2017 phase III 2017 MDS phase II 2017 | Intravenous              | CD33         |
| Vanalimab Vanucizumab     | Humanized monoclonal antibody IgG1\(\lambda\) | Antineoplastic?   | No studies clinical trial or PubMed                      | Intravenous              | STEAP1       |
| Mitazalimab Vantictumab   | Humanized monoclonal antibody IgG2mab | Antineoplastic    | Prostate cancer                                          | Intravenous              | Frizzled receptor |
| Vandalotuzumab Vedolizumab| Humanized monoclonal antibody IgG1\(k\) | Antineoplastic    | NSCLC, breast phase I 2017                               | Intravenous              | Angiopoietin 2/vascular endothelial growth factor A |
| Vapaliximab               | Chimeric monoclonal antibody IgG2\(\kappa\) | No studies in PubMed or clinical trials | Vascular adhesion protein AOC3 (VAP-1)                    |                          |              |
| Varisacumab               | Human monoclonal antibody IgG1\(k\) | No studies in PubMed or clinical trials | VEGF-A                                                    |                          |              |
| Varilumab                 | Human monoclonal antibody IgG1\(k\) | Antineoplastic    | Solid tumors and hematologic malignancies Phase I 2017, phase II 2019/20 Melanoma phase II 2018/21 | Intravenous              | CD27         |
| Vatelizumab               | Humanized monoclonal antibody IgG4 | Disease modifying | UC phase II 2016 MS phase II 2016 withdrawn lack of efficacy |                          | A2\(\beta1\) integrin I domain ITGA2 (CD49b) |
| Vedolizumab LDP02 MLN02   | Humanized monoclonal antibody IgG1\(k\) | Disease modifying | Crohn disease Ulcerative colitis In CD resolution extraintestinal manifestations | Intravenous              | Integrin \(\alpha4\beta7\) Selectively blocks trafficking of Memory T cells to inflamed gut tissue by inhibiting \(a4b7\)-mucosal addressin cell adhesion molecule-1 (MAd-CAM-1) interaction |
| Generic Drug Name | Brand Name | Type of Antibody | AHFS Classification | Dosage Form(s) | Target |
|-------------------|------------|------------------|---------------------|----------------|--------|
| Veltuzumab IMMU-106 HA20 | | Humanized monoclonal antibody IgG1κ | Antineoplastic Non-Hodgkin’s lymphoma phase II 2013 ITP phase II 2016 | Subcutaneous | CD20 |
| Vepalimomab | | Murine monoclonal antibody | | | AOC3 (vascular adhesion protein-1) |
| Vesencumab MNRP1685A | | Human monoclonal antibody IgG1mab | Antineoplastic Solid malignancies Phase I 2011 proteinuria | | Neuropilin1 (NRP1) |
| Visilizumab Nuvion | | Humanized monoclonal antibody IgG2 | Disease modifying Prevent GVHD Not effective in UC | | CD3 |
| Vobarilizumab | | Humanize monoclonal scFv | Disease modifying inflammatory autoimmune diseases | Nothing in PubMed | IL6R |
| Volociximab M200 | | Chimeric monoclonal antibody IgG4κ | Antineoplastic Solid tumors NSCLC phase I/II 2010 Disease modifying phase I AMD terminated no results | | Integrin α5β1 |
| Vopratelimab JTX-2011 | | Humanized monoclonal antibody IgG1κ | Antineoplastic Solid tumors phase II 2022 | Intravenous | Inducible T-cell costimulator (ICOS) |
| Vorsetuzumab mafodotin H1F6 SGN-70 | | Humanized monoclonal antibody | Antineoplastic Phase I 2017 | Intravenous | CD70 |
| Votumumab | HumaSPECT Diagnostic EU 1998 Withdrawn from market 2003 | Human monoclonal antibody | Diagnostic | Human colon cancer imaging | Tumor antigen Cytokeratin tumor-associated antigen (CTAA16.88) |
| Antibody Name     | Type                                    | Disease Type                  | Phase | Route          | Published Information                                                 |
|-------------------|-----------------------------------------|-------------------------------|-------|----------------|-----------------------------------------------------------------------|
| Vunakizumab (SHR-1314) | Humanized monoclonal antibody IgG1     | Disease modifying Psoriasis   | Phase II 2019 | Subcutaneous | Interleukin 17 alpha                                                  |
| Xentuzumab (BI-836845) | Humanized monoclonal antibody          | Antineoplastic Breast, prostate, solid | Phase I 2019 | Intravenous   | Insulin-like growth factor (IGF1, IGF2)                              |
| XMAB-5574         | Humanized monoclonal immunoglobulin fragment κ Fc | Antineoplastic Diffuse large B-cell lymphoma | Phase II 2015/18/19/22, Phase III 2022 | Intravenous | CD19                                                                   |
| Zalutumumab 2F8 (HUMAX-EGFR) | Human monoclonal antibody            | Antineoplastic Squamous cell carcinoma of the head and neck | Phase II 2011, Phase III 2016 | Intravenous | EGFR                                                                   |
| Zanolimumab       | Humanized monoclonal antibody IgG1κ    | Antineoplastic CTCL           | Phase II good results Phase III suspended by company? | Intravenous | CD4                                                                   |
| Zenocutuzumab     | Humanized monoclonal antibody IgG1 bispecific epidermal growth factor receptors her2,her3 | Antineoplastic               | ERBB3, HER3 |                |                                                                       |
| Ziralimumab       | Human monoclonal antibody IgM          | Disease modifying immunosuppressive | No studies clinical trials or PubMed | CD147 (basigin) |                                                                       |
| Zolbetuximab IMAB362 | Chimeric monoclonal antibody IgG1κ ADCC enhance antibody | Antineoplastic gastric cancer | Phase I, IIb, Phase III 2023 | Intravenous | Claudin protein (CLDN18.2)                                            |
| Zolimomab aritoxy H65-RTA ZX-CD5 | Orthoyme CD 5 plus Human monoclonal antibody IgG1 | Disease modifying             | Not effective in preventing GVHD 1994 | CD5 |                                                                       |

Auristatins are water-soluble dolastatin analogs of dolastatin 10. Dolastatin 10 belongs to dolastatin family and it can powerfully bind to tubulin, thus inhibiting polymerization mediated through the binding to the vinca alkaloid-binding domain, and causes cell to accumulate in metaphase arrest.
Ankylosing Spondylitis
Certolizumab pegol is also approved for use with ankylosing spondylitis.

Systemic Lupus Erythematosus
Belimumab (Benlysta) is a human Mab (IgG1) that binds to B-cell activating factor and acts as a B-lymphocyte stimulator-specific inhibitor. It was approved by the FDA in 2011 for treatment of adult patients with active, autoantibody-positive SLE receiving standard therapy. This medication also decreases episodic frequency of lupus nephritis.281–283

Cardiovascular Disease
Despite marked improvement in survival from cardiovascular disease, this illness remains the number one cause of mortality in the US. This process causes injury to the endothelium of blood vessels of the heart secondary to toxins, accumulation of cholesterol, or chronic low-grade inflammation. Treatment has been preventive, primarily during actual injury or following injury. Therapies involve changes in behavior (diet, exercise, and cessation of tobacco use), pharmacologic to control contributing underlying illness (hypercholesterolemia, hypertension, diabetes type I and II), to diminish injury through thrombolytics, stents, vasodilators, supplemental oxygen, or to control sequelae of infarctions (cardiac dysfunction/failure). Passive antibody therapies are being tried to decrease the effects of some of the contributing factors of atherosclerotic plaque formation.

Abciximab (ReoPro) is a chimeric recombinant monoclonal fragment (IgG1 Fab') with specificity to platelet glycoprotein Ib/IIa receptor (CD41 7E3)/Integrin α-Ⅱbβ3 that prevents platelets from binding to fibrinogen. This Mab also prevents coagulation factor XIII from binding to platelets allowing stabilization of clots and are more easily lysed. The Fc portion of the antibody is removed to decrease thrombocytopenias. This antibody is used during high-risk coronary interventional to prevent clot formation and cardiac ischemia.284

Alirocumab (Praluent) is a human Mab (IgG1) with specificity to proprotein convertase subtilisin/kexin type 9. This medication is used to control cholesterol levels in patients at high risk for cardiovascular events and in patients with familial hypercholesterolemia who are not controlled by other agents.285–287

Evolocumab (Repatha) is a human Mab (IgG2a) FDA approved for the treatment of hypercholesterolemia in patients with familial hypercholesterolemia or history of cardiovascular disease. This Mab has specificity to PCSK9. This medication reduced low-density lipoprotein (LDL) and cholesterol levels by 60% even after statin therapy. Hazard ratios for primary and secondary endpoints were less than one (～0.80–0.85) with fewer cardiovascular-related death or infarction and stroke.288,289

Under future watch is frovocimab (LY3015014) a humanized Mab (IgG4k) with specificity to PCSK9 that completed phase I and II trials. There was up to 50% reduction in LDL cholesterol levels. Phase III studies have yet to be performed.290

An additional antibody is lodelcizumab a humanized Mab (IgG1x); however, no studies were found in clinicaltrials.gov or in Pubmed searches.

Bococizumab is a humanized Mab (IgG2x) that was in phase III trial, which was discontinued secondary to primary endpoints not being achieved.291

NEUROLOGIC DISEASES
Besides autoimmune and malignant diseases of the neurologic system, there are also diseases of the central nervous system classified as degenerative. Such diseases include supranuclear palsy (SNP), Alzheimer’s, and Parkinson’s. Alzheimer’s is likely the most common cause of dementia first described in 1907. This disease may be depicted as presenile or senile dementia and progresses at a similar rate no matter age of onset. This disease has a genetic predisposition causing it to occur in younger age groups. Histological changes include diffuse plaques (containing amyloid), neurofibrillary plaques, and neuronal loss especially in the hippocampus and temporal regions. Medical management may reverse some of the symptoms but does not prevent disease progression. Parkinson’s is a mainly sporadic degenerative disease with a gradual progressive course mainly affecting motor function more than memory. It was first described in 1817. This is a disease of the substantia nigra characterized by loss of melanin containing nerve cells and eosinophilic intracytoplasmic inclusions. Aside from emotional support and physical therapy, medical therapy is used to decrease tremors including anticholinergic drugs for tremors at onset, beta blockers for intention tremors, and levodopa for postural imbalance and akinesia. Deep brain stimulation is also used to treat symptoms later on as disease progresses. SNP starts in the same age range as Parkinson’s (middle to later in life) that was first described in 1963 with disturbances in gait and balance secondary to rigidity of trunk muscles. Loss of neurons and gliosis is seen in the midbrain. Medical treatment is relatively unsuccessful. Multiple sclerosis is a demyelinating disease most often seen in young adults. The clinical
manifestations are diverse and the progression can be chronic, acute, or remitting and relapsing. Medications and therapeutic plasma exchange have been used to treat this debilitating disease with limited efficacy. Clinical trials are ongoing looking at Mab therapies for treatment of these four neurologic degenerative diseases.

**Multiple Sclerosis**

Alemtuzumab (Lemtrada) is a humanized Mab (IgG1κ) targeting CD52 that depletes lymphocytes (B and T cell) as reported earlier and is FDA approved for treatment of acute relapsing and remitting multiple sclerosis.

Ocrelizumab (Ocrevus) is a humanized Mab (IgG1κ) with specificity to CD20 (a B-cell membrane protein). In phase II trials, there were decreases in brain lesions on imaging, and decrease rate of disability decline in primary progressive multiple sclerosis.

Natalizumab (Tysabri) is a monoclonal IgG4κ humanized antibody with specificity to cell adhesion molecule (CD62L) that is FDA approved for relapsing multiple sclerosis.

The mabs to watch out for in the future and are in clinical trials include anifrolumab a human monoclonal antibody in phase I trials; elezanumab is a human Mab (IgG1λ) with specificity to repulsive guidance molecule family member-A that is in phase II trials to be completed 2021; and finally inebilizumab (MEDI-551) is a humanized monoclonal antibody (IgG2κ) with specificity to CD19 (a B-cell lymphocyte protein). This Mab mechanism of action is via ADCC and has completed phase I trials with good safety profile and response in decreasing lesions seen on contrast enhanced magnetic resonance imaging. Otilimab (MOR103) is a human Mab (IgG1λ) completing phase I studies with good safety profile that targets granulocyte-macrophage colony-stimulating factor. Ublituximab is in phase II clinical studies to be completed in 2019, and phase III studies are scheduled to be completed in 2021. This Mab is a chimeric Mab (IgG1κ) with specificity to CD20 MS2A1.

Additional Mab have serious adverse effects such as daclizumab a humanized monoclonal (IgG1κ) with specificity to (CD25 {IL-2Rα}); or are ineffective as is opicinumab a human Mab IgG1 with specificity to Leucine-rich repeat and immunoglobulin domain containing neurite outgrowth inhibitor receptor interacting protein-1 which in a phase II trial was no more beneficial than placebo in treating optic neuritis in multiple sclerosis patients.

**Alzheimer’s Disease**

Aducanumab is a human Mab IgG1 with specificity to β-amyloid (N-terminus 3–6) soluble oligomers and insoluble fibers. Phase III clinical trials are ongoing since 2015.

BAN-2401 is a humanized Mab IgG1 with specificity to β-amyloid fibrillary and soluble β amyloid and is in phase IIb clinical studies since 2013.

Gosuranemab (BIIB092, IPN-007) is a humanized Mab IgG4κ with specificity to the tau protein and is in clinical trials to treat Alzheimer’s disease scheduled to be completed in 2021. Gosuranemab is also in phase I studies to treat progressive suranuclear palsy and will be completed in 2020.

Crenezumab (RG7412, MABT5102A) is a humanized Mab IgG4 with specificity to 1–40 β-amyloid and is on phase III studies scheduled to be completed in 2021 and 2022.

Gantenerumab (R04909832, R1450) is a human Mab IgG1κ with targets β-amyloid. This Mab on initial phase III studies was found to be ineffective. Ongoing phase II/III trials are currently in place at higher dosing in a clinical population of people with autosomal dominant form of Alzheimer’s disease.

Solanezumab (LY2062430) is a humanized Mab IgG1 with specificity to beta amyloid. Initial phase III trials discontinued for lack of efficacy in preventing Alzheimer’s disease. Ongoing phase III trials are now in place for secondary prevention of this disease and will be completed in 2021 and 2022.

Mab antibodies studied and were ineffective include bapineuzumab, gantenerumab (R04909832, R1450), and ponezumab (RN1219, PF-04,360,365).

**Parkinson’s Disease**

Prasinezumab (PRX002, RG7935, RO7046015) is a humanized Mab IgG1κ with specificity to α-synuclein. This Mab is in phase II clinical trials to treat Parkinson’s and will be completed in 2021.

**ALLERGIC DISEASES**

Allergic reactions develop because of immunologic stimulation of IgE antibodies followed by their interaction with allergens and mast cells. Effects can be local (dermatitis) or systemic (respiratory, cardiovascular, and gastrointestinal). Treatment is either avoidance of the allergens or supportive therapy in acute allergic reactions including pharmacologic treatment with type 1 and 2 histamine blockers, glucocorticosteroids, and if life-threatening epinephrine. Passive antibody therapies are being studied and approved to curtail severe reactions.
**Asthma**
Asthma affects 24 million individuals in the US, and up to 10% of asthma patients have severe disease that may be uncontrolled despite high doses of standard-of-care asthma medications requiring additional use of chronic oral corticosteroids. Benralizumab (Fensensa) is a humanized Mab (IgG1k) with specificity to CD125 (IL-5Rα). This Mab is approved to treat severe asthma of the eosinophilic subtype in ages 12 and older. Its mechanism of action is to decrease the number of eosinophils via ADCC. Basophils are also depleted.303

**Atopic Dermatitis**
Dupilumab (Dupixent) is a human monoclonal gG4 antibody with specificity to interleukin-4 receptor subunit-alpha (IL-4Rα) that is approved to treat severe atopic dermatitis in adults.304

**COAGULOPATHY AND OTHER BENIGN HEMATOLOGIC DISEASES**
Coagulopathies are usually either autoimmune or genetic. In factor VIII deficiency, recombinant factor VIII is used to replace lack of this protein. However, patients may develop antibodies to factor VIII leading to high titers of inhibitors. Furthermore, patients without deficiency may also develop autoantibodies to factor VIII de novo leading to coagulopathies. Other factor combinations as well as recombinant active factors have been created to overcome these inhibitory antibodies. Mabs with bispecific binding are also being researched as another avenue for treatment.

ITP can lead to critical low platelet levels increasing risk for severe bleeding. ITP can occur in both adult and pediatric settings as it is considered an autoimmune disease. Typically, this is treated with steroids and IVIG. In addition, as mentioned earlier, RhD+ patients have benefitted from polyclonal medications directed against the D antigen. Recently, Mab to treat this disease have been developed and will be discussed next.

Thrombotic thrombocytopenic purpura (TTP) is a blood disorder that does not lead to bleeding but to development of diffuse thrombi in small blood vessels. More often, this disorder is secondary to an inherited deficiency of ADAMTS-13. This patient population with congenital deficiency is managed with transfusion of FFP to replace the deficient enzyme. Acquired TTP is typically treated with therapeutic plasma exchange (TPE). This treatment modality removes the inhibitory antibody and ultralarge vWF multimers. Similarly, TPE will replete the missing enzyme. Immunosuppressive agents may be added if only TPE is not effective. A Mab preventing interaction of vWF and platelets was recently approved for use in treating this disorder.305,306 Caplacizumab-yhdp (Cablivi) is a humanized single-variable-domain immunoglobulin (Nanobody) that inhibits the interaction between ultralarge vWF multimers and platelets and is directed against vWF. It induces a faster response to therapy with TPE and decreases relapse with continued use during TPE. This medication is then used post-TPE treatment until immunological evidence of disease is controlled to prevent relapse.305,307,308 This medication was FDA approved for use in TTP in 2019.

Atypical hemolytic uremic syndrome (aHUS) is a disorder of the complement system due to uncontrolled activation. This disorder presents with thrombocytopenia, thrombi, and renal dysfunction. Historically, this illness was treated with TPE; however, end-stage renal failure occurred in 30% of patients and about 65% mortality in subsequent relapses with increasing incidence of renal failure. There are now two monoclonal antibodies approved for the treatment of aHUS. Refer to Table 16.1.

**Sickle Pain Crisis**
In sickle cell disease, one of the frequent complications is pain crises. This is usually treated with analgesics, oxygen, hydration, and transfusions (simple or exchange). Monoclonal antibodies are being developed to treat pain crises in sickle cell patients in both adult and pediatric populations. Crizanlizumab is a humanized Mab (IgG2k) with specificity to selectin P. One phase II trial was completed in 2016 and three additional phase II studies will be completed between 2021 and 27 to treat vasoocclusive pain crisis. This medication may be under FDA review as early as 2019.309,310

**INFECTIONS**
Antimicrobials have historically been developed against a variety of viral, bacterial, fungal, and parasitic infections. These pharmaceuticals target differences from human cells of these particular organisms such as cell wall or membrane structure, genetic make-up, transcription/translation of genetic material, or metabolic pathways.
Often organisms develop resistance to entire categories of these medications. Earlier in the chapter, passive polyclonal antibodies were discussed in the treatment of some of these infectious agents and we will now discuss research in monoclonal therapies to pathogenic microorganisms.

**Clostridium difficile**

Enterocolitis from *Clostridium difficile* is a community or hospital acquired infection increasing morbidity and mortality in those that acquire it. Treatment is supportive or with fecal transplants or antibiotics. Bezlotoxumab (Zinplava) is a human Mab (IgG1) with specificity to *Clostridium difficile*’s B toxin. It is used to treat pseudomembranous colitis and prevent *C. difficile* re-infection.

Actoxumab, a monoclonal antibody against *C. difficile* toxin A, has shown not to be clinically significant.

**Respiratory Syncytial Virus**

Respiratory syncytial virus (RSV) infects almost all children by 2 years old and poses extra risk in preterm infants. Supportive therapy, RSV-IG or IVIG, and antiviral therapy have been used to mitigate the sequelae of this infection with optimal response yet to be seen. No vaccines have yet to be developed for this infection. Recently, monoclonal antibodies have been FDA approved or are undergoing preclinical trials to treat this infectious process and include palivizumab, Nirsevimab (MEDI8897), TRL3d3 (3D3), and ALX-0171.

Not beneficial or safe in use for RSV: motavizumab, Supatavumab (REGN2222, SAR438584).

**Influenza virus**

Influenza is a worldwide respiratory infectious problem with cyclic epidemics yearly. Supportive therapy, yearly vaccinations, and antivirals are used to decrease the morbidity and mortality caused by this sometimes virulent pathogen. Both polyclonal and monoclonal therapies are being evaluated to better treat these infections. Mabs in preclinical trials include diridavumab (CR6262), firiivumab, gedivumab (RG7745, RO6876802), lesofavumab (RG70026), and Navivumab (CT-P27).

**Rabies**

Rabies is a devastating viral infection with swift mortality if not treated quickly after initial exposure. Vaccines usually react too slowly and have to be combined with polyclonal IVIG infusions. Monoclonal therapy was previously studied but usually the virus mutates quickly and the infection is not controlled. More recently, in clinical trials, cocktails of Mabs are being tried to more closely mimic the benefits of polyclonal therapies. These Mabs include foravirumab, rafivirumab (CR57), and Rmab.

**Hepatitis B virus**

HBV is one of if not the most common infections in the world. Even though antivirals are available and effective, only recently they have they been widely used in the infant population and not just “high”-risk individuals. Mabs to treat this infection that are being investigated include libivirumab. Mab that is not found to be effective is tuvirumab.

**Ebola**

Ebola is a relatively rare but devastating hemorrhagic infection. Most care is supportive with various studies being performed to prevent/mitigate this disease. Vaccines are under development as well as passive polyclonal therapies. Mab therapies being developed or studied include porgaviximab (C2G4), cosfroviximab, and larcaviximab.

For these and other bacterial, fungal, and viral anti-infectious agents, information may be found in Table 16.1.

**IMMUNOMODULATION**

In solid organ transplants, cellular or humoral immunity can develop against the transplant leading to acute or chronic rejection. An additional complication with these and stem cell transplants is severe GVHD. In the past, these transplant complications were treated with high-dose glucocorticosteroids, immunosuppressive medication, chemotherapeutic agents, IVIG, or T-cell lymphocytic specific immunoglobulins. Recently, Mabs have been added to this armamentarium to better control these adverse reactions to transplantations.

Basiliximab (Simulect) is a chimeric Mab (IgG1κ) with specificity to CD25 IL-2α. The only FDA-approved indication for this medication is prophylaxis of acute rejection in renal transplant patients. There are multiple ongoing studies of this biological for other organ transplants including liver, lung, and heart as well as for inflammatory/immunologic diseases such as GVHD following stem cell transplantation, ulcerative colitis, and uveitis.

Belatacept (Nulojix) is a soluble fusion protein consisting of the modified extracellular domain of CTLA-4 fused to the Fc domain of a recombinant human Mab
IgG1. This Mab selectively inhibits T-cell activation through costimulation blockade binding to both CD80 and CD86 while blocking CD28 via tighter binding than its parent antibody abatacept. Refer to Table 16.1.

METABOLIC SYNDROMES
Hypercholesterolemia is associated with increased risk for cardiovascular disease/atherosclerosis secondary to inherited or dietary etiologies. Diet and exercise are used to treat mild forms of these disorders. Medications such as nicotinic acid, fibrates, bile acid binding resins, and 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase inhibitors are used for more severe forms of these disorders. Phase III studies have been completed with monoclonal antibodies for patients’ refractory to the previously mentioned forms of therapy.

Hypophosphatemia
Burosumab (KRN23, Crysvita) is a human Mab IgG1κ with specificity to phosphaturic hormone fibroblast growth factor 23 (FGF 23). This hormone is a regulator of phosphate and vitamin D homeostasis. FGF23 inhibits the enzyme CYP27B1 and stimulates CYP24A1, thereby reducing circulating levels of 1,25-dihydroxyvitamin D (1,25(OH)2D), the active metabolite of vitamin D. This medication is FDA approved for the treatment of X-linked hypophosphatemic rickets.320,321

Osteoporosis
Denosumab (Prolia) is an FDA-approved human Mab (IgG2) that is a receptor activator of nuclear factor κB ligand that inhibits development and activity of osteoclasts. As Prolia, this medication is used to prevent or treat osteoporosis in women.322–324 This medication under the trade name Xgeva is also used to prevent skeletal-related events in adults with bone metastasis from breast, prostate cancers, and multiple myeloma.325,326

ENDOCRINE DISORDERS
Diabetes may be classified as primary or secondary. In this chapter, we will be mainly interested in both insulin-dependent (Type I) and insulin-independent types (Type II). Type I diabetes mellitus is generally secondary to loss of β cells in the islets of Langerhans and subsequent loss of insulin production. Type II typically is secondary to decreased sensitivity to the effects of insulin. In type I, insulin is replaced exogenously depending on glucose levels. In type II, medications are given to stimulate islet cells to produce more insulin. Mabs are being developed to potentially mitigate the autoimmune process leading to Type I diabetes mellitus or the sequela of renal failure often seen with this disease. For type II, Mabs are being investigated to potentially decrease body mass index and thus decrease disease severity. Refer to Table 16.1.

OTHER CLINICAL DISORDERS
Age-related macular degeneration (AMD) is the leading irreversible cause of visual loss affecting the elderly. Two forms include a dry form with deposits in the macula or a wet form involving abnormal growth of blood vessels. The wet form, even though less frequent, is associated with more severe visual acuity loss. Antiangiogenic drugs or laser treatments are used to slow the progression or even partially reverse visual loss. Some trials have been completed while others are ongoing using Mab to treat the wet form of AMD. Brolucizumab was found as good as if not better than aflibercept in a phase III clinical trial.327

Cryopyrin-associated periodic syndromes (including familial cold auto-inflamatory syndrome and Muckle-Wells syndrome); tumor necrosis factor receptor-associated periodic syndrome (TRAPS); hyperimmunoglobulin D Syndrome (HIDS)/mevalonate kinase deficiency and familial Mediterranean fever (FMF) may also respond to canakinumab.328

POTENTIAL FUTURE USES OF MONOCLONAL ANTIBODIES AND THEIR TARGETS
Passive antibody therapy continues to be useful clinically whether polyclonal or monoclonal therapy is implemented. Increased utilization of the classic polyclonal antibody preparations continue especially in the realm of infections. In the past 3 years, monoclonal therapy has evolved and revolutionized treatment in many areas. As targets are identified to modify disease pathology no matter its genre we continue to get a better handle on morbidity and mortality. We are learning that not only is the target important but the portion of the target mediating the effect we intend to modify is also important. Importantly, modification of antibodies to be more compatible with the immune system while decreasing rapidity of clearance also allows for more consistent therapy. There are also many targets yet to be discovered or only now being developed as in the canonical wingless/integrated (WNT) signaling. This receptor family is important in a multitude of diseases not limited to: hereditary colorectal cancer,
### TABLE 16.2
Summary of Polyclonal Antibody Therapies.

| Generic Drug Name | Brand Name | Additional Brand Names | AHFS Classification       | Dosage Form(s)      | Restricted Medication |
|-------------------|------------|------------------------|---------------------------|---------------------|-----------------------|
| Antithymocyte globulin (equine) | Atgam |  | Immunosuppressive agent | Intravenous solution |  |
| Antithymocyte globulin (rabbit) | Thymoglobulin |  | Immunosuppressive agent | Intravenous solution |  |
| Antivenin *Latrodectus mactans* | Black widow Antivenin |  | Serums | Intravenous solution |  |
| Antivenin *micrurus* | Eastern and Texas coral Snake Antivenin |  | Serums | Intravenous solution |  |
| Botulism immune globulin | BabyBIG |  | Serums | Intravenous solution |  |
| Crotalidae polyvalent immune Fab | Crofab |  | Serums | Intravenous solution |  |
| Cytomegalovirus immune globulin | Cytogam |  | Serums | Intravenous solution | Yes |
| Digoxin immune Fab | Digibind |  | Serums | Intravenous solution |  |
| Hepatitis B immune globulin | Hepagam-B |  | Serums | Intramuscular solution, Intravenous solution |  |
| Hepatitis B immune globulin | BayHepB | HepaGam B, Hyper Hep B, Nabi-HB |  | Intravenous solution |  |
| High antibody titer Ebola FFP |  |  |  |  |  |
| High antibody titer influenza FFP |  |  |  |  |  |

*Continued*
| Generic Drug Name      | Brand Name | Additional Brand Names                                                                 | AHFS Classification       | Dosage Form(s)                  | Restricted Medication                                      |
|------------------------|------------|----------------------------------------------------------------------------------------|----------------------------|---------------------------------|-----------------------------------------------------------|
| Immunoglobulin (generic) | Gamunex    | Vivaglobin, Cuvitru, Privigen, gammagard, octagam, gamunex, hizentra, Bivigam, Carimune, Flebogamma, Gamastan, Gamimune, Gammplex, gammar, Panglobulin, Panzyga, Sandoglobulin | Injection, Subcutaneous    | Intravenous, Subcutaneous         | Treat XLA, CVID, Hyper IgM syndromes, Wiskott Aldrich syndrome |
| Rabies immune globulin | Bayrab     | HyperRAB, Imogam rabies, KedRAB                                                      |                            |                                 |                                                           |
| Respiratory syncytial virus immune globulin | RespiGam |                                                                                 |                            |                                 |                                                           |
| Rho (D) immune globulin | WhinRho    | Rhophylac, MicRhoGAM, BatRhoD, HyperRho                                              | Serum,                    | Intravenous, intramuscular solutions |                                                           |
| Rimabotulinumtoxin B   | Myobloc    | Other Miscellaneous Therapeutic agents                                                | Injection solution        |                                 |                                                           |
| Rozrolimupab           | Myobloc    | Anti-RhD                                                                               | Injection solution        |                                 |                                                           |
| Tetanus immune globulin | Baytet     | Hypertet                                                                               |                            |                                 |                                                           |
| Varicella zoster immune globulin | VariZIG |                                                                                  |                            |                                 |                                                           |

Searched sites for table information. Monoclonal. https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm. https://fdasis.nlm.nih.gov/srs/. https://clinicaltrials.gov/ct2/. https://www.ncbi.nlm.nih.gov/pubmed/. https://chem.nlm.nih.gov/chemidplus/m. https://druginfo.nlm.nih.gov/drugportal/. https://www.creativebiolabs.net/.
various types of sporadic cancers, intellectual disability syndrome, Alzheimer’s disease, bipolar disorder, bone diseases, and vascular diseases. One monoclonal antibody rosmantuzumab (OMP-131R10), a humanized Mab (IgG1x), is in phase I trials to treat colorectal cancer. Other disease processes have yet to find their optimal therapy (Alzheimer’s) or are advancing to fuller therapeutic benefit. The future is wide open for this newer class of pharmaceuticals as they continue to develop to full fruition.

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CHAPTER 16 Passive Monoclonal and Polyclonal Antibody Therapies

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