

BIOPHARMACEUTICAL Benchmarks nature biotechnology

Biopharmaceuticals are defined here as recombinant proteins, including recombinant antibody-based products, and nucleic acid-based and genetically engineered cell-based products. They are listed consecutively from most recent approval in each class, with registrations since 2014 in bold and withdrawals in red. Eight categories are shown: recombinant clotting factors; recombinant thrombolytics, anticoagulants and other blood-related products; recombinant hormones; recombinant growth factors; recombinant interferons, interleukins and tumor necrosis factor; recombinant vaccines; monoclonal antibody-based products; and other recombinant products. Where more than one drug in the same category was approved in a single year, they are listed alphabetically by trade name. Several products have been approved for multiple indications, but only the first indication for which it was approved is listed here. Some product entries describe the product as being the same as another listed product. In such instances differences invariably exist in terms of approved indication range or the company holding the marketing authorizations, usually as a result of commercial agreements.

Table 1 Biopharmaceuticals approved in the United States and European Union through end of July 2018			
Product	Company (location)	Therapeutic indication	Date approved
Recombinant clotting factors			
<i>Factor VIII</i>			
Adynovi (rurioctocog alfa pegol), extended half-life PEGylated form of full-length r factor VIII product Advate (see below). Same product as <i>Adynovate</i> (see below)	Baxalta Innovations (Vienna)	Hemophilia A	2018 (EU)
Afstya (onocotocog alfa), B-domain-truncated rh coagulation factor VIII, produced in CHO cells	CSL Behring (Marburg, Germany, & Kanakake, IL, USA)	Hemophilia A	2017 (EU 2016 (US)
Vihuma (simocotocog alfa), rh B-domain-deleted factor VIII, produced in HEK cells. Same product as <i>Nuwiq</i> (see below)	Octapharma (Stockholm)	Hemophilia A	2017 (EU)
Iblitas (octocog alfa), rh coagulation factor VIII, produced in BHK cells using the same expression construct as Bayer's Kogenate and Helixate. Same product as <i>Kovaltry</i> (see below)	Bayer Pharma (Berlin)	Hemophilia A	2016 (EU)
Kovaltry (octocog alfa), rh coagulation factor VIII, produced in BHK cells using the same expression construct as Bayer's Kogenate and Helixate. Same product as <i>Iblitas</i> (see above)	Bayer Pharma Bayer HealthCare (Whippany, NJ, USA)	Hemophilia A	2016 (EU & US)
Novwendin (von Willebrand factor (recombinant)), produced in CHO cells	Baxalta (Westlake Village, CA, USA)	von Willebrand disease	2015 (US)
Nuwiq (simocotocog alfa), B-domain-deleted rh factor VIII, produced in HEK cells. Same product as <i>Vihuma</i> (see above)	Octapharma USA (Hoboken, NJ, USA)	Hemophilia A	2015 (US) 2014 (EU)
Obizur (susocotocog alfa), r B-domain-deleted porcine factor VIII, produced in BHK cells	Baxalta Innovations Baxter Healthcare (Westlake Village, CA, USA)	Acquired hemophilia due to development of autoantibodies against factor VIII	2015 (EU) 2014 (US)
Adynovo (recombinant, PEGylated antihemophilic factor), extended half-life PEGylated form of full-length r factor VIII product Advate (see below). Same product as <i>Adynovi</i> (see above)	Baxalta	Hemophilia A	2015 (US)
Elocta (efmrocotocog alfa) in EU, Eloctate (antihemophilic factor recombinant, Fc fusion protein) in US; rh coagulation factor VIII-Fc fusion protein comprising B-domain-deleted human factor VIII covalently linked to the Fc domain of a human IgG, produced in HEK cells	Swedish Orphan Biotivum (Stockholm)	Hemophilia A	2015 (EU) 2014 (US)
NovoEight (turoctocog alfa), rh factor VIII analog that, when activated, is structurally comparable to endogenous human factor VIIIa, produced in CHO cells	Novo Nordisk (Bagsvaerd, Denmark, & Plainsboro, NJ, USA)	Hemophilia A	2013 (EU & US)
Xyntha (antihemophilic factor), rh coagulation factor VIII, produced in CHO cells	Pfizer/Wyeth (Philadelphia)	Hemophilia A	2008 (US)
Advate (octocog alfa), rh factor VIII, produced in CHO cells	Baxter Healthcare (Vienna & Deerfield, IL, USA)	Hemophilia A	2004 (EU) 2003 (US)
Helixate NexGen (octocog alfa), rh factor VIII, produced in BHK cells	Bayer (Berlin)	Hemophilia A	2000 (EU)
RuFactor (morcotocog alfa), B-domain-deleted rh factor VIII, produced in CHO cells	Pfizer/Wyeth (Sandwich, UK) Genetics Institute (Cambridge, MA, USA)	Hemophilia A	2000 (US) 1999 (EU)
Kogenate , <i>Helixate</i> (antihemophilic factor), rh factor VIII, produced in BHK cells. Sold as <i>Helixate</i> by Aventis Behring through a license agreement	Bayer (Leverkusen, Germany, & Berkeley, CA, USA)	Hemophilia A	2000 (EU) 1993 (US)
Bioclote (antihemophilic factor), rh factor VIII, produced in CHO cells	Aventis Behring (King of Prussia, PA, USA)	Hemophilia A	1993 (US)
Recombinate (antihemophilic factor), rh factor VIII, produced in CHO cells	Baxter Healthcare (Deerfield, IL, USA), Genetics Institute	Hemophilia A	1992 (US)
<i>Other blood factors</i>			
Andexxa (coagulation factor Xa recombinant inactivated-zhzo), r modified human factor Xa, produced in CHO cells	Portola Pharmaceuticals (South San Francisco, CA, USA)	For patients treated with rivaroxaban or apixaban, when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding	2018 (US)
Rebinyr (rh coagulation factor IX) in US, <i>Refusia</i> (nonacog beta pegol) in EU; rh coagulation factor IX, produced in CHO cells and PEGylated	Novo Nordisk	Hemophilia B	2017 (EU & US)
Alprolix (eftreronacog alfa), rh coagulation factor IX fused to a human IgG1 Fc domain, produced in HEK cells	Biogen Idec (Maidenhead, UK, & Cambridge, MA, USA)	Hemophilia B	2016 (EU) 2014 (US)
Ideelvion (albuterpronacog alfa), rh factor IX–albumin fusion protein, produced in CHO cells	CSL Behring	Hemophilia B	2016 (EU & US)
Iunify (coagulation factor IX (recombinant)), rh coagulation factor IX, produced in CHO cells	Aptevo BioTherapeutics (Berwyn, PA, USA)	Hemophilia B	2015 (US)
Rizabizis (nonacog gamma), rh factor IX, produced in CHO cells	Baxalta Innovations (Vienna) Baxter Healthcare (Westlake Village, CA, USA)	Hemophilia B	2014 (EU) 2013 (US)
Tretten in US, <i>Novotwintren in EU (catridecog), rh factor XIII A-subunit, produced in <i>S. cerevisiae</i></i>	Novo Nordisk	Congenital factor XIII A-subunit deficiency	2013 (US) 2012 (EU)
Recothrom (thrombin), rh factor IIa, produced in CHO cells	ZymoGenetics (Seattle)	Control of minor bleeding during surgery	2008 (US)
NovoSeven (eptacog alfa, activated), rh factor VIIa, produced in BHK cells	Novo Nordisk	Some forms of hemophilia	1996 (EU) 1999 (US)
Benefix (nonacog alfa), rh factor IX, produced in CHO cells	Pfizer/Wyeth	Hemophilia B	1997 (EU & US)
Recombinant thrombolytics, anticoagulants and other blood-related products			
<i>Tissue plasminogen activator</i>			
Metalyse (tenecteplase), modified rh tPA, produced in CHO cells	Boehringer Ingelheim (Ingelheim, Germany)	Myocardial infarction	2001 (EU) Withdrawn 2005
TNKase (tenecteplase), modified rh tPA, produced in CHO cells	Roche/Genentech (South San Francisco, CA, USA)	Myocardial infarction	2000 (US)
Eckinase (reteplase), r tPA, produced in <i>Escherichia coli</i> ; differs from human tPA in that 3 of its 5 domains have been deleted	Roche (Welwyn Garden City, UK)	Acute myocardial infarction	1996 (EU) Withdrawn 2000
Rapilysin (reteplase), r tPA (see Eckinase above)	Actavis Group PTC (Hafnarfjörður, Iceland), Roche	Acute myocardial infarction	1996 (EU)
Retavase (reteplase), r tPA (see Eckinase above)	Chiesi USA (Cary, NC, USA)	Acute myocardial infarction	1996 (US)
Activase (alteplase), rh tPA, produced in CHO cells	Roche/Genentech	Acute myocardial infarction	1987 (US)
<i>Hirudin</i>			
Refudjan (tepirudim), r hirudin, produced in <i>S. cerevisiae</i>	Calgene Europe (Windsor, UK) Bayer HealthCare	Anticoagulation therapy for heparin-associated thrombocytopenia	1997 (EU) 1998 (US) Withdrawn 2012 (EU)
Revasc (desirudin), r hirudin, produced in <i>S. cerevisiae</i>	Canyon Pharmaceuticals (London)	Prevention of venous thrombosis	1997 (EU) Withdrawn 2014
<i>Other</i>			
Ruconest (conestat alfa), rh C1 esterase inhibitor, produced in the milk of transgenic rabbits	Santarus (Raleigh, NC, USA) Pharming Group (Leiden, the Netherlands)	Acute angioedema	2014 (US) 2010 (EU)
Jeheta (scirplaximin), r truncated form of human plasmin, produced in <i>P. pastoris</i>	ThromboGenics (Leuven, Belgium)	Symptomatic vitreomacular adhesion, vitreomacular traction	2013 (EU) 2012 (US)
Atryn (rh antithrombin), produced in milk of transgenic goats	Laboratoire français du fractionnement et des biotechnologies (Les Ulis, France), FHO Biologics (Framingham, MA, USA)	Hereditary antithrombin deficiency	2009 (US) 2006 (EU)
Kalbitor (ecallantide), plasma kallikrein inhibitor, produced in <i>P. pastoris</i>	Dyax (Cambridge, MA, USA)	Hereditary angioedema	2009 (US)
Xigris (drotrecogin alfa), rh activated protein C, produced in a human cell line	Eli Lilly (Houten, the Netherlands)	Severe sepsis	2001 (US) 2002 (EU) Withdrawn 2012 (EU)
Recombinant hormones			
<i>Insulins</i>			
Semglee (insulin glargine), r insulin glargine, produced in <i>P. pastoris</i> , biosimilar to Lantus	Mylan (Saint-Priest, France)	Diabetes mellitus	2018 (EU)

Table 1 Continued			
Product	Company (location)	Therapeutic indication	Date approved
Admelg (insulin lispro injection), rapid-acting human insulin analog, produced in <i>E. coli</i>	Sanofi (Bridgewater, NJ, USA)	Diabetes mellitus	2017 (US)
Fiasp (insulin aspart injection), rapid-acting human insulin, produced in <i>S. cerevisiae</i>	Novo Nordisk	Diabetes mellitus	2017 (US)
Insulin lispro Sanofi , produced in <i>E. coli</i> , biosimilar to Humalog	Novo Avenatis (Paris)	Diabetes mellitus	2017 (EU)
Lusdana (insulin glargine), engineered insulin, produced in <i>E. coli</i> , biosimilar to Lantus	Merck Sharp & Dohme (Hoddesdon, UK)	Diabetes mellitus	2017 (EU) 2017 (US, tentative)
Soliqua in EU, <i>Soliqua</i> in US (insulin glargine/fixisenatide), combination of long-acting insulin glargine, produced in <i>E. coli</i> , and a synthetically produced human GLP-1 analog	Sanofi-Aventis (Paris) Sanofi (Bridgewater, NJ, USA)	Diabetes mellitus type 2	2017 (EU) 2016 (US)
Xultophy (insulin degludec/liraglutide), a combination of 2 previously approved products, <i>Victoza</i> and <i>Tresiba</i>	Novo Nordisk	Diabetes mellitus type 2	2016 (US) 2014 (EU)
Abasaglar (previously <i>Abasira</i>) in EU, <i>Abasaglar</i> in US (insulin glargine), produced in <i>E. coli</i> , biosimilar (in EU) to Lantus	Eli Lilly (Indianapolis), Boehringer Ingelheim (Ridgefield, CT, USA) Eli Lilly (Wiemna)	Diabetes mellitus	2015 (US) 2014 (EU)
Ryzodeg 70/30 in US, <i>Ryzodeg</i> in EU (insulin degludec/insulin aspart), combination of two engineered insulins, produced in <i>S. cerevisiae</i>	Novo Nordisk	Diabetes mellitus type 1 and 2	2015 (US) 2013 (EU)
Toujeo (insulin glargine), produced in <i>E. coli</i>	Sanofi (Bridgewater, NJ, USA)	Diabetes mellitus	2015 (US)
Tresiba (insulin degludec), engineered long-acting human insulin analog, produced in <i>S. cerevisiae</i> (see also <i>Ryzodeg</i> above)	Novo Nordisk	Diabetes mellitus type 1 and 2	2015 (US) 2013 (EU)
Afrezza (rh insulin), produced in <i>E. coli</i>	MannKind (Danbury, CT, USA)	Diabetes mellitus	2014 (US)
Novolog max (insulin aspart mix), a 50:50 mixture of engineered rh insulin, produced in <i>S. cerevisiae</i> in soluble and protamine suspension forms	Novo Nordisk	Diabetes mellitus	2008 (US)
Insulin Human Winthrop (rh insulin), produced in <i>E. coli</i>	Sanofi (Frankfurt)	Diabetes mellitus	2007 (EU) Withdrawn 2018
Exubera (inhalable rh insulin), produced in <i>E. coli</i>	Pfizer (Sandwich, UK)	Diabetes mellitus	2006 (EU & US) Withdrawn 2008 (EU)
Levemir (insulin detemir), long-acting rh insulin, produced in <i>S. cerevisiae</i>	Novo Nordisk	Diabetes mellitus	2005 (US) 2004 (EU)
Apidra (insulin glulisine), rapid-acting insulin analog, produced in <i>E. coli</i>	Sanofi (Frankfurt)	Diabetes mellitus	2004 (EU & US)
Actrapid , <i>Velosolin</i> , <i>Monotard</i> , <i>Insulatard</i> , <i>Protaphane</i> , <i>Mixtard</i> , <i>Actraphane</i> , <i>Ultratard</i> : rh insulin formulated as short-, intermediate- or long-acting product, produced in <i>S. cerevisiae</i>	Novo Nordisk	Diabetes mellitus	2002 (EU) Monotard and Ultratard withdrawn 2006
Novolog (insulin aspart), short-acting rh insulin analog, produced in <i>S. cerevisiae</i>	Novo Nordisk	Diabetes mellitus	2001 (US)
Novolog mix 70/30 (contains insulin aspart, a short-acting rh insulin analog, in both soluble and crystalline form) (see also <i>Novomix 30</i> below)	Novo Nordisk	Diabetes mellitus	2001 (US)
Novomix 30 (contains a mixture of insulin aspart, a short-acting rh insulin analog, in both soluble and crystalline form, produced in <i>S. cerevisiae</i>)	Novo Nordisk	Diabetes mellitus	2000 (EU)
Lantus (insulin glargine), long-acting rh insulin analog, produced in <i>E. coli</i>	Sanofi (Frankfurt)	Diabetes mellitus	2000 (EU & US)
Optisulin (insulin glargine), long-acting rh insulin analog, produced in <i>E. coli</i> (see also <i>Lantus</i> above)	Sanofi (Frankfurt)	Diabetes mellitus	2000 (EU)
NovoRapid (insulin aspart), rh insulin analog, produced in <i>S. cerevisiae</i>	Novo Nordisk	Diabetes mellitus	1999 (EU)
Liraglog (insulin lispro), insulin analog, produced in <i>E. coli</i>	Eli Lilly (Houten, the Netherlands)	Diabetes mellitus	1997 (EU) Withdrawn 2001
Insulin (rh insulin), produced in <i>E. coli</i>	Sanofi (Frankfurt)	Diabetes mellitus	1997 (EU)
Humalog (insulin lispro), insulin analog, produced in <i>E. coli</i>	Eli Lilly (Houten, the Netherlands)	Diabetes mellitus	1996 (EU & US)
Novolin (rh insulin), produced in <i>S. cerevisiae</i>	Novo Nordisk	Diabetes mellitus	1991 (US) Withdrawn 2010
Humulin (rh insulin), produced in <i>E. coli</i>	Eli Lilly (Indianapolis)	Diabetes mellitus	1982 (US)
<i>Human growth hormone</i>			
Somatropin (somatotropin) (somatropin), r hGH, produced in <i>S. cerevisiae</i>	Biopartners (Reutlingen, Germany)	Growth failure, growth hormone deficiency	2013 (EU) Withdrawn 2017
Accretropin (somatotropin), r hGH, produced in <i>E. coli</i>	Emergent Biosolutions (Rockville, MD, USA) Cangene (Winnipeg, MB, Canada)	Growth failure or short stature associated with Turner syndrome in children	2008 (US)
Valtropin (somatotropin), r hGH, produced in <i>S. cerevisiae</i> , biosimilar to <i>Humatrope</i>	Biopartners LG Life Sciences (Reutlingen, Germany)	Certain forms of growth disturbance in children and adults	2007 (US) 2006 (EU) Withdrawn 2012 (EU)
Omnitrope (somatotropin), r hGH, produced in <i>E. coli</i> , biosimilar (in EU) to <i>Genotropin</i>	Sandoz (Kundl, Austria) Novartis (Princeton, NJ, USA)	Certain forms of growth disturbance in children and adults	2006 (EU & US)
Somavert (pegvisomant), PEGylated r hGH analog (antagonist), produced in <i>E. coli</i>	Pfizer (Brussels & New York) Nektar Therapeutics (San Francisco)	Acromegaly	2003 (US) 2002 (EU)
Nutropin AQ (somatotropin), r hGH, produced in <i>E. coli</i> , different formulation of <i>Nutropin</i> (see below)	Ipsern Pharma (Boulogne-Billancourt, France)	Growth failure, Turner syndrome	2001 (EU) 1994 (US) Withdrawn 2008 (EU)
Serostim (somatotropin), r hGH, produced in mouse C127 cells	EMD Serono (Geneva)	AIDS-associated catabolism and wasting	1996 (US)
Genotropin (somatotropin), r hGH, produced in <i>E. coli</i>	Pfizer (New York)	hGH deficiency in children	1995 (US)
Norditropin (somatotropin), r hGH, produced in <i>E. coli</i>	Novo Nordisk	Growth failure in children due to inadequate growth hormone secretion	1995 (US)
Tev-Tropin , <i>Bio-tropin</i> (somatotropin), r hGH, produced in <i>E. coli</i>	Teva Pharmaceuticals (North Wales, PA, USA)	hGH deficiency in children	1995 (US)
Nutropin (somatotropin), r hGH, produced in <i>E. coli</i>	Roche/Genentech	hGH deficiency in children	1994 (US)
Humatrope (somatotropin), r hGH, produced in <i>E. coli</i>	Eli Lilly (Indianapolis)	hGH deficiency in children	1987 (US)
Protropin (somatrem), r hGH differing from hGH by an extra N-terminal methionine, produced in <i>E. coli</i>	Genentech	hGH deficiency in children	1985 (US) Withdrawn 2004
<i>Follicle-stimulating hormone</i>			
Rekovele (follitropin delta), rh FSH, produced in <i>PER.C6</i> cells	Ferring Pharmaceuticals (Copenhagen)	Anovulation	2016 (EU)
Bemfola (follitropin alfa), rh FSH, produced in CHO cells, biosimilar to Gonaf	Finox Biotech (Burgdorf, Switzerland)	Anovulation (women), failure of spermatogenesis (men)	2014 (EU)
Ovaleap (follitropin alfa), rh FSH, produced in CHO cells, biosimilar to Gonaf	Teva Pharma (Utrecht, the Netherlands)	Infertility, subfertility	2013 (EU)
Elonva (corifollitropin alfa), a modified rh FSH in which the C-terminal peptide of the β -subunit of human chorionic gonadotropin is fused to the FSH β -chain, produced in CHO cells	Merck Sharp & Dohme	Controlled ovarian stimulation	2010 (EU)
Fertavid (follitropin beta), rh FSH, produced in CHO cells. Active substance same as that in <i>Puregon</i> (see below)	Merck Sharp & Dohme	Infertility	2009 (EU)
Pergoveris (follitropin alfa/follitropin alfa) combination product containing rh FSH and rh luteinizing hormone, both produced in CHO cells	Merck Serono (London)	Stimulation of follicular development in women with severe luteinizing hormone and FSH deficiency	2007 (EU)
Follistim (follitropin beta), rh FSH, produced in CHO cells	Merck (Whitehouse Station, NJ, USA)	Infertility	1997 (US)
Puregon (follitropin beta), rh FSH, produced in CHO cells	Merck Sharp & Dohme (Haarlem, the Netherlands)	Anovulation and superovulation	1996 (EU)
Gonal F (follitropin alfa), rh FSH, produced in CHO cells	Merck Serono EMD Serono (Rockland, MD, USA)	Anovulation and superovulation	1997 (US) 1995 (EU)
<i>Other hormones</i>			
Myalepta in EU, <i>Myalept</i> in US (metreleptin), rh leptin analog, produced in <i>E. coli</i>	Aegerion Pharmaceuticals (Amsterdam & Cambridge, MA, USA)	Some forms of lipodystrophy	2018 (EU) 2014 (US)
Ozempic (semaglutide), human GLP-1 receptor agonist, produced in yeast and covalently modified by attachment of a C18 fatty acid	Novo Nordisk	Diabetes mellitus type 2	2018 (EU) 2017 (US)
Movymia (teriparatide), rh parathyroid hormone fragment, produced in <i>E. coli</i> , biosimilar to <i>Fortseo</i> . Same product as <i>Terosa</i> (see below)	STADA Arzneimittel (Bad Vilbel, Germany)	Osteoporosis	2017 (EU)
Natpar (parathyroid hormone), rh parathyroid hormone, full length, produced in <i>E. coli</i> . Same product as <i>Preducta</i> (see below).	Shire Pharmaceuticals Ireland (Dublin)	Hypoparathyroidism	2017 (EU)
Terosa (teriparatide), rh parathyroid hormone fragment, produced in <i>E. coli</i> , biosimilar to <i>Fortseo</i> . Same product as <i>Movymia</i> (see above)	Gedeon Richter (Budapest)	Osteoporosis	2017 (EU)
Natpara (parathyroid hormone), rh parathyroid hormone, produced in <i>E. coli</i>	Shire-NPS Pharmaceuticals (Lexington, MA, USA)	Hypocalcemia	2015 (US)

Table 1 Continued			
Product	Company (location)	Therapeutic indication	Date approved
Saxenda (liraglutide), human GLP-1 analog, produced in <i>S. cerevisiae</i> and covalently modified by palmitic acid. Active substance same as that in <i>Victoza</i> (see below)	Novo Nordisk	Obesity	2015 (EU)
Eperzan in EU, <i>Tanzeum</i> in US (albiglutide), GLP-1 receptor agonist; two tandem copies of modified human GLP-1 fused to human albumin, produced in <i>S. cerevisiae</i>	GSK (Carrigillan, Ireland, & Research Triangle Park, NC, USA)	Diabetes mellitus type 2	2014 (EU & US)
Trulicity (dulaglutide), fusion protein consisting of a GLP-1 analog linked to a human IgG Fc domain, produced in a mammalian cell line	Eli Lilly (Utrecht, the Netherlands, & Indianapolis)	Diabetes mellitus type 2	2014 (EU & US)
Gattex in US, <i>Revestive</i> in EU (teduglutide), rh GLP-2 analog, produced in <i>E. coli</i>	NPS Pharma (Dublin)	Short bowel syndrome	2012 (EU & US)
Victoza (liraglutide), GLP-1 analog with attached fatty acid, produced in <i>S. cerevisiae</i>	Novo Nordisk	Diabetes mellitus type 2	2010 (US) 2009 (EU)
Preducta , rh parathyroid hormone, produced in <i>E. coli</i>	NPS Pharma	Osteoporosis	2006 (EU) Withdrawn 2014
Fortical , r salmon calcitonin, produced in <i>E. coli</i>	Upsher-Smith Laboratories (Minneapolis)	Postmenopausal osteoporosis	2005 (US)
Luvris (lutropin alfa), rh luteinizing hormone, produced in CHO cells	EMD Serono (Rockland, MA, USA) Merck Europe (Amsterdam)	Some forms of infertility	2004 (US) 2000 (EU)
Forsteo in EU, Forteo in US (teriparatide), r shortened human parathyroid hormone, produced in <i>E. coli</i>	Eli Lilly (Houten, the Netherlands)	Established osteoporosis in some postmenopausal women	2003 (EU) 2002 (US)
Natorec (nesiritide), rh natriuretic peptide, produced in <i>E. coli</i>	Johnson & Johnson/Scios (Titusville, NJ, USA)	Acutely decompensated congestive heart failure	2001 (US)
Ovitrelle in EU, Ovidrel in US (choriogonadotropin alfa) rh chorionic gonadotropin, produced in CHO cells	Merck Serono	Selected assisted reproductive techniques	2001 (EU) 2000 (US)
Thyrogen (thyrotropin alfa), rh thyroid-stimulating hormone, produced in CHO cells	Sanofi Genzyme (Cambridge, MA, USA)	Thyroid cancer (detection and treatment)	1998 (US) 2000 (EU)
Forcaltonin , r salmon calcitonin, produced in <i>E. coli</i>	Unigene UK (Bushey Heath, UK)	Paget disease	1999 (EU) Withdrawn 2008
Glucagon , rh glucagon, produced in <i>S. cerevisiae</i>	Novo Nordisk	Hypoglycemia	1998 (US)
Glucagon (glucagon, recombinant), rh glucagon, produced in <i>E. coli</i>	Eli Lilly (Indianapolis)	Hypoglycemia	1998 (US)
Recombinant growth factors			
<i>Erythropoietin</i>			
Retacrit (epoetin zeta) in EU, epoetin alfa (epo) in US, rh EPO, produced in CHO cells, biosimilar to <i>Eprex</i> and <i>Erypo</i>	Hospira (Royal Leamington Spa, UK) Pfizer (Lake Forest, IL, USA)	Anemia	2018 (US) 2007 (EU)
Biopoin (epoetin theta), rh EPO, produced in CHO cells	Teva (Ulm, Germany)	Anemia	2009 (EU)
Eporatio (epoetin theta), rh EPO, produced in CHO cells	Teva (Ulm, Germany)	Anemia	2009 (EU)
Abseamed (epoetin alfa), produced in CHO cells, biosimilar to <i>Eprex/Erypo</i>	Medice Arzneimittel Pütter (Iserloh, Germany)	Anemia associated with chronic renal failure	2007 (EU)
Binocrit (epoetin alfa), produced in CHO cells, biosimilar to <i>Eprex/Erypo</i>	Sandoz	Anemia associated with chronic renal failure	2007 (EU)
Epoetin alfa Hexal (epoetin alfa), produced in CHO cells, biosimilar to <i>Eprex/Erypo</i>	Hexal (Holzkirchen, Germany)	Anemia associated with chronic renal failure	2007 (EU)
Mircera (methoxy polyethylene glycol-epoetin beta) PEGylated rh EPO, produced in CHO cells	Roche (Welwyn Garden City, UK)	Anemia associated with chronic kidney disease	2007 (EU & US)
Silapo (epoetin zeta), produced in CHO cells, biosimilar to <i>Eprex/Erypo</i>	STADA (Bad Vilbel, Germany)	Anemia associated with chronic renal failure	2007 (EU)
Dynepo (epoetin delta), rh EPO, produced in a human cell line	Shire Pharmaceuticals (Basingstoke, UK)	Anemia	2002 (EU) Withdrawn 2009
Aranesp (darbepoetin alfa), long-acting r EPO analog, produced in CHO cells (see <i>Nespo</i> below)	Amgen (Breda, the Netherlands)	Anemia	2001 (EU & US)
Nespo (darbepoetin alfa), long-acting r EPO analog, produced in CHO cells (see <i>Aranesp</i> above)	Dompé Biotech (Milan)	Anemia	2001 (EU) Withdrawn 2008
Neorecom			

Table 1 Continued	Product	Company (location)	Therapeutic indication	Date approved
	Herzuma (trastuzumab), r humanized IgG1 against HER2, produced in CHO cells, biosimilar to Herceptin	Celtrion Healthcare (Budapest)	Breast and gastric cancers	2018 (EU)
	Hyrimiz (adalimumab), anti-TNF IgG, produced in CHO cells, biosimilar to Humira. Same product as Halimatoz and Hefiya (see above)	Sandoz	Various inflammatory conditions mediated by TNF, including rheumatoid arthritis and plaque psoriasis	2018 (EU)
	Ilumya (trilicicuzumab-asmn), humanized IgG1 that binds the p19 subunit of IL-23, produced in CHO cells	Merck (Whitehouse Station, NJ, USA)	Plaque psoriasis	2018 (US)
	Kanjinti (trastuzumab), r humanized IgG1 against HER2, produced in CHO cells, biosimilar to Herceptin	Amgen Europe (Breda, the Netherlands)	Breast and gastric cancers	2018 (EU)
	Mvasi (bevacizumab in EU, bevacizumab-aww in US), humanized IgG antibody to human VEGF-A1, produced in CHO cells, biosimilar to Avastin	Amgen Europe (Thousand Oaks, CA, USA)	Various cancers	2018 (EU) 2017 (US)
	Mylotarg (gemtuzumab ozogamicin), antibody drug conjugate targeting the CD33 surface antigen, consisting of a humanized IgG4 chemically conjugated to Acetyl-y-calicheamicin, produced in NSO mouse myeloma cells	Pfizer Europe (Brussels) Pfizer (New York, NY, USA) Pfizer/Wyeth (Philadelphia)	Acute myeloid leukemia	2018 (EU) 2000 (US) Withdrawn 2010 (US)
	Ocrevus (ocrelizumab), r humanized IgG1 targeting the CD20 surface antigen, produced in CHO cells	Roche Registration Genentech (South San Francisco, CA, USA)	Multiple sclerosis	2018 (EU) 2017 (US)
	Trazimera (trastuzumab), humanized IgG, produced in a CHO cells, biosimilar to Herceptin	Pfizer (Brussels)	Breast cancer, gastric or gastro-esophageal junction adenocarcinoma	2018 (EU)
	TROGARZO (ibalizumab-uiyk), humanized IgG4 targeting the CD4 domain, produced in NSO cells	TaiMed Biologics (Irvine, CA, USA) Theratechnologies (Montreal)	Human immunodeficiency virus type 1 infection	2018 (US)
	Zessly (infliximab), chimeric anti-TNF IgG1 produced in CHO cells, biosimilar to infliximab	Sandoz	Rheumatoid arthritis and selected additional inflammatory diseases	2018 (EU)
	Amgevita (adalimumab), anti-TNF human IgG1, produced in CHO cells, biosimilar to Humira. Same product as Solybmic and Amjevita (see below)	Amgen Europe	Rheumatoid arthritis and selected additional inflammatory diseases	2017 (EU)
	Bavencio (avelumab), human IgG1 specific for programmed death ligand-1 (PD-L1), produced in CHO cells	Merck Europe (Amsterdam) Pfizer (New York, NY, USA) Pfizer/Wyeth (Philadelphia)	Metastatic Merkel cell carcinoma, urothelial carcinoma	2017 (EU & US)
	Besponsa (inotuzumab ozogamicin), antibody-drug conjugate consisting of a humanized IgG2a specific for human CD22, produced in CHO cells, covalently linked to the cytotoxic agent N-acetyl-y-calicheamicin dimethylhydrazide	Merck Europe (Amsterdam) Pfizer (New York, NY, USA) Pfizer/Wyeth (Philadelphia)	Acute lymphoblastic leukemia	2017 (EU & US)
	Blitzima (rituximab), chimeric IgG1 against cell surface antigen CD20, produced in CHO cells, biosimilar to MabThera. Same product as Ritemisa, Truxima and Rituzena (see below)	Celtrion Healthcare Hungary (Budapest)	Non-Hodgkin lymphoma, CLL, granulomatosis	2017 (EU)
	Cyltezo (adalimumab in EU, adalimumab-sdbm in USA), rh IgG1 against human TNF, produced in CHO cells, biosimilar to Humira	Boehringer Ingelheim (Rhein, Germany) Boehringer Ingelheim (Ridgefield, CT, USA)	Range of inflammatory conditions, including psoriasis, rheumatoid arthritis and Crohn's disease	2017 (EU & US)
	Dinutuximab beta Apeiron (dinutuximab beta), chimeric IgG1 against the disialoganglioside GD2, produced in CHO cells. Same product as Garziba (see below)	Apeiron Biologics (Vienna)	Neuroblastoma	2017 (EU)
	Dupixent (dupilumab), human IgG4 that binds the IL-4 receptor subunit, produced in CHO cells	Sanofi-Aventis (Paris & Bridgewater, NJ, USA), Regeneron Pharmaceuticals (Tarrytown, NY, USA)	Atopic dermatitis	2017 (EU & US)
	Imfinzi (durvalumab), human IgG1 blocking the interaction of programmed cell death ligand-1 (PD-L1) with its receptor PD-1 and CD80, produced in CHO cells	AstraZenca (Wilmington, DE, USA)	Urothelial carcinoma	2017 (US)
	Imrardi (adalimumab), produced in CHO cells, biosimilar to Humira	Samsung Bioepis UK (Chertsey, UK)	Rheumatoid arthritis, selected additional inflammatory diseases	2017 (EU)
	Ixifi (infliximab-qbtk), produced in a mammalian cell line, biosimilar to Remicade	Pfizer (New York)	Various inflammatory conditions, including rheumatoid arthritis, Crohn's disease and psoriasis	2017 (US)
	Kezara (sarilumab), human IgG1 that binds IL-6 receptors, produced in CHO cells	Sanofi-Aventis (Paris & Bridgewater, NJ, USA), Regeneron Pharmaceuticals (Tarrytown, NY, USA)	Rheumatoid arthritis	2017 (EU) 2017 (US)
	Kyntheum in EU, Siliq in US (brodalumab), human IgG2 against human IL-17 receptor A, produced in CHO cells	LEO Pharma (Ballerup, Denmark) Valeant Pharmaceuticals (Bridgewater, NJ, USA)	Psoriasis	2017 (EU) 2017 (US)
	Ogivi (trastuzumab-dkst), produced in CHO cells, biosimilar to Herceptin	Mylan (Morgantown, WV, USA, & Zurich)	Breast and gastric cancers	2017 (US)
	Otruzant, produced in CHO cells, biosimilar to Herceptin	Samsung Bioepis UK (Brentford, UK)	Breast and gastric cancers	2017 (EU)
	Qarziba (dinutuximab beta; previously dinutuximab beta EUSA and dinutuximab beta Apeiron), chimeric IgG1 against carbohydrate disialoganglioside GD2, which is overexpressed by cells of neuroectodermal origin such as neuroblastoma cells, produced in CHO cells	EUSA Pharma (Hemel Hempstead, UK)	Neuroblastoma	2017 (EU)
	Renflexis (infliximab-abda), chimeric IgG1 that binds TNF- α , produced in CHO cells, biosimilar to Remicade. Same product as Fixixabi (see below)	Merck (Kenilworth, NJ, USA)	Crohn's disease and various other inflammatory conditions	2017 (US)
	Ritémisa (rituximab), produced in CHO cells, biosimilar to MabThera. Same product as Blitzima, Rituzena and Truxima (see above and below)	Celtrion Healthcare Hungary	Non-Hodgkin lymphoma, granulomatosis with polyangiitis, microscopic polyangiitis	2017 (EU)
	Rituxan Hycela (rituximab and hyaluronidase human), both produced in CHO cells	Biogen (Cambridge, MA, USA), Genentech	Follicular lymphoma, diffuse large B-cell lymphoma, CLL	2017 (US)
	Rituzena (previously Tuxella) (rituximab), produced in CHO cells, biosimilar to MabThera. Same product as Blitzima, Ritémisa and Truxima (see above and below)	Celtrion Healthcare Hungary	Non-Hodgkin lymphoma, CLL, granulomatosis with polyangiitis	2017 (EU)
	Ritathan (rituximab), chimeric IgG1 against cell surface antigen CD20, produced in CHO cells, biosimilar to MabThera. Same product as Ritímxyo (see below)	Sandoz	Various conditions including non-Hodgkin lymphoma, CLL, rheumatoid arthritis	2017 (EU)
	Ritímxyo (rituximab), chimeric IgG1 against cell surface antigen CD20, produced in CHO cells, biosimilar to MabThera. Same product as Ritathan (see above)	Sandoz	Various conditions including non-Hodgkin lymphoma and rheumatoid arthritis, but excluding CLL	2017 (EU)
	Solybmic (adalimumab), anti-TNF human IgG1 produced in CHO cells, biosimilar to Humira. Same product as Amgevita and Amjevita (see above and below)	Amgen Europe	Rheumatoid arthritis and selected additional inflammatory diseases	2017 (EU)
	Tecentriq (atezolizumab), humanized IgG1 specific for programmed death ligand 1 (PD-L1), engineered to lack Fc glycosylation, produced in CHO cells	Roche Registration (Grenzach-Wyhlen, Germany) Genentech (South San Francisco, CA, USA)	Urothelial carcinoma, non-small cell lung cancer	2017 (EU) 2016 (US)
	Tremfya (guselkumab), human IgG1 that selectively binds the p19 subunit of IL-23, produced in CHO cells	Janssen-Cilag (Beerse, Belgium) Janssen Biotech (Horsham, PA, USA)	Psoriasis	2017 (EU & US)
	Truxima (rituximab) chimeric IgG1 against cell surface antigen CD20, produced in CHO cells, biosimilar to MabThera. Same product as Blitzima, Ritémisa, and Truxima (see above)	Celtrion	Selected cancers and autoimmune disorders	2017 (EU)
	Zinplava (bezlotuzumab), human IgG directed against <i>Clostridium difficile</i> toxin B, produced in CHO cells	Merck Sharp & Dohme Merck (Whitehouse Station, NJ, USA)	C. difficile infection	2017 (EU) 2016 (US)
	Amjevita (adalimumab-atto), rh IgG1 specific for TNF, produced in CHO cells, biosimilar to Humira. Same product as Solybmic and Amgevita (see above)	Amgen (Thousand Oaks, CA, USA)	Rheumatoid arthritis and selected additional inflammatory diseases	2016 (US)
	Antrim (oblitoximab), chimeric IgG1 against <i>Bacillus anthracis</i> toxin, produced in NSO cells	Elyslys Therapeutics (Pine Brook, NJ, USA)	Inhalational anthrax	2016 (US)
	Cinqair in US, Cinqair in EU (reslizumab), humanized IgG4 against IL-5, produced in NSO cells	Teva Respiratory (Frazer, PA USA) Teva (Haarlem, the Netherlands)	Asthma	2016 (US) 2016 (EU)
	Darzalex (daratumumab), human IgG1 against CD-38, produced in CHO cells	Janssen-Cilag Janssen Biotech	Multiple myeloma	2016 (EU) 2015 (US)
	Empliciti (elotuzumab) humanized IgG1 against the cell surface receptor SLAMF7, produced in NSO cells	Bristol-Myers Squibb (Uxbridge, UK, & Princeton, NJ, USA)	Multiple myeloma (in combination with lenalidomide and dexamethasone)	2016 (EU) 2015 (US)
	Fixixabi (infliximab), chimeric IgG1 against TNF- α , produced in CHO cells, biosimilar to Remicade. Same product as Renflexis (see above)	Samsung Bioepis (Chertsey, UK)	Various forms of arthritis, psoriasis, colitis, Crohn's disease, ankylosing spondylitis	2016 (EU)
	Infectax in EU and US, Remsima in EU (infliximab in EU, infliximab-dmyb in US), chimeric IgG1 specific for TNF- α , produced in murine Sp2/O cells, biosimilar to Remicade	Infectra: Hospira (Lake Forest, IL, USA), Celtrion (Incheon, Republic of Korea) and Hospira (Royal Leamington Spa, UK); Remsima: Celtrion (Budapest)	Certain forms of arthritis and psoriasis, Crohn's disease, ulcerative colitis, ankylosing spondylitis	2016 (US) 2013 (EU)
	Lartuvo (olaratumab), rh IgG1 specific for human platelet-derived growth factor receptor- α , produced in NSO cells	Eli Lilly (Utrecht, the Netherlands, & Indianapolis)	Sarcoma	2016 (EU & US)
	Portzaga (nectumumab), human IgG1 against the ligand binding site of human EGF receptor, produced in NSO cells	Eli Lilly (Utrecht, the Netherlands, & Indianapolis)	Non-small-cell lung cancer (in combination with gemcitabine and cisplatin)	2016 (EU) 2015 (US)
	Talzi (teixoviumab), humanized IgG4 against HL-17A, produced in CHO cells	Eli Lilly (Utrecht, the Netherlands, & Indianapolis)	Psoriasis	2016 (EU & US)
	Zibryta (daclizumab), humanized IgG1 against IL-2Ra, produced in NSO cells	Biogen (Cambridge, MA USA) Biogen Idec (Maldenhead, UK)	Multiple sclerosis	2016 (EU & US) Withdrawn 2018 (EU & US)

Table 1 Continued	Product	Company (location)	Therapeutic indication	Date approved
	Bilincyo (bilantemumab), bispecific T-cell engager antibody construct (BiTE), produced in CHO cells	Amgen Europe (Thousand Oaks, CA, USA)	Acute lymphoblastic leukemia	2015 (EU) 2014 (US)
	Co-125y (secukinumab), human IgG1 selectively binding human IL-17A, produced in CHO cells	Novartis Europharm (Camberley, UK) Novartis (East Hanover, NJ, USA)	Moderate to severe plaque psoriasis in adults	2015 (EU & US)
	Keytruda (pembrolizumab), humanized IgG4 capable of binding to the receptor PD-1, produced in CHO cells	Merck Sharp & Dohme Merck (Whitehouse Station, NJ, USA)	Advanced (unresectable or metastatic) melanoma in adults	2015 (EU) 2014 (US)
	Nivolumab BMS (nivolumab), human IgG4 against the receptor PD-1, produced in CHO cells. Same product as Opdivo (see below)	Bristol-Myers Squibb (Uxbridge, UK)	Locally advanced or metastatic squamous non-small-cell lung cancer after prior chemotherapy in adults	July 2015 (EU) Withdrawn November 2015 (US)
	Nucala (mepolizumab), humanized IgG1 capable of binding human IL-5, produced in CHO cells	GlaxoSmithKline (Cork, Ireland) GSK (Research Triangle Park, NC, USA)	Add-on treatment for severe refractory eosinophilic asthma in adult patients	2015 (EU & US)
	Opdivo (nivolumab), human IgG4 against the receptor PD-1, produced in CHO cells. Same product as nivolumab BMS (see above)	Bristol-Myers Squibb (Uxbridge, UK, & Princeton, NJ, USA)	Melanoma (as monotherapy or in combination with ipilimumab), non-small-cell lung cancer, renal cell carcinoma	2015 (EU) 2014 (US)
	Praluent (alirocumab), human IgG1 targeting PCSK9, produced in CHO cells	Sanofi-Aventis (Paris & Bridgewater, NJ, USA) Regeneron Pharmaceuticals (Tarrytown, NY, USA)	Primary hypercholesterolemia or mixed dyslipidemia, as an adjunct to diet	2015 (EU & US)
	Praxbind (idarucizumab), humanized IgG1 Fab fragment capable of binding the anticoagulant drug dabigatran, produced in CHO cells	Boehringer Ingelheim (Rhein, Germany, & Ridgefield, CT, USA)	Rapid reversal agent for the anti-coagulant drug dabigatran	2015 (EU & US)
	Repatha (evolocumab), human IgG2 capable of binding human PCSK-9, produced in CHO cells	Amgen Europe (Thousand Oaks, CA, USA)	Hypercholesterolemia and mixed dyslipidemia	2015 (EU & US)
	Unlutinix (dinutuximab), chimeric IgG1 targeting human disialoganglioside GD2, produced in Sp2/O cells	United Therapeutics (Chertsey, UK, & Silver Spring, MD, USA)	Neuroblastoma (administered in combination with GM-CSF, IL-2 and isotretinoin)	2015 (EU & US) Withdrawn 2017 (EU & US)
	Cyramza (ramucirumab), human mAb that binds the VEGF-2 receptor, produced in NSO cells	Eli Lilly Nederland (Utrecht, the Netherlands) Eli Lilly (Indianapolis)	Gastric cancer	2014 (EU & US)
	Entyvio (vedolizumab), humanized IgG targeting the human α 4 β 7 integrin, produced in CHO cells	Takeda Pharmaceuticals (Deerfield, IL, USA) Takeda Pharma (Taastrup, Denmark)	Ulcerative colitis, Crohn's disease	2014 (EU & US)
	Gazyva in US, Gazvayo in EU (obinituzumab), humanized, glyco-engineered mAb specific for B-cell antigen CD20, produced in CHO cells	Roche/Genentech Roche (Welwyn Garden City, UK)	CLL	2014 (EU) 2013 (US)
	Sylvant (situximab), chimeric mAb that binds human IL-6, produced in CHO cells	Janssen Biotech	Multicentric Castlemann disease	2014 (EU & US)
	Kadcyla (trastuzumab emtansine), humanized mAb specific for HER2 antigen, produced in CHO cells and conjugated to the small molecule cytotoxin DM1	Roche (Welwyn Garden City, UK)	Breast cancer	2013 (EU & US)
	Simponi Aria (golimumab). Active substance same as that in Simponi (see below); different strength and mode of administration	Janssen Biotech	Rheumatoid arthritis	2013 (US)
	Perjeta (pertuzumab), human mAb specific for HER2, produced in CHO cells	Roche/Genentech	Breast cancer	2013 (EU) 2012 (US)
	Abthrax (raxibacumab), human IgG mAb against the protective antigen (PA) of <i>B. anthracis</i> , produced in NSO cells	GSK/Human Genome Sciences (Rockville, MD, USA)	Inhalational anthrax	2012 (US)
	Adcetris (brentuximab vedotin), chimeric mAb conjugate specific for human CD30 (expressed on the surface of lymphoma cells), produced in CHO cells	Takeda Pharma (Roskilde, Denmark)	Lymphoma	2012 (EU) 2011 (US)
	Banlysta (delimumab), human mAb that targets human α 5 β 1 lymphocyte stimulator (BLyS), a B cell survival factor, produced in NSO cells	Human Genome Sciences Giga Group (Greenford, UK)	Lupus	2011 (EU & US)
	Xgeva (denosumab) (see Prolia)	Amgen Europe	Bone loss associated with cancer	2011 (EU) 2010 (US)
	Yervoy (ipilimumab), human mAb binding to CTLA-4 (a negative regulator of T-cell activation), thereby enhancing T cell activation and proliferation, produced in CHO cells	Bristol-Myers Squibb (Uxbridge, UK)	Melanoma	2011 (EU & US)
	Actemra in US, RoActemra in EU (tocilizumab), humanized mAb specific for IL-6, produced in a mammalian cell line	Roche (Welwyn Garden City, UK)	Rheumatoid arthritis	2010 (US) 2009 (EU)
	Arzerra (ofatumumab), human mAb specific for CD20, produced in NSO hybridoma cells	Novartis (East Hanover, NJ, USA), Genmab (Greenford, UK)	CLL	2010 (EU) 2009 (US)
	Prolia (denosumab), human mAb specific for receptor activator of nuclear factor κ B ligand (RANKL), produced in CHO cells	Amgen Europe	Osteoporosis in postmenopausal women	2010 (EU & US)
	Scintimun (besilumab), murine mAb against nonspecific cross-reacting antigen-95 (found on surface of granulocytes), produced in hybridoma cells	CIS Bio International (Gil-sur-Yvette, France)	In vivo diagnosis or investigation of sites of inflammation or infection via scintigraphic imaging	2010 (EU)
	Gimzia (certolizumab pegol), anti-TNF- α humanized and PEGylated antibody Fab' fragment, produced in <i>E. coli</i>	UCB Pharma (Brussels, Belgium)	Crohn's disease, rheumatoid arthritis	2009 (EU) 2008 (US)
	Ilaris (canakinumab), human mAb specific for IL-1 β , produced in Sp2/O cells	Novartis Pharmaceuticals (East Hanover, NJ, USA) Novartis Europharm (Dublin)	Gyopyrin-associated periodic syndromes (GAPS)	2009 (EU & US)
	Removax (catumaxomab), bispecific engineered antibody targeting the human epithelial cell adhesion molecule and human CD3 expressed on T-lymphocytes, produced in hybridoma cells	Novio Biotech (Gräfelfing, Germany)	Malignant ascites in patients with carcinomas expressing epithelial cell adhesion molecule	2009 (EU) Withdrawn 2017 (EU)
	Simponi (golimumab), human mAb specific for TNF- α , produced in Sp2/O cells	Janssen Biologics (Leiden, the Netherlands) Janssen Biotech (Horsham, PA, USA)	Rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis	2009 (EU & US)
	Stelara (ustekinumab), human mAb specific for the p40 subunit of IL-12 and IL-23, produced in Sp2/O cells	Janssen-Cilag	Moderate to severe plaque psoriasis	2009 (EU & US)
	Lucentis (ranibizumab), humanized IgG fragment that binds and inactivates VEGF-A, produced in <i>E. coli</i>	Roche/Genentech	Neovascular (wet) age-related macular degeneration	2007 (EU) 2006 (US)
	Solisris (eculizumab), humanized IgG that binds human C5 complement protein, produced in a murine myeloma cell line	Alexion Pharmaceuticals (Cheshire, CT, USA, & Paris)	Paroxysmal nocturnal hemoglobinuria	2007 (EU & US)
	Vectibix (panitumumab), human mAb that binds human EGF receptor, produced in CHO cells	Amgen Europe Abgenix	EGF receptor-expressing colorectal carcinoma	2007 (EU) 2006 (US)
	Tysabri (natalizumab), humanized mAb against selected leukocyte integrins, produced in murine myeloma cells	Biogen Inc. (Cambridge, MA, USA) Biogen Netherlands (Bathoeverdorp, the Netherlands)	Relapsing forms of multiple sclerosis	2006 (US) 2004 (US) Suspended 2005 (US) Resumed 2006 (US)
	Xolair (omalizumab), humanized mAb that binds IgE at the site of high-affinity IgE receptor binding, produced in CHO cells	Roche/Genentech	Moderate to severe persistent asthma in adults and adolescents	2005 (EU) 2003 (US)
	Zevalin (ibritumomab tiuxetan), murine mAb against the CD20 antigen, produced in CHO cells	Spectrum Pharmaceuticals (Amsterdam)	Non-Hodgkin lymphoma	2004 (EU) 2002 (US)
	Eribix (cetuximab), chimeric mAb against human EGF receptor, produced in Sp2/O cells	Merck KGaA (Darmstadt, Germany) Eli Lilly (Indianapolis)	EGF receptor-expressing metastatic colorectal cancer	2004 (EU & US)
	Raptiva (efalizumab), humanized mAb that binds to LFA-1, which is expressed on all leukocytes, produced in CHO cells	Serono (London, UK) Genentech	Chronic moderate to severe plaque psoriasis in adults	2004 (EU) 2003 (US) Withdrawn 2009 (US)
	Avastin (bevacizumab), humanized mAb against VEGF, produced in CHO cells	Roche/Genentech (Welwyn Garden City, UK)	Metastatic colorectal cancer, glioblastoma, metastatic renal carcinoma	2005 (EU) 2004 (US)
	NeuroSpec (fanlesomab), murine mAb against CD15, a surface antigen of selected leukocytes, produced in hybridoma cells	Palatin Technologies (Cranbury, NJ, USA), Mallinckrodt Pharmaceuticals (Hazelwood, MO, USA)	Imaging of equivocal appendicitis	2004 (US) Withdrawn 2005 (US)
	Humira in EU & US, Truxeda in EU (adalimumab), anti-TNF human mAb, produced in CHO cells	AbbVie (Maldenhead, UK)	Rheumatoid arthritis	2003 (EU) 2002 (US) 2002 (US) 2007 (EU)
	Bexxar (tositumomab), radiolabeled mAb against CD20, produced in murine hybridoma cells	GSK	CD20-positive follicular non-Hodgkin lymphoma	2003 (US) Withdrawn 2014 (US)
	Mabcamph (EU) or Campath (US) (alemtuzumab), humanized mAb against CD52, a surface antigen of B lymphocytes, produced in CHO cells	Genzyme (Naarden, the Netherlands) Millennium (Cambridge, MA, USA)	CLL	2001 (EU & US) Withdrawn 2012 (US)
	Herceptin (trastuzumab), humanized mAb against HER2, produced in a murine cell line	Roche (Welwyn Garden City, UK)	Treatment of metastatic breast cancer overexpressing HER2 protein	2000 (EU) 1998 (US)
	Remicade (infliximab), chimeric mAb against TNF- α , produced in Sp2/O cells	Janssen (Leiden, the Netherlands)	Crohn's disease	1999 (EU) 1998 (US)
	Synagis (palivizumab) humanized mAb directed against an epitope on the surface of respiratory syncytial virus, produced in a murine myeloma cell line	MedImmune (Gaithersburg, MD, USA) AbbVie Deutschland (Ludwigshafen, Germany) Roche (Welwyn Garden City, UK) Biogen (Cambridge, MA, USA)	Prophylaxis of lower respiratory tract disease caused by syncytial virus in children	1999 (EU) 1998 (US)
	Zenapax (daclizumab), humanized mAb against the IL-2 receptor α -chain, produced in NSO cells	Roche (Welwyn Garden City, UK) Biogen (Cambridge, MA, USA)	Prevention of acute kidney transplant rejection	1999 (EU) 1997 (US) Withdrawn 2009 (EU)

Table 1 Continued	Product	Company (location)	Therapeutic indication	Date approved
	Humascept (votumumab), human mAb against cytokeratin tumor-associated antigen, produced in a human lymphoblastoid cell line	KS Biomedex (Farnham, UK)	Detection of carcinoma of the colon or rectum	1998 (EU) Withdrawn 2004 (EU)
	MabThera in EU, Rituxan in US (rituximab), chimeric mAb against CD20 surface antigen of B lymphocytes, produced in CHO cells	Roche (Welwyn Garden City, UK)	Non-Hodgkin lymphoma	1998 (EU) 1997 (US)
	Simulect (basiliximab), chimeric mAb directed against the α -chain of the IL-2 receptor, produced in a murine myeloma cell line	Novartis (Horsham, UK)	Prophylaxis of acute organ rejection in allogeneic renal transplantation	1998 (EU)
	LeukoScan (sulesomab), murine mAb Fab fragment against granulocyte surface nonspecific cross-reacting antigen-90, produced in Sp2/O cells	Immunomedics (Darmstadt, Germany)	Diagnostic imaging for infection and inflammation in bone of patients with osteomyelitis	1997 (EU) Withdrawn 2018 (US)
	Verluma (necatinomab), murine mAb Fab fragment directed against carcinoembryonic antigen, produced in a murine cell line	Boehringer Ingelheim, NeoRx (Seattle)	Detection of small-cell lung cancer	1996 (US) Withdrawn 1999 (US)
	Tecemab KI (antimelanoma Mab fragments), murine mAb fragments (Fab/Fab2 mix) against HMW-MAA, produced in murine ascites culture	Amersham Sorin (Milan)	Diagnosis of cutaneous melanoma lesions	1996 (EU) Withdrawn 2000 (US)
	ProstaSint (capromab pentetate), murine mAb against the tumor surface antigen PSMA, produced in a murine cell line	EUSA Pharma USA (Langhorne, PA, USA)	Detection, staging and follow-up of prostate adenocarcinoma	1996 (US)
	MyoSint (micromerab pentetate), murine mAb fragment directed against human cardiac myosin, produced in a murine cell line	Centocor	Myocardial infarction imaging	1996 (US) Withdrawn 1999 (US)
	CEA-scan (arctimomab), murine mAb Fab fragment against human carcinoembryonic antigen (CEA), produced in mouse ascites culture	Immunomedics	Detection of recurrent or metastatic colorectal cancer	1996 (EU & US) Withdrawn 2005 (EU & US)
	Indimacs 125 (igovomab), murine mAb Fab fragment against the tumor-associated antigen CA125, produced in a murine cell line	CIS Bio (Gil-sur-Yvette, France)	Diagnosis of ovarian adenocarcinoma	1996 (EU) Withdrawn 2009 (US)
	ReoPro (abciximab), Fab fragments derived from a chimeric mAb against the platelet surface receptor GPIIb/IIIa, produced in a mammalian cell line	Janssen Biologics (Leiden, the Netherlands), Centocor	Prevention of blood clots	1994 (US)
	OncoSint CROV (satumomab pendetide), murine mAb against the tumor-associated glycoprotein TAG-72, produced in a murine cell line	Cytogen (Princeton, NJ, USA)	Detection, staging and follow-up of colorectal and ovarian cancers	1992 (US) Withdrawn 2002 (EU)
	Orthoclon OKT3 (muromonab CD3), murine mAb against the T-lymphocyte surface antigen CD3, produced in a murine cell line	Centocor Ortho Biotech Products (Raritan, NJ, USA)	Reversal of acute kidney transplant rejection	1986 (US)
	Other recombinant products			
	Bone morphogenetic proteins			
	Oppegna (eptomerin alfa), rh BMP-7, produced in CHO cells	Olympus Biotech (Limerick, Ireland) Wyeth (Madison, NJ, USA)	Posterolateral lumbar spinal fusion	2009 (EU) Withdrawn 2016 (US)
	Infuse bone graft, containing dibrometerin alfa, a rh BMP-2 produced in CHO cells, placed on an absorbable collagen sponge. Active substance same as that in Infuse (see below)	Medtronic BioPharma (Heerlen, the Netherlands) Wyeth Europa Genzyme Institute	Acute open tibial shaft fracture	2002 (EU)
	Inductos (dibrometerin alfa), rh BMP-2, produced in CHO cells	Medtronic BioPharma (Heerlen, the Netherlands) Wyeth Europa Genzyme Institute	Acute tibia fractures	2002 (EU)
	Infuse (rh BMP2), produced in CHO cells	Medtronic Sofamor Danek (Memphis, TN, USA)	Promotes fusion of lower spine vertebrae	2002 (US)
	OP-1 implant in US, Osgraft in EU (eptomerin alfa), rh BMP-7, produced in CHO cells	Olympus Biotech (Limerick, Ireland) Straker Biotech (Hopkinton, MA, USA)	Non-union of tibia	2001 (EU & US) Withdrawn 2015 (EU)
	Recombinant enzymes			
	BiMarin (pegvaline-papq), r phenylalanine ammonia lyase, produced in <i>E. coli</i> and PEGylated	BioMarin (Novato, CA, USA)	Phenylketonuria	2018 (US)
	Lamzede (velmanase alfa), rh α -mannosidase, expressed in precursor form in CHO cells	Chiesi Farmaceutici (Parma, Italy)	α -mannosidosis	2018 (EU)