

Supplementary Table 1. Traditional biotech product approvals 2014–July 2018. EU approvals are those approved specifically through the centralized approvals process. Due to the European regulatory structure, some additional such products may also have come on the market in individual European countries and hence direct comparison between EU and US listed approvals cannot be made. Omitted from this table are blood cells/whole plasma based products.

Product	Company	Therapeutic Indication	Approved
2018			
Albuminex (5% and 25%) human albumin prepared from donor-pooled plasma.	Bio Products Laboratory, Durham, NC	Hypovolemia, ascites, hypoalbuminemia including from burns, acute nephrosis, acute respiratory distress syndrome and cardiopulmonary bypass	2018 (USA)
Alofisel (darvadstrocel), a suspension of expanded human allogeneic mesenchymal adult stem cells extracted from adipose tissue	Takeda Pharma, Taastrup, Denmark	Rectal fistula	2018 (EU)
Epidiolex (cannabidiol), cannabinoid produced from an extract of <i>Cannabis sativa</i> L. plants	Greenwich Biosciences, Carlsbad, CA	Seizures associated with Lennox-Gastaut syndrome or Dravet syndrome	US NDA granted in June 2018, but pending controlled substance scheduling
Hematopoietic progenitor cells, cord blood (human cord blood	MD Anderson Cord Blood Bank, Houston,	Donor hematopoietic progenitor cell transplantation procedures	2018 (USA)

hematopoietic progenitor cell solution)	TX		
Omegaven (fish oil triglycerides).		Parenteral nutrition-associated cholestasis (PNAC)	2018 (USA)
2017			
Daptomycin Hospira (daptomycin), a cyclic lipopeptide antibiotic produced by fermentation of <i>Streptomyces roseosporus</i> .	Hospira, Hurley, UK	Various infections	2017 (EU)
Fibrin sealant (human) contains human fibrinogen and human thrombin, purified from pooled human plasma.	Instituto Grifols, Barcelona, Spain	Bleeding in adults undergoing surgery	2017 (USA)
Fibryna , Fibrinogen (Human) fibrinogen concentrate purified from pooled human plasma.	Octapharma USA, Hoboken, NJ	Acute bleeding episodes in adults and adolescents with congenital fibrinogen deficiency	2017 (USA)
Haegarda (C1 Esterase Inhibitor Subcutaneous [Human]). C1 Esterase Inhibitor purified from pooled human plasma.	CSL Behring, Kankakee, IL	Hereditary Angioedema	2017 (USA)
Kedrab Rabies Immune Globulin (Human), anti-rabies immunoglobulin prepared from	Kedrion Biopharma, Fort Lee, NJ	Passive post-exposure prophylaxis (PEP) of rabies infection	2017 (USA)

human plasma from donors hyper-immunized with rabies vaccine.			
Odactra House Dust Mite (Dermatophagoides farinae and Dermatophagoides pteronyssinus) Allergen Extract	Merck & Co, Whitehouse station, NJ	House dust mite (HDM)-induced allergic rhinitis,	2017 (USA)
Rydapt (midostaurin), an alkaloid derived, produced by fermentation of <i>Streptomyces staurosporeus</i> ,	Novartis Europharm Ltd, Camberley, UK	Acute myeloid leukaemia, systemic mastocytosis,	2017 (EU)
Spherox (spheroids of human autologous matrix-associated chondrocytes)	CO.DON, Teltow, Germany	Repair of cartilage defects	2017 (EU)
Tacforius (tacrolimus monohydrate) a macrolide produced by fermentation of <i>Streptomyces tsukubaensis</i> .	Teva B.V.Haarlem, the Netherlands.	Prophylaxis of transplant rejection in adult kidney or liver allograft recipients. Treatment of allograft rejection resistant to treatment with other immunosuppressive medicinal products in adult patients.	2017 (EU)
VeraSeal (human fibrinogen, human thrombin), obtained via the Cohn fractionation process of human plasma.	Instituto Grifols, S.A. Barcelona, Spain	Stop bleeding during surgery	2017 (EU)
2016			

Clevecord HPC (Allogeneic cord blood containing hematopoietic progenitor cells)	Cleveland Cord Blood Center, Cleveland, OH.	Hematopoietic progenitor cell transplantation	2016 (USA)
Coagadex (coagulation factor X, purified from human plasma)	Bioproducts laboratory, Hertfordshire, UK Bioproducts laboratory, Durham, NC.	Treatment of individuals with hereditary factor X deficiency	2016 (EU) 2015 (USA)
Cuvitru (IgG preparation purified from pooled human plasma)	Baxalta, Westlake village, CA.	Replacement therapy for primary humoral immunodeficiency	2016 (USA)
Defitelio (defibrotide sodium, an oligonucleotide mixture derived from porcine intestinal tissue)	Jazz pharmaceuticals, Palo Alto, CA	Hepatic veno-occlusive disease (VOD)	2016 (USA)
Enzepi (pancreas powder containing multiple enzymes, extracted from porcine pancreatic glands)	Allergan pharmaceuticals, Dublin, Ireland	Exocrine pancreatic insufficiency	2016 (EU), <u>withdrawn 2017</u>
Episalvan (birch bark extract)	Birken AG, Niefern-oschelbronn, Germany	Wound healing	2016 (EU)
HPC, cord blood (allogenic cord blood containing hematopoietic progenitor cells (HPC), recovered from umbilical cord material and placenta).	Bloodworks, Seattle, WA	Disorders effecting the hematopoietic system	2016 (USA)
Inhixa (enoxaparin sodium, depolymerized heparin sodium extracted from porcine intestinal mucosa)	Techdow Europe, Uppsala, Sweden	Venous thromboembolism & related.	2016 (EU)

Integra omnigraft dermal regeneration matrix (Omnigraft; also marketed as Integra dermal regeneration template), consists of a porous matrix comprised of bovine collagen and chondroitin-6-sulfate)	Integra life sciences, Plainsboro, NJ.	Neuropathic diabetic foot ulcers, thermal injuries	2016 (USA)
Juvederm volbella XC (an injectable gel consisting of cross-linked hyaluronic acid produced by a <i>Streptococcus</i> strain)	Allergan, Irvine, CA.	Lip augmentation, and correction of perioral rhytids	2016 (USA)
MACI (autologous cultured chondrocytes on a porcine collagen membrane)	Vericel, Cambridge, MA	Cartilage defects of the knee	2016 (USA)
Thorinane (enoxaparin sodium, depolymerized heparin sodium extracted from porcine intestinal mucosa. Approved as a biosimilar product.	Pharmathen, Athens, Greece	Venous thromboembolism	2016 (EU)
Vaxchora (Cholera vaccine, live, oral).	PaxVax, Redwood city, CA	Immunization against <i>Vibrio cholerae</i>	2016 (USA)
2015			
Anavip (crotalidae immune F (ab') ₂). Antibody fragment-based rattlesnake antivenin, from equine blood.	Rare Disease Therapeutics, Franklin, TN/ AnovoRx distribution, Memphis, TN.	Treatment of North American rattlesnake bites	2015 (USA)

Anthrasil (anthrax immune globulin, intravenous, human). Polyclonal antibody preparation purified from the plasma of human donors previously immunized with the BioThrax anthrax vaccine.	Cangene, Winnipeg, Manitoba, Canada	Treatment of inhalational Anthrax	2015 (USA)
Coagadex (Coagulation factor X, purified from human plasma)	Bioproducts laboratory, Durham, NC.	Treatment of individuals with hereditary factor X deficiency	2015 (USA)
Fluad (influenza vaccine, adjuvanted). Trivalent vaccine prepared from influenza viral strains propagated in embryonated hen's eggs.	Seqiris Inc., NC, USA	Influenza vaccine	2015 (USA)
Holoclar (<i>ex vivo</i> expanded autologous human corneal epithelial cells containing stem cells)	Chiesi Farmaceutici SpA, Parma, Italy	Limbal stem cell deficiency due to physical or chemical ocular burns.	2015 (EU)
Quadracel (diphtheria and tetanus toxoids and acellular pertussis absorbed and inactivated poliovirus vaccine.	Sanofi Pasteur, Swiftwater, PA	Active immunization of children against diphtheria, tetanus, pertussis and poliomyelitis	2015 (USA)
Raplixa (human fibrinogen/human thrombin, isolated directly from human plasma)	Mallinckrodt, Dublin, Ireland The medicines company, Parsippany, NJ	Used as a supportive treatment where standard surgical techniques are insufficient for improvement of haemostasis.	2015 (EU & USA)

Respreeza (human alpha 1 proteinase inhibitor, purified from pooled human plasma)	CSL Behring, Marburg, Germany	Emphysema in adults with documented severe alpha 1-proteinase inhibitor deficiency	2015 (EU)
2014			
Bellafill PMMA collagen dermal filler (dermal filler consisting of bovine collagen, as well as polymethylmethacrylate beads)	Suneva Medical, SanDiego, CA	To smooth smile lines and approve appearance of acne scars	2014 (USA)
Duavive (contains conjugated oestrogens extracted from the urine of pregnant mares)	Pfizer, Kent, UK	Treatment of oestrogen deficiency symptoms in postmenopausal women	2014 (EU)
Fluzone intradermal quadrivalent vaccine (inactivated vaccine prepared from influenza viruses propagated in embryonated chicken eggs)	Sanofi Pasteur, Swiftwater, PA	Active immunization against influenza	2014 (USA)
Gel-syn (purified sodium hyaluronate produced via fermentation of selected <i>streptococci</i>)	Institut Biochimique, Pambio-Noranco, Switzerland	Pain relief and lubricant function in patients with moderate osteoarthritis of the knee	2014 (USA)
Grastek (Timothy grass pollen allergen extract)	Merck, Whitehouse station, NJ	Treatment of grass pollen-induced allergic rhinitis	2014 (USA)
Hyqvia (blood derived human immune globulin)	Baxter	Primary immunodeficiency	2014 (USA)

Monovisc (chemically cross-linked hyaluronic acid derived from bacterial fermentation (<i>Streptococcus equi</i>).	Anika therapeutics, Bedford, MA	Treatment of pain in patients with moderate osteoarthritis of the knee	2014 (USA)
Oralair (sweet vernal, orchard, perennial rye, timothy and Kentucky blue grass mixed pollens allergen extract)	Greer laboratories, Lenoir, NC	Treatment of grass pollen-induced allergic rhinitis caused by any of the 5 grass species listed	2014 (USA)
Ragwitek (short ragweed pollen allergen extract)	Merck, whitehouse station, NJ	Treatment of short ragweed pollen-induced allergic rhinitis	2014 (USA)
Restylane silk injectable gel (chemically cross-linked hyaluronic acid derived from bacterial (<i>streptococcus</i>) fermentation)	Valeant pharmaceuticals, Bridgewater, NJ	May help increase the volume of patient's lips, and may smooth wrinkles around the mouth	2014 (USA)