

## **Supplementary information**

### **Article title**

Absorption, Distribution, Metabolism, and Excretion (ADME) of Therapeutic Proteins: Current Industry Practices and Future Perspectives

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**Table S2. Summary of Therapeutic Protein BLA Submission Packages Reviewed from 2011 through 2020**

Year	Therapeutic Protein	Company	TP Class	Indication	Dose Route	PK Species
2011	Aflibercept	Regeneron	Fc fusion protein	Neovascular wet AMD	IVT	Mo, Rt, Rb
	Belatacept	Bristol Myers Squibb	Fc fusion protein	Prophylaxis of organ rejection in kidney transplants	IV	Mo, Rt, Rb
	Belimumab	Human Genome Sciences	IgG1 mAb	Systemic Lupus Erythematosus (SLE)	IV	Mo, Mu
	Ipilimumab	Bristol Myers Squibb	IgG1 mAb	Unresectable or metastatic melanoma	IV	Mo
2012	Glucarpidase	BTG International	Enzyme	Reduce toxic methotrexate concentrations in patients with delayed methotrexate clearance due to renal impairment	IV	Mo, Dog, Mu, Rt, Rb
	Ocriplasmin	ThromboGenics	Enzyme	Symptomatic vitreomacular adhesion including macular holes	IVT	NA
	Pertuzumab	Genentech	IgG1 mAb	HER2+ metastatic breast cancer	IV	Mo
	Raxibacumab	Human Genome Sciences	IgG1 mAb	Inhalational anthrax due to Bacillus anthracis	IV	Rb
	Tbo-filgrastim	Teva Pharmaceuticals	Recombinant protein	Neutropenia	SC	Mo, Rt
	Ziv-aflibercept	Sanofi-aventis	Fusion protein	Metastatic colorectal cancer	IV	Mo
2013	Coagulation factor IX, recombinant	Baxter Healthcare Corporation	Recombinant protein	Hemophilia B	IV	Rt, Mo, Mu
	Recombinant coagulation factor XIII A-subunit	NovoNordisk	Recombinant protein	Prophylaxis treatment of congenital FXIII deficiency	IV	Mo
	Tocilizumab	Genentech-Roche	mAb	Rheumatoid arthritis; juvenile idiopathic arthritis	IV, SC	Mo, Pig
	Obinutuzumab	Genentech-Roche	mAb	Chronic lymphocytic leukemia in combo with chlorambucil	IV	Mo
2014	Ramucirumab	Eli Lilly	mAb	Advanced gastric cancer or gastro-esophageal junction adenocarcinoma	IV	Mo
	Elosulfase alfa	BioMarin	Recombinant protein/enzyme	Mucopolysaccharidosis type IVA (MPS IVA; Morquio A syndrome)	IV	Mu
	Metreleptin	Amylin	Recombinant protein	Complications of leptin deficiency in patients with congenital or acquired generalized lipodystrophy	SC	Dog, Mu

	Siltuximab	JNJ	mAb	Multicentric Castleman's disease	IV	Mo
	Pembrolizumab	Merck	mAb	Unresectable or metastatic melanoma	IV	Mo
	Nivolumab	Bristol Myers Squibb	mAb	Advanced squamous non-small cell lung cancer after prior platinum-based therapy	IV	Mo
	Blinatumomab	Amgen	Fab (bispecific Ab)	Philadelphia chromosome negative relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL)	IV	Mo
	Albiglutide	GlaxoSmithKline	Fusion protein	Type II diabetes	SC	Mo, Mu
	Vedolizumab	Takeda	mAb	Ulcerative colitis; Crohn's disease	IV	Mo
	Peginterferon beta-1a	Biogen Idec	Cytokine	Multiple sclerosis	SC	Mo
	Dulaglutide	Eli Lilly	Fc fusion	Type II diabetes	SC	Mo
	Coagulation factor IX	Biogen	Fc fusion	Hemophilia B	IV	Mu, Dog, Mo, Rt
	Antihemophilic factor	Biogen	Fc fusion	Hemophilia A	IV	Mu, Dog, Mo, Rt
	Antihemophilic factor porcine	Baxter Healthcare	Recombinant protein	Treatment of bleeding episodes in adults with acquired hemophilia A	IV	Dog, Mo
<b>2015</b>	Secukinumab	Novartis	mAb	Psoriasis	SC	Mo
	Dinutuximab	United Therapeutics	mAb	High-risk neuroblastoma	IV	Mo, Rt
	Alirocumab	Sanofi	mAb	High Cholesterol	SC	Mo, Rt
	Evolocumab	Amgen	mAb	High Cholesterol	SC	Mo, Ham
	Mepolizumab	GlaxoSmithKline	mAb	Severe Asthma	SC	Mo
	Daratumumab	Janssen	mAb	Multiple myeloma	IV	Mo, Chimp
	Necitumumab	Eli Lilly	mAb	Squamous non-small cell lung cancer	IV	Mo, Mu
	Elotuzumab	Bristol Myers Squibb	mAb	Multiple myeloma	IV	Mo, Mu
	Idarucizumab	Boehringer Ingelheim	Fab	Uncontrolled bleeding	IV	Mo, Rt
	Asfotase-a	Alexion	Fc Fusion GP	Hypophosphatasia	SC	Mo, Mu, Rt, Rb
	Sebelipase-a	Alexion	enzyme	LAL Deficiency	IV	Mo, Rt, Rb
	Parathyroid hormone	Shire Pharmaceuticals	hormone	Hypoparathyroidism	SC	Mo, Rt, Dog, Rb
<b>2016</b>	Daclizumab	Biogen	mAb	MS	SC	Mo
	Obiltoximab	Elusys Therapeutics	mAb	Anti-Anthrax	IV	Mo, Rb
	Reslizumab	Teva	mAb	Asthma	IV	Mo, Mu
	Atezolizumab	Genentech	mAb	Urothelial carcinoma; NSCLC, TNBC, SCLC, HCC, Melanoma	IV	Mo

	Olaratumab	Eli Lilly	mAb	Soft tissue sarcoma	IV	Mo, Mu
	Bezlotoxumab	MSD	mAb	Clostridium difficile infection	IV	Mu
	Ixekizumab	Eli Lilly	mAb	Psoriasis	SC	Mo
<b>2017</b>	Emicizumab	Roche/Genentech Inc	Bispecific Ab	Hemophilia A	SC	Mo, Mu
	Vestronidase Alfa-vjvk	Ultragenyx Pharm Inc	Enzyme	Mucopolysaccharidosis type VII	IV	Mo, Rt, Mu, Rb
	Benralizumab	AstraZeneca	mAb	Severe Asthma	SC	Mo
	Guselkumab	Janssen/Johnson & Johnson	mAb	Plaque Psoriasis	SC	Mo, GP
	Sarilumab	Sanofi/Regeneron	mAb	Rheumatoid Arthritis	SC	Mo, Rt, Mu
	Durvalumab	AstraZeneca	mAb	Urothelial Carcinoma	IV	Mo
	Cerliponase Alfa	BioMarin Pharmaceutical	Enzyme	Batten Disease (Tripeptidyl peptidase 1 deficiency)	ICV	Mo, Dog
	Ocrelizumab	Roche/Genentech Inc	mAb	Relapsing or primary progressive forms of Multiple Sclerosis	IV	Mo, Rt, Mu
	Dupilumab	Regeneron/Sanofi	mAb	Atopic Dermatitis	SC	Mo, Rt, Mu
	Avelumab	Merck KGaA/Pfizer	mAb	Merkel Cell Carcinoma	IV	Mo, Mu
	Brodalumab	Valeant Pharmaceuticals	mAb	Plaque psoriasis	SC	Mo
	Coagulation Factor IX (Recombinant), GlycoPEGylated	Novo Nordisk, Inc.	Recombinant pegylated protein	Hemophilia B in children and adults	IV	Dog, Mu, Pig
<b>2018</b>	Ravulizumab	Alexion	mAb	Paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS)	IV	Mo, Rb
	Tagraxofusp-erzs	Stemline	Fusion protein	Blastic plasmacytoid dendritic cell neoplasm (BPDCN)	IV	Mo
	Calaspargase pegol	Servier	Engineered protein - enzyme	Acute lymphoblastic leukemia	IV	Rt, Dog
	Emapalumab	Novimmune	mAb	Hemophagocytic lymphohistiocytosis	IV	Mo
	Elapegedemase-lvlr	Leadiant Biosciences	Enzyme	Adenosine deaminase-severe combined immunodeficiency (ADA-SCID)	IM	Rt, Dog
	Cemiplimab-rwlc	Regeneron	mAb	Metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC	IV	Mo
	Galcanezumab-gnlm	Eli Lilly	mAb	Prophylaxis of migraine	SC	Rt, Mo

	Fremanezumab-vfrm	Teva	mAb	Prophylaxis of migraine	SC	Rt, Mo, Mu, Rb
	Moxetumomab pasudotox-tdfk	AstraZeneca	Fusion protein	Hairy cell leukemia	IV	Mo, Mu, Rt
	Lanadelumab	Shire	mAb	Types I and II hereditary angioedema	SC	Mo, Rt
	Cenefermine	Dompe Farmaceutici	Recombinant protein	Neurotrophic keratitis	Ocular (topical)	Rt, Rb
	Mogamulizumab-kpkc	Kyowa Kirin	mAb	Relapsed or refractory mycosis fungoides (MF) or Sézary syndrome (SS)	IV	Mo
	Pegvaliase-pqpz	BioMarin	Enzyme	Phenylketonuria (PKU)	SC	Rt, Mo, Mu
	Erenumab-aooe	Amgen/Novartis	mAb	Migraine	SC	Mo
	Burosumab-twza	Kyowa Kirin	mAb	x-Linked hypophosphatemia (XLH), a rare, inherited form of rickets	SC	Rb, Mo
	Tildrakizumab	Merck	mAb	Plaque psoriasis	SC	Mu, Mo
	Ibalizumab-uiyk	TaiMed Biologics	mAb	HIV	IV	Mo
<b>2019</b>	Turoctocog alfa pegol	Novo Nordisk, Inc.	Pegylated recombinant protein	Hemophilia A	IV	Mo, Rt, Mu, Rb, Dog
	Crizanlizumab	Novartis Pharmaceuticals Corporation	Humanized IgG2	Sickle cell disease	IV	Mo
	Brolucizumab	Novartis Pharmaceuticals Corporation	Humanized scFv	Macular degeneration	IVT	Mo, Rb
	Risankizumab	Abbvie Inc	Humanized IgG1	Plaque psoriasis	IV, SC	Mo
	Romosozumab-aqqg	Amgen	Humanized IgG2	Osteoporosis in postmenopausal women at risk of fracture	SC	Mo, Rt, Rb
<b>2020</b>	Tafasitamab-cxix	MorphoSys AG	mAb; Humanized	Diffuse Large B-Cell Lymphoma	IV	Mo
	Inebilizumab	Viel Bio	Humanized IgG1	Neuromyelitis optica and neuromyelitis optica spectrum disorders	SC	Mu
	Teprotumumab-trbw	Horizon Therapeutics Ireland DAC	Human IgG1	Thyroid eye disease	IV	Mo
	Isatuximab	Sanofi	Chimeric IgG1	Multiple myeloma	IV	Mo, Mu
	Eptinezumab-jjmr	Lundbeck	Humanized IgG1	Migraine prevention	IV	Mo, Rt, Rb
	Satralizumab-mwge	Genentech	mAb	Neuromyelitis optica spectrum disorder	SC	Mo

Atoltivimab, Aftivimab, and Odesivimab-ebgn	Regeneron	mAb	Treatment of infection caused by Zaire ebolavirus	IV	Mo
Naxitamab-gqgk	Y-mAbs Therapeutics, Inc.	mAb	High-risk refractory or relapsed neuroblastoma	IV	Rt
Margetuximab-cmkb	MacroGenics	mAb	Metastatic HER2-positive breast cancer	IV	Mo
Ansuvimab-zykl	Ridgeback Biotherapeutics	mAb	Treatment of infection caused by Zaire ebolavirus	IV	Mo
Somapacitan	Novo Nordisk Inc.	protein conjugate	Replacement of endogenous GH in adults with growth hormone deficiency	SC	Rt, Mo, Mu, Rb, Pig

Abbreviations: IVT = intravitreal injection, IV = intravenous, SC = subcutaneous, mAb = monoclonal antibody, Ab = antibody; Mo = monkey, Rt = rat, Mu = murine, Rb = rabbit, Ham = hamster, GP = Guinea pig, IgG1 = immunoglobulin G1, IgG2 = immunoglobulin G2.