PRODUCT PIPELINE | FACTOR CONCENTRATES (DECEMBER 8, 2017)

NAME	COMPANY	TYPE	CLINICAL TRIALS	DESCRIPTION
Bax 111 (vonicog alfa) (Vonvendi in the U.S.)	Baxalta (now part of Shire)	Recombinant von Willebrand factor	In August 2015, Baxalta announced the publication of pivotal Phase III study results of Bax 111 with 37 patients with Type 3 VWD. Bleeding was treated successfully in all patients. In December 2015, the U.S. FDA granted Baxalta a biologics license for Vonvendi. In June 2017, the European Medicines Agency approved Vonvendi for use in adults with VWD.	This is a recombinant von Willebrand factor that preserves ultra-high molecular weight multimers for the treatment of VWD. Its mean half-life is 21.9 hours.
N8-GP (turoctocog alfa pegol)	Novo Nordisk	Recombinant factor VIII	The pathfinderT2 Phase III trial for hemophilia A patients aged 12 years or older was completed in March 2014. 175 patients were treated prophylactically (50 IU/kg every 4 days, resulting in a mean trough level of 8%) and 11 patients were treated on demand. One inhibitor developed among the 186 patients treated.	This glycopegylated rFVIII was shown to have a half-life of 18.4 hours, approximately 1.5 times most current treatments.
BAY94-9027	Bayer	Recombinant factor VIII	In February 2014, Bayer announced positive results from its *Protect VIII* Phase III trial in 134 adolescents and adults, who received FVIII every 7, 5 or 3.5 days. The study met its primary objective of protection from bleeds with fewer infusions. No inhibitors were reported. In October 2017, Bayer submitted a Biologics License Application to the U.S. FDA, which is now being reviewed.	This is a pegylated, long-acting plasma/albumin free, full-length rFVIII. The goal is to increase half-life and reduce the frequency of infusions.
Adynovate (Bax 855)	Baxalta (now part of Shire)	Recombinant factor VIII	In August 2014 Baxalta reported positive results from its pivotal Phase III trial that included 137 adolescent and adult patients. No inhibitors or allergic reactions were reported. The U.S. FDA approved Adynovate for adults and adolescents, aged 12 years and over, in November 2015. Health Canada approved Adynovate for bleeding, prophylaxis and surgery in persons 12 years and older in November 2016. The European medicines Agency did the same in November 2017.	This is a pegylated, long-acting plasma/albumin free, full-length rFVIII. The goal is to increase half-life and reduce the frequency of infusions. The Phase III trial showed a half-life of 1.4 times that of Advate. None of the patients in the trial developed an inhibitor.

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rVIII-SingleChain (Afstyla in the U.S. and Canada)	CSL Behring	Recombinant factor VIII	In June 2015 CSL announced results of its Affinity Phase I/III study with 175 subjects over the age of 12. In July 2016, CSL released results of a Phase III study in children under 12. It showed that 2- or 3-times weekly prophylaxis resulted in a 0.0 mean annual bleed rate (ABR) for "spontaneous" hemorrhages and a 3.69 overall ABR. Afstyla was appoved for use in children and adults by the U.S. FDA in May 2016 and by Health Canada in December 2016.	This is a novel recombinant single-chain factor VIII design that uses a strong, covalent bond to von Willebrand factor to reduce clearance and extend half-life compared to traditional factor VIII. Mean half-life in adults is 14 hours. No inhibitors developed after 14,000 exposure days in 175 study subjects.
BAX 826	Baxalta, now part of Shire	Recombinant factor VIII	In March 2016, Baxalta reported dosing of the first patient in its Phase I clinical trial of BAX 826. In May 2017, Shire announced a pre-defined once-weekly dosing target was not met.	BAX 826 uses proprietary polysialic acid (PSA) technology to extend its circulating half-life.
NN79 (N9-GP; Refixia in Europe)	Novo Nordisk	Recombinant factor IX	A Phase III trial (paradigm 2) was completed in May 2013. In January 2016, Novo Nordisk filed a license application with the European Medicines Agency, which was approved in June 2017 for persons 12 years and over. The EMA wrote: "… part of the active substance in Refixia (called PEG) may accumulate in the body, including in a structure in the brain called choroid plexus, following long-term treatment. Since this could potentially cause problems especially in children below 12 years of age, Refixia is only approved for use in in adults and children from 12 years of age.	Prolonged half-life is obtained by site-direction of glycoPEGylation. A 40-kDa polyethylene glycol molecule is attached to the activation peptide of FIX. Half-life was reported to be five times longer than the standard FIX. In the Phase III trials, once-weekly administration of Refixia maintained factor IX activity levels above 15 percent, and reduced the median annualized bleeding rate to 1.0. No inhibitors were reported.
CB2679d/ISU304	Catalyst Biosciences, Inc. & ISU Abxis	Recombinant factor IX	In April 2017, the company announced it had received approval from the Korean Ministry of Food and safety to begin human clinical trials for its new investigational drug CB2679dISU304. In September 2017, the company reported on Phase I/II trial results, which showed a potency 22 times that of Benefix in IV transfusions, demonstrating proof-of-concept.	The company claims that CB 2679d/ISU304, a highly potent next-generation coagulation Factor IX variant, has demonstrated the potential to normalize human Factor IX levels with a daily subcutaneous injection in preclinical studies.

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Coagadex (Factor X)	Bio Products Laboratory (BPL)	A plasma-derived factor X concentrate to treat hereditary factor X deficiency	In April 2015, BPL announced results from its pivotal Phase III trial. Control of bleeding was excellent or good in 98% of bleeding episodes in 16 patients. No adverse events caused withdrawal from the trial. In October 2015, the U.S. FDA approved Coagadex for use. In February 2016, the European Medicines Agency recommended to grant market authorization.	Human coagulation factor X is a protein derived from human plasma.