

PRODUCT PIPELINE | NON-FACTOR COAGULATION PRODUCTS (FEBRUARY 22, 2018)

NAME	COMPANY	TYPE	CLINICAL TRIALS	DESCRIPTION
<p>Emicizumab - Anti-factor IXa/X bispecific antibody (called Hemlibra in the U.S. and previously called ACE910)</p>	<p>Chugai Pharmaceutical Co, Genentech & Roche</p>	<p>A monoclonal antibody that acts as a FVIII-mimetic cofactor</p>	<p>In November 2017, the U.S. FDA licensed emicizumab, under the brand name Hemlibra, for on-demand and prophylactic treatment of patients with hemophilia A and inhibitors with weekly sub-cutaneous injections. The label includes a “black box” warning around the use of activated prothrombin complex concentrate (FEIBA) because of the risk of thrombotic complications.</p> <p>In late November 2017, Roche(Genentech) announced positive results for its Phase III trial (HAVEN III) in patients with hemophilia A without inhibitors. The once-weekly Hemlibra therapy reported superiority in reducing treated bleeds to factor VIII prophylaxis in an intra-patient comparison.</p> <p>In December 2017, Roche announced Phase III study results with 57 patients with inhibitors, showing very low annual bleeding rates with once-weekly subcutaneous injections.</p>	<p>Emicizumab is a bi-specific antibody that mimics coagulation factor VIII with a half-life of three weeks. It offers an alternative option for patients with hemophilia A with inhibitors, through user-friendly, sub-cutaneous routine prophylaxis.</p>
<p>Fitusiran (ALN-AT3)</p>	<p>Alnylam Pharmaceuticals Inc. (in alliance with Genzyme), soon to be taken over by Sanofi</p>	<p>A subcutaneously delivered RNAi therapeutic. It has the potential to be used in a number of bleeding disorders.</p>	<p>The FDA has granted orphan drug status to this compound for both hemophilia A and B.</p> <p>In December 2016, Alnylam announced that once-monthly subcutaneous administration of fitusiran at two fixed dose levels, 50 mg (6 patients) and 80 mg (10 patients), achieved potent and dose-dependent lowering of antithrombin (AT) and increases in thrombin generation in patients with hemophilia A or B with inhibitors. Median annual bleeding rates fell dramatically.</p> <p>During a Phase III trial in mid-2017, however, the company announced the death of one of the 33 trial subjects due to an intracranial clot. The trial was put on temporary hold.</p> <p>In November 2017, Alnylam announced it had agreed with the regulator, the U.S. FDA, to stricter safety measures and risk mitigation strategies. The trial will re-start in 2018.</p>	<p>ALN-AT3 aims to correct the hemostatic imbalance in hemophilia by reducing antithrombin, an endogenous anticoagulant, thus increasing thrombin generation and improving hemostasis. with once-a-month subcutaneous dosing.</p>