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Product Snapshot

Pipeline

SB-525 (giroctocogene fitelparvovec)

Provided to you by FormularyDecisions
Last updated 06/16/2022
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Product Overview

Manufacturer	Pfizer Inc. and Sangamo Therapeutics, Inc.
Status	• No PDUFA date at this time • Fast Track status: 5/16/2017; Orphan Drug designation: 5/3/2017; Regenerative Medicine Advanced Therapy designation: 7/5/2019
Proposed indication	Hemophilia A
Therapeutic class	Gene therapy
Mechanism of action	• SB-525 comprises a recombinant AAV6 encoding the complementary deoxyribonucleic acid for B domain deleted human Factor VIII to optimize both the vector manufacturing yield and liver-specific Factor VIII protein expression[1] ○ The SB-525 transcriptional cassette incorporates multi-factorial modifications to the liver-specific promoter module, Factor VIII transgene, synthetic polyadenylation signal, and vector backbone sequence • SB-525 aids in the correction of the disease-causing mutation in the endogenous copy of the Factor VIII gene

Formulation	Solution for injection
Dose and administration	• Dosing: 9e11 vg/kg to 3e13 vg/kg have been studied[1] • Route of administration: IV infusion[1] • Setting of administration: Not yet determined
Epidemiology of disease	• Incidence: In 2015, about 1/5,000 to 1/6,000 people (approximately 400 babies) in the US were born with hemophilia A (based on 2015 NORD data and 2016 CDC data)[2,3] • Prevalence: In 2016, there was an estimated 20,000 people in the US with hemophilia (based on 2016 CDC data); however, the exact number of people living with hemophilia A in the US is unknown[3]
Relevant ICD-10-CM code	D66 (hereditary Factor VIII deficiency)
Distinguishing factors of product	• Unique MOA: Designed to deliver a copy of the Factor VIII gene to a patient's liver cell to induce Factor VIII expression and thus raise Factor VIII levels[1] • Study results have shown that SB-525 can safely induce durable clotting Factor VIII activity in patients with severe hemophilia A as demonstrated in the phase 1/2 Alta clinical trial[1]
Relevant disease background and treatment guidelines	• Hemophilia is a hereditary bleeding disorder characterized by an underlying defect in the ability to generate adequate levels of thrombin needed for effective clotting, such as a deficiency in coagulation FVIII (hemophilia A) or coagulation FIX (hemophilia B)[4] • Prophylaxis is the standard of care for people with severe hemophilia and for some with moderate hemophilia[5] • Prophylaxis with CFCs is always recommended over episodic therapy and should be individualized, taking into account patient bleeding phenotype, joint status, individual pharmacokinetics, and patient preference[5] • Management of acute bleeding necessitates CFC replacement therapy and should be carried out in consultation with a hemophilia treatment center and staff experienced in inhibitor treatment[5] • World Federation of Hemophilia: Guidelines for the Management of Hemophilia (3rd Edition, August 2020)[5]
Competitive landscape	• FDA-approved agents for the treatment of hemophilia A include HEMLIBRA® (emicizumab-kxwh), NOVOEIGHT® (antihemophilic factor, recombinant), and XYNTHA® (antihemophilic factor [recombinant]); this list is not all-inclusive[6-8] • Investigational agents

	BMN-270[9,10] (valoctocogene roxaparvovec)	SAR-439774[11] (fitusiran)
Manufacturer	BioMarin Pharmaceutical Inc	Sanofi
Mechanism of action	Gene therapy	siRNA
Phase of development	BLA resubmission expected Q2 2022	3
PDUFA	Unknown	Unknown

Key: AAV6 – adeno-associated virus serotype 6 vector; BLA – Biologics License Application; CDC – Centers for Disease Control and Prevention; CFC – clotting factor concentrate; FVIII – Factor VIII; IV – intravenous; MOA – mechanism of action; NORD – National Organization for Rare Disorders; PDUFA – Prescription Drug User Fee Act; siRNA – small interfering ribonucleic acid.

Key Comparators

	SB-525 (giroctocogene fitelparvovec)[1]	NOVOEIGHT (antihemophilic factor, recombinant)[6]	XYNTHA (antihemophilic factor [recombinant])[7]	HEMLIBRA (emicizumab-kxwh)[8]
Manufacturer	Pfizer Inc. and Sangamo Therapeutics, Inc.	Novo Nordisk Inc.	Wyeth Pharmaceuticals	Genentech, Inc.
Indications	Proposed indication: Severe hemophilia A	Adults and children with hemophilia A for: On-demand treatment and control of bleeding episodes Perioperative management Routine prophylaxis to reduce frequency of bleeding episodes	Adults and children with hemophilia A for: Control and prevention of bleeding episodes and for perioperative management	Adults and children with hemophilia A for: Routine prophylaxis to prevent or reduce frequency of bleeding episodes
Dosing	Route: IV injection Dosages studied ranged from 9e11 vg/kg to 3e13 vg/kg	IV injection Dosage required (IU) = body weight (kg) x desired Factor VIII increase (IU/dL or % normal) x 0.5 (IU/kg per IU/dL) Frequency determined by type of bleeding episode and recommendation of treating physician	Route: IV injection Dose: Required units = body weight (kg) x desired Factor VIII rise (IU/dL or % of normal) x 0.5 (IU/kg per IU/dL) Frequency of administration is determined by type of bleeding episode and recommendation of treating physician	3 mg/kg SC once weekly for the first 4 weeks, followed by one of the following: 1.5 mg/kg once weekly 3 mg/kg once every 2 weeks 6 mg/kg once every 4 weeks
Available or anticipated pricing[12]	TBD	AWP: $2.40 WAC: $2.00 (1 IU)	AWP: $1.91 WAC: $1.59 (1 IU)	AWP: $18,948.01 WAC: $15,790.01 150 mg/mL (1 mL SOL)

Key: AWP – average wholesale price; SC – subcutaneous; SOL – solution; TBD – to be determined; WAC – wholesale acquisition cost.

Clinical Trials

High-level overview:

- The SB-525 clinical development program consists of an open-label, adaptive, and dose-ranging phase 1/2 study for hemophilia A, an open-label, lead-in study for hemophilia A and B, and a phase 3 pivotal AFFINE trial evaluating SB-525 in adult male participants with moderately severe or severe hemophilia A[13-16]
- Initial results of the Alta study demonstrate that SB-525 has the potential to be a predictable and reliable treatment that may bring clinical benefit to patients with hemophilia A
    - SB-525 was generally well tolerated and demonstrated a dose-dependent increase in Factor VIII activity levels

NCT / Study ID	Study description	Study population	Phase, study design, sample size	Status	Highlights
NCT03061201[14] ALTA	Open-label, adaptive, dose-ranging study assessing the safety and tolerability of SB-	• Inclusion: Males aged ≥18 years diagnosed with severe hemophilia A treated or exposed to Factor VIII	Phase 1/2, OL N=11 (actual)	• Active, not recruiting • Estimated study completion date: July 23, 2024	• All patients (N=4) treated with the SB-525 dose of 3e13 vg/kg did not experience any

NCT / Study ID	Study description	Study population	Phase, study design, sample size	Status	Highlights
	525 in patients with severe hemophilia A	concentrates or cryoprecipitate for at least 150 EDs; ≥12 bleeding episodes if receiving on-demand therapy over preceding 12 months • Exclusion: Presence of neutralizing antibodies; evidence of any bleeding disorder in addition to hemophilia A; markers of hepatic inflammation or acute kidney injury		• Initial results presented in 2019[17]	spontaneous bleeding episodes ≥3 weeks post-treatment and did not require Factor VIII replacement therapy following initial prophylactic period post-SB-525 administration[17] • SB-525 showed dose-dependent increases in Factor VIII activity levels across all dose cohorts evaluated[17] • SB-525 was generally well tolerated, with treatment-related significant AEs of hypotension (grade 3, N=1) and fever (grade 2, N=3) only occurring in patients on the 3e13 vg/kg dose, which resolved with treatment within 24 hours[17] • At 104 weeks, 5 patients in the highest dose 3e13 vg/kg cohort had mean Factor VIII activity of 25.4% via chromogenic clotting assay[18] • The mean ABR through 1 year post-infusion was 0 and was 1.4 through the total duration of follow-up as of the October 1, 2021 cutoff date; all bleeding events occurred after 69 weeks post-infusion[18]

NCT / Study ID	Study description	Study population	Phase, study design, sample size	Status	Highlights
NCT03587116[15]	Open-label, multicenter, lead-in study to assess the efficacy and safety of SB-525 in patients with hemophilia A or B	• Inclusion: Males aged ≥18 and <65 years diagnosed with severe hemophilia A or B; previous experience with Factor IX or VIII therapy; no known hypersensitivity to Factor IX or VIII replacement product • Exclusion: Anti-AAV-Spark100 neutralizing antibody titer above or equal to 1:1 in hemophilia B patients or Anti-SB-525 capsid AAV6 neutralizing antibody titer (above or equal to lowest detectable titer) in hemophilia A patients; diagnosis of hepatitis B or C; currently on antiviral therapy for hepatitis B or C; pre-existing diagnoses of portal hypertension, splenomegaly, or hepatic encephalopathy; diagnosis of HIV; history of chronic infection; previously on fidanacogene elaparvovec, SB-525, or any AAV gene-based therapy; planned procedure requiring Factor IX or VIII surgical prophylactic factor treatment in next 24 hours	Phase 3, OL, MC N=250 (estimated)	• Recruiting • Estimated study completion date: May 14, 2023	• Primary endpoints include ABR and incidence of serious AEs • Events of special interest include inhibitor against Factor IX or VIII, thrombotic events, and Factor IX or VIII hypersensitivity reactions
NCT04370054[16,18] AFFINE	Open-label, multicenter, pivotal study to evaluate the efficacy and safety of giroctocogene fitelparvovec in adult male participants with moderately severe or severe hemophilia A for	• Inclusion: Males who have been followed on routine Factor VIII prophylaxis therapy during the lead-in study and have ≥150 documented EDs to a Factor VIII protein product; moderately severe to severe hemophilia A; suspension of	Phase 3, OL, MC N=63 (estimated)	• Active, not recruiting • Estimated study completion date: September 16, 2027	• Primary endpoint is the ABR[16] • Events of special interest include Factor VIII activity levels, annualized infusion rate, annualized Factor VIII consumption, change in

NCT / Study ID	Study description	Study population	Phase, study design, sample size	Status	Highlights
	the study duration of 5 years	Factor VIII prophylaxis therapy post-study drug infusion • Exclusion: Anti-AAV6 neutralizing antibodies; history of inhibitor to Factor VIII; laboratory values at screening visit that are abnormal or outside acceptable study limits; significant and/or unstable liver disease, biliary disease, or significant liver fibrosis; planned surgical procedure requiring Factor VIII prophylactic factor treatment 12 months from screening visit; active hepatitis B or C; serological evidence of HIV-1 or HIV-2 with CD4+ cell count ≤200 mm^3 and/or viral load >20 copies/mL			joint health, patient-reported outcome instruments, and incidence and severity of AEs[16]

Key: AAV – adeno-associated viral; AAV6 – adeno-associated virus serotype 6 vector; ABR – annual bleeding rate; AE – adverse event; CD4+ – cluster of differentiation 4 positive; ED – exposure day; MC – multicenter; N – sample size; NCT / Study ID – National Clinical Trial / study identifier; OL – open-label.

P&T Considerations

Factors affecting uptake	• Giroctocogene fitelparvovec would be the first or second gene therapy FDA approved for hemophilia A, depending on the regulatory path for valoctocogene roxaparvovec • No information on drug cost is available
Formulary criteria	Potential prior authorization criteria for consideration: • Diagnosis of severe hemophilia A • Aged ≥12 years • Male gender • Prescriber is a hematologist • Previous trial of factor concentrates or bypassing agents • No previous receipt of gene therapy for hemophilia A • Appropriate dosing
Contracting	Payers may consider entering into a value-based outcome agreement with the manufacturer; possible outcomes may include ABR over a set number of months or years

Key: ABR – annual bleeding rate; FDA – Food and Drug Administration.

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