



March 1, 2016

SBC-103 (rhNAGLU enzyme) Shows a 26.2 Percent Mean Reduction in Heparan Sulfate in Cerebrospinal Fluid at the Highest Dose Studied in Patients with Mucopolysaccharidosis IIIB (MPS IIIB) in Phase 1/2 Study at Six Months

-Data Presented as Late-Breaker at WORLDSymposium™ 2016-

NEW HAVEN, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (Nasdaq: ALXN) announced today that researchers presented 24-week results from an ongoing open-label, Phase I/II trial of intravenous SBC-103 (rhNAGLU enzyme), an investigational enzyme replacement therapy, in children with mucopolysaccharidosis IIIB (MPS IIIB, also known as Sanfilippo B syndrome), a genetic, progressive, and devastating rare lysosomal storage disease. Data from this study showed a 26.2 percent mean reduction from baseline in total heparan sulfate (HS) levels in cerebrospinal fluid (CSF) at 24 weeks in the highest dose studied (3 mg/kg every other week [qow]).¹ These data were presented in a late-breaking poster at the 12th Annual WORLDSymposium™ in San Diego.

MPS IIIB is caused by genetic mutations that result in a marked decrease in N-acetyl- α -D-glucosaminidase (NAGLU) enzyme activity, leading to abnormal accumulation of HS in the brain and other organs. This results in severe neurocognitive decline, behavioral disturbances, speech loss, increasing loss of mobility, and premature death.²

"MPS IIIB is a severe and progressive disorder characterized by systemic and central nervous system (CNS) morbidities, with devastating and life-threatening outcomes for affected children. SBC-103 is manufactured with our proprietary protein expression platform, and we are encouraged by its potential to be administered intravenously and cross the blood-brain barrier to provide both systemic and CNS clinical benefits for patients suffering from MPS IIIB," said Martin Mackay, Ph.D., Executive Vice President and Global Head of R&D at Alexion. "These 24-week results, coupled with the increased dose response observed in animal models, support dose escalation for all patients in the study."

Eleven children with MPS IIIB (ages 2 years to 10 years at study entry) were enrolled in the first-in-human study, which included three parallel dosing groups of intravenous SBC-103 (0.3, 1.0 and 3.0 mg/kg qow). The primary endpoint of the ongoing trial is safety and tolerability, and key secondary endpoints presented at WORLDSymposium include changes from baseline in HS levels in CSF and serum as well as pharmacokinetics (PK) and pharmacodynamics (PD). Additional secondary endpoints related to neurocognitive outcomes, brain structure, and changes in HS levels in urine are also being evaluated.

Most adverse events (AEs) in the study were mild and unrelated to SBC-103, and no patient discontinued the study. Of 11 patients in the study, two patients experienced a total of four serious AEs (bacteremia, pyrexia, staphylococcal bacteremia, and cyanosis [pre-treatment]) that were deemed not related to SBC-103. Six infusion-associated reactions occurred in three patients (pyrexia, chills, hypertension, and tachycardia).¹

At 24 weeks of treatment, the analysis showed a 26.2 percent mean reduction from baseline in total HS CSF in the 3 mg/kg (N=4) dosing cohort. These data are directionally consistent with reductions in brain HS observed in the NAGLU -/- mouse model. Patients in the 0.3 mg/kg (N=3) and 1.0 mg/kg (N=4) groups had a 10.9 percent mean increase and a 0.4 percent mean decrease in HS CSF, respectively. Additionally, researchers reported mean reductions in total serum HS at 24 weeks of 39.6 percent, 53.9 percent, and 40.5 percent at 0.3, 1.0 and 3.0 mg/kg, respectively. These findings are directionally consistent with reductions in liver HS observed in the NAGLU -/- mouse model. Researchers also reported PK findings for SBC-103 at 24 weeks, noting that individual HS CSF reduction levels were linearly correlated with an increase in serum PK exposures.¹

An interim 12-week analysis from the Phase 1/2 study reported in December 2015 showed a dose-dependent reduction of HS levels in CSF in the three dosing cohorts (mean reductions of 3 percent, 6 percent and 11 percent at 0.3 mg/kg [N=3], 1.0 mg/kg [N=4], and 3.0 mg/kg [N=3], respectively). One patient who received only one 3 mg/kg and one 1 mg/kg dose (instead of 6 doses at 3 mg/kg) due to an unrelated SAE was excluded from this analysis, and restarted treatment at week 8.

About Mucopolysaccharidosis IIIB (MPS IIIB)

MPS IIIB (also known as Sanfilippo B syndrome) is a genetic, progressive, and devastating rare lysosomal storage disease.

In patients with MPS IIIB, genetic mutations result in a marked decrease in N-acetyl- α -D-glucosaminidase (NAGLU) enzyme activity, which leads to the accumulation of heparan sulfate (HS) in the brain and other organs. The accumulation of abnormal HS leads to progressive brain atrophy, neurocognitive decline, behavioral disturbances, speech loss, increasing loss of mobility, and premature death.² MPS IIIB typically presents in children during the first few years of life, and patients have a greater than 50 percent mortality rate by 17 years of age.³

There are no approved treatments for patients with MPS IIIB. Current supportive care is palliative for behavioral problems, sleep disturbances, seizures, and other complications, and does not address the root cause of MPS IIIB or stop disease progression.^{2,3}

About SBC-103

SBC-103 (rhNAGLU enzyme) is an enzyme replacement therapy being investigated in a Phase 1/2 trial for patients with MPS IIIB. It is a recombinant form of the N-acetyl- α -D-glucosaminidase (NAGLU) enzyme intended to reduce accumulated heparan sulfate by replacing the missing or deficient NAGLU enzyme. SBC-103 was granted orphan designation by the U.S. Food and Drug Administration (FDA) in April 2013 and by the European Medicines Agency (EMA) in June 2013. It received Fast Track designation by the FDA in January 2015.

SBC-103 utilizes Alexion's proprietary protein expression platform, a novel production process that has the potential to enable enzyme replacement therapies (ERTs) to cross the blood-brain barrier. Alexion is evaluating the use of this platform in the development of ERTs for severe and devastating lysosomal storage diseases that have central nervous system manifestations.

About Alexion

Alexion is a global biopharmaceutical company focused on developing and delivering life-transforming therapies for patients with devastating and rare disorders. Alexion developed and commercializes Soliris[®] (eculizumab), the first and only approved complement inhibitor to treat patients with paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS), two life-threatening ultra-rare disorders. As the global leader in complement inhibition, Alexion is strengthening and broadening its portfolio of complement inhibitors, including evaluating potential indications for eculizumab in additional severe and ultra-rare disorders. Alexion's metabolic franchise includes two highly innovative enzyme replacement therapies for patients with life-threatening and ultra-rare disorders, Strensiq[®] (asfotase alfa) to treat patients with hypophosphatasia (HPP) and Kanuma[™] (sebelipase alfa) to treat patients with lysosomal acid lipase deficiency (LAL-D). In addition, Alexion is advancing the most robust rare disease pipeline in the biotech industry with highly innovative product candidates in multiple therapeutic areas. This press release and further information about Alexion can be found at: www.alexion.com.

[ALXN-G]

Forward-Looking Statements

This news release contains forward-looking statements, including statements related to potential medical benefits of SBC-103 for mucopolysaccharidosis IIIB (MPS IIIB). Forward-looking statements are subject to factors that may cause Alexion's results and plans to differ from those expected, including for example, risks and uncertainties of drug development, decisions of regulatory authorities regarding marketing approval or material limitations on the marketing of SBC-103 for MPS IIIB, delays in arranging satisfactory manufacturing capabilities and establishing commercial infrastructure for SBC-103 for MPS IIIB, the possibility that results of clinical trials are not predictive of safety and efficacy results of SBC-103 in broader or different patient populations, the risk that estimates regarding the number of patients with MPS IIIB are inaccurate, and a variety of other risks set forth from time to time in Alexion's filings with the Securities and Exchange Commission, including but not limited to the risks discussed in Alexion's Annual Report on Form 10-K for the period ended December 31, 2015. Alexion does not intend to update any of these forward-looking statements to reflect events or circumstances after the date hereof, except when a duty arises under law.

References

1. Whitley CB, Escolar ML, Vijay S, et al. Initial, 24 Week Results of Heparan Sulfate Levels in Cerebrospinal Fluid (CSF) and Serum in an Open Label, Phase I/II, First-in-Human Clinical Trial of Intravenous SBC-103 in Mucopolysaccharidosis IIIB. Poster presented at WORLDSymposium Annual Meeting 2016, San Diego, February 29-March 4. Abstract LB-33.
2. Wijburg FA, Wegrzyn G, Burton BK, Tytki-Szymanska A. "Mucopolysaccharidosis type III (Sanfilippo syndrome) and misdiagnosis of idiopathic developmental delay, attention deficit/hyperactivity disorder or autism spectrum disorder." *Acta Paediatr.* 2013;102(5):462-70.
3. Heron, B., et al. *Am. J. Med. Genet Part A.* 2011;155:58-68.

View source version on [businesswire.com](http://www.businesswire.com/news/home/20160301006917/en/): <http://www.businesswire.com/news/home/20160301006917/en/>

Alexion Pharmaceuticals, Inc.

Media

Stephanie Fagan, 203-271-8223

Senior Vice President, Corporate Communications

OR

Amanda Fahey, 203-699-7240

Associate Director, Corporate Communications

OR

Investors

Elena Ridloff, CFA, 203-699-7722

Vice President, Investor Relations

Source: Alexion Pharmaceuticals, Inc.

News Provided by Acquire Media