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## **Alexion Presents New SBC-103 (rhNAGLU enzyme) Phase 1/2 Data on Brain MRI and Neurocognitive Assessments in Patients with Mucopolysaccharidosis IIIB (MPS IIIB)**

*Preliminary evidence suggest the potential for dose-dependent disease stabilization in MPS IIIB patients treated with SBC-103 at six months*

*Data Presented at 14<sup>th</sup> International Symposium on MPS and Related Diseases 2016*

NEW HAVEN, Conn.--(BUSINESS WIRE)-- Alexion Pharmaceuticals, Inc. (Nasdaq:ALXN) announced today that researchers presented new data from an ongoing open-label, Phase 1/2 trial of intravenous (IV) SBC-103 (rhNAGLU enzyme), an investigational enzyme replacement therapy, in children with mucopolysaccharidosis IIIB (MPS IIIB, also known as Sanfilippo syndrome type B), a genetic, progressive, and devastating rare lysosomal storage disease. Preliminary evidence, based on brain scans (MRI) and neurocognitive assessments at 24 weeks, showed the potential for disease stabilization in patients with MPS IIIB treated with SBC-103.<sup>1</sup> These data were presented at the 14<sup>th</sup> International Symposium on MPS and Related Diseases in Bonn, Germany.

MPS IIIB is caused by genetic mutations that result in a marked decrease in N-acetyl- $\alpha$ -D-glucosaminidase (NAGLU) enzyme activity, leading to abnormal accumulation of heparan sulfate (HS) in the brain and other organs, as well as progressive brain atrophy with cortical gray matter (CGM) volume loss.<sup>2-5</sup> This results in severe neurocognitive decline, behavioral disturbances, speech loss, increasing loss of mobility, and premature death.<sup>6</sup> At present there is no treatment for this disorder. MPS IIIB typically presents in children during the first few years of life, and these children have a greater than 50 percent mortality rate by 17 years of age.<sup>7</sup>

"MPS IIIB is a devastating and life-threatening disorder, with no available treatments, and has a severe and progressive impact on the cognitive function of children suffering with the disease," said Martin Mackay, Ph.D., Executive Vice President and Global Head of R&D at Alexion. "These new data presented today suggest the potential of SBC-103 to cross the blood-brain barrier when administered intravenously and provide preliminary evidence of potential dose-dependent disease stabilization at 24 weeks in children with MPS IIIB."

Researchers presented preliminary results for volumetric brain MRI and neurocognitive assessments performed after 24 weeks of IV SBC-103 at 0.3, 1, or 3 mg/kg every other week (QOW). MRI scans for those dosed at 3 mg/kg showed that 3 out of 4 patients had an increase or no change (-1% to +1%) in CGM volume compared to baseline suggesting a potential for disease stabilization at this dose. In the 1 mg/kg group and 0.3 mg/kg group, MRI scans showed that 2 out of 3 and 0 out of 3 patients respectively had an increase or no change in CGM volume compared to baseline. In the neurocognitive assessments for the 3 mg/kg group, 3 out of 4 patients had an increase in both mental age equivalent (AEq) and developmental quotient (DQ) compared to baseline. For the 1 mg/kg group, 2 out of 4 patients had an increase in both AEq and DQ compared to baseline, and for 0.3 mg/kg group, 1 out of 3 patients had an increase in both AEq and DQ compared to baseline. Overall, response profiles among the 3 mg/kg treatment groups suggest a potential dose effect as compared to the 0.3 mg/kg and 1 mg/kg groups.<sup>1</sup>

"These new preliminary data from the brain MRI and neurocognitive assessments of children with MPS IIIB show, for the first time, the potential for disease stabilization following intravenous administration of SBC-103," said Chester B. Whitley, Ph.D., M.D., Department of Pediatrics, University of Minnesota, Minneapolis, U.S. "In addition to the evidence of heparan sulfate reduction in cerebrospinal fluid, these findings support the continued advancement of this clinical program, and dose escalation to 5 mg/kg and 10 mg/kg for all patients in the study with this severe and progressive rare disease."

Eleven children with MPS IIIB (ages 2 years to 10 years at study entry) were enrolled in this 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 *MPS 2016* include effect of SBC-103 on total HS levels in cerebrospinal fluid (CSF) and serum, brain structures (MRI) and neurocognitive status, and pharmacokinetic (PK) profile of SBC-103.

During 24 weeks of treatment with SBC-103 at the highest dose of 3 mg/kg, most adverse events (AEs) were mild in severity and no patient discontinued 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. Seven infusion-

associated reactions occurred in three patients (pyrexia, chills, hypertension, and tachycardia).<sup>1</sup>

As previously presented at the 12<sup>th</sup> Annual *WORLD Symposium*<sup>TM</sup>, patients treated with SBC-103 had a 26.2 percent mean reduction from baseline in total HS levels in CSF at 24 weeks in the highest dose studied (3 mg/kg QOW). Additionally, at week 24, patients in the 0.3 mg/kg and 1.0 mg/kg groups had a 10.9 percent mean increase and a 0.4 percent mean decrease in HS CSF, respectively. HS reduction in CSF was linearly correlated with SBC-103 serum PK exposures. Total change from baseline in serum HS was -39.6 percent, -53.9 percent and -40.5 percent for 0.3 mg/kg, 1 mg/kg, and 3 mg/kg groups, respectively.<sup>8</sup>

### **About Mucopolysaccharidosis IIIB (MPS IIIB)**

MPS IIIB (also known as Sanfilippo syndrome type B) 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- $\alpha$ -D-glucosaminidase (NAGLU) enzyme activity, which leads to the accumulation of heparan sulfate (HS) in the brain and other organs, as well as progressive brain atrophy with cortical gray matter (CGM) volume loss.<sup>2-5</sup> The accumulation of abnormal HS results in neurocognitive decline, behavioral disturbances, speech loss, increasing loss of mobility, and premature death.<sup>6</sup> 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.<sup>7</sup>

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.<sup>6,7</sup>

### **About SBC-103**

SBC-103 (rhNAGLU enzyme) is an enzyme replacement therapy (ERT) being investigated in a Phase 1/2 trial for patients with MPS IIIB. It is a recombinant form of the N-acetyl- $\alpha$ -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 Commission 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 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, including those 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 is the global leader in complement inhibition and has developed and commercializes 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. In addition, Alexion's metabolic franchise includes two highly innovative enzyme replacement therapies for patients with life-threatening and ultra-rare disorders, hypophosphatasia (HPP) and lysosomal acid lipase deficiency (LAL-D). 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](http://www.alexion.com)

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### **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, the possibility that clinical trials of our product candidates could be delayed or that additional research and testing is required by regulatory agencies, 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 Quarterly Report on Form 10-Q for the period ended March 31, 2016 and in our other filings with the U.S. Securities and Exchange Commission.*

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, Brain Structural MRI and Neurocognitive Evaluations in a Phase I/II, First-in-Human Clinical Trial of Intravenous SBC-103 in Mucopolysaccharidosis IIIB. Poster presented at 14<sup>th</sup> International Symposium on MPS and Related Diseases 2016, Bonn, Germany, July 14-17. Abstract 99.
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6. 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.
7. Heron B, et al. Incidence and natural history of mucopolysaccharidosis type III in France and comparison with United Kingdom and Greece. *Am. J. Med. Genet Part A*. 2011;155:58-68.
8. 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 *WORLD Symposium Annual Meeting 2016*, San Diego, February 29-March 4. Abstract LB-33.

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