Jazz Pharmaceuticals Announces Positive Results from the Phase 2/3 EXPRESS Study of Xyrem in Pediatric Patients with Narcolepsy with Cataplexy

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Abstract Accepted for Oral Presentation at the 31st Annual Meeting of the Associated Professional Sleep Societies LLC (APSS) in June 2017

DUBLIN, April 24, 2017 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced positive top-line efficacy results from the global, double-blind, placebo-controlled, randomized-withdrawal, multicenter Phase 2/3 study evaluating Xyrem® (sodium oxybate) oral solution, CIII, in the treatment of cataplexy in pediatric patients with narcolepsy. Xyrem demonstrated statistically significant differences in the primary and key secondary efficacy endpoints that measured the change in the weekly number of cataplexy attacks, the Clinical Global Impression of Change scale (CGIc) for the severity of cataplexy, and the Epworth Sleepiness Scale (ESS) for children and adolescents (CHAD) score compared to placebo. The preliminary safety results were consistent with the results previously observed in Xyrem studies in adults and our Xyrem post-marketing experience.

"More than half of all narcolepsy patients report that their symptoms began as teenagers or in childhood. Although narcolepsy in children is characterized by the same symptoms as adults, pediatric narcolepsy is frequently under-recognized and under-diagnosed," said Karen Smith, M.D., Ph.D., global head of research and development and chief medical officer of Jazz Pharmaceuticals. "We look forward to presenting the results from this large pivotal Xyrem pediatric study in narcolepsy at the APSS meeting in June. We expect to submit a supplemental NDA to the FDA in support of the use of Xyrem in pediatric patients in the fourth quarter of 2017, subject to completion of the full data analysis."

About the Global Phase 2/3 EXPRESS[1] Study

The EXPRESS study is a double-blind, placebo-controlled, randomized-withdrawal, multicenter study evaluating the efficacy and safety of Xyrem with an open-label pharmacokinetic evaluation and safety extension for at least one year in pediatric patients with narcolepsy with cataplexy. The study enrolled 106 patients aged seven to seventeen with narcolepsy with cataplexy. The study design included a titration period (if necessary), a Xyrem stable-dose period of two to three weeks, followed by a 1:1 randomization to either Xyrem or placebo for 2 weeks. After the completion of the double-blind, placebo-controlled treatment period, patients have the opportunity to receive Xyrem in an open-label treatment phase for at least one year. After a pre-planned interim analysis, efficacy on the primary endpoint was demonstrated. As a result, randomization to placebo was discontinued, and the study remains ongoing with open-label Xyrem treatment.

The primary efficacy endpoint was the change in the weekly number of cataplexy attacks from the last 2 weeks of the stable-dose period to the 2 weeks of the double-blind placebo-controlled treatment period. The key secondary endpoints measured the CGIc for cataplexy severity and the ESS (CHAD) score from the end of the stable-dose period to the end of the double-blind placebo-controlled treatment period.

About Narcolepsy

Narcolepsy is a debilitating neurological disorder characterized by excessive sleepiness, and the inability to regulate sleep-wake cycles normally. It affects an estimated one in 2,000 people in the United States, and more than half of narcolepsy patients report that their symptoms began as teenagers or in childhood.[2] It is estimated that 50 percent or more patients with narcolepsy have not been diagnosed. Studies have shown it may take 10 years or more for people with narcolepsy to receive a correct diagnosis. Of the five key symptoms of narcolepsy, excessive daytime sleepiness and cataplexy are the most common symptoms.

About Jazz Pharmaceuticals

Jazz Pharmaceuticals plc (Nasdaq: JAZZ) is an international biopharmaceutical company focused on improving patients' lives by identifying, developing and commercializing meaningful products that address unmet medical needs. The company has a diverse portfolio of products and product candidates, with a focus in the areas of sleep and hematology/oncology. In these areas, Jazz Pharmaceuticals markets Xyrem® (sodium oxybate) oral solution, Erwinaze® (asparaginase *Erwinia chrysanthemi*) and Defitelio® (defibrotide sodium) in the U.S. and markets Erwinase® and Defitelio® (defibrotide) in countries outside the U.S. For more information, please visit www.jazzpharmaceuticals.com.

About Xyrem

Xyrem oral solution, CIII, is indicated for the treatment of cataplexy in narcolepsy and for the treatment of excessive daytime sleepiness (EDS) in narcolepsy. Xyrem may only be dispensed to patients enrolled in the Xyrem REMS Program. Xyrem was first approved in the U.S. in 2002, based on clinical trial data in adults. The current USPI for Xyrem indicates that safety and effectiveness in pediatric patients have not been established. Therefore, subject to completion of the full data analysis, Jazz plans to submit a supplemental NDA to FDA in the fourth quarter of 2017, with revised proposed labeling to include these data, consistent with the Agency's pediatric written request.

IMPORTANT SAFETY INFORMATION

Xyrem is a central nervous system (CNS) depressant. In clinical trials at recommended doses obtundation and clinically significant respiratory depression occurred in Xyrem-treated patients. Almost all of the patients who received Xyrem during clinical trials in narcolepsy were receiving central nervous system stimulants.

Xyrem is the sodium salt of gamma hydroxybutyrate (GHB). Abuse of GHB, either alone or in combination with other CNS depressants, is associated with CNS adverse reactions, including seizure, respiratory depression, decreases in the level of consciousness, coma, and death.
Because of the risks of CNS depression, abuse, and misuse, Xyrem is available only through a restricted distribution program called the Xyrem REMS Program, using the central pharmacy that is specially certified. Prescribers and patients must enroll in the program. For further information go to www.XYREMREMS.com or call 1-866-XYREM88® (1-866- 997-3688).

Xyrem is contraindicated in combination with sedative hypnotics or alcohol and in patients with succinic semialdehyde dehydrogenase deficiency.

Caution should be used when considering the concurrent use of Xyrem with other CNS depressants. Healthcare providers should caution patients against hazardous activities requiring complete mental alertness or motor coordination within the first 6 hours of dosing or after first initiating treatment until certain that Xyrem does not affect them adversely. The rapid onset of sedation, coupled with the amnestic features of Xyrem, particularly when combined with alcohol, has proven to be dangerous for the voluntary and involuntary user (e.g. assault victim). Patients should be monitored for emergent or increased depression and suicidality and for impaired motor/cognitive function. Episodes of sleepwalking should be fully evaluated and appropriate interventions considered. The amount of daily sodium intake in each dose of Xyrem should be considered in patients sensitive to salt intake. The most common adverse reactions were nausea, dizziness, vomiting, somnolence, enuresis, and tremor.

Please click here to see the full Prescribing Information for Xyrem, including BOXED Warning.

Reference:

[1] EXPRESS stands for the Effect of Xyrem in Pediatric naRcolEpSy patientS

[2] Dauvilliers Y, Montplaisir J, Molinari N, Carlander B, Ondze B, Besset A, Billiard M. Age at onset of narcolepsy in two large populations of patients in France and Quebec. Neurol 2001; 57:2029-2033.

"Safe Harbor" Statement under the Private Securities Litigation Reform Act of 1995

This press release contains forward-looking statements, including, but not limited to, statements related to the expected presentation of results from the company's Phase 2/3 pediatric narcolepsy study evaluating narcolepsy with cataplexy, the company's plans for submission of a supplemental NDA with the FDA for the use of Xyrem in pediatric patients, the timing of such events and activities, and other statements that are not historical facts. These forward-looking statements are based on the company's current plans, objectives, estimates, expectations and intentions and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks and uncertainties associated with: pharmaceutical product development and clinical success thereof and the regulatory approval process, including the risk that the company may be unable to obtain approval by the FDA of its supplemental NDA for Xyrem in a timely manner or at all; and other risks and uncertainties affecting the company and its development programs, including those described from time to time under the caption "Risk Factors" and elsewhere in Jazz Pharmaceuticals plc's Securities and Exchange Commission filings and reports (Commission File No. 001-33500), including the company's Annual Report on Form 10-K for the period ended December 31, 2016 and future filings and reports by the company. Other risks and uncertainties of which the company is not currently aware may also affect the company's forward-looking statements and may cause actual results and the timing of events to differ materially from those anticipated. The forward-looking statements herein are made only as of the date hereof or as of the dates indicated in the forward-looking statements, even if they are subsequently made available by the company on its website or otherwise. The company undertakes no obligation to update or supplement any forward-looking statements to reflect actual results, new information, future events, changes in its expectations or other circumstances that exist after the date as of which the forward-looking statements were made.

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