Jazz Pharmaceuticals Announces FDA Acceptance of Supplemental New Drug Application for Xyrem® (sodium oxybate) to Treat Cataplexy and Excessive Daytime Sleepiness in Pediatric Narcolepsy Patients

June 27, 2018

DUBLIN, June 27, 2018 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the U.S. Food and Drug Administration (FDA) accepted for priority review its supplemental new drug application (sNDA) seeking revised labeling for Xyrem® (sodium oxybate) oral solution, CIII, to include an indication to treat cataplexy and excessive daytime sleepiness (EDS) in pediatric narcolepsy patients. The Prescription Drug User Fee Act (PDUFA) goal date for an FDA decision is October 27, 2018.

"There has been a great deal of interest from the narcolepsy community in understanding the safety and efficacy of Xyrem in pediatric patients. We look forward to the FDA review and the potential for a new Xyrem indication specific to cataplexy and EDS in children and adolescents," said Jed Black, M.D., senior vice president, Sleep and CNS Medicine at Jazz Pharmaceuticals and adjunct professor, Stanford Center for Sleep Sciences and Medicine. "Jazz continues to strive to address unmet needs within the sleep community."

About Xyrem
Xyrem oral solution, CIII, is indicated for the treatment of cataplexy in narcolepsy and for the treatment of 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 United States Package Insert (USPI) for Xyrem indicates that safety and effectiveness in pediatric patients have not been established. Jazz filed an sNDA on April 27, 2018 to expand the currently approved indication to include pediatric narcolepsy patients. With collaboration and a Pediatric Written Request from the FDA, Jazz initiated the global Phase 2/3 EXPRESS study in 2014 to assess the safety, efficacy and pharmacokinetics of Xyrem in pediatric patients, seven to 17 years of age.

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.

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 begin when they are teenagers or in childhood.[1] 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 plc
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*), Defitelio® (defibrotide sodium) and Vyxeos® (daunorubicin and cytarabine) liposome for injection in the U.S. and markets Erwinase® and Defitelio® (defibrotide) in countries outside the U.S. For country-specific product information, please visit www.jazzpharmaceuticals.com/products. For more information, please visit www.jazzpharmaceuticals.com and follow us on Twitter at @JazzPharma.

"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 potential for a new Xyrem indication

specific to cataplexy and EDS in children and adolescents, 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 the regulatory approval process, including the risk that the company is unable to obtain FDA approval of its sNDA 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 Quarterly Report on Form 10-Q for the quarter ended March 31, 2018 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.

References:

1. 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

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SOURCE Jazz Pharmaceuticals plc

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