Jazz Pharmaceuticals Presents Long-Term Safety and Efficacy Data for Xyrem® (sodium oxybate) in Pediatric Patients with Narcolepsy with Cataplexy

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DUBLIN, June 3, 2018 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that Xyrem® (sodium oxybate) oral solution, CIII, demonstrated long-term efficacy for up to one year in reducing cataplexy and excessive daytime sleepiness (EDS) in the global Phase 2/3 EXPRESS study of pediatric patients seven to 17 years of age with narcolepsy. The results were presented in a poster today at the 32nd Annual Meeting of the Associated Professional Sleep Societies and will be featured in an oral presentation on June 5 at 2:45 p.m. ET.

"Although the symptoms of narcolepsy typically begin during childhood, there are no cataplexy treatments approved for patients under the age of eighteen," 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 has studied *Xyrem* extensively in the pediatric population as part of our commitment to addressing unmet needs in sleep medicine, and we recently filed a supplemental new drug application to the U.S. Food and Drug Administration seeking revised labeling for *Xyrem* to include an indication to treat cataplexy and EDS in pediatric patients with narcolepsy."

In the EXPRESS study, after a two-week double-blind, placebo-controlled withdrawal period (DB), participants entered an open-label safety period for up to 47 weeks, for a total study duration of up to one year. Seventy-nine participants completed ≥6 months, and 46 completed one year. Change in weekly number of cataplexy attacks was calculated from daily cataplexy diaries. EDS was assessed by the Epworth Sleepiness Scale for Children and Adolescents (ESS-CHAD) at each study visit.

The efficacy of sodium oxybate for cataplexy and EDS in pediatric narcolepsy was demonstrated after the two-week double-blind placebo-controlled treatment period and was maintained during open label treatment. The median (Q1, Q3) change from baseline in weekly number of cataplexy attacks was 0.0 (-2.25, 4.17) at study end, with little change throughout. Similarly, the median (Q1, Q3) change from baseline in ESS-CHAD score was 0.0 (-3.0, 3.0) at study end.

The safety profile of sodium oxybate in children and adolescents in this study is similar to that reported in adults, and no new safety concerns were identified following the use of sodium oxybate for up to one year. The most common Treatment-Emergent Adverse Events (TEAEs) (≥5%) were enuresis, nausea, vomiting, headache, decreased weight, decreased appetite, nasopharyngitis and dizziness. Two serious TEAEs occurred (acute psychosis and suicidal ideation), both in sodium oxybate-naïve participants during the open-label titration period. Both events resolved after reducing the dose or discontinuing sodium oxybate, respectively.

Safety assessments included measures of anxiety (Multidimensional Anxiety Scale for Children 10-item [MASC-10]), depressive symptoms (Children's Depression Inventory 2nd Edition Self-Report Short Version [CDI 2:SR(S)]) and suicidality (Columbia-Suicide Severity Rating Scale [C-SSRS]), in addition to TEAEs. T-scores on the MASC-10 were within the average range throughout the study in both sodium oxybate-naïve and on-sodium oxybate participants. T-scores on the CDI 2:SR(S) were within the average range throughout the study in both sodium oxybate-naïve and on-sodium oxybate participants; a slight downward trend was observed in mean CDI 2:SR(S) T-scores over time.

Top-line efficacy results and preliminary safety findings from the EXPRESS study were recently published in *The Lancet Child & Adolescent Health.*

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.

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 began as 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 Xyrem as a potential treatment for cataplexy and EDS in pediatric narcolepsy patients 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 U.S. Food and Drug Administration approval of its supplemental new drug application 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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