Jazz Pharmaceuticals Presents Data for the Phase 3 TONES 2 Study of JZP-110 in Patients with Excessive Sleepiness Associated with Narcolepsy

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Data were presented in a poster presentation at the annual SLEEP Meeting; JZP-110 U.S. NDA submission planned for later this year

DUBLIN, June 6, 2017 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today presented the positive efficacy results from its global multicenter study of JZP-110 in adult patients with excessive sleepiness associated with narcolepsy. The data were presented today in a poster session at the 31st Associated Professional Sleep Societies (APSS) Annual SLEEP Meeting in Boston.

"Excessive sleepiness is a significant and serious symptom for patients with narcolepsy," said Karen Smith, M.D., Ph.D., executive vice president of research and development and chief medical officer of Jazz Pharmaceuticals. "This study demonstrated that JZP-110 could be an important treatment option for patients who suffer from excessive sleepiness as a result of narcolepsy. It also further highlights our deep commitment to our sleep therapeutic area and our significant investment in research and development to bring innovative treatments to patients with important unmet medical needs."

"This study demonstrated statistically significant effects of both 150 mg and 300 mg doses of JZP-110 on the co-primary endpoints of change in mean sleep latency on the Maintenance of Wakefulness Test and change in Epworth Sleepiness Scale score from baseline to week 12," said Michael J. Thorpy, M.D.,Ch.B., Professor of Clinical Neurology, The Saul R. Korey Department of Neurology, Albert Einstein College of Medicine. "The effects seen in this study were maintained over the full 12 weeks of the study. This is a potentially important development for patients with narcolepsy who experience excessive sleepiness."

The Treatment of OSA and Narcolepsy Excessive Sleepiness (TONES) Phase 3 program is comprised of four studies, one study evaluating excessive sleepiness in adult patients with narcolepsy (TONES 2), two studies evaluating excessive sleepiness in adult patients with OSA (TONES 3 and TONES 4), and an open-label, long-term safety and maintenance of efficacy study (TONES 5) in the treatment of excessive sleepiness in patients with narcolepsy or OSA.

About the Global Phase 3 TONES 2 Study

TONES 2 was a 12-week, 4-arm, parallel-group, double-blind, placebo-controlled, randomized Phase 3 study that evaluated the safety and efficacy of JZP-110 in adults with excessive sleepiness in narcolepsy. Patients (N=239) were randomized 1:1:1:1 to JZP-110 300 mg (n=60), 150 mg (n=60), 75 mg (n=59) and placebo (n=60). The co-primary endpoints were the change in mean sleep latency on the Maintenance of Wakefulness Test (MWT) and in the Epworth Sleepiness Scale (ESS) score from baseline to week 12. The key secondary endpoint was the percentage of patients who reported improvement on the Patient Global Impression of Change (PGIc) scale, a patient-reported measure in overall condition from baseline to week 12.

In patients with narcolepsy, JZP-110 150 mg and 300 mg doses significantly increased mean sleep latency relative to placebo at week 12 on the MWT and these effects were observed as early as week one and continued throughout the 12 weeks of the study ($p<0.0001$). JZP-110 significantly decreased ESS scores relative to placebo at all doses at week 12 ($p<0.0001$ for 150 mg and 300 mg doses and $p<0.05$ for 75 mg dose). The JZP-110 75 mg dose reached statistical significance on the co-primary endpoint of the ESS, but not the MWT. On the key secondary endpoint of PGIc, JZP-110 significantly increased the percentage of patients who reported improvement in their overall condition at all doses relative to placebo at week 12 ($p<0.0001$ for 150 mg and 300 mg doses and nominal p-value of $p<0.05$ at the 75 mg dose as the co-primary endpoint of MWT was not met at this dose).

The modified intent-to-treat (mITT) population for the efficacy analysis consisted of 231 patients.

The estimated changes from baseline to week 12 were:

	Change (SE) from Baseline to Week 12			
TONES 2 Study Results (mITT population)	**JZP-110 300 mg** (N=59)	**JZP-110 150 mg** (N=55)	**JZP-110 75 mg** (N=59)	**Placebo** (N=58)
Mean Sleep Latency on Maintenance of Wakefulness Test (MWT): Increased ability to stay awake	12.3 min (1.4) *p<0.0001*	9.8 min (1.3) *p<0.0001*	4.7 min (1.3) *p=0.1595*	2.1 min (1.3)
Epworth Sleepiness Scale (ESS) score: Decreased subjective sleepiness	-6.4 (0.7) *p<0.0001*	-5.4 (0.7) *p<0.0001*	-3.8 (0.7) *p<0.05*	-1.6 (0.7)
Patient Global Impression-Change (PGIc): Minimal, much, or very much improvement	84.7% *p<0.0001*	78.2% *p<0.0001*	67.8% *p<0.05^*	39.7%

^There was a nominal p-value at 75 mg because both co-primary endpoints were not positive at 75 mg in the statistical hierarchy.

The safety and tolerability of JZP-110 were consistent with the previous Phase 2 studies in patients with narcolepsy. Of the 239 subjects randomized, 195 completed the 12-week treatment. Ten patients discontinued due to treatment emergent adverse events (TEAEs). Discontinuations due to TEAEs were greater than placebo (n=1, 1.7%) in the JZP-110 150 (n=3, 5.1%) and 300 mg (n=5, 8.5%) groups, and the same in the JZP-110 75 mg dose group (n=1, 1.7%). The most commonly reported TEAEs across all doses of JZP-110 (occurring ≥5% of patients across all JZP-110 groups)

were headache, nausea, decreased appetite, nasopharyngitis, dry mouth, and anxiety. There was one subject with two serious adverse events (non-cardiac chest pain and anxiety) on JZP-110 that were considered not treatment related as assessed by the investigator.

Full details of the APSS annual SLEEP meeting can be found at http://www.sleepmeeting.org/.

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, with symptoms typically appearing in early adulthood. 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. Excessive sleepiness is the primary symptom of narcolepsy and is present in all people with the disorder. Excessive sleepiness is characterized by the inability to stay awake and alert during the day resulting in unplanned lapses into sleep or drowsiness.

About JZP-110

JZP-110 is a selective dopamine and norepinephrine reuptake inhibitor (DNRI) in development for treatment of excessive sleepiness in adult patients with narcolepsy, OSA, and Parkinson's disease. In 2014, Jazz Pharmaceuticals acquired a license to develop and commercialize JZP-110 from SK Biopharmaceuticals, which discovered the compound. Jazz Pharmaceuticals has worldwide development, manufacturing, and commercialization rights to JZP-110, excluding certain jurisdictions in Asia. SK Biopharmaceuticals maintains rights in Korea, Japan, China, Taiwan, Singapore, Indonesia, India, Philippines, Thailand, Malaysia, Vietnam, and Hong Kong. JZP-110 has orphan drug designation in the United States for narcolepsy.

Across the entire JZP-110 development program, over 2,000 subjects have enrolled in 20 studies. The JZP-110 Phase 3 clinical program includes one study evaluating excessive sleepiness in adult patients with narcolepsy (TONES 2), two studies evaluating excessive sleepiness in adult patients with OSA (TONES 3 and TONES 4), and an open-label, long-term safety and maintenance of efficacy study (TONES 5) in the treatment of excessive sleepiness in patients with narcolepsy or OSA. Enrollment is complete in all studies that are expected to support Jazz Pharmaceuticals' planned JZP-110 New Drug Application (NDA) submission to the U.S. Food and Drug Administration (FDA) in late 2017.

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.

"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 JZP-110 as a potential treatment for excessive sleepiness in adult patients with narcolepsy, the company's significant investment in research and development to bring innovative treatments to patients with important unmet medical needs, the company's plans for submission of an NDA for JZP-110 with the FDA and the timing thereof, 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; the regulatory approval process, including the risk that the company may be unable to obtain approval by the FDA for JZP-110 in a timely manner or at all; and effectively commercializing JZP-110; 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, 2017 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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