Jazz Pharmaceuticals Announces Positive Results from the Phase 3 TONES 2 Study of JZP-110 in Narcolepsy Patients with Excessive Sleepiness

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

DUBLIN, April 26, 2017 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced positive efficacy results from the global multicenter study of JZP-110 in adult patients with excessive sleepiness associated with narcolepsy. Based on the preliminary safety analysis, the most commonly reported adverse events (AEs) in this study were generally consistent with those previously observed in the Phase 2 clinical studies evaluating JZP-110 in narcolepsy.

"Excessive sleepiness in narcolepsy remains an important unmet medical need, and we believe that the statistically and clinically significant effect observed in this study indicates that JZP-110 could be an important treatment option for patients," said Karen Smith, M.D., Ph.D., global head of research and development and chief medical officer of Jazz Pharmaceuticals. "Subject to completion of the data analysis and our regulatory discussions with FDA, we expect to submit the JZP-110 NDA for excessive sleepiness in obstructive sleep apnea and narcolepsy in late 2017. We are grateful to the patients and investigators who contributed to this successful study. This study exemplifies our ongoing and increasing commitment to R&D, as demonstrated by the large number of important clinical and regulatory activities that we have underway to bring new therapies to patients."

"Patients with narcolepsy struggle with excessive sleepiness, which is the symptom of narcolepsy that patients report as having the most significant impact on their daily lives," said Michael Thorpy, M.D., Director of the Sleep-Wake Disorders Center at the Montefiore Medical Center, Bronx, New York. "Excessive sleepiness occurs in all patients with narcolepsy and when combined with frequent irresistible sleep attacks, can lead to a considerable burden of illness and adverse effect on patients' health."

The Treatment of OSA and Narcolepsy Excessive Sleepiness (TONES) Phase 3 program is comprised of four studies, two in obstructive sleep apnea (OSA) (TONES 3 and TONES 4 studies), one in narcolepsy (TONES 2 study) and one open-label, long-term safety and maintenance of efficacy study. The TONES 2 study enrolled 240 patients. The company plans to present the results from the TONES 2, TONES 3 and TONES 4 studies assessing the effect of JZP-110 on excessive sleepiness in narcolepsy and OSA at the APSS meeting in June.

Efficacy and Preliminary Safety Results of TONES 2 Study

The TONES 2 study, or 14-002, is a 4-arm, parallel-group study evaluating three doses of JZP-110 (300 mg, 150 mg, and 75 mg) compared to placebo for a 12-week period.

In TONES 2, JZP-110 demonstrated highly statistically significant improvement in the co-primary endpoints of the Maintenance of Wakefulness Test (MWT) and the Epworth Sleepiness Scale (ESS) and in the key secondary endpoint of the Patient Global Impression of Change (PGIc) scale at the 300 mg and 150 mg doses compared to placebo. These effects were maintained throughout the course of the study. The JZP-110 75 mg dose reached statistical significance on the co-primary endpoint of ESS, but did not reach statistical significance on the co-primary endpoint of MWT.* The endpoints of MWT and ESS measure patients' ability to stay awake and patients' subjective levels of sleepiness, respectively.

Based on a preliminary safety analysis, the most commonly reported adverse events across all doses in TONES 2 were headache, nausea, decreased appetite, nasopharyngitis, dry mouth, and anxiety. There was one patient with two serious adverse events (SAEs) on JZP-110 that were considered not treatment related as assessed by the investigator. The open-label, long-term safety and maintenance of efficacy study is ongoing, and the results will be included in the planned New Drug Application (NDA) submission.

About the Global Phase 3 TONES 2 Study

TONES 2 is a 12-week, 4-arm, parallel-group, double-blind, placebo-controlled, randomized Phase 3 study evaluating the safety and efficacy of JZP-110 in adults with excessive sleepiness in narcolepsy. Patients were randomized 1:1:1:1 to JZP-110 300 mg, 150 mg, 75 mg and placebo. The co-primary endpoints are the change in mean sleep latency on the MWT and the change in the ESS score from baseline to week 12. The key secondary endpoint is the percentage of patients who report improvement on the PGIc scale, a patient-reported measure of improvement, worsening, or no change in overall condition from baseline to week 12. The TONES 2 study enrolled 240 patients.

For information about the TONES 3 and TONES 4 studies, refer to the company's press release dated March 20, 2017 at www.jazzpharmaceuticals.com.

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 late-stage development for treatment of excessive sleepiness in adult patients with narcolepsy or OSA. In 2014, Jazz Pharmaceuticals plc acquired a world-wide license (except in certain countries in Asia) to develop and commercialize JZP-110 from SK Biopharmaceuticals, who 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 two studies evaluating excessive sleepiness in adult patients with OSA (TONES 3 and TONES 4), one study evaluating excessive sleepiness in adult patients with narcolepsy (TONES 2) and an open-label, long-term safety and maintenance of efficacy study. Enrollment is complete in all studies that are expected to support the planned JZP-110 NDA submission to the U.S. Food and Drug Administration (FDA).

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 expected presentation of JZP-110 study results at APSS, the company's plans for submission of an NDA for JZP-110 with the FDA, 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; 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 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.

To view the original version on PR Newswire, visit:http://www.prnewswire.com/news-releases/jazz-pharmaceuticals-announces-positive-results-from-the-phase-3-tones-2-study-of-jzp-110-in-narcolepsy-patients-with-excessive-sleepiness-300446560.html

SOURCE Jazz Pharmaceuticals plc

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* This information was corrected on April 28, 2017. The original version stated that the 75mg dose reached statistical significance on the co-primary endpoint of MWT and did not reach statistical significance on the co-primary endpoint of ESS.