Jazz Pharmaceuticals Presents Long-Term Safety and Efficacy Data from Phase 3 TONES 5 Study of Solriamfetol for Excessive Sleepiness in Narcolepsy or Obstructive Sleep Apnea

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DUBLIN, June 3, 2018 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that its investigational treatment solriamfetol demonstrated long-term maintenance of efficacy and a tolerable safety profile in the open-label Phase 3 TONES 5 study of excessive sleepiness (ES) in patients with narcolepsy or obstructive sleep apnea (OSA). Data from the study 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 at the meeting on June 5 at 1:30 p.m. ET.

"As a leader in sleep medicine, Jazz is focused on addressing the needs of the sleep community through the research and development of new treatment options, and we are pleased that the results of this long-term study are consistent with the safety and efficacy that we have seen across the breadth of our clinical program for solriamfetol," 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. "If approved by the U.S. Food and Drug Administration, solriamfetol would offer patients the first new chemical entity for the treatment of excessive sleepiness in narcolepsy and OSA in the U.S. in nearly 10 years."

In the TONES 5 study, patients with ES due to narcolepsy or OSA, including those who had completed prior studies with solriamfetol, began treatment with solriamfetol in the two-week titration phase followed by a maintenance phase of up to 50 weeks. A subset of patients participated in a two-week placebo-controlled Randomized Withdrawal (RW) phase after approximately six months of treatment. The primary endpoint in the RW phase was change in Epworth Sleepiness Scale (ESS) from beginning to end of the RW. Secondary endpoints were Patient and Clinician Global Impression of Change (PGI-C and CGI-C, respectively).

In this trial, 643 patients (226 narcolepsy; 417 OSA) were administered solriamfetol and included in the safety population, and 458 completed the study. Two hundred and eighty-two patients were entered into the RW phase, and 280 completed this phase (141 receiving placebo and 139 receiving solriamfetol), representing the modified intent-to-treat population. At the end of the RW phase, patients who received solriamfetol remained improved, whereas those who were switched to placebo worsened. The Least Squares (LS) mean change in ESS score was 1.6 with solriamfetol compared with 5.3 with placebo, resulting in a LS mean difference of –3.7 (95% CI –4.80, –2.65; P<0.0001).

For both secondary endpoints (PGI-C and CGI-C), significantly greater percentages of patients who were switched to placebo were rated by their physicians and themselves as worse in their overall condition at the end of the RW compared with the solriamfetol group (both *P*<0.0001).

Long-term maintenance of efficacy was also demonstrated during the open-label period for up to one year by sustained reductions in mean ESS scores and improvements on the PGI-C and CGI-C scales.

The most frequent treatment-emergent serious adverse events (AEs; ≥5%) with solriamfetol were headache, nausea, insomnia, nasopharyngitis, dry mouth, and anxiety; 27 (4.2%) patients experienced one or more serious treatment-emergent adverse events. There was one death due to sepsis in a 70-year-old immunosuppressed male with OSA on solriamfetol 300 mg. The death was considered unrelated to study drug by the investigator.

About OSA and Excessive Sleepiness

OSA is a prevalent disease (as high as 14% in men and 5% in women) in which ES is a major presenting complaint in many cases.[1-2] ES in OSA is associated with impairments in cognitive function, safety, productivity, interpersonal relationships, and overall quality of life. Positive Airway Pressure (PAP) therapy, with its most common form being Continuous Positive Airway Pressure (CPAP), has been shown to be an effective therapy for sleep-related airway obstruction, with frequent improvement in ES in many patients; however, not all patients tolerate CPAP therapy and among those who do, usage is highly variable. It is estimated that ES persists in 12%–65% of people utilizing CPAP for OSA.[3-6]

About Narcolepsy

Narcolepsy is a debilitating neurological disorder characterized by ES, and the inability to regulate sleep-wake cycles normally.[7] It affects an estimated one in 2,000 people in the United States, with symptoms typically appearing in early adulthood. It is estimated that more than 50% of patients with narcolepsy have not been diagnosed.[8] Studies have shown it may take 10 years or more for people with narcolepsy to receive a correct diagnosis.[9] ES is the primary symptom of narcolepsy and is present in all people with the disorder.[2] ES is characterized by the inability to stay awake and alert during the day, resulting in unplanned lapses into sleep or drowsiness.[2,7,10]

About Solriamfetol

Solriamfetol (JZP-110) is a selective dopamine and norepinephrine reuptake inhibitor (DNRI) in development for treatment of ES in adult patients with narcolepsy, OSA, and Parkinson's disease. In 2014, Jazz Pharmaceuticals acquired a license to develop and commercialize solriamfetol from Aerial Biopharma. Jazz Pharmaceuticals has worldwide development, manufacturing, and commercialization rights to solriamfetol, excluding certain jurisdictions in Asia. SK Biopharmaceuticals, the discoverer of the compound (also known as SKL-N05), maintains rights in 12 Asian markets, including Korea, China and Japan. Solriamfetol has orphan drug designation in the United States for narcolepsy.

On March 2, 2018, Jazz announced that the U.S. Food and Drug Administration (FDA) accepted for filing with standard review the company's New Drug Application (NDA) seeking marketing approval for solriamfetol for the treatment of ES in adult patients with narcolepsy or OSA. The NDA for solriamfetol is underpinned by the Treatment of OSA and Narcolepsy Excessive Sleepiness (TONES) Phase 3 program, which was comprised of four studies that evaluated solriamfetol in:

- ES in adult patients with narcolepsy (TONES 2)
- ES in adult patients with OSA (TONES 3 and TONES 4), and
- The long term safety and maintenance of efficacy for the treatment of ES in patients with narcolepsy or OSA (TONES 5).

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 solriamfetol as a potential treatment for ES in adult patients with narcolepsy or OSA 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 for solriamfetol in a timely manner or at all; and effectively commercializing solriamfetol; 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.

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