Jazz Pharmaceuticals Presents New Data from a Human Abuse Liability (HAL) Study for JZP-110, an Investigational Treatment for Excessive Sleepiness in Patients with Narcolepsy or with Obstructive Sleep Apnea, at 30th Annual SLEEP Meeting

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DUBLIN, June 14, 2016 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced results from a Human Abuse Liability (HAL) study of JZP-110, an investigational wake-promoting agent in Phase 3 development for the treatment of excessive sleepiness (ES) in adult patients with narcolepsy or with obstructive sleep apnea (OSA). The data will be presented today at the 30th Associated Professional Sleep Societies (APSS) Annual SLEEP Meeting, taking place June 11-15, 2016 in Denver, Colorado.

"The new data from the HAL study demonstrated that each of the doses of JZP-110 that were studied, including the high therapeutic dose of 300 mg and the supratherapeutic doses of 600 mg and 1200 mg, had consistently lower ratings on the primary endpoint of Peak Liking at the Moment and on the secondary endpoints of Overall Drug Liking and willingness to Take the Drug Again compared to the Schedule IV stimulant phentermine at 90 mg," said Jack Henningfield, Ph.D., vice president at Pinney Associates and professor at Johns Hopkins University School of Medicine. "JZP-110 has a mechanism of action that is distinct from traditional stimulants and these data showed that the abuse potential of JZP-110 differed from that of a traditional stimulant as well."

"Despite current therapies, many patients with narcolepsy and patients with OSA continue to experience excessive sleepiness. The new HAL data help further our understanding of JZP-110's potential to fill an unmet need for new wake-promoting treatment options," said Karen Smith, M.D., Ph.D., global head of research and development and chief medical officer at Jazz Pharmaceuticals.

About the HAL Study
HAL studies are clinical studies that help assess the relative abuse potential of a medicine. The HAL study was a randomized, double-blind, placebo-controlled, six-sequence crossover study evaluating the abuse potential of JZP-110 relative to the Schedule IV stimulant phentermine in 43 adults with a recent history of recreational polydrug use, including stimulants, who met study entry criteria. Subjects were randomized to one of six test sequences, in which they received a single treatment with one of the six study drugs (JZP-110 at 300 mg, 600 mg, and 1200 mg; phentermine at 45 mg and 90 mg; and placebo), with a two-day washout period between each treatment.

The study evaluated effects that are predictive of abuse potential. The primary endpoint was Liking at the Moment across the first 12 hours after drug administration based on a subject-reported 100-point bipolar liking/disliking visual analog scale (VAS), a standard measure of abuse potential in HAL studies. Key secondary endpoints were retrospective VAS ratings at 24 hours after drug administration for Overall Next Day Drug Liking and how much the participant would like to Take the Drug Again.

Results
On the primary endpoint, all doses of JZP-110 had significantly lower ratings of peak (E_{max}) Liking at the Moment compared to 90 mg of phentermine ($P<0.05$) and had significantly greater ratings of peak Liking at the Moment compared to placebo ($P<0.001$). On the secondary endpoint of Overall Next Day Drug Liking, JZP-110 at 600 mg and at 1200 mg had significantly lower measures compared to both doses of phentermine ($P<0.05$). JZP-110 at 300 mg was not statistically different from 45 mg of phentermine ($p=0.070$). JZP-110 at 600 mg and at 1200 mg did not have any statistical difference in Overall Next Day Drug Liking measures compared to placebo. JZP-110 at 300 mg had higher measures of Overall Next Day Drug Liking at 24 hours compared to placebo ($p=0.021$). On the secondary endpoint of willingness to Take the Drug Again, JZP-110 at all doses had significantly lower measures compared to both doses of phentermine ($P<0.05$). All doses of JZP-110 had higher ratings of willingness to Take the Drug Again relative to placebo ($P<0.05$).

Of the 43 adult subjects, 37 completed all six test treatment phases. Two subjects discontinued for treatment emergent adverse events (TEAEs) after receiving 1200 mg of JZP-110. TEAEs were dose-dependent for JZP-110 and phentermine and none were serious or severe. The most frequent TEAEs at the 1200 mg dose of JZP-110 were: hypervigilance, elevated mood, dry mouth, nausea, feelings of relaxation, decreased appetite, hyperhidrosis, insomnia, headache, restlessness, and palpitations.

These data were also presented at the College on Problems of Drug Dependence meeting in Palm Springs, California on June 13, 2016.

New data from a post-hoc analysis from the Phase 2 studies of JZP-110 on its effect on wakefulness was also presented in an oral presentation on June 13 and will be presented in a poster session today at APSS.

Full details of the APSS annual meeting can be found here
[http://www.sleepmeeting.org/home]

About JZP-110
JZP-110 is a late-stage investigational wake-promoting agent being developed as a treatment of ES in adult patients with narcolepsy or with OSA. JZP-110 acts as a selective Dopamine and Norepinephrine Reuptake Inhibitor (DNRI). Jazz Pharmaceuticals has worldwide development, manufacturing, and commercialization rights to JZP-110, excluding certain jurisdictions in Asia. JZP-110 has orphan drug designation in the United States (U.S.) for narcolepsy. The enrollment in the Phase 3 safety and efficacy studies of JZP-110 in the treatment of ES in narcolepsy and OSA patients is ongoing. The proof of concept for moving into the Phase 3 clinical development program was based on consistent results from two Phase 2 clinical studies of JZP-110 as a potential treatment of ES in adult patients with narcolepsy.

Data from the Phase 2b study of JZP-110 has been accepted and will be published in the journal *Sleep*. The data show that at doses of 150 mg to 300 mg/day, JZP-110 significantly improved the ability of adults with narcolepsy to stay awake compared to placebo as measured on the Maintenance of Wakefulness Test and significantly reduced subjective symptoms of ES relative to placebo as measured using the Epworth Sleepiness Scale. In this

study, JZP-110 had a safety profile that appeared to be consistent with other wake-promoting agents. The most common AEs with JZP-110 vs placebo were insomnia, headache, nausea, diarrhea, decreased appetite, and anxiety. These data were previously presented at a late breaker session during the 28th Annual Meeting of APSS on June 2, 2014.

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 the therapeutic potential of Jazz Pharmaceuticals' product candidate, JZP-110, 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 could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, among others, risks and uncertainties associated with the difficulty and uncertainty of pharmaceutical product development and the uncertainty of clinical success; 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, 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 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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SOURCE Jazz Pharmaceuticals

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