Jazz Pharmaceuticals Announces Positive Top-line Results from Phase 3 Study of JZP-258 in Adult Narcolepsy Patients with Cataplexy and Excessive Daytime Sleepiness

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JZP-258 achieves primary and key secondary endpoints demonstrating highly statistically significant differences in weekly number of cataplexy attacks and Epworth Sleepiness Scale scores compared to placebo

DUBLIN, March 26, 2019 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced positive top-line results from the global, double-blind, placebo-controlled, randomized-withdrawal, multicenter Phase 3 study evaluating the efficacy and safety of JZP-258 for the treatment of cataplexy and excessive daytime sleepiness (EDS) in adult patients with narcolepsy. JZP-258 is a novel oxybate product candidate with a unique composition of cations resulting in 92% less sodium than Xyrem® (sodium oxybate).

The Phase 3 study demonstrated highly statistically significant differences in the primary endpoint that measured the change in the weekly number of cataplexy attacks and the key secondary endpoint of change in Epworth Sleepiness Scale (ESS) score with JZP-258 compared to placebo. In this study, patients were randomized to either continue JZP-258 or to receive placebo. Patients randomized to JZP-258 showed clinically meaningful maintenance of efficacy for both cataplexy and EDS, while a statistically significant worsening for both cataplexy and ESS endpoints was observed in the placebo group compared with JZP-258.

The safety profile of JZP-258 is consistent with sodium oxybate. The most commonly reported treatment-emergent adverse events that occurred in ≥ 5% of patients who received JZP-258 were headache, nausea, dizziness, cataplexy, nasopharyngitis, decreased appetite, influenza, diarrhea and vomiting. Two patients experienced serious adverse events (SAEs) that were considered by the investigator to be treatment related.

Jazz will submit the Phase 3 study data for presentation at an upcoming medical meeting. Data from the completed Phase 3 study and interim data from the ongoing 24-week open-label, safety study will be included in the planned submission of a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA).

"Jazz is committed to developing new treatment options that serve unmet needs for patients living with sleep disorders, including JZP-258, a novel oxybate product candidate with 92% less sodium than sodium oxybate," said Jed Black, M.D., senior vice president, Sleep and CNS Medicine at Jazz Pharmaceuticals and adjunct professor, Stanford University Medical Center, Stanford Center for Sleep Sciences and Medicine. "We are deeply grateful to the patients and investigators who participated in this study, and we will meet with the FDA to discuss the Phase 3 results in narcolepsy and our NDA submission plans, with the goal of making JZP-258 available to narcolepsy patients."

"Narcolepsy is a chronic, debilitating disease and is associated with an increased risk of comorbidities," said Michael Thorpy, M.D., director, Sleep-Wake Disorders Center, Montefiore Health System in Bronx, New York. "An extensive body of evidence has established that excessive consumption of sodium is linked with an increased risk of stroke, cardiovascular disease and other adverse outcomes. Patients with narcolepsy may require lifelong medication, and there is a need for a new, low-sodium oxybate formulation."

About the Phase 3 Study

The Phase 3 study of JZP-258 was a global, double-blind, placebo-controlled, randomized-withdrawal, multicenter study evaluating the efficacy and safety of JZP-258 in the treatment of cataplexy in adult patients with narcolepsy. The primary endpoint was the change in the weekly number of cataplexy attacks and the key secondary endpoint was the change in the ESS score from JZP-258 and placebo over the randomized-withdrawal period. The study enrolled 201 patients and randomized 134 patients, comprising a heterogeneous patient population which included those previously treated with Xyrem, naïve to Xyrem, and with or without other anti-cataplectic treatments. A randomized-withdrawal study design aims to measure efficacy – specifically, maintenance of effect – for patients who remain on active treatment and worsening for patients who switch to placebo.

The study design included a titration period of up to 12 weeks, a JZP-258 stable-dose period of two weeks, followed by a 1:1 randomization to either JZP-258 or placebo for 2 weeks. After the completion of the double-blind, placebo-controlled treatment period, patients had the opportunity to receive JZP-258 in an optional 24 week open-label safety extension period. More information about the study design is available at www.clinicaltrials.gov (identifier: NCT03030599).

About JZP-258

JZP-258 is an investigational product being evaluated in adult patients for the treatment of cataplexy and excessive daytime sleepiness in narcolepsy, as well as for the treatment of idiopathic hypersomnia. JZP-258 is a novel oxybate product candidate with a unique composition of cations resulting in 92% less sodium than Xyrem® (sodium oxybate). The mechanism of action of JZP-258 is not fully understood, but it is hypothesized that the therapeutic effects of JZP-258 on sleep/wake symptoms are mediated through modulation of $GABA_B$ during sleep.

About Narcolepsy

Narcolepsy is a chronic, debilitating neurological disorder characterized by excessive daytime sleepiness, and the inability to regulate sleep-wake cycles normally.[1] It affects an estimated one in 2,000 people in the United States, with symptoms typically appearing in childhood. It is estimated that more than 50% of patients with narcolepsy have not been diagnosed.[2] Studies have shown it may take 10 years or more for people with narcolepsy to receive a diagnosis.[3] Excessive daytime sleepiness is the primary symptom of narcolepsy and is present in all people with the disorder.[4] There are five primary symptoms of narcolepsy, including excessive daytime sleepiness, cataplexy, hallucinations, sleep paralysis and sleep disruption.[5] While all patients with narcolepsy experience excessive daytime sleepiness, they may not experience all five symptoms.[6,7] Excessive daytime sleepiness is characterized by the inability to stay awake and alert during the day resulting in unplanned lapses into sleep or drowsiness.[2,4,8]

About Cataplexy

Cataplexy, the most specific symptom of narcolepsy, is the sudden, generally brief (<2 minutes) loss of muscle tone with retained consciousness. It is usually triggered by strong emotions, such as laughter, surprise, or anger.[6,7,9] Although many emotions can potentially lead to cataplexy, those associated with mirth are usually the most potent.[6] Cataplexy occurs in about 70% of patients with narcolepsy.[10] Presentation differs widely among patients, ranging from sporadic partial attacks triggered by laughter to frequent complete collapse brought about by a variety of emotions.[6,7] Complete collapse is generally less common.[7] More commonly, episodes of cataplexy involve only certain muscle groups, such as arms and legs (e.g., knees buckling), the head and neck (e.g., head dropping), or the face and jaw (e.g., sagging, slurred speech, eyelid drooping).[6,7,9,10]

About Jazz Pharmaceuticals plc
Jazz Pharmaceuticals plc (Nasdaq: JAZZ), a global biopharmaceutical company, is dedicated to developing life-changing medicines for people with limited or no options. As a leader in sleep medicine and with a growing hematology/oncology portfolio, Jazz has a diverse portfolio of products and product candidates in development, and is focused on transforming biopharmaceutical discoveries into novel medicines. 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®, Defitelio® (defibrotide) and Vyxeos® 44 mg/100 mg powder for concentrate for solution for infusion in countries outside the U.S. For country-specific product information, please visit www.jazzpharmaceuticals.com/medicines. 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 the company's planned submission of an NDA for JZP-258 with the FDA, the company's goal of making JZP-258 available to 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: 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 of its planned NDA for JZP-258 in a timely manner or at all; effectively commercializing JZP-258; 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'sSecurities and Exchange Commission filings and reports (Commission File No. 001-33500), including the company's Quarterly Report on Form 10-K for the year ended December 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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