Jazz Pharmaceuticals Presents JZP-110 Phase 2b Data For The Treatment Of EDS Symptoms In Adults With Narcolepsy

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Study Demonstrated Robust Alerting Effect Consistent with Phase 2a Results
Planning Phase 3 Clinical Development Program

DUBLIN, June 2, 2014 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today presented data from the Phase 2b study evaluating JZP-110 (formerly known as ADX-N05) as a potential new treatment for the symptoms of excessive daytime sleepiness (EDS) in adults with narcolepsy. In the study, all primary and secondary endpoints were met and patients treated with JZP-110 experienced statistically significant improvements in objective and subjective symptoms of EDS. Based on these data, Jazz Pharmaceuticals plans to evaluate JZP-110 in Phase 3 clinical studies in patients with EDS associated with narcolepsy and in patients with EDS associated with obstructive sleep apnea (OSA), pending discussions with regulatory agencies.

These data were presented today at a late-breaker session during SLEEP 2014, the 28th Annual Meeting of the Associated Professional Sleep Societies (APSS), in Minneapolis, Minn. The annual SLEEP meeting is the premier U.S. conference for healthcare professionals, advocates and industry partners involved in sleep medicine.

"We are committed to developing and commercializing new and differentiated therapies that address unmet patient needs in sleep medicine, and we believe, based on the encouraging results from early clinical trials, that JZP-110 has the potential to significantly help people with narcolepsy and OSA who are experiencing EDS," said Jeffrey Tobias, M.D., executive vice president, research and development, and chief medical officer, Jazz Pharmaceuticals. "As one of the newest additions to our growing sleep clinical development pipeline, we look forward to advancing the Phase 3 clinical program for this product candidate."

About the Study
This Phase 2b, double-blind, placebo-controlled, parallel-group, multicenter study evaluated the safety and efficacy of JZP-110 over 12 weeks in 93 subjects aged 18-70 years with an ICSD-2[1] diagnosis of narcolepsy. The study was sponsored by Aerial BioPharma, LLC, from which Jazz Pharmaceuticals acquired the rights to JZP-110 in early 2014. Subjects were randomized to once-daily placebo (n=49) or JZP-110 (n=44). JZP-110 was administered at a dose of 150 mg/day during weeks one through four and at a dose of 300 mg/day during weeks five through 12.

Co-primary efficacy endpoints measuring JZP-110's effect on EDS were change from baseline to last assessment in the length of time it took to fall asleep as measured by the average sleep onset latency (SOL) on the Maintenance of Wakefulness Test (MWT), an objective measure of the severity of EDS, and symptom improvement as measured by the Clinical Global Impression-Change (CGIC), a subjective physician-completed scale. The change from baseline at weeks four and 12 on the Epworth Sleepiness Scale (ESS), a subjective patient-completed measure of sleepiness, was a secondary endpoint.

Patients treated with JZP-110 experienced statistically significant results in both primary endpoints and the secondary endpoint (ESS) at weeks four and 12 compared to those receiving placebo.

Patients who received treatment experienced the following results:

Phase 2b Study Results Treated Population = subjects with ≥ 1 post-randomization assessment	**Week 4**		**Week 12**	
	JZP-110 *(150 mg)*	**Placebo**	**JZP-110** *(150 mg through week 4 followed by 300 mg for 8 weeks)*	**Placebo**
Sleep Onset Latency (SOL) on the Maintenance of Wakefulness Test (MWT): Increase in time to fall asleep	9.5 minutes N=40	1.4 minutes N=45	12.8 minutes N=40	2.1 minutes N=45
	p<0.0001		*p<0.0001*	
Clinical Global Impression-Change (CGIC): Symptoms "much improved" or "very much improved"	80% N=43	51% N=47	86% N=43	38% N=47
	p<0.0066		*p<0.0001*	
Epworth Sleepiness Scale (ESS): Decrease in overall sleepiness	-5.6 points N=43	-2.4 points N=47	-8.5 points N=43	-2.5 points N=47
	p=0.0038		*p<0.0001*	

"These results are highly consistent with the robust alerting effects seen in the Phase 2a clinical study and add to the body of evidence supporting the potential clinical benefit of JZP-110 for patients suffering from EDS," said Jed Black, M.D., vice president, sleep medicine, Jazz Pharmaceuticals, and consulting associate professor, Stanford University Medical Center, Stanford Center for Sleep Sciences and Medicine. "We believe this is an important development program for the sleep community because many patients with EDS experience an inadequate response to, or difficulty tolerating, their currently prescribed alerting medications."

In this study, JZP-110 was generally well-tolerated. Most adverse events (AEs) were mild to moderate in severity. The most common AEs (>=10%) more frequently observed with JZP-110 than with placebo were headache, nausea, diarrhea, insomnia, decreased appetite and anxiety. Two subjects in the JZP-110 group reported serious AEs (conversion disorder and acute cholecystitis) that were attributed by the investigators as unlikely to be related to the compound. Three subjects (6.8%) in the JZP-110 group and two subjects (4%) in the placebo group discontinued due to adverse events (AEs). The three subjects in the JZP-110 group discontinued for the following reasons: one subject with conversion disorder; one subject with bruxism, insomnia and anxiety; and the third subject with palpitations and initial insomnia.

Other Data at APSS
In addition to the JZP-110 oral presentation, the following posters related to studies involving Xyrem® (sodium oxybate) oral solution will also be presented during the meeting:

- **Abstract 1029:** Development of Definition of Responder to Narcolepsy Treatment; Poster 151; Presentation on Monday, June 2, 2014, 4:00-6:00 PM CDT, Exhibit Hall B.
- **Abstract 0667:** Time to Response with Xyrem® (sodium oxybate) for the Treatment of EDS and Cataplexy in Patients with Narcolepsy; Poster 266; Presentation on Tuesday, June 3, 2014, 4:00-6:00 PM CDT, Exhibit Hall B.
- **Abstract 0666:** A 12-Week Open-Label, Multicenter Study Evaluating the Safety of Xyrem® (sodium oxybate) in Patients with Narcolepsy; Poster 265; Presentation on Tuesday, June 3, 2014, 4:00-6:00 PM CDT, Exhibit Hall B.

Jazz Pharmaceuticals Clinical Development Pipeline in Narcolepsy and Sleep
Jazz Pharmaceuticals continues to expand its clinical development pipeline in the areas of narcolepsy and sleep. Current clinical investigations include:

- **Xyrem® (sodium oxybate) oral solution in Children and Adolescents:** In working with the Food and Drug Administration (FDA), Jazz Pharmaceuticals has received a *Pediatric Written Request* from the FDA to study Xyrem in children and adolescents. The company is preparing to conduct a Phase 3 clinical trial to assess the safety and efficacy of sodium oxybate in children and adolescents aged seven to 17 years who have narcolepsy with cataplexy and plans to initiate clinical sites for this study in the second half of 2014.
- **JZP-110:** Jazz Pharmaceuticals is currently planning a Phase 3 clinical development program for this investigational compound for the treatment of EDS in adults with narcolepsy and for the treatment of EDS in adults with OSA.
- **JZP-386**: Pre-clinical trials are underway with a deuterium-modified analog of sodium oxybate. Jazz Pharmaceuticals expects the first-in-human study to begin in Europe in 2014, subject to the availability of clinical trial material.

About Narcolepsy
Narcolepsy is a sleep disorder that involves the brain's inability to regulate sleep-wake cycles normally.[2] It affects an estimated 1 in 2,000 people in the United States,[3] with symptoms typically appearing in early adulthood.[1] It is estimated that 50 percent or more patients with narcolepsy have not been diagnosed.[3] Studies have shown it may take 10 years or more for people with narcolepsy to receive a correct diagnosis.[4],[5] EDS is the primary symptom of narcolepsy and is present in all people with the disorder.[1],[6] EDS is characterized by the inability to stay awake and alert during the day resulting in unplanned lapses into sleep or drowsiness.[1],[6]

About Xyrem
Xyrem® (sodium oxybate) oral solution, CIII, is indicated for the treatment of cataplexy in narcolepsy and for the treatment of EDS in narcolepsy. Xyrem may only be dispensed to patients enrolled in the Xyrem Success Program®. Xyrem was first approved in the United States in 2002. Safety and effectiveness in pediatric patients have not been established.

IMPORTANT SAFETY INFORMATION

XYREM is a Central Nervous System (CNS) depressant. In clinical trials at recommended doses, obtundation and clinically significant respiratory depression occurred in XYREM-treated patients. Almost all of the patients who received XYREM during clinical trials in narcolepsy were receiving CNS stimulants.

XYREM is the sodium salt of gamma hydroxybutyrate (GHB). Abuse of GHB, either alone or in combination with other CNS depressants, is associated with CNS adverse reactions, including seizure, respiratory depression, decreases in the level of consciousness, coma, and death.

Because of the risks of CNS depression, abuse, and misuse, XYREM is available only through a restricted distribution program called the XYREM Success Program®, using a centralized pharmacy. Prescribers and patients must enroll in the program. For further information go to www.XYREM.com or call 1-866-XYREM88® (1-866-997-3688).

Xyrem is contraindicated in combination with sedative hypnotics or alcohol and in patients with succinic semialdehyde dehydrogenase deficiency. Use caution when considering the concurrent use of Xyrem with other CNS depressants. Healthcare providers should caution patients against hazardous activities requiring complete mental alertness or motor coordination within the first 6 hours of dosing or after first initiating treatment until certain that Xyrem does not affect them adversely. Xyrem is a Schedule III controlled substance. The rapid onset of sedation, coupled with the amnestic features of Xyrem, particularly when combined with alcohol, has proven to be dangerous for the voluntary and involuntary user (e.g. assault victim). Monitor patients for emergent or increased depression and suicidality and for impaired motor/cognitive function. Episodes of sleepwalking should be fully evaluated and appropriate interventions considered. Consider the amount of daily sodium intake in each dose of Xyrem in patients sensitive to salt intake.

In three controlled clinical trials, the most common adverse reactions (incidence ≥5% and twice the rate of placebo) in Xyrem-treated patients were nausea (20%), dizziness (15%), vomiting (11%), somnolence (8%), enuresis (7%) and tremor (5%).

Please click here to see the full Prescribing Information for Xyrem, including BOXED Warning.

About Jazz Pharmaceuticals plc
Jazz Pharmaceuticals plc (Nasdaq: JAZZ) is a specialty biopharmaceutical company focused on improving patients' lives by identifying, developing and commercializing differentiated products that address unmet medical needs. The company has a diverse portfolio of products and/or product candidates in the areas of sleep, hematology/oncology, pain and psychiatry. The company's U.S. marketed products in these areas include: Xyrem® (sodium oxybate) oral solution, Erwinaze® (asparaginase Erwinia chrysanthemi), Prialt® (ziconotide) intrathecal infusion, Versacloz™ (clozapine) oral suspension, FazaClo® (clozapine, USP) HD and FazaClo LD. Jazz Pharmaceuticals also has a number of products marketed outside the United

States, including Erwinase® and Defitelio® (defibrotide). 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 Jazz Pharmaceuticals' planned clinical trials, the expected timing of those trials, the potential benefits to patients of JZP-110, and other statements that are not historical facts. These forward-looking statements are based on Jazz Pharmaceuticals' current expectations 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 difficulty and uncertainty of pharmaceutical product development, including the timing thereof, the uncertainty of clinical success, such as the risk that results from early clinical trials may not be predictive of results obtained in later and larger clinical trials, the risk that the company may not be able to obtain and supply sufficient product to meet requirements for clinical trial supplies, and the uncertainty of regulatory approval, and those other risks detailed 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 Quarterly Report on Form 10-Q for the quarter ended March 31, 2014 and future filings and reports by the company. Jazz Pharmaceuticals undertakes no duty or obligation to update any forward-looking statements contained in this press release as a result of new information, future events or changes in its expectations.

[1] American Academy of Sleep Medicine. The International Classification of Sleep Disorders. 2nd ed. Westchester, IL: American Academy of Sleep Medicine; 2005.
[2] National Institute of Neurologic Disorders and Stroke. NINDS Narcolepsy Information Page. Accessed Sept. 27, 2013 http://www.ninds.nih.gov/disorders/narcolepsy/narcolepsy.htm.
[3] Ahmed I, Thorpy M. Clinical features, diagnosis and treatment of narcolepsy. Clin Chest Med. 2010;31(2):371- 381.
[4] Morrish E, King MA, Smith IE, Shneerson JM. Factors associated with a delay in the diagnosis of narcolepsy. Sleep Med. 2004;5(1):37-41.
[5] US Modafinil in Narcolepsy Multicenter Study Group. Randomized trial of modafinil as a treatment for the excessive daytime somnolence of narcolepsy. Neurology. 2000;54(5):1166-1175.
[6] Scammell TE. The neurobiology, diagnosis, and treatment of narcolepsy. Ann Neurol. 2003;53(2):154-166.

SOURCE Jazz Pharmaceuticals plc

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