Jazz Pharmaceuticals Announces FDA Acceptance and Priority Review of Supplemental New Drug Application for Xywav™ (calcium, magnesium, potassium, and sodium oxybates) Oral Solution in Idiopathic Hypersomnia

April 12, 2021

Final FDA decision anticipated by August 12
Phase 3 study results to be presented during AAN Annual Meeting Clinical Trials Plenary Session on April 20
Company to host investor webcast to review Phase 3 data on April 20 at 12:30 PM ET

DUBLIN, April 12, 2021 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the U.S. Food and Drug Administration (FDA) has granted Priority Review designation and confirmed the acceptance for substantive review of the supplemental New Drug Application (sNDA) seeking approval for Xywav™ (calcium, magnesium, potassium, and sodium oxybates) oral solution in adult patients with idiopathic hypersomnia. The sNDA will be filed by the FDA on April 13, 2021 and a PDUFA goal date for an FDA decision has been set for August 12, 2021.

Jazz submitted to FDA the clinical study report for the Phase 3 study of *Xywav* in a double-blind, multicenter, placebo-controlled, randomized withdrawal study evaluating the efficacy and safety of *Xywav* in adult patients with idiopathic hypersomnia in December 2020 under rolling review, and completed the rolling submission of the sNDA in February 2021. The trial met its primary endpoint of clinically meaningful improvements in the Epworth Sleepiness Scale (ESS) p-value <0.0001 and the key secondary endpoints of Patient Global Impression of change (PGIc) p-value <0.0001 and Idiopathic Hypersomnia Severity Scale (IHSS) p-value <0.0001.

The Phase 3 study results will be presented during the Clinical Trials Plenary Session of the 2021 American Academy of Neurology (AAN) Annual Meeting on April 20, 2021, with an investor webcast to follow.

Webcast/conference call details
The company will host an audio webcast on April 20, 2021 at 12:30 PM ET to review the Phase 3 idiopathic hypersomnia data being presented at the 2021 AAN Annual Meeting. The live webcast may be accessed from the Investors section of the company's website at www.jazzpharmaceuticals.com. Investors may participate in the conference call by dialing (855) 353-7924 in the U.S. or (503) 343-6056 outside the U.S., and entering passcode 8075156.

An archived version of the webcast will be available for at least one week on the Investors section of the company's website. An audio replay will be available through April 27, 2021 by dialing (855) 859-2056 in the U.S. or (404) 537-3406 outside the U.S., and entering passcode 8075156.

About Idiopathic Hypersomnia
Idiopathic hypersomnia is an often debilitating, neurologic sleep disorder characterized by chronic excessive daytime sleepiness (the inability to stay awake and alert during the day resulting in the irrepressible need to sleep or unplanned lapses into sleep or drowsiness) that is not caused by other medical, behavioral or psychiatric conditions.[1,2,3,4] Symptoms may also include a prolonged main sleep episode of more than 9 hours or a sleep duration of 11 hours or longer over a 24-hour period, prolonged, non-restorative nighttime sleep and long and unrefreshing naps, and severe sleep inertia (prolonged difficulty waking, with frequent reentries into sleep, confusion, and irritability).[1,2,3,4] Idiopathic hypersomnia is a condition with its own specific diagnostic criteria.[1] Idiopathic hypersomnia is a debilitating illness that can significantly affect social, school and occupational functioning.[4,5] Insurance claims data suggest the number of people diagnosed with idiopathic hypersomnia and actively seeking healthcare is 37,000 patients in the U.S.; however, given that idiopathic hypersomnia is often misdiagnosed, in addition to the lack of an FDA-approved treatment, many people with idiopathic hypersomnia remain undiagnosed indicating that the unmet need may be significantly greater.

More information about Xywav, including Full Prescribing Information and Medication Guide, is available here. <http://pp.jazzpharma.com/pi/xywav.en.USPI.pdf>

About Xywav™ (calcium, magnesium, potassium, and sodium oxybates) oral solution
Xywav, also known as JZP-258, is a lower-sodium oxybate approved by the U.S. Food and Drug Administration (FDA) for the treatment of cataplexy or excessive daytime sleepiness in patients 7 years of age and older with narcolepsy. It is an investigational product being evaluated for the treatment of idiopathic hypersomnia in adult patients. While the exact mechanism of action of *Xywav* is unknown, it is hypothesized that the therapeutic effects of *Xywav* on cataplexy and excessive daytime sleepiness are mediated through $GABA_B$ actions during sleep at noradrenergic and dopaminergic neurons, as well as at thalamocortical neurons. *Xywav* received Fast Track designation by the FDA in September 2020 for the treatment of idiopathic hypersomnia.[6]

Important Safety Information
WARNING: Taking XYWAV with other central nervous system (CNS) depressants such as medicines used to make you or your child fall asleep, including opioid analgesics, benzodiazepines, sedating antidepressants, antipsychotics, sedating anti-epileptic medicines, general anesthetics, muscle relaxants, alcohol, or street drugs, may cause serious medical problems, including trouble breathing (respiratory depression), low blood pressure (hypotension), changes in alertness (drowsiness), fainting (syncope), and death.

The active ingredient of XYWAV is a form of gamma hydroxybutyrate (GHB). Abuse or misuse of illegal GHB alone or with other drugs that cause changes in alertness (or consciousness) has caused serious side effects. These effects include seizures, trouble breathing (respiratory depression), changes in alertness (drowsiness), coma, and death. Call your doctor right away if you or your child has any of these serious side effects. Because of these risks, you have to go through the XYWAV and XYREM REMS Program to have your or your child's prescription for XYWAV filled.

Do not take XYWAV if you take or your child takes other sleep medicines or sedatives (medicines that cause sleepiness), drinks alcohol, or has a rare problem called succinic semialdehyde dehydrogenase deficiency.

Keep XYWAV in a safe place to prevent abuse and misuse. Selling or giving away XYWAV may harm others, and is against the law. Tell your doctor if you have ever abused or been dependent on alcohol, prescription medicines, or street drugs.

Anyone who takes XYWAV should not do anything that requires them to be fully awake or is dangerous, including driving a car, using heavy machinery, or flying an airplane, for at least 6 hours after taking XYWAV. Those activities should not be done until you know how XYWAV affects you or your child.

XYWAV can cause serious side effects, including the following:

- **Breathing problems, including** slower breathing, trouble breathing, and/or short periods of not breathing while sleeping (sleep apnea). People who already have breathing or lung problems have a higher chance of having breathing problems when they use XYWAV.
- **Mental health problems, including** confusion, seeing or hearing things that are not real (hallucinations), unusual or disturbing thoughts (abnormal thinking), feeling anxious or upset, depression, thoughts of killing yourself or trying to kill yourself, increased tiredness, feelings of guilt or worthlessness, or difficulty concentrating. Tell your doctor if you or your child have or had depression or have tried to harm yourself or themselves. **Call your doctor right away if you have or your child has symptoms of mental health problems or a change in weight or appetite.**
- **Sleepwalking**. Sleepwalking can cause injuries. Call your doctor if you or your child starts sleepwalking. Your doctor should check you or your child.

The most common side effects of XYWAV in adults include headache, nausea, dizziness, decreased appetite, parasomnia (a sleep disorder that can include abnormal dreams, abnormal rapid eye movement (REM) sleep, sleep paralysis, sleep talking, sleep terror, sleep-related eating disorder, sleep walking, and other abnormal sleep-related events), diarrhea, excessive sweating (hyperhidrosis), anxiety and vomiting.

The most common side effects of XYWAV in children include bedwetting, nausea, headache, vomiting, weight decrease, decreased appetite, and dizziness.

XYWAV can cause physical dependence and craving for the medicine when it is not taken as directed. These are not all the possible side effects of XYWAV.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

About Jazz Pharmaceuticals plc

Jazz Pharmaceuticals plc (Nasdaq: JAZZ) is a global biopharmaceutical company dedicated to developing life-changing medicines for people with serious diseases — often with limited or no options. We have a diverse portfolio of marketed medicines and novel product candidates, from early- to late-stage development, in key therapeutic areas. Our focus is in neuroscience, including sleep medicine and movement disorders, and in oncology, including hematologic malignancies and solid tumors. We actively explore new options for patients including novel compounds, small molecule advancements, biologics and innovative delivery technologies. Jazz is headquartered in Dublin, Ireland and has employees around the globe, serving patients in more than 90 countries. For more information, please visit www.jazzpharmaceuticals.com and follow @JazzPharma on Twitter.

"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 goal date for an FDA decision on the sNDA submission and the potential timing of the availability of *Xywav* for people with idiopathic hypersomnia; and other statements that are not historical facts. These forward-looking statements are based on Jazz Pharmaceuticals' 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; the regulatory approval process, including the risk that the company may be unable to obtain approval by the FDA of its sNDA for *Xywav* in a timely manner or at all; effectively commercializing *Xywav*; 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 Jazz Pharmaceuticals' Annual Report on Form 10-K for the year ended December 31, 2020 and future filings and reports by Jazz Pharmaceuticals. Other risks and uncertainties of which Jazz Pharmaceuticals is not currently aware may also affect Jazz Pharmaceuticals' 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 Jazz Pharmaceuticals on its website or otherwise. Jazz Pharmaceuticals 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.

1. 2015 Review article in Chest, by Khan/Trotti et al, "Central Disorders of Hypersomnolence: Focus on the Narcolepsies and Idiopathic Hypersomnia" https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4694150/
2. 2016 Sleep Medicine Review article, by Billiard/Sonka et al, "Idiopathic Hypersomnia" https://www.ncbi.nlm.nih.gov/pubmed/26599679
3. International Classification of Sleep Disorders, Third Edition (ICSD 3): http://www.aasmnet.org/store/product.aspx?pid=849
4. Diagnostic and Statistical Manual of Mental Disorders (DSM-V) p. 368-372 Hypersomnolence Disorder: https://www.psychiatry.org/psychiatrists/practice/dsm
5. G Hess, R Mehra, G Carls, J Profant, J Altenburger, O Pasenchenko, J F Acquavella, 0625 US Prevalence of Narcolepsy

and Other Sleep Disorders From 2013–2016: A Retrospective, Epidemiological Study Utilizing Nationwide Claims, Sleep, Volume 41, Issue suppl_1, April 2018, Page A232, https://doi.org/10.1093/sleep/zsy061.624
6. Xywav (calcium, magnesium, potassium and sodium oxybates) oral solution Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.

Media Contact:
Jacqueline Kirby, Vice President, Corporate Affairs & Government Relations
Ireland +353 1 697 2141 U.S. +1 215 867 4910

Investor Contact:
Andrea N. Flynn, Ph.D., Vice President, Head, Investor Relations
Ireland +353 1 634 7887 U.S. +1 650 496 2717

View original content to download multimedia:http://www.prnewswire.com/news-releases/jazz-pharmaceuticals-announces-fda-acceptance-and-priority-review-of-supplemental-new-drug-application-for-xywav-calcium-magnesium-potassium-and-sodium-oxybates-oral-solution-in-idiopathic-hypersomnia-301266604.html

SOURCE Jazz Pharmaceuticals plc