Jazz Pharmaceuticals to Present from Expanding Neuroscience Portfolio Epidiolex® (cannabidiol) Oral Solution Data at the 2021 American Epilepsy Society Annual Meeting

December 1, 2021

Data from six abstracts advancing cannabidiol (CBD) research to be presented, including two abstracts which highlight results from a U.S. caregiver survey that provides insight on real-world seizure and non-seizure outcomes in patients taking Epidiolex

Additional key abstract demonstrates Epidiolex's utility in improving seizure frequency and seizure-free intervals in patients with Tuberous Sclerosis Complex (TSC) as part of post-hoc analysis of a Phase 3 trial

DUBLIN, Dec. 1, 2021 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that six company-sponsored Epidiolex® (cannabidiol) oral solution presentations, including one late-breaking abstract, will be debuted at the upcoming 2021 American Epilepsy Society (AES) annual meeting, which will be held December 3 to 7, 2021 in Chicago, IL.

"With the successful integration of GW Pharmaceuticals this year, Jazz is excited to present at the AES meeting for the first time and meet with physicians and patient advocacy groups to better understand patient needs and build on GW's progress in epilepsy," said Robert Iannone, M.D., M.S.C.E., executive vice president, research and development and chief medical officer of Jazz Pharmaceuticals. "The GW cannabinoid platform enhances our neuroscience R&D portfolio and, coupled with our development capabilities, will accelerate our cannabinoid development programs to potentially treat additional neurological conditions. The latest research being presented at AES adds to the body of clinical evidence supporting *Epidiolex*, as well as survey data from people living with rare forms of epilepsy that provides additional understanding on reduced seizure frequency and improvements in cognition, emotional functioning and executive function following treatment initiation."

Epidiolex, a pharmaceutical formulation of cannabidiol (CBD), is the first prescription, plant-derived cannabis-based medicine approved by the U.S. Food and Drug Administration. It is indicated for the treatment of patients with seizures associated with Lennox-Gastaut syndrome (LGS), Dravet syndrome (DS) and tuberous sclerosis complex (TSC) in patients aged 1 year and older.

Presentation highlights include:

- **BECOME (BEhavior, COgnition, and More with *Epidiolex*) Caregiver Survey Results:** Two posters will be presented from the U.S.-based BECOME global outcomes caregiver survey of nearly 500 responders, characterizing and quantifying real-world seizure and non-seizure outcomes in patients with LGS or DS. Findings of the survey indicated a reported improvement in emotional functioning, cognition and executive function, and language and communication since initiating treatment, in addition to decreased seizure frequency.
- **Effect of Add-on CBD on Seizure Frequency and Seizure-Free Intervals in Patients With Seizures Associated With Tuberous Sclerosis Complex (TSC): Phase 3 Trial GWPCARE6 Post Hoc Analysis:** A post-hoc analysis of the pivotal placebo-controlled Phase 3 *Epidiolex* trial in patients with TSC (NCT02544763). The analysis evaluated reduction in seizure frequency as cumulative distribution function to determine the proportion of patients, treated with CBD 25 mg/kg/d (CBD25) or placebo, who reached all continuous responder rate thresholds and the longest seizure-free intervals. The findings also provide more insight into the effects of *Epidiolex* in patients with treatment-resistant epilepsy associated with TSC.

The AES abstracts are available online at <https://www.aesnet.org/education/annual-meeting/aes-abstract-search#?wst=c0af36fb10161c568cd26bd07e9858ab>.

A full list of Jazz-sponsored AES presentations follows:

Presentation Topic	Author	Presentation Details
Seizure Related Outcomes With Real-World Use of CBD in Lennox-Gastaut Syndrome and Dravet Syndrome: BECOME, A Caregiver Survey	Dixon-Salazar, et al.	**POSTER** **Date:** Monday, December 6; 1:00 PM EST (12:00 PM CST) **Presentation Number:** 3.3
Non-Seizure Related Outcomes With Real-World Use of CBD in Lennox-Gastaut Syndrome and Dravet Syndrome: BECOME, A Caregiver Survey	Berg, et al.	**POSTER** **Date:** Monday, December 6; 1:00 PM EST (12:00 PM CST) **Presentation Number:** 3.304
Effect of Add-on CBD on Seizure Frequency and Seizure-Free Intervals in Patients With Seizures Associated With Tuberous Sclerosis Complex: Phase 3 Trial GWPCARE6 Post Hoc Analysis	Thiele, et al.	**POSTER** **Date:** Monday, December 6; 1:00 PM EST (12:00 PM CST) **Presentation Number:** 3.283

Efficacy and Safety of CBD Dose Adjustment in Patients with Lennox-Gastaut Syndrome: Post Hoc Analysis of Phase 3 Trial GWPCARE3 and Open-Label Extension (OLE) Trial GWPCARE5	Saurer, et al.	**POSTER** **Date:** Saturday, December 4; 1:00 PM EST (12:00 PM CST) **Presentation Number:** 1.42
Non-Seizure-Related Benefits of CBD Among Individuals with Dravet or Lennox-Gastaut Syndromes: A Qualitative Study	Bowditch, et al.	**VIRTUAL POSTER** **Date:** Thursday, December 9; 1:00 PM EST (12:00 PM CST) **Presentation Number:** 2.243
Pharmacokinetic Drug-Drug Interaction with Coadministration of CBD and Everolimus in a Phase 1 Healthy Volunteer Trial	Wray, et al.	**VIRTUAL POSTER** **Date:** Thursday, December 9; 1:00 PM EST (12:00 PM CST) **Presentation Number:** 3.299

About Tuberous Sclerosis Complex

Tuberous sclerosis complex (TSC) is a rare genetic condition.[1] The condition causes mostly benign tumors to grow in vital organs of the body including the brain, skin, heart, eyes, kidneys and lungs[2] and is a leading cause of genetic epilepsy.[3] People with TSC may experience a variety of seizure types. One of the most common is infantile spasms that typically present in the first year of life; focal (or partial) seizures are also very common.[4] TSC is associated with an increased risk of autism and intellectual disability[5] and the severity of the condition can vary widely. In some children the disease is very mild, while others may experience life-threatening complications.[2] Epilepsy is present in about 85 percent of patients with TSC and may progress to become intractable to medication.[4,6,7] More than 60 percent of individuals with TSC do not achieve seizure control[8] with standard treatments such as antiepileptic drugs, epilepsy surgery, ketogenic diet, or vagus nerve stimulation[6] compared to 30-40 percent of individuals with epilepsy who do not have TSC who are drug resistant.[9,10]

About Dravet Syndrome

Dravet syndrome (DS) is a rare genetic condition that appears during the first year of life with frequent fever-related seizures (febrile seizures). Later, other types of seizures typically arise, including myoclonic seizures (involuntary muscle spasms). Additionally, status epilepticus, a potentially life-threatening state of continuous seizure activity requiring emergency medical care, may occur. Children with DS typically experience poor development of language and motor skills, hyperactivity and difficulty relating to others.

About Lennox-Gastaut Syndrome

Lennox-Gastaut syndrome (LGS) begins in childhood. It is characterized by multiple types of seizures. People with LGS begin having frequent seizures in early childhood, usually between ages 3 and 5. More than three-quarters of affected individuals have tonic seizures, which cause the muscles to contract uncontrollably. Almost all children with LGS develop learning problems and intellectual disability. Many also have delayed development of motor skills such as sitting and crawling. Most people with LGS require help with usual activities of daily living.

About Epidiolex®/Epidyolex® (cannabidiol)

Epidiolex®/Epidyolex® (cannabidiol), the first prescription, plant-derived cannabis-based medicine approved by the U.S. Food and Drug Administration (FDA) for use in the U.S., the European Commission (EC) for use in Europe, the Medicines and Healthcare products Regulatory Agency (MHRA) for use in Great Britain, the Therapeutic Goods Administration for use in Australia, Swissmedic for use in Switzerland, and the Food & Nutrition Services of the Israel Ministry of Health for use in Israel, is an oral solution which contains highly purified cannabidiol (CBD). In the U.S., *Epidiolex* is indicated for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS), Dravet syndrome (DS) or tuberous sclerosis complex (TSC) in patients one year of age and older. *Epidiolex* has received approval in the European Union under the tradename *Epidyolex* for adjunctive use in conjunction with clobazam to treat seizures associated with LGS and DS in patients two years and older, and for adjunctive use to treat seizures associated with TSC, in patients two years of age and older. *Epidyolex* has received Orphan Drug Designation from the European Medicines Agency (EMA) for the treatment of seizures associated LGS, DS and TSC.

Important Safety Information & Indications

Contraindication: Hypersensitivity

EPIDIOLEX (cannabidiol) oral solution is contraindicated in patients with a history of hypersensitivity to cannabidiol or any ingredients in the product.

Warnings & Precautions

Hepatocellular Injury:

EPIDIOLEX can cause dose-related transaminase elevations. Concomitant use of valproate and elevated transaminase levels at baseline increase this risk. Transaminase and bilirubin levels should be obtained prior to starting treatment, at one, three, and six months after initiation of treatment, and periodically thereafter, or as clinically indicated. Resolution of transaminase elevations occurred with discontinuation of EPIDIOLEX, reduction of EPIDIOLEX and/or concomitant valproate, or without dose reduction. For patients with elevated transaminase levels, consider dose reduction or discontinuation of EPIDIOLEX or concomitant medications known to affect the liver (e.g., valproate or clobazam). Dose adjustment and slower dose titration is recommended in patients with moderate or severe hepatic impairment. Consider not initiating EPIDIOLEX in patients with evidence of significant liver injury.

Somnolence and Sedation:

EPIDIOLEX can cause somnolence and sedation that generally occurs early in treatment and may diminish over time; these effects occur more commonly in patients using clobazam and may be potentiated by other CNS depressants.

Suicidal Behavior and Ideation:

Antiepileptic drugs (AEDs), including EPIDIOLEX, increase the risk of suicidal thoughts or behavior. Inform patients, caregivers, and families of the risk

and advise to monitor and report any signs of depression, suicidal thoughts or behavior, or unusual changes in mood or behavior. If these symptoms occur, consider if they are related to the AED or the underlying illness.

Withdrawal of Antiepileptic Drugs:
As with most AEDs, EPIDIOLEX should generally be withdrawn gradually because of the risk of increased seizure frequency and status epilepticus.

Adverse Reactions:
The most common adverse reactions in patients receiving EPIDIOLEX (≥10% and greater than placebo) include transaminase elevations; somnolence; decreased appetite; diarrhea; pyrexia; vomiting; fatigue, malaise, and asthenia; rash; insomnia, sleep disorder and poor-quality sleep; and infections. Hematologic abnormalities were also observed.

Pregnancy:
EPIDIOLEX should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Encourage women who are taking EPIDIOLEX during pregnancy to enroll in the North American Antiepileptic Drug (NAAED) Pregnancy Registry.

Drug Interactions:
Strong inducers of CYP3A4 and CYP2C19 may affect EPIDIOLEX exposure. EPIDIOLEX may affect exposure to CYP2C19 substrates (e.g., clobazam, diazepam, stiripentol), orally administered P-gp substrates, or other substrates (see full Prescribing Information). Consider dose reduction of orally administered everolimus, with appropriate therapeutic drug monitoring, when everolimus is combined with EPIDIOLEX. A lower starting dose of everolimus is recommended when added to EPIDIOLEX therapy. Concomitant use of EPIDIOLEX and valproate increases the incidence of liver enzyme elevations. Pneumonia was observed more frequently with concomitant use of EPIDIOLEX and clobazam. Dosage adjustment of EPIDIOLEX or other concomitant medications may be necessary.

Indications:
EPIDIOLEX (cannabidiol) oral solution is indicated for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS), Dravet syndrome (DS), or tuberous sclerosis complex (TSC) in patients 1 year of age and older.

Please refer to the EPIDIOLEX full Prescribing Information for additional important information here.

About Jazz Pharmaceuticals plc
Jazz Pharmaceuticals plc (Nasdaq: JAZZ) is a global biopharmaceutical company whose purpose is to innovate to transform the lives of patients and their families. We are dedicated to developing life-changing medicines for people with serious diseases – often with limited or no therapeutic options. We have a diverse portfolio of marketed medicines and novel product candidates, from early- to late-stage development, in neuroscience and oncology. Within these therapeutic areas, we are identifying new options for patients by actively exploring small molecules and biologics, and through innovative delivery technologies and cannabinoid science. Jazz is headquartered in Dublin, Ireland and has employees around the globe, serving patients in nearly 75 countries. For more information, please visit www.jazzpharma.com and follow @JazzPharma on Twitter.

Caution Concerning Forward-Looking Statements
This press release contains forward-looking statements, including, but not limited to, statements related to the *Epidiolex* for people with tuberous sclerosis complex, Lennox-Gastaut syndrome, Dravet syndrome and the potential impact on that community 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, 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' Quarterly Report on Form 10-Q for the quarter ended September 30, 2021 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.

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