Jazz Pharmaceuticals to Present Data Demonstrating Advancements in Epilepsy Outcomes at the 2022 American Epilepsy Society Annual Meeting

November 28, 2022

Data from six abstracts to be presented, including new long-term Phase 3 results and two real-world analyses of U.S. caregiver-reported seizure and non-seizure outcomes in patients prescribed Epidiolex ®(cannabidiol)

DUBLIN, Nov. 28, 2022 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that six company-sponsored Epidiolex® (cannabidiol) oral solution presentations, including three late-breaking abstracts, will be shared at the upcoming 2022 American Epilepsy Society (AES) annual meeting, which will be held December 2-6, 2022, in Nashville, TN.

"We understand the significant, lifelong implications of severe, childhood-onset epilepsy on both patients and their families. We continually strive to improve patient outcomes and are proud to present data that includes caregiver-reported insight into *Epidiolex*'s effects on seizure and non-seizure outcomes in both children and adults living with Lennox-Gastaut Syndrome and Dravet Syndrome," said Kelvin Tan, MB BCh, MRCPCH, senior vice president and chief medical officer of Jazz Pharmaceuticals. "In addition, we are sharing long-term Phase 3 trial findings which demonstrate *Epidiolex's* ability to reduce tuberous sclerosis complex-related seizures over the course of three years of treatment – further underscoring that *Epidiolex* is an important treatment option in an area with significant unmet patient need."

Epidiolex, a pharmaceutical formulation of highly-purified cannabidiol (CBD), is the first prescription, plant-derived cannabis-based medicine approved by the U.S. Food and Drug Administration (FDA). 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:

- **Two Late Breaker Abstracts Featuring Subgroup Analysis of BECOME (BEhavior, COgnition, and More with Epidiolex) Caregiver Survey Results:** While onset of LGS and DS is typically in infancy or childhood, these conditions are lifelong diseases with symptoms that evolve over time. The BECOME survey is a global outcomes survey of caregivers of patients with LGS or DS that characterized and quantified the seizure and non-seizure outcomes of Epidiolex treatment. The results from both poster presentations demonstrate that a substantial proportion of the caregivers of people with LGS or DS treated with Epidiolex reported improvements in many patients' seizure and non-seizure outcomes, regardless of age group (patients aged <18 years and >18 years).[1,2]
- **Long-term Safety and Efficacy of Add-on Cannabidiol (CBD) for Seizures Associated with Tuberous Sclerosis Complex (TSC): 3-Year Results From GWPCARE6 Open-Label Extension (OLE):** Final data from the Phase 3 trial GWPCARE6 OLE evaluates the long-term efficacy and safety of add-on *Epidiolex* in patients with TSC-associated seizures across three years. Findings suggest that long-term, add-on *Epidiolex* treatment was well tolerated and demonstrated sustained reductions in TSC-associated seizures in patients for up to 156 weeks.[3]
- **REST LGS TOOL: Real World Use to Screen for LGS and Improve Access to Care:** LGS is frequently undiagnosed in the adult population due to the lack of transfer of prior medical history to adult providers and the evolution of the symptoms of LGS over time. The Refractory Epilepsy Screening Tool for LGS patients (REST-LGS) was designed to improve identification and treatment of patients with LGS. This retrospective chart review of 100 patients aged 18 and older with drug-resistant epilepsy (DRE) and Intellectual and Development Disabilities (IDD) sought to further validate the REST-LGS. Using REST-LGS, this study identified that over half of the individuals without a previous LGS diagnosis should be referred for further diagnostic evaluation at a specialized epilepsy center, and further validated the REST-LGS for the identification of potential LGS patients with DRE and IDD.[4]

The AES abstracts are available online at https://www.aesnet.org/education/annual-meeting/aes-abstract-search.

A full list of Jazz-sponsored AES presentations follows:

Presentation Topic	Author	Presentation Details
Seizure-Free Days as a Novel and Meaningful Outcome in Patients with Lennox-Gastaut Syndrome: Post Hoc Analysis of Patients Receiving Cannabidiol (CBD) in GWPCARE3 and GWPCARE4	Auvin, S. et al.	**POSTER** **Date:** Saturday, December 3, 12:00 PM - 2:00 PM **Presentation Number:** 1.285
Long-term Safety and Efficacy of Add-on Cannabidiol (CBD) for Seizures Associated with Tuberous Sclerosis Complex (TSC): 3-Year Results From GWPCARE6 Open-Label Extension (OLE)	Thiele, E. et al.	**POSTER** **Date:** Sunday, December 4, 12:00 PM - 2:00 PM **Presentation Number:** 2.237
REST LGS TOOL: Real World Use to Screen for LGS and Improve Access to Care	Wolf, S. et al.	**POSTER** **Date:** Sunday, December 4, 12:00 PM - 2:00 PM

		Presentation Number: 2.106
Late-Breaker Abstracts		
Nonseizure Outcomes With Cannabidiol (CBD) in Pediatric Versus Adult Patients With Lennox-Gastaut Syndrome (LGS) and Dravet Syndrome (DS): Subgroup Analysis of BECOME, a Caregiver Survey	Dixon-Salazar, T. et al.	**POSTER** **Date:** Monday, December 5, 12:00 PM - 1:45 PM **Presentation Number:** 3.429
Seizure Outcomes With Cannabidiol (CBD) in Pediatric Versus Adult Patients With Lennox-Gastaut Syndrome (LGS) and Dravet Syndrome (DS): Subgroup Analysis of BECOME, a Caregiver Survey	Saurer, T.B. et al.	**POSTER** **Date:** Monday, December 5 12:00 PM - 1:45 PM **Presentation Number:** 3.428
Dravet Syndrome Natural History: Placebo-Treated Patients in Clinical Trials Rationale	Nabbout, R. et al.	**POSTER** **Date:** Monday, December 5 12:00 PM - 1:45 PM **Presentation Number:** 3.414

About Tuberous Sclerosis Complex

Tuberous sclerosis complex (TSC) is a rare genetic condition.[5] The condition causes mostly benign tumors to grow in vital organs of the body including the brain, skin, heart, eyes, kidneys and lungs[6] and is a leading cause of genetic epilepsy.[7] 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.[8] TSC is associated with an increased risk of autism and intellectual disability[9] and the severity of the condition can vary widely. In some children the disease is very mild, while others may experience life-threatening complications.[6] Epilepsy is present in about 85 percent of patients with TSC and may progress to become intractable to medication.[8,10,11] More than 60 percent of individuals with TSC do not achieve seizure control[12] with standard treatments such as antiepileptic drugs, epilepsy surgery, ketogenic diet, or vagus nerve stimulation[8] compared to 30-40 percent of individuals with epilepsy who do not have TSC who are drug resistant.[13,14]

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).[15] 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.[16] 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, 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. Please visit www.jazzpharmaceuticals.com for more information.

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, including as a potential treatment option in an area with significant unmet patient need, 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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