Jazz Pharmaceuticals Presents New Findings From Caregiver Survey on Outcomes of Epidiolex® (cannabidiol) for Adult and Pediatric Patients With Severe, Childhood-Onset Epilepsies

December 5, 2022

Real-world data from the BECOME (BEhavior, COgnition, and More with Epidiolex) Caregiver Survey presented at the 2022 American Epilepsy Society Annual Meeting expands evidence behind Epidiolex treatment in adult and pediatric patients

Caregivers of Lennox-Gastaut Syndrome and Dravet Syndrome patients reported seizure and non-seizure related outcomes across age groups

DUBLIN, Dec. 5, 2022 /PRNewswire/ -- Jazz Pharmaceuticals plc (NASDAQ: JAZZ) today announced new real-world data from the BECOME (BEhavior, COgnition, and More with Epidiolex ®) Caregiver Survey that showed a substantial proportion of caregivers of adult and pediatric patients with Lennox-Gastaut Syndrome (LGS) and Dravet Syndrome (DS) prescribed Epidiolex® (cannabidiol) oral solution reported improvements in patients' seizure and non-seizure outcomes across all age groups.[1,2] These data were presented at the 2022 American Epilepsy Society (AES) annual meeting taking place December 2–6, 2022, in Nashville, TN.

"At Jazz, we strive to continually deepen our understanding of the benefits of *Epidiolex* across the patient experience. The data from the BECOME Caregiver Survey provide important insights into the reported effects of *Epidiolex* on both seizure and non-seizure outcomes," said Kelvin Tan, MB BCh, MRCPCH, senior vice president and chief medical officer of Jazz Pharmaceuticals. "These data expand our understanding of the multifaceted experience of people living with epilepsy and their caregivers and could ultimately refine the *Epidiolex* treatment paradigm across age groups. The BECOME study ensures that patients and caregiver lived experience is front and center in clinical research."

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

"Severe, childhood-onset epilepsies like LGS and DS are lifelong conditions that have significant, long-term impacts on both caregivers and patients. These results are critical in broadening the knowledge base of the potential benefits of *Epidiolex* treatment across all age groups and identifying additional seizure and non-seizure outcomes to explore in future studies," said lead author and investigator Timothy B. Saurer, Medical Affairs Director of Jazz Pharmaceuticals. "We look forward to additional insights from the BECOME survey as we work to further characterize the specific effects of *Epidiolex* in both adult and pediatric patients living with rare, treatment-resistant epilepsy conditions."

Results

The results from both poster presentations suggest 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). Limitations to the survey included retrospective caregiver accounts, post-hoc analyses that were not pre-specified, and selection bias due to study design. In addition, the studies were not blinded and there were no comparator arms.

Seizure-Related Outcomes by Age (Poster 3.428)

The seizure-related outcome analysis found a large majority of caregivers reported patient seizure improvements as measured by decreased frequency in at least one seizure type (84% aged <18 years and ≥18 years) and severity (77% aged <18 years; 75% in ≥18 years).[1] Respondents reported patient improvements in specific seizure types: convulsive seizures (72% each), drop seizures (71% each), non-convulsive/non-drop seizures (66% aged <18 years; 69% in ≥18 years) and night-time seizures (61% and 63%).[1]

Many respondents also reported reductions in use of rescue medications (57%), emergency room visits (56% and 51%), hospitalizations (55% and 50%) and occurrence of seizure-related injuries (48% and 49%).[1]

Non-Seizure-Related Outcomes by Age (Poster 3.429)

A substantial proportion of caregivers of patients with LGS or DS, regardless of age, reported improvements in alertness, cognition and executive function, emotional and social function, language and communication, physical function, sleep, and daily activities since initiating *Epidiolex* treatment.[2]

A significant proportion of respondents in both age groups (patients aged <18 years and ≥18 years) reported any improvement (possible, minor, definite) in one or more questions regarding the following non-seizure outcome areas: Alertness, cognition, and executive function (87% and 81%) and emotional and social function (82% and 80%).[2]

In patients aged <18 years, the most frequently reported improvement was the ability to learn new things (76%). For patients ≥18 years, the most frequently reported improvement was in alertness (70%).[2]

Rates of worsening varied by behavior and ranged from 0% to 20% of respondents.[2]

The most common side effects for *Epidiolex* include: sleepiness, decreased appetite, diarrhea, increase in liver enzymes, feeling very tired or weak, rash, sleep problems, fever, vomiting and infections.[3]

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

About the BECOME (BEhavior, COgnition, and More with *Epidiolex*) Caregiver Survey

The U.S.-based survey, BECOME (global outcomes survey assessing changes in BEhavior, Cognition, and More with Epidiolex®), characterized and quantified real-world seizure and non-seizure outcomes in patients with LGS (80 percent) or DS (20 percent) treated with *Epidiolex* for three or more months. The investigators conducted an online survey of 498 caregivers (97 percent parents). The caregivers were asked to compare the past month to the period prior to initiation of *Epidiolex* treatment by answering questions with answers that were multiple choice or ranked on worsening-to-improving scales. All of the questions were based on those from validated measures and other previously published caregiver reports. *Epidiolex*-associated adverse events were not assessed in this survey. Limitations to the survey included retrospective caregiver accounts and selection bias due to study design.

About Tuberous Sclerosis Complex

Tuberous sclerosis complex (TSC) is a rare genetic condition.[4] The condition causes mostly benign tumors to grow in vital organs of the body including the brain, skin, heart, eyes, kidneys and lungs[5] and is a leading cause of genetic epilepsy.[6] 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.[7] TSC is associated with an increased risk of autism and intellectual disability[8] and the severity of the condition can vary widely. In some children the disease is very mild, while others may experience life-threatening complications.[4] Epilepsy is present in about 85 percent of patients with TSC and may progress to become intractable to medication.[4,9,10] More than 60 percent of individuals with TSC do not achieve seizure control[11] 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.[12,13]

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).[14] 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.[15] 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 is a prescription, plant-derived cannabis-based medicine administered as an oral solution which contains highly purified cannabidiol (CBD). Cannabidiol, the active ingredient in EPIDIOLEX, is a cannabinoid that naturally occurs in the *Cannabis sativa* L. plant. The precise mechanisms by which EPIDIOLEX exerts its anticonvulsant effect in humans are unknown. *Epidiolex* was 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 potential benefits of *Epidiolex* treatment across all age groups and identify additional seizure and non-seizure outcomes to explore in further studies, 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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References

[1] Saurer, T.B. et al. 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. American Epilepsy Society 2022 Annual Meeting. Nashville, TN, United States. https://www.aesnet.org/education/annual-meeting/aes-abstract-search. Accessed November 27, 2022.

[2] Dixon-Salazar, T. et al. 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. American Epilepsy Society 2022 Annual Meeting. Nashville, TN, United States. https://www.aesnet.org/education/annual-meeting/aes-abstract-search. Accessed November 27, 2022.

[3] U.S. Prescribing Information. https://pp.jazzpharma.com/pi/epidiolex.en.USPI.pdf#page=32. Accessed November 9, 2022

[4] TS Alliance. What is TSC? https://www.tsalliance.org/about-tsc/what-is-tsc/. Accessed November 9, 2022.

[5] NIH Tuberous Sclerosis Fact Sheet. https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Tuberous-Sclerosis-Fact-Sheet Accessed November 9, 2022.

[6] TS Alliance Website. https://www.tsalliance.org/. Accessed November 9, 2022.

[7] Kingswood JC, d'Augères GB, Belousova E, et al. TuberOus SClerosis registry to increase disease Awareness (TOSCA) - baseline data on 2093 patients. 2017;12(1):2.

[8] de Vries PJ, Belousova E, Benedik MP, et al. TSC-associated neuropsychiatric disorders (TAND): findings from the TOSCA natural history study. *Orphanet J Rare Dis*. 2018;13(1):157.

[9] Tuberous Sclerosis Alliance. Diagnosis, Surveillance and Management for Healthcare Professionals. https://www.tscalliance.org/healthcare-professionals/diagnosis/. Accessed November 7, 2022.

[10] Jeong A, Wong M. Systemic disease manifestations associated with epilepsy in tuberous sclerosis complex. *Epilepsia*. 2016;57(9):1443-1449.

[11] Chu-Shore CJ, Major P, Camposano S, Muzykewicz D, Thiele EA. The natural history of epilepsy in tuberous sclerosis complex. *Epilepsia*. 2010;51(7):1236-1241.

[12] Kwan P, Brodie MJ. Early identification of refractory epilepsy. *N Engl J Med*. 2000;342(5):314-319.

[13] French JA. Refractory epilepsy: clinical overview. *Epilepsia*. 2007;48 Suppl 1:3-7.

[14] Epilepsy Foundation. Dravet Syndrome. https://www.epilepsy.com/what-is-epilepsy/syndromes/dravet-syndrome. Accessed November 9, 2022.

[15] NORD. Rare Disease Database. https://rarediseases.org/rare-diseases/lennox-gastaut-syndrome/. Accessed November 9, 2022

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