Jazz Pharmaceuticals to Showcase New Real-World Evidence Reinforcing Epidiolex® (cannabidiol) Benefits and Broad-Spectrum Efficacy in Treatment-Resistant Epilepsies at the American Epilepsy Society 2024 Annual Meeting

December 06, 2024

Data from nine abstracts to be presented, including first data from the EpiCom Trial, a prospective evaluation of behavioral outcomes in patients with tuberous sclerosis complex, which suggests improvements in severity of behavioral symptoms

Real-world data from the BECOME (BEhavior, COgnition and More with Epidiolex®) surveys, which show outcomes reported by long-term care facility nurses and tuberous sclerosis complex caregivers

For U.S. media and investors only

DUBLIN, Dec. 6, 2024 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced nine company-sponsored Epidiolex® (cannabidiol) posters are being presented at the American Epilepsy Society (AES) 2024 Annual Meeting, being held December 6-10 in Los Angeles, California.

Data presented at the meeting includes updated analyses of real-world data from the BECOME-TSC (BEhavior, COgnition, and More with *Epidiolex*) caregiver survey, which characterizes and quantifies seizure and non-seizure outcomes in patients with epilepsy and tuberous sclerosis complex (TSC) treated with *Epidiolex*. An additional presentation showcases data from the BECOME-LTC survey, which evaluated the perspectives of nurses who care for patients with epilepsy in long-term care (LTC) facilities and group homes, reporting improvements in seizure frequency and in certain non-seizure outcomes associated with *Epidiolex* treatment. Further, the first presentation of data from the EpiCom trial, a prospective, interventional trial evaluating the impact of adjunctive *Epidiolex* on TSC-associated neuropsychiatric disorders (TAND), revealed improvements in behavioral symptom severity following treatment initiation.

"Our real-world data presentations at AES 2024, including novel findings from the BECOME-LTC, BECOME-TSC and EpiCom studies, demonstrate the meaningful impact of *Epidiolex* in the treatment of patients with rare epilepsies," said Sarah Akerman, MD, head of neuroscience global medical and scientific affairs of Jazz Pharmaceuticals. "These findings increase our understanding of *Epidiolex's* benefits beyond seizure control, addressing unmet needs across a range of epilepsy syndromes for people living with rare epilepsies and demonstrating reproducibility and consistency of effect across different populations."

Data highlights include:

- A prespecified three-month analysis of the EpiCom trial reporting TSC-associated neuropsychiatric disorders (TAND)-associated outcomes demonstrated improvements after initiating adjunctive *Epidiolex* treatment in the severity of behavioral problems in patients with TSC as reported by the TAND Self-Report Quantified Checklist and Aberrant Behavior Checklist.
- Two updated analyses of real-world outcomes from the BECOME-TSC study showed that, of 55 caregivers who completed the survey, 89% planned to continue *Epidiolex* treatment for their loved one. The most important stated reasons for continuing *Epidiolex* included seizure and non-seizure benefits such as reduced seizure frequency and severity/duration, as well as TAND-related improvements in cognition and language/communication.
- Results from the BECOME-LTC (BEhavior, COgnition, and More with *Epidiolex* in the Long-Term Care Setting) survey found that, among 102 nurses surveyed, 85% reported a reduction in overall frequency of any seizure type after *Epidiolex* initiation, with 49% reporting a greater than 50% reduction. Improvements were also observed across different seizure subtypes as well as in non-seizure outcomes, with nurses reporting improvements in emotional functioning, sleep, cognitive abilities, ability to communicate, and physical functioning.
- Results from CARE-EpiC (Caregiver Analysis of Real-world *Epidiolex* in Epilepsy Context), a cross-sectional caregiver survey, demonstrated reduced caregivers' need for additional support of their dependents' physical, emotional, and behavioral care after *Epidiolex* initiation and characterized improvements in their dependents' well-being as well as caregivers' experiences.
- A subgroup analysis evaluating treatment outcomes in patients with TSC (TSC group) versus other types of focal epilepsy (non-TSC group) treated with *Epidiolex* in the U.S. Expanded Access Program, found *Epidiolex* has similar effectiveness in TSC and other focal epilepsies, regardless of focal epilepsy type, further reinforcing the clinical profile of *Epidiolex* as a broad-spectrum agent. In the TSC group, *Epidiolex* was associated with a median reduction from baseline of 51%–87% in focal seizures and 44%–87% in total seizures. In the non-TSC group, *Epidiolex* was also associated with a median reduction from baseline of 46%–75% in focal and 46%–74% in total seizures.

Epidiolex is indicated for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS), Dravet syndrome or TSC in patients one year of age and older. All AES 2024 abstracts are available online at the following link: https://aesnet.org/education/annual-meeting/aes-abstract-search.

A full list of Jazz Pharmaceuticals' presentations follows below:

Presentation Title	Presenting Author	Poster Number / Date & Time (PT)
Cannabidiol has antiseizure and antitumor effects in preclinical models of tuberous sclerosis complex through mTORC1-independent mechanisms	A.R. Tee	Poster Number: 1.052 Session Date/Time: Saturday, December 7th, 12:00 – 2:00 PM
Caregiver-Reported Nonseizure Outcomes with Real-World Use of Cannabidiol (CBD) in Tuberous Sclerosis Complex (TSC): Results From the BECOME-TSC Survey	D. Samanta	Poster Number: 1.433 Session Date/Time: Saturday, December 7th, 12:00 – 2:00 PM
Caregiver-Reported Real-World Use of Cannabidiol (CBD) and Effects on Seizures and Caregiver Burden: Results From the CARE-EpiC Survey	M. Faithe	Poster Number: 1.434 Session Date/Time: Saturday, December 7th, 12:00 – 2:00 PM
Caregiver-Reported Seizure Outcomes with Real-World Use of Cannabidiol (CBD) in Tuberous Sclerosis Complex (TSC): Results From the BECOME-TSC Survey	D. Krueger	Poster Number: 1.435 Session Date/Time: Saturday, December 7th, 12:00 – 2:00 PM
Effects of Cannabidiol (CBD) on Audiogenic Seizures in the DBA/1 Mouse Model of Sudden Unexpected Death in Epilepsy (SUDEP)	C.L. Faingold	Poster Number: 2.354 Session Date/Time: Sunday, December 8th, 12:00 – 2:00 PM
Real-World Outcomes of Cannabidiol (CBD) in Tuberous Sclerosis Complex (TSC) and Other Focal Epilepsies: Experience from the Expanded Access Program (EAP)	E.A. Thiele	Poster Number: 2.369 Session Date/Time: Sunday, December 8th, 12:00 – 2:00 PM
Tuberous Sclerosis Complex (TSC)–Associated Neuropsychiatric Disorders (TAND) Outcomes Following Add-on Cannabidiol (CBD) Treatment: 3-Month Analysis of Open-Label Phase 3b/4 Trial EpiCom	A. van Eeghen	Poster Number: 2.377 Session Date/Time: Sunday, December 8th, 12:00 – 2:00 PM
Clinical Characteristics and Treatment Patterns in Patients with Dravet Syndrome and Lennox-Gastaut Syndrome Who Are Prescribed Cannabidiol (CBD)	S. Kothare	Poster Number: 2.406 Session Date/Time: Sunday, December 8th, 12:00 – 2:00 PM
Nurse-Reported Outcomes of Cannabidiol (CBD) Treatment in the Long-Term Care (LTC) Setting: Results From the BECOME-LTC Survey	A. Fowler	Poster Number: 2.411 Session Date/Time: Sunday, December 8th, 12:00 – 2:00 PM

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.[4] 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[8] 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).[11] 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.[12] 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, the Food & Nutrition Services of the Israel Ministry of Health for use in Israel, and the New Zealand Medicines and Medical Devices Safety Authority for use in New Zealand, 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. *Epidiolex* has received Orphan Drug Designation (ODD) from the U.S. FDA for the treatment of seizures associated with LGS, DS, and TSC. Similarly, *Epidyolex* received ODD from the European Medicines Agency (EMA) for the same indications.

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

Hepatic Injury:
EPIDIOLEX can cause dose-related transaminase elevations. Concomitant use of valproate and elevated transaminase levels at baseline increase this risk. Obtain transaminase and bilirubin levels prior to starting treatment, at 1, 3, and 6 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. There have been postmarketing reports of cholestatic or mixed patterns of liver injury. Elevated ammonia levels were reported in some patients with transaminase elevations; most taking concomitant valproate, clobazam, or both. Consider discontinuation or dose adjustment of valproate or clobazam if ammonia is elevated.

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 them 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 EPIDIOLEX Pregnancy Surveillance Program and 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 read the EPIDIOLEX full Prescribing Information for additional important information here.

About Jazz Pharmaceuticals
Jazz Pharmaceuticals plc (Nasdaq: JAZZ) is a global biopharma company whose purpose is to innovate to transform the lives of patients and their families. We are dedicated to developing potentially life-changing medicines for people with serious diseases — often with limited or no therapeutic options. We have a diverse portfolio of marketed medicines, including leading therapies for sleep disorders and epilepsy, and a growing portfolio of cancer treatments. Our patient-focused and science-driven approach powers pioneering research and development advancements across our robust pipeline of innovative therapeutics in oncology and neuroscience. Jazz is headquartered in Dublin, Ireland with research and development laboratories, manufacturing facilities and employees in multiple countries committed to serving patients worldwide. Please visit www.jazzpharmaceuticals.com for more information.

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