Jazz Pharmaceuticals to Present Long-Term and Real-World Data Emphasizing Commitment to Treatment-Resistant Epilepsy at the 2023 American Epilepsy Society Annual Meeting

December 01, 2023

Data from nine abstracts to be presented, including real-world outcomes of Epidiolex® (cannabidiol) in treatment-resistant focal epilepsies

Presentations include data on U.S. caregiver-reported seizure and non-seizure outcomes in patients with tuberous sclerosis complex prescribed Epidiolex

DUBLIN, Dec. 1, 2023 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that nine company-sponsored presentations, including five late-breaking abstracts, will be shared at the 2023 American Epilepsy Society (AES) annual meeting, being held December 1-5 in Orlando, Florida.

Late-breaking presentations include a post-hoc analysis examining real-world outcomes of Epidiolex® (cannabidiol) in treatment-resistant focal epilepsies within the Expanded Access Program (EAP), as well as a post-hoc analysis of the GWPCARE6 Open-Label Extension (OLE) trial evaluating the effectiveness of *Epidiolex* as add-on therapy against focal seizures in tuberous sclerosis complex (TSC). Two additional late-breaking abstracts will feature interim results from the BECOME-TSC (BEhavior, COgnition, and More with *Epidiolex*) Survey of caregivers of patients with TSC. These abstracts will report seizure and non-seizure outcomes with real-world use of *Epidiolex* in TSC and further expand the results of the original BECOME survey conducted among caregivers of people with Dravet syndrome (DS) or Lennox-Gastaut syndrome (LGS) that were presented at the 2022 AES meeting.

"Multiple presentations at the 2023 AES meeting continue to build the scientific evidence in support of *Epidiolex* and improve understanding around the treatment's full impact," said Kelvin Tan, MBBCh, MRCPCH, senior vice president and chief medical officer of Jazz Pharmaceuticals. "In addition to seizure outcomes, the BECOME studies are also designed to assess non-seizure benefits of *Epidiolex,* such as cognition and executive function, emotional and social function, and language and communication. We are determined to not only address seizure outcomes for patients living with rare epilepsies, but also improve the day-to-day lives for both patients and their loved ones."

Data highlights at the 2023 AES annual meeting include:

- A post-hoc analysis of patients diagnosed with treatment-resistant focal epilepsy within the EAP that demonstrated *Epidiolex* was associated with a sustained reduction in focal-onset seizures through 144 weeks. Notably, a second post-hoc analysis investigated the effectiveness and safety results of *Epidiolex* in adult patients from the EAP which found similar outcomes among patients with treatment-resistant epilepsies, including focal seizures. The EAP was an initiative launched in 2014 to provide add-on *Epidiolex* to patients with treatment-resistant epilepsy at 35 U.S. epilepsy centers.
- A post-hoc analysis of the GWPCARE6 OLE trial evaluating the effectiveness of *Epidiolex* as add-on therapy against focal seizures in TSC. At least 50% reduction was reported by the majority of patients across focal seizure types through 144 weeks. Additionally, responder rates for focal seizure subtypes were consistent with the overall focal seizure responder rates, and the safety profile observed in the analysis was consistent with that observed in its overall clinical development program.
- Interim results of the BECOME-TSC survey, in which the majority of caregivers reported patient improvements in overall seizure frequency and severity, as well as improvements in patients' cognition, emotional functioning, and communication domains.

The 2023 AES 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	**Lead Author**	**Poster Number / Date & Time (ET)**
Late-Breaking Abstracts		
Real-World Outcomes of Cannabidiol (CBD) in Treatment-Resistant Focal Epilepsies: Experience From the Expanded Access Program (EAP)	A. D. Patel	Poster Number: 2.493 Session Date/Time: Sunday, December 3rd, 12:00-2:00 PM
Long-Term Effectiveness of Cannabidiol Against Focal Seizures in Tuberous Sclerosis Complex: Results From the GWPCARE6 Open-Label Extension Trial	J.Y. Wu	Poster Number: 2.498 Session Date/Time: Sunday, December 3rd, 12:00-2:00 PM
Caregiver-Reported Nonseizure Outcomes with Real-World Use of Cannabidiol (CBD) in Tuberous Sclerosis Complex (TSC): Interim Results From the BECOME-TSC Survey	S. Wilson	Poster Number: 2.499 Session Date/Time: Sunday, December 3rd, 12:00-2:00 PM

Caregiver-Reported Seizure Outcomes with Real-World Use of Cannabidiol (CBD) in Tuberous Sclerosis Complex (TSC): Interim Results from the BECOME-TSC Survey	M.K. Koenig	Poster Number: 2.503 Session Date/Time: Sunday, December 3rd, 12:00-2:00 PM
Cannabidiol and Sodium Valproate Demonstrate Pharmacodynamic Synergism in an Acute Mouse Model of Generalised Seizures	R.R. Rohini	Poster Number: 3.479 Session Date/Time: Monday, December 4th, 12:00-1:45 PM
Abstracts		
Efficacy and Safety of Cannabidiol (CBD) for Seizures Associated With Tuberous Sclerosis Complex (TSC) in Pediatric and Adult Patients From GWPCARE6: A Phase 3 Trial With Open-Label Extension (OLE)	E.A. Thiele	Poster Number: 3.266 Session Date/Time: Monday, December 4th, 12:00-1:45 PM
Change in Antiseizure and Anxiolytic Medications Pre- and Post-Cannabidiol Initiation	G. Fang	Poster Number: 3.287 Session Date/Time: Monday, December 4th, 12:00-1:45 PM
Long-term Effectiveness of Cannabidiol (CBD) Against Focal-Onset Seizures in Treatment-Resistant Epilepsies (TRE)	Y.D. Park	Poster Number: 3.291 Session Date/Time: Monday, December 4th, 12:00-1:45 PM
Real-world Safety and Effectiveness of Cannabidiol (CBD) in Adults With Treatment-Resistant Epilepsies: Long-term Results From the United States Expanded Access Program (EAP)	J.P. Szaflarski	Poster Number: 3.293 Session Date/Time: Monday, December 4th, 12:00-1:45 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,* 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. 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* received Orphan Drug Designation from the U.S. FDA for the treatment of seizures associated with LGS, DS and TSC. *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. A Phase 3 study is ongoing in Japan evaluating cannabidiol in patients with 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.

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