JAMA Neurology Publishes Results from Positive Phase 3 Trial of EPIDIOLEX® (cannabidiol) oral solution in Children with Seizures Associated with Dravet Syndrome

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EPIDIOLEX significantly reduced convulsive seizure frequency in children taking multiple anti-epileptic drugs with poor seizure control

CARLSBAD, Calif., March 02, 2020 (GLOBE NEWSWIRE) -- GW Pharmaceuticals plc (NASDAQ: GWPH, GW, the Company or the Group), the world leader in the science, development, and commercialization of cannabinoid prescription medicines, along with U.S. subsidiary Greenwich Biosciences, announced today that *JAMA Neurology* has published results from the second positive Phase 3 trial (GWPCARE2) of EPIDIOLEX® (cannabidiol) oral solution CV in children with seizures associated with Dravet syndrome. The article has been published online and will be included in the May 2020 print issue of the journal. 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) for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome in patients two years of age or older.

In the study, two doses of EPIDIOLEX, 10 and 20 mg/kg/day, significantly reduced convulsive seizure frequency compared to placebo in children two to 18 years of age with highly treatment-resistant Dravet syndrome, meeting the study's primary endpoint. The primary endpoint outcomes for the 10 and 20 mg/kg/day arms were similar, with seizure reductions of 49% and 46% from baseline, respectively, vs 27% for placebo (10 mg/kg/day, p=0.0095 and 20 mg/kg/day, p=0.0299).

"Dravet syndrome is one of the most difficult-to-treat forms of epilepsy and patients are highly individualized in their symptoms and dosing needs," said Ian Miller, M.D., Chief of Neurology at Nicklaus Children's Hospital in Miami, FL and lead author. "The data published by *JAMA Neurology* show that EPIDIOLEX 10 and 20 mg/kg/day were both efficacious and significantly reduced convulsive seizures. Drug-resistant seizures are common with Dravet syndrome and it is valuable to have a range of approved doses that offer physicians the flexibility to adjust treatment to a patient's specific needs."

Results from key secondary endpoints also showed:

- Significant reductions in total seizure frequency from baseline: 56% for 10 mg/kg/day and 47% for 20 mg/kg/day vs 30% for placebo (p=0.0003 and p=0.0255, respectively).
- Significantly more patients taking EPIDIOLEX (44% on 10 mg/kg/day and 49% on 20 mg/kg/day) achieved a 50 percent or greater reduction in convulsive seizures from baseline during the treatment period compared to placebo (26%; p=0.0332 and p=0.0069, respectively).
- Compared with placebo, caregivers of patients treated with EPIDIOLEX were significantly more likely to report an improvement in overall condition as measured by the Caregiver Global Impression of Change (CGIC) scale at last visit (10 mg/kg/day, p=0.0009 and 20 mg/kg/day, p=0.0279).

The most common adverse reactions in the study (occurring in at least 10% of patients in any group) included decreased appetite, diarrhea, somnolence, pyrexia, and fatigue. Elevated liver transaminases occurred more frequently on 20 mg/kg/day than 10 mg/kg/day cannabidiol, with all affected patients on concomitant valproate.

"EPIDIOLEX continues to represent an important advancement in the treatment of difficult-to-treat pediatric-onset epilepsies such as Dravet syndrome where there are few FDA-approved therapies," said Justin Gover, GW CEO. "We are pleased that the full results of our GWPCARE2 study in Dravet syndrome are now available to the greater neurology community. The continued publication of our data is a testament to our groundbreaking research in the field of cannabinoids, which we plan to continue to advance in an effort to bring more novel treatments to patients in need."

Study Overview

The pivotal Phase 3 study of EPIDIOLEX – GWPCARE2 – was a randomized, double-blind placebo-controlled trial of patients aged 2-18 years with a confirmed diagnosis of drug-resistant Dravet syndrome currently uncontrolled on one or more concomitant anti-epileptic drugs (AEDs). The trial randomized 199 patients into three arms, where EPIDIOLEX 10 mg/kg/day (n=67), EPIDIOLEX 20 mg/kg/day (n=67), or placebo (n=65) was added to current AED treatment. On average, patients were taking three AEDs, having previously tried and discontinued on average, four other AEDs. The average age of trial participants was 9 years. The median baseline convulsive seizure frequency per month was 12 and the median baseline total seizure frequency per month was 35.

"When scientific research is validated by esteemed journals like *JAMA Neurology*, it's a win for every member of the Dravet community seeking more information and a greater understanding of treatments for their condition," said Mary Anne Meskis, Executive Director of the Dravet Syndrome Foundation. "Patients and their families are in need of treatment options that work for this devastating illness and it's exciting to see further proof that EPIDIOLEX has the potential to make a meaningful difference in patients' lives."

Results from the first positive Phase 3 pivotal trial of EPIDIOLEX in patients with Dravet syndrome were published in *The New England Journal of*

Medicine.[1] The EPIDIOLEX clinical program now includes five positive randomized, controlled Phase 3 clinical trials in Lennox-Gastaut Syndrome, Dravet syndrome and tuberous sclerosis complex.

About Dravet Syndrome

Dravet syndrome is a rare, severe, lifelong form of epilepsy that typically begins in the first year of life with frequent and/or prolonged seizures.[2] Previously known as severe myoclonic epilepsy in infancy (SMEI), it affects between 1 in 20,000 to 1 in 40,000 people.[3,4] About 80 percent of people with this syndrome have a gene mutation that causes problems in the way the brain works.[2]

Children with Dravet syndrome can develop many different seizure types and approximately 15 percent die within 10 years of diagnosis due to issues such as SUDEP (sudden unexpected death in epilepsy), prolonged seizures (status epilepticus), seizure-related accidents such as drowning, or infections.[2,5] Additionally, the majority will develop moderate to severe intellectual and developmental disabilities[6] and require lifelong supervision and care.[2]

About EPIDIOLEX® (cannabidiol) oral solution, CV

EPIDIOLEX® (cannabidiol) oral solution CV, a pharmaceutical formulation of highly purified cannabidiol (CBD), is the first in a novel class of anti-epileptic medications and the first prescription, plant-derived cannabis-based medicine approved by the U.S. Food and Drug Administration (FDA). In the U.S., EPIDIOLEX is indicated for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome in patients two years of age or older. A supplemental New Drug Application (sNDA) has been submitted to the FDA for the treatment of seizures associated with tuberous sclerosis complex (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 Dravet syndrome. EPIDIOLEX/EPIDYOLEX has received Orphan Drug Designation from the FDA and the EMA for the treatment of seizures associated with Dravet syndrome, LGS and TSC, each of which are severe childhood-onset, drug-resistant syndromes.

Important Safety Information

Important safety information for EPIDIOLEX is available at EPIDIOLEX.com.

About GW Pharmaceuticals plc and Greenwich Biosciences, Inc.

Founded in 1998, GW is a biopharmaceutical company focused on discovering, developing and commercializing novel therapeutics from its proprietary cannabinoid product platform in a broad range of disease areas. The Company's lead product, EPIDIOLEX ® (cannabidiol) oral solution, CV, is commercialized in the U.S. by its U.S. subsidiary Greenwich Biosciences for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome in patients two years of age or older. This product has received approval in the European Union under the tradename EPIDYOLEX®. The Company has submitted a supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) seeking to expand the indication for EPIDIOLEX to include seizures associated with tuberous sclerosis complex (TSC), for which it has reported positive Phase 3 data, and is carrying out a Phase 3 trial in Rett syndrome. The Company has a deep pipeline of additional cannabinoid product candidates, in particular nabiximols, for which the Company is advancing multiple late-stage clinical programs in order to seek FDA approval in the treatment of spasticity associated with multiple sclerosis and spinal cord injury, as well as for the treatment of PTSD. The Company has additional cannabinoid product candidates in Phase 2 trials for autism and schizophrenia. For further information, please visit www.gwpharm.com.

Forward-looking statements

This news release contains forward-looking statements that reflect GW's current expectations regarding future events, including statements regarding financial performance, the timing of clinical trials, the timing and outcomes of regulatory or intellectual property decisions, the relevance of GW products commercially available and in development, the clinical benefits of EPIDIOLEX®/EPIDYOLEX® (cannabidiol) oral solution CV and Sativex® (nabiximols), and the safety profile and commercial potential of both medicines. Forward-looking statements involve risks and uncertainties. Actual events could differ materially from those projected herein and depend on a number of factors, including (inter alia), the success of GW's research strategies, the applicability of the discoveries made therein, the successful and timely completion and uncertainties related to the regulatory process, and the acceptance of EPIDIOLEX®/EPIDYOLEX®, Sativex® and other products by consumer and medical professionals. A further list and description of risks and uncertainties associated with an investment in GW can be found in GW's filings with the U.S. Securities and Exchange Commission. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. GW undertakes no obligation to update or revise the information contained in this press release, whether as a result of new information, future events or circumstances or otherwise.

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