

EPIDIOLEX: FROM PLANT TO PROMISING PHARMACEUTICAL

GW Pharmaceuticals, which operates in the U.S. through its subsidiary GREENWICH Biosciences, is developing Epidiolex[®], the first pharmaceutical formulation of cannabidiol (CBD) derived from the cannabis plant. Epidiolex is currently in Phase 3 studies for the treatment of two rare, severe childhood-onset seizure disorders, Dravet syndrome and Lennox-Gastaut syndrome (LGS) for which, in 2016, the Company completed three successful Phase 3 trials. GW is also evaluating Epidiolex in patients with tuberous sclerosis complex (TSC), the leading genetic cause of epilepsy,¹ and in patients with infantile spasms (IS), another severe, early-onset, treatment-resistant epilepsy syndrome. The company also has a global pipeline of clinical-stage cannabinoid candidates for both orphan and non-orphan indications with a focus on neurological conditions.

A large percentage of these patients are resistant to treatment and experience multiple types of seizures, as well as intellectual, behavioral and physical disabilities. These conditions are difficult to manage and treatment options are currently limited, particularly in Dravet syndrome and TSC for which there are no FDA-approved treatments. The day-to-day impact of these devastating conditions is significant and, with high rates of early mortality, there is considerable unmet need for novel new therapies.²⁻⁸

WHAT IS CANNABIDIOL (CBD)?

The cannabis plant contains more than 100 cannabinoids; the two best characterized are CBD and tetrahydrocannabinol (THC). CBD is a non-psychoactive component of the cannabis plant which, in clinical trials, has shown medical benefit.⁹ CBD is being studied for a number of chronic conditions, including epilepsy, due to its potential anticonvulsant properties.¹⁰ CBD is unlike THC, the component of the marijuana plant that makes people "high." The fact that Epidiolex is a purified pharmaceutical formulation of plant-derived CBD is of particular importance as Epidiolex is expected to be indicated for use in children, as well as adults.

WHAT IS PHARMACEUTICAL CBD?

Pharmaceutical CBD is a consistent, standardized formulation of CBD that meets chemical purity and quality measures and is studied in randomized, controlled clinical trials with oversight from a recognized regulatory authority, such as the U.S. Food and Drug Administration (FDA) to ensure safety and efficacy. To date, there are no plant-derived CBD products that meet FDA standards.

EPIDIOLEX IS **NOT** MEDICAL MARIJUANA

Epidiolex is not medical marijuana; it is a pharmaceutical formulation of purified CBD that is derived from the cannabis plant. Medical marijuana

is the use of the marijuana or cannabis plant or its basic extracts to attempt to treat symptoms of illness and other conditions. It can come in different forms which may contain all or various components of the cannabis plant such as THC, CBD and other cannabinoids. The FDA has not recognized or approved the marijuana plant or any extract from it as a pharmaceutical medicine.

While a growing number of states have legalized marijuana for medical use, medical marijuana differs from pharmaceutical treatments in that even legal forms are not regulated. For this reason, there is no way to ensure consistency between batches or that there is accurate labeling. In addition, there is no standardization in terms of how these products are prescribed or dosed for specific conditions. Finally, there are no large, carefully conducted, controlled studies to determine the benefits and risks of medical marijuana products for patient use.

WHAT IS EPIDIOLEX AND HOW IS IT DIFFERENT?

- Epidiolex is a pharmaceutical formulation of purified CBD, administered orally in liquid form. If approved, it will be the first in a new class of CBD anti-epileptic drugs (AEDs) and the first FDA-approved prescription product derived from the cannabis plant.
- The active ingredient in Epidiolex is CBD. The plants used to develop Epidiolex are specifically bred for medical purposes and have a high concentration of CBD, a non-psychoactive component of the cannabis plant.
- The therapy would be the first FDA-approved drug for Dravet syndrome.
- Epidiolex is also being studied in additional severe, early-onset, treatment-resistant epilepsy syndromes including LGS, TSC and IS where there are limited treatment options.
- Over 1,500 patients have been exposed to Epidiolex treatment.
- Epidiolex is being studied in large, well-controlled clinical trials with the goal of producing a high-quality, substantial volume of safety and efficacy data to submit as part of a New Drug Application to FDA in the middle of 2017. To meet the FDA standards, a series of additional research must also be conducted to study pharmacokinetics and drug-drug interactions.
- Epidiolex is manufactured in compliance with Good Manufacturing Practice (GMP) standards and meets FDA standards for pharmaceutical products, which ensures consistent formulation and reliable dosing. Epidiolex is produced using a highly scalable and consistent growing and manufacturing process that is designed to ensure adequate supply of the medication.

¹ <http://www.tsalliance.org/>

² Dravet C. The core Dravet syndrome phenotype. *Epilepsia*. 2011;52(Suppl. 2):3-9.

³ Bourgeois B, Douglass L, Sankar R. Lennox-Gastaut syndrome: a consensus approach to differential diagnosis. *Epilepsia*. 2014;55(Suppl. 4):4-9.

⁴ van Rijckevorsel K. Treatment of Lennox-Gastaut syndrome: overview and recent finding. *Neuropsychiatr Dis Treat*. 2008;4(6):1001-1019.

⁵ Skluzacek J, Watts KP, Parsy O, Wical P, Camfield P. Dravet syndrome and parent associations: The IDEA League experience with comorbid conditions, mortality, management, adaptation, and grief. *Epilepsia*. 2011;52(Suppl. 2):95-101.

⁶ Hancock EC, Cross JH. Treatment of Lennox-Gastaut syndrome. *Cochrane Database of Syst Rev*. 2013;Feb 28;(2):CD003277.

⁷ Autry AR, Trevathan E, Van Naarden Braun K, Yeargin-Allsopp M. Increased risk of death among children with Lennox-Gastaut syndrome and infantile spasms. *J Child Neurol*. 2010;25(4):441-447.

⁸ <http://www.tsalliance.org/about-tsc/signs-and-symptoms-of-tsc/brain-and-neurological-function/epilepsy-and-seizure-disorders/>

⁹ <http://ir.gvpharm.com/releasedetail.cfm?ReleaseID=1002552>

¹⁰ <https://www.ncbi.nlm.nih.gov/pubmed/?term=7%3A09Rosenberg+EC%2C+T sien+RW%2C+W halley+B%2C+Devinsky+O.+Cannabinoids+and+epilepsy.+Neurotherapeutics.+2015%3B12%3A747-768>