

# EPIDIOLEX: FROM PLANT TO PROMISING PHARMACEUTICAL

GREENWICH Biosciences, the U.S. subsidiary of GW Pharmaceuticals, plc, is developing Epidiolex<sup>®</sup>, the first pharmaceutical formulation of cannabidiol (CBD) derived from the cannabis plant. The U.S. Food and Drug Administration (FDA) is currently reviewing a New Drug Application (NDA) for Epidiolex as an add-on therapy for the treatment of seizures associated with Dravet syndrome and Lennox-Gastaut syndrome (LGS), two rare, severe childhood-onset seizure disorders. Epidiolex is also being evaluated in patients with tuberous sclerosis complex (TSC), the leading genetic cause of epilepsy,<sup>1</sup> and in patients with infantile spasms (IS), another severe, early-onset, treatment-resistant epilepsy syndrome. These conditions are difficult to manage and treatment options are currently limited, particularly in Dravet syndrome for which there is no FDA-approved treatment.<sup>2-8</sup> 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. 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.

## WHAT IS CANNABIDIOL (CBD)?

The cannabis plant contains more than 100 cannabinoids; the two best characterized are CBD and tetrahydrocannabinol (THC). CBD is a component of the cannabis plant<sup>9</sup> lacking euphoric side effects<sup>10</sup> that is being studied for epilepsy, due to its potential anticonvulsant properties.

## 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, placebo-controlled clinical trials to ensure safety and efficacy. To date, there are no plant-derived CBD products that have been approved by the FDA.

## 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 refers to the use of the marijuana (cannabis) plant 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<sup>11</sup> such as THC, CBD and other cannabinoids, terpenes, flavonoids, and other plant material and unwanted residual material

absorbed by the plant.<sup>12</sup> The FDA has not recognized or approved the marijuana plant or any extract from it, though three synthetic cannabinoid products have been FDA approved.

While a growing number of states have removed or lessened restrictions to obtaining medical marijuana, even unrestricted forms are not regulated. For this reason, there is no way to ensure consistency, stability, or accurate labeling.<sup>10</sup> In addition, there is no standardization in terms of how these products are prescribed or dosed for specific conditions.<sup>10</sup> 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?

- 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 anti-epileptic drugs (AEDs) and the first FDA-approved prescription product derived from the cannabis plant.
- The active ingredient in Epidiolex is cannabidiol (CBD). The plants used to develop Epidiolex are specifically bred for medical purposes and have a high concentration of CBD, a component of the cannabis plant.
- The therapy would be the first FDA-approved drug to treat seizures associated with 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.
- Approximately 1,500 patients have been exposed to Epidiolex treatment.
- Epidiolex was 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 an NDA to FDA (October 2017). To meet the FDA standards, a series of additional research has been and will 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 and stable 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 Curatolo P, Jóźwiak S, Nabbout R. Management of epilepsy associated with tuberous sclerosis complex (TSC): Clinical recommendations. *European Journal of Paediatric Neurology* 6, 582–586 (2012).

2 Dravet, C. The core Dravet syndrome phenotype. *Epilepsia* 52 Suppl 2, 3–9 (2011).

3 Bourgeois BF, Douglass LM & Sankar R. Lennox-Gastaut syndrome: a consensus approach to differential diagnosis. *Epilepsia* 55 Suppl 4, 4–9 (2014).

4 van Rijeckvoersel K. Treatment of Lennox-Gastaut syndrome: overview and recent findings. *Neuropsychiatric disease and treatment* 4, 1001–1019 (2008).

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

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. *Journal of Child Neurology* 25, 441–447 (2010).

8 TS Alliance. Epilepsy and Seizures Disorders. Available at <http://www.tsalliance.org/about-tsc/signs-and-symptoms-of-tsc/brain-and-neurological-function/epilepsy-and-seizure-disorders/>. Accessed December 22, 2017.

9 Rosenberg E, Tsien R, Whalley B, Devinsky O. *Cannabinoids and Epilepsy*. *Neurotherapeutics* 12, 747–768 (2015).

10 Russo EB. Current Therapeutic Cannabis Controversies and Clinical Trial Design Issues. *Frontiers in Pharmacology*. 7:309 (2016)

11 Chandra S, Lata H, ElSohly M, Walker L, Potter W. Cannabis cultivation: Methodological issues for obtaining medical-grade product. *Epilepsy Behavior* 70, 302–312 (2017).

12 Russo EB. Cannabidiol Claims and Misconceptions. *Trends in Pharmacological Sciences* 38, 198–201 (2017).