TECHNOLOGY

Cannabidiol (CBD), a non-psychoactive component of Cannabis, has demonstrated efficacy in reducing seizures in epileptic patients. Epidiolex is a CBD formulation manufactured by GW Pharmaceuticals, approved in by the FDA in 2018 to treat certain forms of epilepsy. However, due to the physicochemical properties of CBD, Epidiolex is formulated with sesame oil and given at high doses, leading to poor bioavailability and side effects. The Agrithera team is developing CBD prodrugs, new chemical entities that metabolize to CBD in the body. These prodrugs are synthesized by attaching benign chemical groups to the CBD molecule, resulting in improved physicochemical properties that would allow for a daily oral pill formulation with reliable blood and brain concentrations.

MARKET NEED

There are 3.4 million patients with epilepsy in the US, representing a total of 1.2% of the US population. This includes 3 million adults and 470,000 children. Existing standard medications fail to appropriately manage epilepsy in about one third of adults and approximately 20-25% of children (~1.1 million individuals), leading to what is known as drug-resistant or refractory epilepsy.

Epilepsy has traditionally been treated with anticonvulsants, many of which target the same inhibitory pathways. CBD acts on molecular targets distinct to those of anticonvulsants and has shown beneficial effects on preclinical models of seizures. It is typically used in combination with other anticonvulsant drugs. However, CBD’s nonideal physicochemical properties result in problems in formulation, pharmacokinetics, and biodistribution, which is why it is administered at high doses formulated with sesame oil, leading to side effects.

STATUS

The Agrithera team has synthesized over 120 prodrugs and is currently working on lead candidate optimization. Their compounds have demonstrated enhanced solubility, stability, and penetration across the blood-brain barrier. They are evaluating pharmacokinetics and tissue distribution, as well as analyzing off-target effects and toxicology prior to preclinical efficacy studies in relevant animal models.