"Cannabinoid Receptor Drug for Lung Delivery with Phase I/II Data" VCU #98-70

Applications

Treatment for:

- Nausea
- Emesis
- Decreased appetite
- Migraine
- Neuropathic pain
- Anxiety
- Seizures and epilepsy
- Inflammation

Advantages

- Faster and improved systemic delivery compared to oral administration
- Pharamceutically-acceptable alternative to inhaled marijuana

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Market Need

Chronic pain is an emerging public health issue, particularly in view of the aging populations of industrialized nations. Over 38 million Americans suffer from chronic pain.

Technology Summary

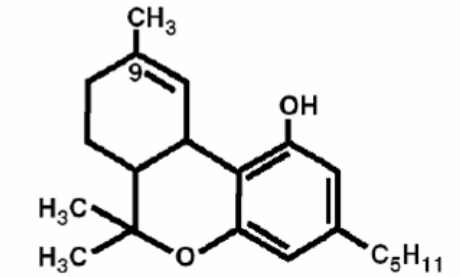
A pressurized metered dose inhaler (pMDI) for the pulmonary delivery of delta-9-tetrahydrocannabinol (THC) supported by an extensive patent estate, inhalation toxicity testing in rats and dogs and Phase 1 and early Phase II clinical results in humans.

- Pharmacology: cannabinoid receptor agonist
- Route of administration: oral inhalation
- Dosage form: CFC-free pressurized metered dose inhaler (multiple strengths)

Potential use includes multiple therapeutic indications and neuroprotection.

Clinical Testing

Maximally-tolerated dose (MTD) inhalation toxicology studies along with long-term 1-month and 3-month studies have been completed in both rats and dogs. The results of these studies and kinetic data revealed no development-limiting findings. All three doses tested in Phase I were found to be safe and well tolerated. Phase II studies completed in migraine sufferers showed efficacy vs. placebo.



$C_{21}H_{30}O_2$ (molecular weight = 314.47)

Chemical Structure of THC

Technology Status

This technology is protected by an extensive patent estate composed of both U.S. and foreign issued patents

and patent applications. Among the aspects covered are the aerosolized formulation of THC, the use of THC in pulmonary delivery, and formulations of THC for pulmonary delivery. (See US patents 6,509,005, 6,713,048)

This technology is available for licensing to industry for further development and commercialization.

Dosage Form

Pulmonary THC is delivered and inhaled via an aerosol cloud formed from a pressurized metered dose inhaler (pMDI), formulated as a drug solution. The inactive ingredients include dehydrated alcohol (10%) and HFA 134a propellant (88.0-89.5%). Each pMDI contains 100 actuations of either 0.3 mg (0.5%) or 1.2 mg (2.0%) THC. The primary closure system is an aluminum canister and metered dose valve, which is packaged with a polypropylene actuator and dust cap. Pulmonary THC appears to provide faster and improved systemic delivery of the API. Systematic studies have been performed to optimize the formulation and fine particle fraction of the aerosol cloud, assess compatibility of packaging components, and evaluate the effects of oxygen and moisture on the stability of the API in the formulated product.

Clinical Experience with THC Pmdi

Phase I – Three Phase I Studies Completed

S1751103. This study was a parallel-group, crossover, double-blind, placebo-controlled, single rising dose tolerance study in healthy volunteers. Six inhaled single dose levels of 0.3, 1.2, 2.4, 3.6, 7.2, 9.6 mg per puff were used. General Conclusions: Product was safe and tolerated at single doses between 0.3 and 9.6 mg; psychotropic effects were evident at the 7.2 and 9.6 mg doses; well described heart rate increases occurred at higher doses; systemic absorption was rapid.

S1751104. This was a double-blind-placebo-controlled, multiple rising dose tolerability study. Eighteen healthy subjects were enrolled in this pharmacokinetic and tolerability study of 2 doses (1.2 and 3.6 mg per puff given 3 times daily) for up to 14 days. General Conclusions: Product was safe and well-tolerated after single and multiple doses at the 1.2 and 3.6 mg doses; cough was the most common adverse effect; systemic absorption was rapid. After multiple dosing the effect of dose-related HR increase was less evident.

S1751110. This was a double-blind, placebo-controlled multiple dose study of 3 pMDI doses (3.6, 4.8, 6.0 mg/puff) in healthy volunteers. General Conclusions: All three doses were found to be safe and well tolerated.

Phase II – One Study Completed in Migraine Sufferers

S1752103. This was a double-blind, placebo-controlled, parallel-group study in 240 migraine sufferers at 1.2, 2.4, 3.6 mg vs. placebo. The treatment was administered 2 hours within onset followed by assessment of pain response (1º) and associated symptoms (nausea, etc.). The adverse effects evaluated included cardiovascular, nervous system and psychoactive. Headline Results: 3.6 mg dose was effective for symptomatic treatment of nausea; the 2.4 and 3.6 mg doses providing some pain relief; coughing and throat irritation were most commonly reported adverse effects; CNS effects were generally low and there were no significant differences in CV, CNS and psychoactive effects among active groups, or between active and placebo; there were no unexpected effects.