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# FSD Pharma Receives U.S. FDA Approval to design a Phase 2a Clinical Trial to Treat Patients with Suspected or Confirmed COVID-19 Diagnosis

TORONTO, June 3, 2020 /CNW/ - **FSD Pharma Inc.** (Nasdaq: HUGE) (CSE: HUGE.CN) (FRA: 0K9A) ("**FSD Pharma**" or the "**Company**") today announced that the U.S. Food and Drug Administration (FDA) has given the company permission to submit an Investigational New Drug Application (IND) for the use of FSD-201 (ultramicrozized palmitoylethanolamide, or ultramicrozized PEA) to treat COVID-19, the disease caused by the SARS-CoV-2 virus. Severe COVID-19 is characterized by an over-exuberant inflammatory response that may lead to a cytokine storm and ultimately death. FSD Pharma is focused on developing FSD-201 for its anti-inflammatory properties to avoid the cytokine storm associated with acute lung injury in hospitalized COVID-19 patients.



"FDA's permission to design a proof-of-concept study in COVID-19 patients evaluating clinical doses of FSD-201 is a paradigm shift for FSD Pharma and is the result of outstanding work conducted by Dr. Edward Brennan, President FSD BioSciences, and his team," said Raza Bokhari, MD, Executive Co-Chairman & CEO. "We contacted the FDA in late-March 2020 after becoming aware that several Italian physicians and scientists were advocating for use of ultramicrozized PEA for patients suffering from symptoms of COVID-19, based on the drug's mechanism of action as a potent and safe anti-inflammatory agent that reduces the production of pro-inflammatory cytokines. Numerous studies over the past 40 years also validate the efficacy and safety of ultramicrozized PEA in the treatment and prophylactic effects in respiratory infections. These studies also pointed out that the ease of application of PEA offers the possibility to have a quick therapeutic answer ready in case of a flu epidemic."

## **COVID-19 Trial Design**

Based on the FDA feedback received to date, we expect the trial will be a randomized, controlled, double-blind, U.S. multicenter study to assess the efficacy and safety of FSD-201 dosed 600mg or 1200mg twice-daily plus standard of care (SOC) versus SOC alone in symptomatic patients with clinical presentation compatible with COVID-19. Eligible patients will present with symptoms consistent with influenza/coronavirus signs (fever, dry cough, malaise, difficulty breathing) and/or newly documented positive COVID-19 disease.

The primary endpoint is to determine if FSD-201 plus SOC provides a significant improvement in clinical status (i.e., shorter time to symptom relief). Key secondary objectives include determining if FSD-201 plus SOC demonstrates additional benefit in terms of safety, objective assessments such as length of time to normalization of fever, length of time to improvement of oxygen saturation and length of time to clinical progression including time to mechanical ventilation or hospitalization, and length of hospital stay. The exploratory endpoint is cytokine clearance as measured by Enzyme Linked Immunosorbent Assay (ELISA).

The treatment period is expected to be 14 days. All patients who experience clinical benefit are expected to continue to receive their assigned treatment until study completion.

## **Rationale for Ultramicronized PEA in COVID-19**

More than 600 scientific papers attest to the physiological properties of PEA and its role as an endogenous modulator, as well as its pharmacological and therapeutic effects, specifically its anti-inflammatory profile.

PEA acts via multiple mechanisms either directly to activate PPAR- $\alpha$  and GPR55 or indirectly through the inhibition of FAAH, which increases endogenous levels of anandamide (AEA) and 2-arachidonoyl-glycerol (2-AG). These endocannabinoids directly activate CB2 (or CB1) receptors and TRPV1 channels (entourage effect). PEA may also activate TRPV1 channels via PPAR- $\alpha$ .

AEA has been shown to inhibit tumor necrosis factor- $\alpha$ -induced NF-kappa B activation, independent of CB1 and CB2. Saturated acylethanolamides such as PEA (an endogenous congener of AEA) may act in an analogous fashion to modify chronic inflammation in autoimmune disorders.

Nobel laureate Rita Levi-Montalcini described the importance of the activation of the inflammatory cascade and in 1993 discovered that PEA functions as a mast cell modulator by reducing mast cell migration and degranulation; thus, PEA reduces the pathological overactivation of these cells and the activity of proinflammatory cytokines (such as TNF- $\alpha$  and IL6), cyclooxygenase and iNOS. It is this excess immune response activity that contributes to the physiologic derangement induced by influenza viruses and sets up the pathogenesis of the "cytokine storm."

In summary, PEA down regulates hyperactive mast cells, inhibits iNOS expression and nuclear NF-kappa B translocation. It is theorized that coronavirus activates the cellular IKK/NF-kappa B signaling pathway for replication; therefore, PEA as a PPAR- $\alpha$  agonist may ameliorate oxidative/nitrosative stress induced by NF-kappa B and may be a suitable agent

for antiviral intervention.

In addition, PEA has repeatedly been shown to down-modulate excess immune response activity that contributes to the physiologic derangement induced by viruses and help mitigate the pathogenesis of the "cytokine storm."

The detailed description of the role of PEA in viral pathogenesis via multiple mechanistic pathways can be found in Jan MKH, Theca AMH (2017) Palmitoyl Ethanol Amide in Prophylaxis and Treatment of Viral Infections. *Infect Dis Diag Treat* 2017: J103.

Between 1969 and 1979, PEA was marketed as Impulsin by a pharmaceutical manufacturer in the former Czechoslovakia to treat influenza and the common cold. During this period, clinical trials were conducted for these indications that involved nearly 4,000 patients and volunteers across six randomized, double-blind, placebo-controlled trials. Together, these clinical trials demonstrate that PEA has clear treatment and prophylactic effects in respiratory infections, and is safe in its use. Side effects were not reported, and study authors explicitly stated that "No side effects were registered after several years of clinical testing of Impulsin in military and civilian communities." They also pointed out that the ease of application of PEA offers the possibility to have a quick therapeutic answer ready in case of a flu epidemic.

In addition, since 2004 PEA has been dispensed in Italy and Spain as a prescription-based medical food supplement. More recently, the Company was made aware that several Italian physician-scientists are advocating for the use of ultramicronized-PEA for patients suffering from symptoms of COVID-19, and that several are using ultramicronized PEA to treat COVID-19 patients in Italy on a compassionate use basis.

## **Background on Ultramicronized PEA**

FSD Pharma acquired worldwide rights (ex-Italy and Spain) to ultramicronized PEA from Epitech Group, an Italian pharmaceutical company that invented and holds the patents until 2034 for ultramicronized PEA (defined as 0.6 -10 $\mu$ M particle size). PEA is a naturally occurring fatty acid amide that was first discovered in the yolks of chicken eggs. It is biosynthesized from a membrane phospholipid and is degraded to palmitic acid and ethanolamine, and serves as an anti-inflammatory modulator within the cell.

Epitech markets ultramicronized PEA as a prescription-based "Food for Special Medical Purposes" in Italy under the brand name Normast® 600mg oral tablets, for several chronic pain and inflammatory conditions, including sciatic pain and diabetic neuropathy.

FSD is focused on developing ultramicronized-PEA (FSD-201) for its anti-inflammatory properties. A first-in-human safety and tolerability study is currently progressing in Australia led by principal researcher Jason Lickliter, MD, Chief Medical Officer of Nucleus Network.

Many clinical trials assessing the safety and efficacy of ultramicronized PEA on chronic pain have been published in the last decade. A number of studies have demonstrated that ultramicronized PEA at doses up to 2700mg/day administered to patients with various chronic pain syndromes induced a significant decrease in pain intensity, compared with control groups. In addition, clinical studies have demonstrated that ultramicronized PEA is generally very well tolerated. More than 1,500 patients have received either ultramicronized

or micronized PEA in clinical studies and no serious adverse events were reported in the vast majority of these studies at doses as high as 2700mg/day.

## **About FSD Pharma**

FSD Pharma Inc. (Nasdaq: HUGE; CSE: HUGE.CN; FRA: 0K9A) is a publicly traded holding company, since May 2018.

FSD BioSciences Inc., a wholly-owned subsidiary, is a specialty biotech pharmaceutical R&D company focused on developing over time a robust pipeline of FDA-approved synthetic compounds targeting the endocannabinoid system of the human body to treat certain diseases of the central nervous system and autoimmune disorders of the skin, GI tract and the musculoskeletal system.

Through our acquisition of Prismic Pharmaceuticals in 2Q19, the Company is also making an effort to help address the opioid crisis by developing opioid-sparing prescription drugs utilizing the ultramicrosized formulation of palmitoylethanolamide (PEA).

The Company has a Phase 1 first-in-human safety and tolerability trial for its lead candidate, FSD-201, currently underway in Australia

FSD's wholly-owned subsidiary, FV Pharma, is a licensed producer under Canada's Cannabis Act and Regulations, having received its cultivation license on October 13, 2017, and its full Sale for Medical Purposes license on June 21, 2019. The Company is licensed to cultivate cannabis in approximately 25,000 square feet of its facility in Cobourg, Ontario.

## **Forward-Looking Statements**

Neither the Canadian Securities Exchange nor its regulation services provider accept responsibility for the adequacy or accuracy of this release.

The Company's subject area experts continue to review the scientific evidence/claims/research relevant to the application of PEA and ultra-micro PEA and thus far have no reason to doubt the authenticity of the material reviewed that has been quoted in the press release. The company is not making any express or implied claims that its product has the ability to eliminate, cure or contain the Covid-19 (or SARS-2 Coronavirus) at this time.

Certain statements contained in this press release constitute "forward-looking information" and "forward-looking statements" within the meaning of applicable Canadian and U.S. securities laws (collectively, "Forward-Looking Information"). Forward-Looking Information includes, but is not limited to, information with respect to FSD Pharma's strategy, plans or future financial or operating performance, receipt of any U.S. Food and Drug Administration ("FDA") approvals, including the approval of our IND submission, the completion of any trials regarding the use of FSD-201 to treat COVID-19 or whether FSD-201 may be effective in treating COVID-19, the costs associated with such planned trials, our ability to obtain required funding and the terms and timing thereof, development of any FDA approved synthetic compounds, the successful treatment of diseases by such compounds, the ability to address the opioid crisis, the development of opioid sparing prescription drugs utilizing the micronized formulations of palmitoylethanolamide ("PEA"), and the objectives and timing of

the initiation of Phase 1 first-in-human safety and tolerability trials for FSD 201. micro-PEA. The use of words such as "budget", "intend", "anticipate", "believe", "expect", "plan", "forecast", "future", "target", "project", "capacity", "could", "should", "focus", "proposed", "scheduled", "outlook", "potential", "estimate" and other similar words, and similar expressions and statements relating to matters that are not historical facts, or statements that certain events or conditions "may" or "will" occur, are intended to identify Forward-Looking Information and are based on FSD Pharma's current beliefs or assumptions as to the outcome and timing of such future events. Such beliefs or assumptions necessarily involve known and unknown risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such Forward-Looking Information. Certain of these risks and uncertainties are described in the Company's continuous disclosure filings available under the Company's SEDAR profile at [www.sedar.com](http://www.sedar.com). Forward-Looking Information is not a guarantee of performance. The Forward-Looking Information contained in this press release is made as of the date hereof, and FSD Pharma is not obligated to update or revise any Forward-Looking Information, whether as a result of new information, future events or otherwise, except as required by law. Because of the risks, uncertainties and assumptions contained herein, investors should not place undue reliance on Forward Looking-Information. The foregoing statements expressly qualify any Forward-Looking Information contained herein.

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