Press release

Aelis Farma announces the inclusion of the 1st patient in a phase 2b study of AEF0117 for the treatment of cannabis use disorder (CUD)

- **AEF0117 is the most advanced drug candidate of the new pharmacological class, the CB_1-SSi, developed by Aelis Farma.**
- **AEF0117 aims to treat disorders related to excessive cannabis use (addiction and psychosis), which are increasing significantly worldwide.**
- **The phase 2b study will investigate the efficacy of AEF0117 for the treatment of cannabis use disorders (CUD), the current medical definition of cannabis addiction.**
- **The study will be coordinated by Columbia University and conducted at 9 clinical centers in the United States. It is expected to include approximately 330 patients and provide results in 2024.**

Bordeaux (France), June 1st, 2022 – 8:45 am CEST - Aelis Farma (ISIN: FR0014007ZB4 - Mnemonic: AELIS), a clinical-stage biopharmaceutical company specializing in the development of treatment for brain diseases, announces the enrollment of the 1st patient in the phase 2b study of AEF0117 for the treatment of cannabis use disorder (CUD), the current medical definition of cannabis addiction.

AEF0117 is the first drug candidate of a proprietary new class of drugs developed by Aelis Farma, the Signaling Specific inhibitors of the CB_1 receptor, the "CB_1-SSi". The CB_1 is the principal receptor of the endocannabinoid system and one of the most expressed neurotransmitter receptors of the brain. This receptor is involved in the regulation of several brain functions, and it is also the main target of the active ingredient of cannabis, THC. CB_1-SSi, by mimicking a recently discovered natural defense mechanism of the brain[1] has the potential to treat various brain pathologies without disrupting normal brain functions and behavior.

Dr Frances Levin, principal investigator of the study and Professor of Psychiatry at Columbia University, said: *"We are delighted to initiate this phase 2b trial of AEF0117. Disorders linked to excessive cannabis use are a growing health and societal problem in Western countries. In the United States alone almost 50 million people used cannabis in 2020[2], of whom 14.2 million have been diagnosed with CUD. Often the negative impact of cannabis use is underappreciated. Excessive cannabis use may cause various behavioral disorders such as psychosis, cognitive impairment with a loss of up to 8 IQ points[3] and worsen other psychiatric disorders such as depression. AEF0117, developed by Aelis Farma, has shown positive results in a phase 2a study and we look forward to continuing its evaluation in a larger population in this new study."*

The phase 2b clinical trial aims to demonstrate the efficacy of AEF0117 for the treatment of cannabis use disorder. The study is expected to include approximately 330 patients at 9 participating clinical centers in the United States. This double-blind, placebo-controlled study will include four separate

[1] "Pregnenolone can protect the brain from cannabis intoxication." (Science, January 3, 2014)
[2] Substance Abuse and Mental Health Services Administration. (2021). Key substance use and mental health indicators in the United States: Results from the 2020 National Survey on Drug Use and Health (HHS Publication No. PEP21-07-01-003, NSDUH Series H-56). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Retrieved from https://www.samhsa.gov/data/.
[3] Grant et al. 2012; Meier et al. 2012

patient arms, which will be administered either a placebo or one of the three test doses of AEF0117 (0.1 mg, 0.3 mg and 1 mg) once daily for 3 months. The primary objective of the study is to demonstrate if AEF0117 reduces cannabis use, as measured by the increase in the proportion of subjects with a response of ≤1 day of cannabis use per week compared to placebo. The proportion of patients reaching other levels of reduction of use and the potential improvement of their quality of life will also be investigated. The results of the study are expected in 2024.

Dr. Pier Vincenzo Piazza, Co-founder and CEO of Aelis Farma, commented: *"The inclusion of the 1st patient in AEF0117's phase 2b study is a key event for Aelis Farma, which, once completed, would enable AEF0117 to enter into confirmatory Phase 3 trials. This achievement is the result of several months of effort from the team dedicated to this project. I would like to thank all of them, our employees, and the investigators at the clinical centers, who have enabled us to achieve this milestone well within the time frame announced to the market. This study is of major importance for several reasons. It represents real hope for the growing number of people suffering from the pathological consequences of excessive cannabis use. These pathologies, for which there is no available effective and safe pharmacological treatment, have a serious societal impact and are increasing significantly in parallel with the wave of cannabis legalization observed in many Western countries, and could become the next drug epidemic. This study also represents the cornerstone of our cooperation with Indivior which, if AEF0117 proves to be efficacious, will accelerate the development and market access of this promising new treatment."*

This phase 2b study is part of the clinical development program of AEF0117 that has received a total of $7.8 million in grants from the National Institutes of Health (NIH) of which $4.5 million was allocated at the end of 2021 for this new phase of development. A previous phase 2a study in subjects with cannabis use disorder, performed at Columbia University (NY) by Dr. Margaret Haney, provided preliminary evidence of the efficacy of AEF0117 with a good safety profile.

Based on encouraging phase 2a results, in June 2021, Aelis Farma entered in an exclusive option and license agreement with Indivior PLC, an international leader in addiction medicine, for the development and commercialization of AEF0117 as a treatment for disorders linked to excessive cannabis use. As part of this collaboration, Aelis Farma received $30 million (option payment). If Indivior exercises the license option at the end of the phase 2b study, Indivior will pay Aelis Farma $100 million to acquire the license (potentially in 2024) and up to an additional $340 million if development, regulatory and commercial milestones are achieved, as well as royalties on net sales of AEF0117 of between 12% and 20%. Following the exercise of the option, all development, registration, and commercialization costs of AEF0117 will be borne by Indivior.

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About AELIS FARMA

Founded in 2013, Aelis Farma is a biopharmaceutical company that has developed a new class of drugs, the Signaling Specific inhibitors of the CB_1 receptor of the endocannabinoid system (CB_1-SSi). These new molecules hold great potential in the treatment of many brain diseases. CB_1-SSi were developed by Aelis Farma on the basis of the discovery of a new natural defense mechanism of the brain made by the team of Dr. Pier Vincenzo Piazza, CEO of the Company, when he was Director of the Inserm Magendie Neurocenter in Bordeaux. For these discoveries, Dr. Piazza was awarded the Inserm Grand Prix and the Grand Prix of Neurology of the French Academy of Sciences, which are among the most prestigious French awards in medicine and neurology.

Aelis Farma is developing two first-in-class drug candidates that are at the clinical stage, AEF0117 and AEF0217, and has a portfolio of innovative CB_1-SSi for the treatment of other diseases associated with dysregulation of CB_1 receptor activity.

AEF0117, which targets disorders linked to excessive cannabis use (addiction and psychosis), has completed a phase 2a trial that showed positive signs of efficacy and is undergoing a phase 2b trial in the United States. Aelis Farma has entered an exclusive option and license agreement with Indivior PLC, a leading pharmaceutical group in the treatment of addiction, for the development and commercialization of AEF0117 for disorders linked to excessive cannabis use. As part of this collaboration, Aelis Farma received $30 million (option payment). If Indivior exercises the license option at the end of the phase 2b study, Aelis Farma will receive a $100 million license fee (potentially in 2024) and up to $340 million in additional payments contingent upon the achievement of development, regulatory and commercial milestones, as well as royalties on net sales of AEF0117 ranging from 12% to 20%.

AEF0217, which targets various cognitive disorders including those associated with Down syndrome, is progressing successfully in its phase 1/2 program and could provide the first evidence of efficacy in early 2023. This compound has been the subject of extensive preclinical proof-of-concept studies using highly innovative and highly predictive tests to assess cognitive functions. In this context, AEF0217 has demonstrated its ability to completely reverse deficits in several models of cognitive disorders such as Down's syndrome and Fragile X syndrome, as well as in certain cognitive deficits associated with aging.

Based in Bordeaux, within the Magendie Neurocenter, Aelis Farma has a team of 24 highly qualified employees and has benefited from investments from the Nouvelle-Aquitaine Region, Inserm Transfert Initiative, Bpifrance, regional funds ACI, NACO and Aqui-invest and IRDI Capital Investissement.

For more information: www.aelisfarma.com

ISIN: FR0014007ZB4
Mnemonic: AELIS
Compartment B of Euronext Paris

Contacts

AELIS FARMA
Pier Vincenzo Piazza
Co-founder and CEO
contact@aelisfarma.com

NewCap
Dusan Oresansky/Marine de Fages
Investor Relations
aelis@newcap.eu
+33 1 44 71 94 92

NewCap
Nicolas Merigeau
Media Relations
nmerigeau@newcap.fr
+33 1 44 71 94 98

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