Press Release

Aelis Farma announces the results of its clinical Phase 2B Study with AEF0117, among participants with Cannabis Use Disorder (CUD)

- **The main objective of this phase 2B study was to demonstrate that AEF0117 reduces cannabis use and to determine the endpoints as well as the optimal dosage of AEF0117 for use in future studies.**
- **AEF0117 was well tolerated, and no safety concerns were identified.**
- **The primary and secondary endpoints, which measured the percentage of participants who reduced the number of days of use per week within a specified threshold: ≤1 day per week (primary endpoint); ≤2 days per week; and full abstinence, were not met by AEF0117. The placebo effect was surprisingly very small for these endpoints.**
- **At the highest dose of 1 mg/day AEF0117 showed consistent trends of a quantitative reduction in the overall amount of cannabis used per week, some of which were statistically significant in participants with moderate CUD.**
- **Currently, Aelis Farma is investigating these quantitative improvements further in order to determine the best course of strategic and regulatory actions.**
- **Indivior has communicated that it does not intend to exercise the option on AEF0117 before seeing the additional analysis of the clinical data.**

Two videoconferences will be held today, September 4, 2024, the first in French at 10:30 am CEST and the second in English at 3:30 pm CEST / 9:30 am EDT.

To participate, please register here:

Videoconference in French

Videoconference in English

Bordeaux, France, September 4, 2024 – 7:00 am CEST – Aelis Farma (ISIN: FR0014007ZB4 – Ticker: AELIS), a clinical-stage biopharmaceutical company specializing in the development of treatments for brain diseases, today announces results from the clinical Phase 2B trial conducted by Aelis Farma with AEF0117[1], evaluating its efficacy and safety in treatment-seeking participants with moderate to severe Cannabis Use Disorder (CUD) that used cannabis ≥5 days/week at baseline. In this study population, 82% of the participants had severe CUD.

The purpose of this pioneering phase 2B trial was to show that AEF0117 lowers cannabis use and to determine the endpoints and optimal dosage of AEF0117 for use in future studies. Three doses of AEF0117 (0.1, 0.3, 1mg once a day for 12 weeks) were evaluated and several endpoints (primary, secondary, and exploratory) measuring changes in cannabis use and their consequences for the participants were analysed.

AEF0117 was well tolerated, and no safety concerns were observed. The type and frequency of adverse events were similar across all treatment groups including placebo.

The primary endpoint, the proportion of participants who reduced their cannabis use to ≤1 day per week, as well as secondary endpoints measuring the proportion of participants reaching either complete abstinence or reducing cannabis use to ≤2 day per week did not differ from placebo. It is noteworthy that there was a very low placebo effect for these endpoints, suggesting that CUD participants in this study may be resistant to change the number of days per week of use.

At the highest dose of AEF0117 (1 mg/day), encouraging and consistent positive trends were observed on several quantitative endpoints measuring the total amount of cannabis used, including the urine concentrations of the THC metabolite THC-COOH, an objective measure of cannabis use. Some of these decreases were statistically significant in participants with moderate CUD. These data are in agreement with the positive results of the phase 2A[2], in which only quantitative endpoints were measured, and the largest population of participants had a moderate CUD.

At the end of the treatment period, AEF0117 (1 mg/day) improved, with a nearly statistically significant effect, anxiety and depression scores on the Hamilton scales and sleep quality. These findings suggest that AEF0117's pharmacological profile differs from that of CB_1 receptor antagonists, including rimonabant, which have been shown to increase anxiety and depression.

These data indicate that AEF0117 is pharmacologically active, providing a supplementary validation of the new pharmacological class developed by Aelis Farma, the "Signalling Specific Inhibitors of the CB_1 receptor (CB_1-SSi)".

Aelis Farma continues to explore the results of the study further in order to determine the best course of strategic and regulatory actions.

This clinical Phase 2B study is part of the strategic collaboration between Aelis Farma and Indivior, which includes an exclusive option for Indivior to license the global rights to AEF0117, a first-in-class synthetic Signaling Specific Inhibitor ("SSI") engineered to inhibit the cannabinoid type 1 ("CB_1") receptor ("CB_1-SSI").[2] Indivior has communicated Aelis Farma that it does not intend to exercise the option on AEF0117 before seeing the additional analysis of the clinical data.

About AEF0117 and the Clinical Phase 2B Study

The Phase 2B study is part of Aelis Farma clinical development program of AEF0117.

The completed Phase 2B trial (NCT05322941) performed by Aelis Farma was a randomized, double-blind, placebo-controlled, 4-arm, parallel-group, prospective, multicentre study ("Effect of AEF0117 on Treatment-seeking Patients with Cannabis Use Disorder (CUD) (SICA2)").[1] Participants were recruited across eleven clinical centres throughout the United States. Three hundred thirty-three treatment-seeking participants with moderate to severe CUD were treated once daily for 12 weeks, with either 1.0mg, 0.3mg, and 0.1mg of AEF0117 or placebo. The primary endpoint was the proportion of participants who reduced their cannabis use to ≤1 day per week. Secondary endpoints included improvement in complete abstinence, the proportion of participants with modest cannabis use (≤2 days per week), a quantitative improvement in quality of life, and overall reduction of days of cannabis use per week. Exploratory endpoints included reduction in cannabis craving and in the amount of cannabis consumed per day of use, as measured by the amount of $ spent on cannabis per day.

About AELIS FARMA

Founded in Bordeaux in 2013, Aelis Farma is a biopharmaceutical company that is developing a new class of drugs, the Signaling-Specific inhibitors of the CB_1 receptor of the endocannabinoid system (CB_1-SSi). CB_1-SSi have been developed by Aelis Farma based on the discovery of a natural regulatory mechanism of CB_1 hyperactivity made by the team led by Dr. Pier Vincenzo Piazza, the Company's CEO, when he was the director of the Neurocentre Magendie of INSERM in Bordeaux. By mimicking this natural mechanism, CB_1-SSi appear to selectively inhibit the disease-related activity of the CB_1 receptor without disrupting its normal physiological activity.[2] CB_1-SSi have consequently the potential to provide new safe treatments for several brain diseases.

Aelis Farma is currently developing two first-in-class clinical-stage drug candidates: AEF0117 for the treatment of cannabis related disorders, that has just completed a Phase 2B study in the United States in CUD, and AEF0217 for cognitive disorders, including those of Down Syndrome (Trisomy 21), currently in a Phase 1/2 study in Spain in people with Down syndrome, which results are expected in Q4-2024. The Company also has a portfolio of new innovative CB_1-SSi for the treatment of other disorders associated with a dysregulation of the activity of the CB_1 receptor. The different drugs developed by the company belong to the same general pharmacological class, the CB_1-SSi, but have distinct functional effects allowing to target different types of dysregulations of the CB_1 receptor.

Aelis Farma draws on the talents of more than 25 highly qualified employees.
For more information, visit www.aelisfarma.com and follow us on LinkedIn and Twitter.

Upcoming communication:

- **Half-year financial results 2024:** September 26, 2024 (after market close)

References:

1. National Library of Medicine (U.S.) (2022, April). *Effect of AEF0117 on treatment-seeking patients with cannabis use disorder (CUD) (SICA2).* Identifier NCT05322941 https://www.clinicaltrials.gov/study/NCT05322941
2. Haney M, Vallée M, Fabre S, Collins Reed S, Zanese M, Campistron G, Arout CA, Foltin RW, Cooper ZD, Kearney-Ramos T, Metna M, Justinova Z, Schindler C, Hebert-Chatelain E, Bellocchio L, Cathala A, Bari A, Serrat R, Finlay DB, Caraci F, Redon B, Martín-García E, Busquets-Garcia A, Matias I, Levin FR, Felpin FX, Simon N, Cota D, Spampinato U, Maldonado R, Shaham Y, Glass M, Thomsen LL, Mengel H, Marsicano G, Monlezun S, Revest JM, Piazza PV. Signaling-specific inhibition of the CB1 receptor for cannabis use disorder: phase 1 and phase 2a randomized trials. Nat Med. 2023 Jun;29(6):1487-1499. https://doi.org/10.1038/s41591-023-02381-w

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Forward-looking statements

Some information contained in this press release are forward-looking statements, not historical data. These forward-looking statements are based on current beliefs, expectations, and assumptions, including, but not limited to, assumptions about Aelis Farma's current and future strategy and the environment in which Aelis Farma operates. They involve known and unknown risks, uncertainties, and other factors, which may cause actual results, performance, or achievements, or industry results or other events, to differ materially from those described or implied by such forward-looking statements. These risks and uncertainties include those set out and described in detail in Chapter 3 "Risk Factors" of Aelis Farma's Universal Registration Document approved by the *Autorité des Marchés Financiers* on April 24, 2024, under number R.24-004.

These forward-looking statements are made only as of the date of this press release and Aelis Farma expressly disclaims any obligation or undertaking to release any updates or corrections to the forward-looking statements included in this press release to reflect any change in expectations or events, conditions, or circumstances on which any such forward-looking statement is based. Forward-looking information and statements are not guarantees of future performance and are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond Aelis Farma's control. Actual results could differ materially from those described in, or implied or projected by, forward-looking information and statements