Press release

Aelis Farma announces the recruitment of the first patient for the phase 1/2 clinical trial of its drug candidate AEF0217 for the treatment of cognitive disorders in Down syndrome

The trial should include around 45 participants with Down syndrome (trisomy 21) and should be completed in the second quarter of 2023

Bordeaux, December 16, 2022 – 7:00 a.m. CET – Aelis Farma (ISIN: FR0014007ZB4 – Ticker: AELIS, PEA-PME eligible), a clinical-stage biopharmaceutical company specializing in the development of treatments for brain diseases, announces today the recruitment of the first patient for its phase 1/2 trial of AEF0217 in participants with Down syndrome.

AEF0217 is Aelis Farma's second drug candidate. It belongs to a new class of drugs discovered by the company, signaling-specific inhibitors of the CB_1 receptor of the endocannabinoid system (CB_1-SSi), a receptor implicated in many brain disorders. AEF0217 is being developed as the first treatment of cognitive impairments caused by a hyperactivity of the CB_1 receptor and, as a first indication, of those associated with Down syndrome (trisomy 21). AEF0217, like other CB_1-SSis, is able to inhibit only certain components of CB_1's activity, which seems to enable this compound to counteract a pathological hyperactivity of the receptor without altering its normal physiological functions and, as a consequence, without causing major side effects.

Aelis Farma recently published the positive results of the phase 1 clinical trials analyzing the safety and pharmacokinetics of AEF0217 in healthy volunteers. These studies have confirmed the particularly favorable safety profile of CB_1-SSi, a particularly important characteristic for fragile populations such as those with Down syndrome. The results of these trials showed that all doses of AEF0217 were well tolerated without any serious adverse effects and that AEF0217 has a favorable pharmacokinetic profile. These positive results allow now to administer AEF0217 to people with Down syndrome.

The phase 1/2 clinical trial with AEF0217 is a monocentric, double-blind study comparing one dose of AEF0217 to placebo, after 28 days of treatment once a day in approximately 45 participants with Down syndrome. The main objective of the trial is to assess the safety and absorption of AEF0217 and it could also provide the first indications of activity as a treatment for the cognitive impairments of Down syndrome.

The first patient has been recruited by the teams of Prof. Rafael de la Torre Fornell at the Hospital del Mar Medical Research Institute (IMIM) in Barcelona (Spain). Depending on the rate of recruitment, the study should be completed in the second quarter of 2023.

Prof. Rafael de la Torre Fornell, the trial's principal investigator, explains*: "Administering AEF0217 for the first time to a person with Down syndrome is a key event for me and my teams. It is a crucial step towards developing a treatment that can improve the cognitive abilities of these charming and unique people that desperately need it".*

Pier Vincenzo Piazza, CEO of Aelis Farma, concludes: *"I would like to congratulate the teams of Prof. Rafael de la Torre Fornell and of Aelis Farma for this major step forward in the development of AEF0217, a drug candidate based on our innovative approach that allows to selectively inhibit only part of the activity of the CB_1 receptor. If the results are favorable, we will be significantly closer to having a*

promising therapy that could considerably improve the quality of life of people with Down syndrome, and also potentially pave the way for the treatment of other cognitive impairments".

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About the AEF0217 clinical program for the treatment of cognitive disorders in Down syndrome: the European ICOD project.

The phase 1/2 trial of AEF0217 is part of the European H2020 ICOD project (*Improving COgnition in Down syndrome, Grant Agreement ID 899986*), and is being run in collaboration with the Hospital del Mar Medical Research Institute (IMIM) in Barcelona (Spain) and Prof. Rafael de la Torre Fornell, project coordinator and principal investigator of the trial. In February 2021, the ICOD project received funding of €6 million from the European Commission to finance the clinical development of AEF0217 for the treatment of cognitive impairments of Down syndrome.

About AELIS FARMA

Founded 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). These new molecular entities 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 Magendie Neurocenter of Inserm in Bordeaux. By reproducing this natural mechanism, CB_1-SSi appear to be able to selectively inhibit the disease-related activity of the CB_1 receptor, without disrupting its normal physiological activity. 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 a dysregulation of the activity of the CB_1 receptor.

AEF0117, which targets disorders due to excessive cannabis use (addiction and psychosis), has shown indications of efficacy in a phase 2a clinical trial and has entered a phase 2b clinical trial in Q2 2022, which will include 330 patients in 9 clinical centers in the United States. Aelis Farma has an exclusive option-license agreement with Indivior PLC, a leading pharmaceutical company in the treatment of addiction, for the development and commercialization of AEF0117 for disorders due to excessive cannabis use. As part of this agreement, Aelis Farma has already received $30 million (option payment). If Indivior exercises the license option at the end of the phase 2b, Aelis Farma will receive a $100 million license fee (potentially in 2024) and Indivior will carry any additional development costs. The agreement also includes up to $340 million in additional payments contingent on the achievement of development, regulatory and commercial milestones, as well as royalties on net sales of AEF0117 ranging between 12% and 20%.

AEF0217, which targets various cognitive disorders including those associated with Down syndrome (trisomy 21), has successfully completed safety and pharmacokinetic trials (phase 1 clinical program) in healthy volunteers and started in December 2022 a phase 1/2 trial in people with Down syndrome. This new study will assess the safety and the pharmacokinetics of AEF0217 and could also provide the first indications of its activity as a treatment of cognitive disorders. The results are expected in Q2 2023. AEF0217 has undergone an extensive preclinical proof-of-concept program using highly innovative tests to assess cognitive functions in animals. In this context, AEF0217 demonstrated its ability to completely reverse the cognitive impairments observed in several animal models of cognitive disorders, such as Down 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 23 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 from IRDI Capital Investissement.

For more information: www.aelisfarma.com

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Forward-looking statements

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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.