Press release

Aelis Farma announces the successful start of the recruitment of the Phase 2B clinical trial with AEF0217 for the treatment of behavioral and cognitive impairments of people with Down syndrome (Trisomy 21)

- **AEF0217 is a *first-in-class* Signalling Specific inhibitor of the CB_1 receptor (CB_1-SSi) developed as a treatment for impairments in adaptive behaviours and cognition in neurodevelopmental disorders, with Down syndrome as the first indication.**
- **On World Down syndrome Day, Aelis Farma is happy to announce that the three countries involved in a Phase 2B clinical trial with AEF0217 in Down syndrome, are now actively recruiting.**
- **This Phase 2B trial is expected to enroll 188 participants with down syndrome aged 16 to 32 years in clinical centers across France, Italy and Spain and evaluate the effects of AEF0217 on the behavioral and cognitive impairments of people with Down syndrome.**

Bordeaux, France, March 21, 2026 – 9:00 a.m. CET – Aelis Farma (ISIN: FR0014007ZB4 – Ticker: AELIS), a clinical-stage biopharmaceutical company specialized in the development of treatments for brain and peripheral diseases involving the CB_1 receptor, announces today, on World Down Syndrome Day, the successful launch of its Phase 2B clinical trial with AEF0217 for the treatment of the behavioral and cognitive impairments associated with Down syndrome (Trisomy 21), with recruitment now underway across the three countries involved (Spain, France and Italy).

The first patient first visit (FPFV) was performed in December 2025 shortly after receiving initial regulatory approval, reflecting the Company's ability to execute its clinical roadmap and the strong engagement of investigators, participants and families. On this World Down Syndrome Day, Aelis Farma is pleased to announce that screening and recruitment are now actively progressing across the centres of the three participating countries.

The protocol of this Phase 2B was submitted through the EU Clinical Trials Information System (CTIS) and has received the required approvals from the European Medical Agency (EMA, the relevant national competent authorities and ethics committees in France, Italy and Spain under Regulation (EU) No 536/2014 (EU CT number: 2025-521013-10-00).

AEF0217: a potential first pharmacological treatment for adaptive behaviour and cognitive impairments in Down syndrome

People with Down syndrome frequently present lifelong impairments in adaptive behaviors and cognition for which no pharmacological treatment is currently approved; standard of care relies primarily on educational, behavioral and supportive interventions that are usually insufficient to enable full autonomy and an adequate quality of life.

An inhibition of the CB_1 receptor of the endocannabinoid system has been proposed as a new target for improving cognitive deficits associated with several conditions. Down syndrome seems associated with an hyperactivity of the CB_1 receptor, and an inhibition of the CB_1 has been shown to improve cognitive performance and neurobiological activity in several genetic animal models of neurodevelopmental disorders, including Down syndrome.

AEF0217 is a first-in-class Signalling Specific inhibitor of the CB_1 receptor (CB_1-SSi), a new pharmacological class developed by Aelis Farma. AEF0217 and the CB_1-SSi class are designed to selectively inhibit the disease-related activity of the CB_1 while preserving the physiological activity of the receptor. This molecular selectivity provides the first pharmacological approach allowing to obtain the positive effects of a CB_1-inhibition without the adverse effects that halted the development of the previous-generation of CB_1 antagonists, which blocked the whole activity of the CB_1.

In a prior Phase 1/2 randomized, double-blind, placebo-controlled study in young adults with Down syndrome (29 participants aged 18 to 32 years), AEF0217 showed a very favorable safety and pharmacokinetic profile. In addition, AEF0217 induced a statistically significant improvement in key adaptative behaviours, as measured by the Vineland Adaptive Behaviour Scales (VABS), such as the ability to communicate, to take care of oneself and to develop social interactions, paralleled by an improvement in brain activity

Aelis Farma's Phase 2B trial with AEF0217 for the treatment of behavioral and cognitive impairments associated with Down syndrome.

This international multicenter Phase 2B clinical trial (AEF0217-201) is designed to confirm and extend the Phase 1/2 findings in a larger population (188 vs 29 participants) and over a longer treatment duration (six-month vs one-month). It is a randomized, double-blind, placebo-controlled, parallel-group study expected to enroll 188 participants aged 16 to 32 years across 10 specialized expert centers (five in France, three in Italy and two in Spain). Participants will be randomized 1:1:1:1 to receive once-daily oral AEF0217 (0.1 mg, 0.2 mg or 0.6 mg) or placebo for 24 weeks, followed by an 8-week treatment free follow-up.

The primary endpoint of the study is the change from baseline after six months of treatment in adaptive behaviors, assessed using the normalized raw scores of the nine subdomains of the Vineland Adaptive Behaviour Scales, Third Edition (VABS-3). Secondary endpoints include measures of cognition (fluid and crystallized), quality of life and sleep efficiency. Safety will be closely monitored throughout the study period, and an independent data monitoring committee (IDMC) will perform an interim safety analysis after at least 40 participants have completed 12 weeks of treatment.

Recruitment is expected to be completed by the end of 2026, and preliminary results are expected in the second half of 2027. Aelis Farma's current cash runway (Q1 2028) extends well beyond the end of this study, allowing the Company to take full advantage of the Phase 2B results.

Prof. Rafael de la Torre Fornel, the principal investigator at IMIM (Barcelona, Spain) and global coordinator of the study, commented: *"We are delighted to participate in this landmark study, which aims to prove the efficacy of a promising treatment to improve adaptive functioning, daily living skills and ultimately the independence of people with Down syndrome. The successful start of the trial and the ongoing recruitment reflect the meticulous preparation and professionalism of the site teams as well as the strong mobilization of people with Down syndrome and their families. We would like to thank all of them for their outstanding support. There is currently no approved pharmacological option to improve adaptive behaviour and cognition in people with Down syndrome. This study is a key step toward potentially delivering a treatment providing tangible benefits for individuals with Down syndrome and their families."*

Pier Vincenzo Piazza, CEO of Aelis Farma, concludes: *"The successful start of recruitment of our Phase 2B trial marks an important milestone in the clinical development of AEF0217 and is a concrete demonstration that Aelis Farma is executing its roadmap with operational efficiency. I would like to thank the investigators and the teams of the clinical sites for their outstanding commitment, and all the participants and their families for their trust and engagement. Last but not least, my thanks go to the team of Aelis Farma for their fantastic commitment and hard work. Our collective ambition is clear: develop the first treatment able to improve the quality of life and independence of people with Down syndrome. This study with AEF0217 could materialize our hope to help people with Down syndrome*

and could open the way to the treatment of a broader spectrum of conditions associated with cognitive impairments."

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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. CB_1-SSi have consequently the potential to provide new safe treatments for several brain and peripheral organ diseases.

Aelis Farma currently has two first-in-class clinical-stage drug candidates. AEF0117 for the treatment of cannabis use disorders (CUD), that has shown to be able to decrease cannabis use across two studies. AEF0217 for cognitive disorders, which has shown in a Phase 1/2 to be safe and able to improve adaptive behaviour in young adults with Down syndrome (Trisomy 21) and has started a Phase 2B in Europe aiming to confirm its efficacy and safety in people with Down syndrome. The clinical results obtained with these 2 compounds have confirmed the safety and therapeutic activity of CB_1-SSi in humans. The Company also develops 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, including diseases involving peripheral organs, such as obesity and related metabolic conditions. 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 and guaranteeing that the different compounds are not substitutable one with the others.

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Contacts

AELIS FARMA
Pier Vincenzo Piazza
Chief Executive Officer
contact@aelisfarma.com

NewCap
Dusan Oresansky/Thomas Cozzolino
Investor Relations
aelis@newcap.eu
+33 1 44 71 94 92

NewCap
Arthur Rouillé
Media Relations
aelis@newcap.fr
+33 1 44 71 00 15

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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.