

Press Release

Aelis Farma receives a second positive recommendation from the Independent Data Monitoring Committee for its Phase 2b study with AEF0217 in people with Down syndrome

- **After analyzing the safety data of the Phase 2b clinical study with AEF0217 in people with Down syndrome, the Independent Data Monitoring Committee (IDMC) identified no safety concerns and recommended that the study continue without any modification to the protocol.**

- **The safety data from 74 participants, including 54 who completed at least 12 weeks of treatment, were analyzed in a blinded manner by the IDMC. These data further support the favorable safety and tolerability profile of AEF0217, which is an important characteristic for a treatment intended for populations with underlying health vulnerabilities, such as people with Down syndrome.**

- **The IDMC also issued a positive recommendation for the potential initiation of a 12-month open-label extension study.**

- **The Phase 2b study is progressing according to plan, with results expected by the end of 2027.**

Bordeaux, France, November 16, 2026 – 07:30 AM CET – Aelis Farma (ISIN: FR0014007ZB4 – Ticker: AELIS), a clinical-stage biopharmaceutical company specializing in the development of treatments for diseases involving the CB_1 receptor, today announces a second positive recommendation from the Independent Data Monitoring Committee ("IDMC") reviewing the safety data of the ongoing Phase 2b study with AEF0217 in adults and older adolescents (16-17 years of age) with Down syndrome.

Following this review, the IDMC recommended that the study continue according to the current protocol, without modification. The Committee also provided a favorable recommendation for the potential initiation of a 12-month open-label extension study that could follow the end of the current Phase 2b.

A second positive safety review confirming the favorable tolerability profile of AEF0217

The IDMC is an independent committee composed of experts in clinical pharmacology, clinical research, pediatrics and Down syndrome. Its role is to periodically review the safety and tolerability data generated during the Phase 2b study with AEF0217 in Down syndrome and provide independent recommendations regarding its continuation.

The first IDMC safety review of the Phase 2b study, based on data from 42 participants of whom 32 had completed four weeks of treatment, also resulted in a positive recommendation, announced in July 2026.

This second review was based on a comprehensive evaluation of the available safety data from 74 randomized participants, including 54 who had completed at least 12 weeks of treatment. The population included young adults (18 to 32 years of age) and older adolescents (16 to 17 years of age, 19% of randomized participants).

The review included adverse events, treatment exposure, clinical laboratory parameters, vital signs,

electrocardiographic assessments and other safety measures collected throughout the study.

The overall findings confirmed a favorable safety and tolerability profile, with no serious or severe adverse events, a low incidence of treatment-related adverse events and no safety concerns requiring changes to the study.

Low frequency of adverse events, predominantly mild and unrelated to treatment

Among the 74 randomized participants included in the safety analysis at the cut-off date (14 September 2026), 23 participants (31.1%) experienced a total of 42 treatment-emergent adverse events (TEAEs).

Nearly all reported events (41 out of 42; 97.6%) were mild in intensity. Only one event of moderate intensity, a transient vasovagal episode, was reported during the heatwave of the summer and was considered unrelated to the investigational treatment by the investigator.

Importantly, no serious adverse events (SAEs), no severe adverse events and no treatment discontinuations or study withdrawals due to adverse events were reported.

The vast majority of adverse events were considered unrelated to the investigational treatment by the investigators. Only two mild events, vomiting and acne, were assessed as potentially treatment-related.

Adverse events were distributed across different organ systems, without evidence of an unexpected pattern or concentration of events in any particular system. Most events were transient, generally lasting only a few days, and resolved without sequelae or the need for changes in study treatment.

These observations are particularly encouraging given the characteristics of the study population, which includes individuals with Down syndrome who may have pre-existing medical conditions and concomitant treatments.

No clinically significant safety signals identified from laboratory, cardiovascular or other assessments

In addition to adverse events, the review included a comprehensive evaluation of clinical laboratory results, vital signs and electrocardiographic assessments.

Laboratory evaluations, including hematology, clinical chemistry, coagulation and urinalysis, showed no consistent pattern suggestive of a treatment-related safety signal. Most abnormal laboratory findings were isolated or considered not clinically significant by investigators.

Vital signs, including blood pressure, heart rate and body temperature, remained generally stable throughout the period evaluated.

Electrocardiographic monitoring also showed no evidence of a consistent treatment-related cardiac safety signal. No clinically significant deterioration in ECG findings was identified over the 12-week evaluation period.

Overall, these assessments did not identify any new safety concern or signal requiring additional monitoring or modifications to the ongoing study.

Favorable tolerability also observed in older adolescents with Down syndrome

An important feature of this Phase 2b study is the inclusion of older adolescents aged 16 and 17 years, in addition to adults aged up to 32 years.

Among the 74 randomized participants, 14 were older adolescents. The incidence of treatment-emergent adverse events was comparable between the adolescent and adult populations, with 4 adolescents (28.6%) and 19 adults (31.7%) reporting at least one TEAE.

No serious or severe adverse events were reported in either age group, and no apparent difference in overall tolerability was identified between adolescents and adults.

These observations provide encouraging initial safety information in older adolescents with Down syndrome, a population not included in the previous Phase 1/2 study.

An increasingly consistent safety profile across the clinical development program

This second positive IDMC recommendation follows the initial favorable review announced in July 2026, which was based on safety data from 42 randomized participants, including 32 who had completed at least four weeks of treatment.

The new findings extend these earlier observations to a larger participant population and a longer treatment exposure, confirming the absence of serious or severe adverse events and a low incidence of adverse events considered related to treatment.

They are also consistent with the favorable safety and tolerability profile observed in previous clinical studies of AEF0217, including the Phase 1 program in healthy volunteers and the randomized Phase 1/2 trial in young adults with Down syndrome.

It is noteworthy that since the data cut-off for the second IDMC review (September 14, 2026), no serious adverse events or new safety concerns have been reported.

Taken together, these successive safety assessments provide growing support for the favorable clinical tolerability profile of AEF0217 and are consistent with the expected properties of Aelis Farma's innovative CB_1-SSi pharmacological approach.

Positive recommendation for a 12-month open-label extension study

The IDMC also reviewed whether the available safety data were sufficient to support the initiation of a 12-month open-label extension study that could follow the Phase 2b trial.

The Committee issued a favorable recommendation for the initiation of an extension study, with continued independent safety monitoring.

This favorable recommendation further derisks the clinical development program of AEF0217, supporting the potential initiation of a one-year open-label study that would accelerate the collection of long-term safety and tolerability data necessary for marketing authorization applications.

Phase 2b clinical development is progressing, with results expected by the end of 2027

The Phase 2b continues to progress, with 108 participants randomized as of November 4, 2026, representing more than half of the planned enrollment of 188 participants. Among them, 38 participants have already completed the 24-week treatment period.

Clinical results of the Phase 2b study are expected by the end of 2027, in line with the previously announced timeline.

These upcoming results will represent a major milestone in the clinical development of AEF0217, with the objective of confirming the encouraging efficacy findings previously observed in the Phase 1/2 study and supporting the next stages of its clinical and regulatory development.

Pier Vincenzo Piazza, Co-founder and CEO of Aelis Farma, stated:

"We are extremely pleased with this second positive recommendation from the independent monitoring committee, which confirms the encouraging safety and tolerability profile of AEF0217 and allows our Phase 2b study to continue without modification.

The safety findings are particularly reassuring, as they now cover a larger number of participants and a longer treatment period, including older adolescents. These observations are consistent with the expected safety profile of our innovative CB_1-SSi pharmacological approach, designed to selectively inhibit pathological CB_1 receptor signaling while preserving its normal physiological functions.

We are also very encouraged by the Committee's favorable recommendation regarding the potential initiation of an open-label extension study, which represents another important step in the clinical development of AEF0217.

Following the recently announced positive results of our retrospective study, suggesting that the benefits previously observed with AEF0217 translate into meaningful improvements in everyday life,

this new positive safety assessment further strengthens our confidence in the therapeutic potential of AEF0217.

We remain fully focused on the successful completion of our Phase 2b study, with results expected by the end of 2027, and are deeply grateful to the participants, their families, caregivers and clinical teams contributing to this important research."

Prof. Rafael de la Torre Fornell, Coordinating Investigator of the Phase 2b, commented:

"This second positive evaluation by the independent monitoring committee is very encouraging from a clinical perspective.

The absence of serious or severe adverse events and the favorable overall tolerability observed to date, including in older adolescents with Down syndrome, are particularly important when developing a treatment intended for potential long-term use in this population.

The Committee's recommendation to continue the study without modification, together with its favorable assessment regarding the planned extension study, provides additional reassurance as we progress with the clinical evaluation of AEF0217.

There is a significant unmet medical need for treatments capable of improving cognitive abilities and adaptive functioning in people with Down syndrome. We look forward to completing this important study and determining whether the encouraging results previously observed with AEF0217 can be confirmed in this larger population."

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About AEF0217

AEF0217 is a first-in-class drug candidate developed by Aelis Farma for the treatment of a broad spectrum of cognitive impairments. It belongs to a novel pharmacological class discovered by the Company, the Signaling Specific inhibitors of the CB_1 receptor (CB_1-SSi).

AEF0217 selectively inhibits specific components of CB_1 receptor intracellular signaling that seem to be associated with pathological states while preserving normal physiological functioning of the receptor, which predicts good tolerability and efficacy.

AEF0217 has shown in preclinical studies the ability to restore a broad spectrum of cognitive impairments associated with neurodevelopmental disorders, autism and aging.

The first clinical proof of concept of AEF0217 efficacy has been obtained in people with Down syndrome in a placebo-controlled, multicentric, randomized Phase 1/2 clinical trial. As predicted, AEF0217 has also demonstrated a very favorable safety and tolerability profile both in healthy volunteers and in people with Down syndrome.

AEF0217 ongoing Phase 2b clinical trial

Building on the positive safety and efficacy findings obtained so far with AEF0217, Aelis Farma is currently conducting an international, multicenter, randomized, double-blind, placebo-controlled Phase 2b clinical study in people with Down syndrome.

The study is designed to further evaluate the safety and efficacy of AEF0217 and confirm its ability to improve adaptive behaviors and cognitive functions.

The trial plans to enroll 188 participants aged 16 to 32 years across clinical centers in France, Spain and Italy, with participants receiving placebo or one of three doses of AEF0217 (0.1, 0.2 or 0.6 mg) once daily for six months.

In July and November 2026, following the first and second scheduled safety reviews, respectively, the Independent Data Monitoring Committee identified no safety concerns and recommended that the study continue without modification to the protocol.

This Phase 2b study is part of the European ICOD (Improving Cognition in Down syndrome) project, supported by the European Union's Horizon 2020 research and innovation program (Grant Agreement No. 899986).

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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 consequently are predicted to be both safe and efficacious to treat many diseases of the brain and peripheral organs.

Aelis Farma currently has two first-in-class drug candidates. Clinical results obtained with both compounds have confirmed the safety and therapeutic efficacy of CB_1-SSi in humans. The first candidate, AEF0117, for the treatment of cannabis use disorder (CUD), has shown its ability to reduce cannabis use in two studies. The second candidate, AEF0217, for the treatment of cognitive impairments, showed a good safety profile and an improvement in adaptive behavior in young adults with Down syndrome in a Phase 1/2 study. On this basis, a Phase 2b study has started in Europe to confirm the efficacy and safety of AEF0217 in a larger cohort of participants with Down syndrome. The Company also has a platform developing a portfolio of innovative CB_1-SSi for the treatment of other diseases involving the brain and peripheral organs. The new compounds share the same core mechanism of action but have distinct structures and functional effects enabling them to target different disease areas and ensuring that they are not substitutable for one another.

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C Compartment of Euronext Paris

Contacts

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

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

NewCap
Nicolas Mérigeau
Media Relations
aelis@newcap.eu
+33 1 44 71 94 98

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Forward-looking statements

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in detail in Chapter 3 "Risk Factors" of Aelis Farma's Universal Registration Document filed with the *Autorité des Marchés Financiers* on April 23, 2026, under number D.26-0284.

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.