Press release

NFL Biosciences outlines its development plan for NFL-101 in smoking cessation following receipt of scientific advice from several European agencies and the U.S. FDA

- **Confirmation by several European agencies and the U.S. FDA of the relevance of the continuous abstinence validation criteria which showed statistical significance (p=0.02) in the Phase 2 CESTO II study**

- **In Europe, a single Phase 3 trial could therefore be sufficient for the approval of NFL-101 in smoking cessation, with continuous abstinence over 12 months as the primary endpoint; in the United States, a second study in addition to the European trial will be required, with a 6-month follow-up period and a primary efficacy endpoint measured at 4 weeks**

- **Additional characterization and mechanism-of-action studies (CEA, HEGP, McLean/Harvard) are expected to enable the submission of clinical trial applications by mid-2026 and to meet the expectations of pharmaceutical companies**

Montpellier, France, October 20, 2025 at 6:00 pm CEST – NFL BIOSCIENCES (Euronext Growth Paris – FR0014003XT0 – ALNFL), (Euronext Growth Paris – FR0014003XT0 – ALNFL), a biopharmaceutical company developing innovative botanical drugs for the treatment of addictions, today announces having received convergent and constructive scientific advice from several regulatory agencies, including the Belgian, Dutch, UK, and German authorities, as well as the U.S. FDA, as part of the development of NFL-101. The project was unanimously perceived as particularly innovative and relevant given the impact of smoking on public health.

Clinical validation and efficacy criteria

All agencies confirmed the relevance of validating continuous abstinence through urinary cotinine measurement, as well as the reclassification as smokers of any participants using e-cigarettes or nicotine substitutes during the study. Under these conditions, the Phase 2 CESTO II trial demonstrated statistically significant results, **with continuous abstinence over 4 weeks in 24.1% of participants treated with NFL-101 (100 µg) compared to 12.9% under placebo, representing a relative risk of 1.87 (p=0.02).**

In Europe, a two-part study could be conducted, with the first part designed to de-risk the second. The expected primary endpoint for the second part would be continuous abstinence over 12 months, with the possibility that a single Phase 3 study could suffice depending on the robustness of the results. The potential inclusion of an active comparator arm (such as a nicotine patch) in addition to the NFL-101 and placebo arms remains under discussion. **In the United States, a second study will be required, with the primary endpoint measured at 4 weeks and a secondary endpoint at 6 months.**

Preparatory steps toward Phase 3 initiation

Additional work **to provide clarifications requested by regulatory agencies** regarding composition, mechanism of action, and manufacturing has already been initiated. The aim is to secure the NFL-101 development plan and strengthen its consistency. This work is **an essential component of the NFL-101 project's value proposition to the pharmaceutical companies** with which the Company is discussing licensing agreements. This work represents an additional investment of approximately €1 million, which is fully justified by the additional value it will help to create.

NFL Biosciences has initiated **complementary analyses of product** composition with specialized Contract Research Organizations (CROs) to further characterize NFL-101. These studies, combined with additional **mechanistic research** conducted with the CEA, the European Georges-Pompidou Hospital (HEGP), and McLean Hospital / Harvard Medical School in Boston, are designed to better understand the interactions between NFL-101, the immune system, and the central nervous system, thereby establishing a link between product composition and its mechanism of action. This approach is intended to confirm that the preclinical toxicity studies already conducted are fully applicable and to ensure that the Phase 3 batches will demonstrate reproducible efficacy.

The first additional characterization data are expected to be available in the coming weeks, while the initial results on the mechanism of action are expected in early 2026. All these studies represent a key milestone ahead of the manufacturing of the Phase 3 clinical batches with Fareva and Synerlab/Meribel Pharma, followed by the submission of clinical trial applications scheduled for mid-2026.

Bruno Lafont, Chief Executive Officer of NFL Biosciences, commented: *"The feedback received from the European agencies and the U.S. FDA confirms the scientific and regulatory strategy we have implemented. The additional work requested is already fully integrated into our roadmap — including in-depth characterization and a better understanding of the mechanism of action. These additional investments strengthen the attractiveness of the NFL-101 program for the pharmaceutical companies with whom we are discussing potential strategic partnerships. We approach the next steps with confidence, with the clear objective of initiating Phase 3 studies in 2026 and bringing NFL-101 closer to its ambition: to become the reference solution in the fight against tobacco addiction."*

About NFL Biosciences: www.nflbiosciences.com

NFL Biosciences is a biopharmaceutical company based in the Montpellier region of France, developing plant-based drug candidates for the treatment of addictions. NFL Biosciences' ambition is to bring new, safer and more effective natural therapeutic solutions to the entire world population, including low- and middle-income countries. Its most advanced product, NFL-101, is a standardized tobacco leaf extract protected by three patent families. NFL Biosciences intends to offer smokers wishing to quit a natural, safe, easy-to-administer and personalized alternative. NFL Biosciences is also developing NFL-301, a natural drug candidate for the reduction of alcohol consumption and has a drug development project for the treatment of cannabis use disorders.

NFL Biosciences shares are listed on Euronext Growth Paris (FR0014003XT0 - ALNFL). The company is qualified as an "Innovative Company" eligible for FCPI investment. More information on www.nflbiosciences.com

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