



Press release

NFL Biosciences announces results from a new study conducted with the CEA providing further insight into the effects of NFL-101, its *first-in-class* treatment for tobacco addiction, and highlighting its prolonged activity

- **A more comprehensive study conducted with the CEA enabled a more detailed characterization of NFL-101's effects**
- **The study model confirmed the prolonged activity of NFL-101**
- **The unique and original nature of NFL-101's effect is clearly demonstrated**

Montpellier, France, May 5, 2025, à 8:30 am CEST – NFL BIOSCIENCES (Euronext Growth Paris - FR0014003XT0 - ALFNL), a biopharmaceutical company developing innovative botanical medicines for the treatment of addiction, today announced the results of a new study conducted with the CEA, providing a deeper understanding of the effects of NFL-101, its drug candidate for tobacco addiction.

"These results enable a more precise identification of the brain regions targeted by NFL-101. They reveal a global and long-lasting effect on the neurobiological mechanisms involved in tobacco withdrawal, setting NFL-101 apart from conventional treatments that act solely on nicotinic receptors and require repeated administration to maintain efficacy. These are particularly compelling additional elements in the context of our ongoing discussions with pharmaceutical companies regarding a strategic partnership." commented **Bruno Lafont, Chief Executive Officer of NFL Biosciences.**

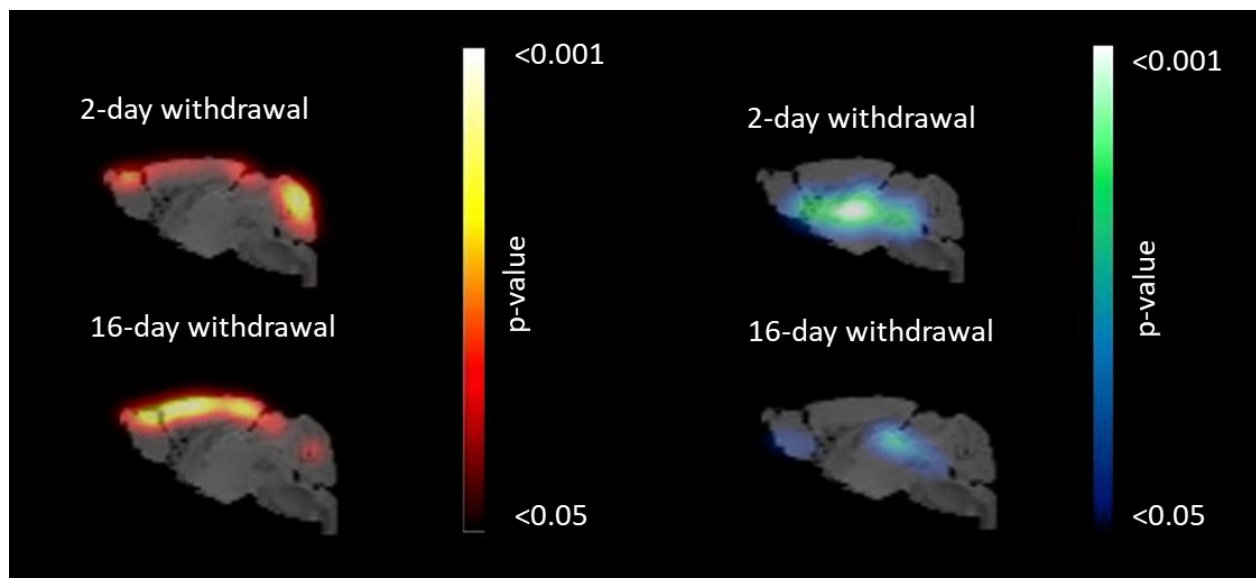
NFL-101 is an innovative drug candidate for smoking cessation, administered in just two doses. Its efficacy was demonstrated versus placebo in the Phase 2 CESTO2 study, with continuous abstinence rates of 24.1% for dose 1 versus 12.9% for placebo ($p = 0.038 < 0.05$) over the primary endpoint period, from day 15 to day 43, confirmed through urinary cotinine measurement. NFL-101's mechanism of action is based on a novel immune-based approach. Its activity was first tested in a mouse model developed by the CEA ([press release dated January 30, 2024](#)), in a molecular imaging study that highlighted the restoration of normal thalamic activity in the brain region associated with the urge to smoke under withdrawal conditions.

In order to confirm the results obtained, to further refine the identification of the targeted brain regions, and to assess any potential persistence of the effects, **NFL Biosciences commissioned the CEA to conduct a second, more in-depth study using its tobacco exposure mouse model.**

The study was conducted by the Pharmacological Neuroimaging team at the CEA's Frédéric Joliot Hospital Service (SHFJ) in Orsay. It involved tracking, via positron emission tomography (PET), the changes in brain function associated with the development of tobacco dependence in mice, in order to highlight the central effects of treatment with NFL-101 in this context.

This new study involved a larger number of mice and allowed for more refined comparisons at 2 and 16 days after the administration of treatments to mice under tobacco withdrawal conditions. In the previous study, the persistence of the effect at 16 days could not be evaluated due to protocol constraints. This new study identified brain regions that were significantly affected—that is, either overactivated or underactivated—at 2 or 16 days after withdrawal.

NFL-101 significantly restores activity in these brain regions at both 2 and 16 days, with a particularly marked effect on **the cortex, thalamus, hippocampus, and striatum**.



Restoration of brain activity by NFL-101 in a mouse model compared with placebo (red = hyperactivation / blue = hypoactivation)

These four brain regions play a central role in the difficulty of quitting smoking. The **cortex**, involved in cognitive and emotional regulation, displays functional alterations during tobacco withdrawal, contributing to reduced executive control and heightened sensitivity to craving-related stimuli. The **thalamus**, rich in nicotinic receptors, is involved in sensory integration and the transmission of motivational signals, playing an active role in the craving mechanism. The **hippocampus**, for its part, is essential for contextual memory and links familiar environments with tobacco use. This facilitates the reactivation of smoking-related memories when exposed to certain contexts, intensifying cravings and increasing the risk of relapse during withdrawal. Finally, the **striatum**, at the center of reward and habit circuits, plays a role in reinforcing addictive behaviors in response to dopamine release induced by nicotine. During withdrawal, disruptions in its dopaminergic activity contribute to withdrawal symptoms, loss of motivation, and persistence of automated behaviors linked to tobacco use, making cessation particularly difficult.

The observation of an effect at 16 days suggests that the treatment provides long-lasting activity in an animal with an extremely rapid metabolism—nicotine’s plasma half-life is approximately 6 to 7 minutes in mice, compared to 2 hours in humans—and an average lifespan of about 2 years.

This study not only demonstrates that NFL-101 acts specifically on the addiction-related brain regions involved in tobacco use, but also that the effect occurs rapidly after administration and is sustained over time—an observation consistent with the clinical experience gained in the CESTO2 study.

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 Paris (FR0014003XT0 - ALNFL).

Contacts:

NewCap

Investor Relations / Media Relations

Mathilde Bohin / Arthur Rouillé

Tel: +33 (0)1 44 71 94 94

E-mail: nfl@newcap.eu

NFL Biosciences

Bruno Lafont

Tel: +33 (0)4 11 93 76 67

E-mail: info@nflbiosciences.com