



## Press release

### **NFL Biosciences publishes positive results from a complementary program confirming the excellent safety profile of NFL-101, its first-in-class treatment for tobacco addiction**

- **Positive results attesting to the safety and tolerability of NFL-101, with doses tested up to more than 600 times the clinical dose**
- **Confirmation of NFL-101's superior safety profile compared to current treatments, further enhancing the product's benefit-risk ratio, as expected by potential industrial partners.**
- **Validation of a new milestone in the development of NFL-101, strengthening the product's file in regards to discussions with regulatory authorities to establish a Phase 3 development plan**

**Montpellier, France, February 4<sup>th</sup>, 2025, 7 a.m. CET** – NFL BIOSCIENCES (Euronext Growth Paris - FR0014003XT0 - ALFNL), a biopharmaceutical company developing botanical drugs for the treatment of addictions, today announced the positive results of a new toxicity study evaluating extreme doses, as well as an associated genotoxicity and mutagenicity program for NFL-101, its proprietary drug indicated for the treatment of tobacco addiction.

NFL Biosciences conducted this extended toxicity program to strengthen its case during discussions with regulatory authorities, to secure NFL-101's late-stage clinical development, and to meet the expectations of potential industrial partners. The program aimed to evaluate the administration of higher doses of NFL-101, using daily administrations compared with the weekly administrations of the previous program which had been conducted before the start of clinical trials. It also included genotoxicity and mutagenicity tests, carried out at the maximum doses permitted by these kinds of tests.

The toxicity study evaluated daily subcutaneous administration of increasing doses of NFL-101 in Sprague Dawley rats for 14 days. The maximum cumulative dose tested was 630 times greater than the cumulative dose assessed in humans, and induced no signs of systemic or local toxicity.

By way of comparison, the maximum cumulative doses safely evaluated in rats for nicotine, cytosine and varenicline - in relation to their respective clinical doses - were 4.8, 8.9 and 95 times higher respectively<sup>1</sup>. The results of this new study demonstrate a significantly better safety profile than currently available treatments. Furthermore, the CESTO 2 study demonstrated efficacy comparable to that of varenicline (Champix) and superior to that of nicotine substitutes, suggesting that NFL-101 may offer the best benefit-risk ratio. The complete absence of adverse effects and signs of toxicity at the doses assessed in this study also suggests that the actual safety threshold of NFL-101 may be even higher. Genotoxicity and

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<sup>1</sup> Baumung C, Rehm J, Franke H, Lachenmeier DW. Comparative risk assessment of tobacco smoke constituents using the margin of exposure approach: the neglected contribution of nicotine. *Sci Rep.* 2016 Oct 19;6:35577. doi: 10.1038/srep35577. PMID: 27759090; PMCID: PMC5069659. / Gotti C, Clementi F. Cytosine and cytosine derivatives. More than smoking cessation aids. *Pharmacol Res.* 2021 Aug;170:105700. doi: 10.1016/j.phrs.2021.105700. Epub 2021 Jun 2. PMID: 34087351. / Xi ZX. Preclinical Pharmacology, Efficacy and Safety of Varenicline in Smoking Cessation and Clinical Utility in High Risk Patients. *Drug Healthc Patient Saf.* 2010 Apr 1;2010(2):39-48. doi: 10.2147/DHPS.S6299. PMID: 21278851; PMCID: PMC3028205. / CDER 2006 Center For Drug Evaluation And Research, Varenicline - Aproval package for Application Number NDA 21-928

mutagenicity studies were perfectly conclusive at the maximum doses tested, showing no deleterious effect on DNA or induction of genetic mutations.

*“The results of this new complementary safety evaluation program for NFL-101 confirm the safety of our treatment at a level never before achieved by a smoking cessation treatment,” said Bruno Lafont, Chief Executive Officer of NFL Biosciences. “These new data will have a positive impact on our ongoing discussions with regulatory authorities, as they contribute to maximizing the benefit-risk ratio of our product, an essential criterion taken into account by regulatory agencies when approving and reimbursing therapeutic products. We are convinced that NFL-101 has the potential to significantly improve the management and support of people wishing to treat their tobacco addiction. These results also facilitate our discussions with players in the pharmaceutical industry, for whom product safety is an essential criterion. We are actively pursuing these exchanges in order to guarantee the success of the Phase 3 program and ensure that our product reaches the market in the next few years”.*

[The results published in September 2024 from the Phase 2 clinical trial, CESTO II](#), evaluating NFL-101 in the treatment of tobacco addiction, demonstrated for the first time the efficacy of a single-dose drug in the treatment of tobacco addiction. NFL-101 could thus become an effective, natural and safe alternative to current treatments, while presenting a lighter and simpler administration method for smokers. Given its unique mechanism of action, NFL-101 could also be administered to any smoker using another smoking cessation medication.

NFL Biosciences is currently pursuing discussions with the regulatory authorities to establish the best possible development plan to enable NFL-101 to reach the market, and is continuing its industrial development to produce GMP batches for use in Phase 3, [based on the manufacturing process validated by the recent production of an engineering batch](#).

**About NFL Biosciences:** [www.nflbiosciences.com](http://www.nflbiosciences.com)

NFL Biosciences is a biopharmaceutical company based in the Montpellier area which develops botanical drug candidates for the treatment of addictions. NFL Biosciences' ambition is to bring new, natural, safer and more effective therapeutic solutions to the entire world population, including low- and middle-income countries. Its most advanced product, called NFL-101, is a standardized, nicotine free tobacco leaf extract protected by two patent families. NFL Biosciences intends to offer smokers who want 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 disorder.

The shares of NFL Biosciences are listed on Euronext Growth Paris (FR0014003XT0 - ALNFL).

#### **Contacts:**

##### **NewCap**

Investors relations / Media relations

Mathilde Bohin / Arthur Rouillé

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

E-mail: [nfl@newcap.eu](mailto:nfl@newcap.eu)

##### **NFL Biosciences**

Bruno Lafont

Tél.: +33 (0)4 11 93 76 67

E-mail: [info@nflbiosciences.com](mailto:info@nflbiosciences.com)