Press release

NFL Biosciences submits an application for authorization of the Phase 2 TONIC clinical trial evaluating NFL-102 in smoking cessation

- **A Phase 2 clinical trial involving 310 smokers, designed to confirm the safety profile of NFL-102, determine its optimal dose, and evaluate its efficacy**

- **An adaptive design that allows for the gradual selection of the dose with the best benefit-risk profile at predefined stages of the study**

Montpellier, France, July 28, 2026 – at 5:45 pm CEST – NFL BIOSCIENCES (Euronext Growth Paris – FR0014003XT0 – ALNFL), a biopharmaceutical company developing innovative botanical drugs for the treatment of addictions, today announced that it has submitted an application to the French National Agency for Medicines and Health Products Safety (ANSM) and the Committee for the Protection of Human Subjects (CPP) for authorization of its TONIC clinical trial, the first study to evaluate NFL-102 in smokers seeking to quit smoking permanently.

This Phase 2, multicenter, randomized, double-blind, placebo-controlled study will include 310 smokers recruited from about ten centers in France. Its objective is to confirm the safety of NFL-102, determine its optimal dose, and evaluate its efficacy in achieving sustained smoking abstinence for four weeks between days 15 and 43, as confirmed by urinary cotinine levels. The follow-up period, limited to 43 days, allows for a shorter study while still evaluating an established efficacy endpoint. This decision is also based on the results of the CESTO2 study, which showed that sustained abstinence at four weeks was a good predictor of long-term abstinence.

A study designed to gradually identify the optimal dose.

The TONIC study is based on an adaptive design that allows for the gradual identification of the most effective dose during the study.

It will begin by comparing **three doses of NFL-102** to placebo.

1. After the **first 40 participants** are enrolled, an initial dose will be eliminated based on safety and efficacy data analyzed by an Independent Data Monitoring Committee (IDMC).

2. After enrolling **an additional 150 participants** (50 per arm, randomized between the two selected dose arms and placebo), an interim analysis conducted by the IDMC will be used to select the most effective dose.

3. The study will then continue exclusively with this selected dose compared to placebo, with the enrollment of **an additional 120 participants** (60 per arm, randomized between the selected dose and placebo).

At the conclusion of the study, the final comparison will include 110 participants who received the selected dose and 110 participants who received placebo, providing the statistical power necessary to assess sustained abstinence over 4 weeks.

A protocol optimized compared to the initial design

The protocol submitted today represents a significant optimization compared to the design presented in January 2026. The initial protocol called for the enrollment of 450 participants, with a final comparison involving 90 participants per arm for each dose and the placebo. The new design reduces the total enrollment to 310 participants, while increasing the final comparison to 110 participants per arm between the selected dose and the placebo.

This change allows for a gradual focus of resources on the most promising dose, limits participants' exposure to the doses not selected, and improves the statistical robustness of the primary analysis, all while reducing the total number of participants.

Bruno Lafont, Chief Executive Officer and co-founder of NFL Biosciences, stated: *"The filing of TONIC marks the first clinical evaluation of NFL-102. We are launching it with a design that we have carefully optimized: by progressively focusing the study on the most promising dose, we are enhancing statistical power while reducing the number of participants by nearly 30%. This makes the study more efficient and more attractive to future partners."*

Next Steps

Subject to obtaining the required regulatory authorizations, **the TONIC study is expected to begin in the second half of 2026 and run for approximately one year**. An initial analysis of data from the first 40 patients will be conducted by the IDMC to identify the two most promising doses of NFL-102 based on their benefit-risk profile. A second analysis by the IDMC will then be conducted after the enrollment of an additional 150 participants to select the final dose. The study will then continue with the enrollment of 120 additional patients, randomized to receive either this dose or a placebo, to confirm its efficacy and safety. **Each decision made by the IDMC will be announced.**

The first 40 participants will be enrolled at the Eurofins Optimed clinical center in Grenoble (France).

The next 270 participants will be enrolled at approximately ten clinical centers in France. Seven have already been selected: La Pitié-Salpêtrière Hospital in Paris, Lyon Sud Hospital (HCL), Infirmerie Protestante in Lyon, Louis Pasteur Hospital in Chartres, Eurofins Optimed in Grenoble, the Clinical Investigation Center (CIC) at Limoges University Hospital, and the CIC at Rouen University Hospital. Three additional centers will be selected shortly. Operational management and coordination of the study will be handled by the Lyon-based CRO RCTs, under the supervision of NFL Biosciences.

About NFL Biosciences: www.nflbiosciences.com

NFL Biosciences is a biopharmaceutical company based in the Montpellier region (France) developing botanical drug candidates for the treatment of addictions. NFL Biosciences' ambition is to provide new natural therapeutic solutions that are safer and more effective for people worldwide, including in low- and middle-income countries. NFL-101 and NFL-102 are standardized tobacco leaf extracts protected by five patent families. NFL Biosciences aims to offer smokers who wish to quit a natural, safe, easy-to-administer and personalized alternative. NFL Biosciences is also developing NFL-301, a natural drug candidate intended to reduce alcohol consumption and has a drug development program targeting cannabis use disorders.

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

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