

NFL BIOSCIENCES: PROMISING RESULTS OF THE PRECESTO CLINICAL TRIAL REVEALING A PROLONGED EFFECT FOR NFL-101 AND MODIFICATION OF THE STRATEGY FOR COMMUNICATING THE CESTO II STUDY RESULTS

The PRECESTO clinical trial shows a clinically relevant reduction in smoking satisfaction among smokers who do not want to quit with a more prolonged effect than expected. This further strengthens the therapeutic potential of NFL-101.

To maximize the potential of the CESTO II results, the NFL Biosciences management team intends to maintain the blind during the 12-month period following the end of recruitment. The CESTO II results would then be published in July 2024 without any preliminary reporting in the fourth quarter of 2023. This proposal is subject to validation by the Board of Directors on October 5, 2023.

NFL BIOSCIENCES (Euronext Growth Paris – FR0014003XT0 – ALNFL), a biopharmaceutical company developing botanical drugs for the treatment of addictions, is announcing that on Thursday September 21 it obtained the results of the PRECESTO study, which set out to better describe the effect of NFL-101. Alongside this, the management team will submit a proposal to the Board of Directors on October 5, 2023 in order to modify the strategy for communicating the CESTO II results, by maintaining the blind for the duration of the study. The results would be announced in July 2024.

Promising results for PRECESTO

For Bruno Lafont, Chief Operating Officer and co-founder of NFL Biosciences: *“The PRECESTO results provide a first placebo-controlled demonstration of the efficacy of NFL-101. The effect observed was more prolonged than initially expected, which is also a very positive sign as we continue moving forward with our clinical development. NFL-101 could be administered on its own or in combination with nicotine replacement therapies in order to increase their efficacy. For smokers who do not want to quit, NFL-101 could enable them to start considering an approach to quit, by generating a prolonged effect following a single dose. We would like to sincerely thank the participants in this study, the Eurofins Optimed clinical center in charge of the study’s operational deployment, and Bpifrance for its financial support”.*

PRECESTO is a placebo-controlled, randomized and double-blind Phase 2a exploratory study, with a crossover covering two periods of 28 days each, including 34 smokers who do not want to quit and have high smoking satisfaction. Each participant is his or her own control and receives, on a random and alternating basis, either NFL-101 or the placebo at the start of each of the two periods. At the end of the study, all the participants received one dose of NFL-101 and one dose of the placebo. For each participant, the order in which NFL-101 and

the placebo were administered was kept secret. For each period, the participants received the treatments on day 1 (D1) then answered the questionnaire on days 4 (D4), 7 (D7), 14 (D14), 21 (D21) and 28 (D28).

Maximum effect for NFL-101 at 28 days

Based on the observations made during the first CESTO study (phase 1), the maximum effect on reducing smoking satisfaction was expected to be recorded on D4, followed by a dissipation over around 10 days. This had determined the primary criteria chosen for PRECESTO on D4. The analysis of the PRECESTO results shows a prolonged effect with a maximum level reached at the end of the observation period (D28). This prolonged duration of action is even more promising for the future of NFL-101.

The p-value analysis for the primary criterion is combined with a post hoc analysis (calculation of exploratory p-values) over the entire period monitored. These values relate to the reduction in smoking satisfaction and show that:

- the effect of NFL-101 compared to placebo is higher over the entire monitoring period from D4 to D28 ($p < 0.01$);
- the effect of NFL-101 compared to placebo is higher ($p=0.16$) on D4, but not significant ($p > 0.05$);
- the effect of NFL-101 compared to placebo is maximal at the end of the observation period on D28 ($p < 0.01$).

Considering the study's exploratory nature, the effect on D4 will not impact the development of NFL-101 because the effect observed with PRECESTO is more prolonged, and therefore more relevant from a clinical perspective, than the expected effect.

In conclusion, the PRECESTO study shows that among participants who do not want to quit:

- NFL-101 reduces smoking satisfaction by more than a placebo;
- the effect of NFL-101 is more prolonged than expected.

Therapeutic potential confirmed by the more prolonged effect

From a clinical perspective, the more prolonged effect than expected following a single dose confirms the therapeutic potential of NFL-101, particularly since this was observed among smokers who did not want to quit. This is an extremely positive development, especially since all current smoking cessation drugs have been developed on and for smokers who want to quit. Many smokers who do not want to quit can sometimes be convinced to try a cessation method but then show low levels of observance of their treatments and quickly abandon this process. NFL-101 would offer a different solution because a single administration would generate a prolonged effect that could then be capitalized on more effectively to initiate a process to stop smoking.

These results corroborate the clinical results already mentioned in the patent application filed in the United States in October 2022. It covers the administration of NFL-101 for all smokers and particularly those who do not initiate a process to quit or those who will initiate a process to quit potentially in combination with another smoking cessation method such as nicotine replacement therapies.

Unlike PRECESTO, the Phase 2b clinical trial underway - CESTO II - is based on between two and four administrations of NFL-101 and includes smokers who want to quit and who are committed to trying to stop. The participants are expected to capitalize on this effect to succeed with their attempts to stop smoking and then remain abstinent.

Modification of the strategy for reporting the CESTO II study results

The Phase 2b CESTO II clinical trial is a placebo-controlled, randomized, double-blind study with 318 participants, monitored over 12 months, conducted at nine clinical investigation centers. The final participant was included in May 2023.

Under the planned reporting strategy, the analysis of continued abstinence rates based on the data for the first six months monitored would involve unblinding the study. This would limit the opportunities to capitalize on the data collected between the 6th and 12th months, which would be considered as open data. Maintaining the blind during the planned 12 months of monitoring would enable the CESTO II study to be taken into account in its entirety by the regulatory agencies. This could optimize the global clinical development plan.

The CESTO II results would then be published in July 2024 and there would be no interim reporting on the results.

Ignacio Faus, Chairman of the Board and Chief Executive Officer of NFL Biosciences, concludes: *“We are very satisfied with the PRECESTO results. They show a more prolonged effect than expected, which is very encouraging. They confirm our confidence in our development program. To maximize our value creation around NFL-101, we will therefore be proposing to the Board of Directors to not open the blind of CESTO II before the end of the monitoring period (12 months). The opposite approach would reduce the relevance of the data collected after six months and their use”.*

This management decision is subject to approval by the Board of Directors on October 5, 2023. The decision will be announced on October 5, 2023 in connection with the half-year earnings press release (after close of trading).

About NFL Biosciences

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). Find out more at www.nflbiosciences.com

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