PRESS RELEASE
Montpellier, October 5, 2023 - 7:00pm CET

NFL BIOSCIENCES: 2023 FIRST-HALF BUSINESS AND EARNINGS UPDATE

Promising results for the PRECESTO Phase 2a exploratory study: detailed analysis

CESTO II clinical trial (phase 2b, underway) for the drug candidate NFL-101 for smoking cessation: results to be released in July 2024

Co-development of NFL-301, a drug candidate to reduce alcohol consumption. New formulation developed and patent application filed

€3m fundraising round in January 2023 and up to €1.9m of non-dilutive financing secured in February 2023 (Bpifrance, France Relance 2030 stimulus plan)

Cash position: €3.6m as of September 30, 2023. Cash horizon secured through to the end of 2024.

NFL BIOSCIENCES (Euronext Growth Paris – FR0014003XT0 – ALNFL), a biopharmaceutical company developing botanical drugs for the treatment of addictions, is reporting its results for the first half of 2023, approved by the Board of Directors on October 5, 2023. On this occasion, NFL Biosciences looks back on its recent progress, including the promising results of the PRECESTO exploratory study, and confirms that the strategy for reporting the CESTO II results will make it possible to take into account the entire study, which will remain double blind through to 12 months of monitoring, with the results of this Phase 2b study expected in July 2024.

October 12, 2023 at 2:30 pm CET - Webinar for shareholders and investors
NFL Biosciences will discuss the promising results of the Phase 2a PRECESTO exploratory study, which demonstrated a clinically relevant effect of NFL-101 on the reduction of satisfaction with cigarettes, and the development strategy of CESTO II, its Phase 2b clinical study to evaluate the efficacy of NFL-101, currently underway on 318 smokers in 8 clinical investigation centers. NFL Biosciences executives will also discuss the development of NFL-301, a drug candidate to reduce alcohol consumption. >> Click here to register[1].

Promising results for the PRECESTO clinical trial

PRECESTO is the second study after CESTO which highlights the effect of NFL-101 in terms of reducing smoking satisfaction. The clinically relevant effect is also more prolonged than expected.

These results confirm the therapeutic interest of NFL-101 administered on its own or in combination with nicotine replacement therapies, which reduce withdrawal symptoms. They corroborate the results of the patent application filed in the United States in October 2022, increasing the probability of a patent being issued that would offer protection through to 2042 as a minimum.

A detailed presentation of the results is appended.

Optimization of the strategy for reporting on the CESTO II clinical trial

Reminder: What is the CESTO II study?

CESTO II is a multicentric, randomized, double blind and placebo-controlled phase 2b clinical trial. The trial is being conducted as follows:

- Three arms (two dose arms and one placebo arm);
- 318 smokers, aged 18 and over;
- Monitoring over 12 months (CESTO2, NCT04571216);

[1] Or type this webpage address in your browser: https://www.boursedirect.fr/fr/formations#webinaires

- The subjects receive two initial subcutaneous injections one week apart. Additional follow-up injections could be provided after three and six months for subjects who have not stopped smoking by these dates.

This study's primary objectives are to select the best dose and assess the efficacy of NFL-101 versus placebo. The main criterion is continued abstinence for four weeks and the key secondary criterion is continued abstinence for six months, measured from 15 days after the first administration and confirmed by measuring exhaled CO. Other secondary criteria are also being studied, including continued abstinence for three months, nine months and 12 months, continued abstinence at the end of the treatment for three months and six months, and continued abstinence during the last three months of the study. A number of exploratory criteria will then be analyzed.

The recruitment of subjects started in January 2022, gradually mobilizing a total of eight Clinical Investigation Centers (CIC) at CHU university hospital centers (Bordeaux, Clermont-Ferrand, Dijon, Lorient, Marseille, Montpellier, Poitiers and Rennes), as well as the Eurofins-Optimed research institute (Grenoble). The final and 318th randomization was carried out at the start of May 2023.

Data analysis and strategy for reporting the results

An analysis of the results had been announced after reaching six months of monitoring for the 318th subject. Under this reporting strategy, the analysis of continued abstinence rates based on the data for the first six months monitored involved unblinding the study. This limited 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 make it possible to maximize the use of all the data collected during the CESTO II study.

The observation of a more prolonged effect than expected during the PRECESTO study calls for a certain level of caution concerning an early review of the results leading to an unblinding before the end of the planned 12-month monitoring period. If an immune response is triggered by the administration of NFL-101, this could, in addition to an immediate effect that would support the success of an attempt to stop smoking, result in a longer-term effect in terms of preventing or managing relapses.

The CESTO II study includes a hierarchy within the criteria for analysis: there is one primary criterion, then one key secondary criterion, six secondary criteria and a number of exploratory criteria. Each of the secondary criteria has a high level of clinical relevance. Maintaining the blind during the 12 months of monitoring will then make it possible to fully capitalize on the results obtained concerning these secondary criteria.

For these three reasons, and because the CESTO II study has been the focus of the majority of the Company's resources for a total of around €8m, the decision has been taken to maximize the use of the data generated. This involves maintaining the blind through to the end of the planned observation period.

The provisional schedule is as follows:

- Final visit for the final subject included: start of May 2024
- Completion of the audits of the centers and review of the data collected: end-June 2024
- Unblinding and transfer of data for statistical analysis: mid-July 2024
- Reporting of results for the primary criterion, the key secondary criterion and the secondary criteria: end-July 2024

It is important to remember that the Company continues to be subject to the blind condition, in the same way as the subjects, the clinical centers and the Eurofins Optimed CRO.

Collaboration with the CEA to study the mechanism of action of NFL-101

In February 2023, NFL Biosciences set up a research partnership with the French Alternative Energies and Atomic Energy Commission (CEA) to study the mechanism of action of its drug candidate NFL-101.

This study is being led by the CEA's Paris-Saclay Pharmacological Neuroimaging team. It will focus on following, by positron emission tomography (PET) imaging, the modifications in the cerebral function associated with the development of tobacco addiction in mice, in order to highlight the central effects of NFL-101 treatment.

The results are expected before the end of the first quarter of 2024.

Co-development of NFL-301, a drug candidate to reduce alcohol consumption

Under the co-development agreement set up at the start of 2022, NFL Biosciences and its industrial partner Athena Pharmaceutiques have developed a prolonged-release form of kudzu plant extracts in microgranule form, NFL-301. NFL Biosciences aims to develop the first oral delivery drug based on kudzu extracts to tackle excessive alcohol consumption.

NFL is preparing a pre-IND in the United States, which is expected to be submitted before the end of the fourth quarter of 2023, with a view to obtaining FDA approval for the manufacturing process, product quality and development strategy through to the MA.

There are no plans for any significant spending on the development of NFL-301 over the next nine months. The current work primarily concerns regulatory and consultation aspects.

Extension of intellectual property

NFL Biosciences has continued moving forward with its intellectual property protection strategy for NFL-101 and NFL-301.

Patent application for NFL-301: a patent application has been filed in the United States for the formulation of NFL-301 with a commitment to extending this globally. This first patent application for NFL-301 aims to protect prolonged-release formulations of extracts of kudzu, a plant used in traditional Chinese medicine, as well as their uses for the treatment of alcohol consumption reduction.

Patent approval on NFL-101: NFL Biosciences has three patent families granting it extensive international protection for its drug candidate NFL-101, including Europe, the United States, China and Japan.

Partnership strategy

Looking beyond the studies underway (CESTO-II and the collaboration with CEA-Saclay), NFL BIOSCIENCES will focus on continuing to develop NFL-101 in partnership with pharmaceutical companies that are interested in the addiction field. As part of its normal business operations, the Company has already had discussions with several international pharmaceutical companies. Considering the positive results seen with PRECESTO, these discussions could be ramped up.

Regarding the partnership with THEMIS PHARMACEUTICALS in India, the development strategy in this country is also being reassessed following the results of the PRECESTO clinical trial.

NFL Biosciences has been invited to attend two major business conferences over the coming months, where its discussions with pharmaceutical companies and institutional investors will continue:

- Jefferies Healthcare annual conference (London, November 14-16, 2023)
- JP Morgan Healthcare annual conference (San Francisco, January 8-11, 2024)

Diversified sources of financing set up at the start of 2023: cash runway to the fourth quarter of 2024

At the start of 2023, NFL Biosciences successfully rolled out its financing strategy by applying for various grants and advances, and calling on the financial markets. In total, €4.2m were received during the first quarter of 2023 and €0.7m are still to be received as findings are generated confirming the success of the trials, representing a total secured amount of €4.9m (€3m through a capital increase and €1.9m of repayable advances or grants). This has enabled NFL Biosciences to secure financing to drive progress with its priority projects, and it has a cash horizon that now runs through to the fourth quarter of 2024.

NFL Biosciences will continue to benefit from an organization with limited fixed costs. Looking further ahead, NFL Biosciences will need additional financing which, independently or combined, may come from (1) capital increases, (2) non-dilutive financing and (3) partnerships with pharmaceutical companies.

Governance changes

On February 27, 2023, the Board of Directors appointed Dr Ignacio Faus, the Company's Chief Executive Officer, as Chairman of the Board of Directors for a period that will not exceed his term of office as a director, i.e. through to the end of the Ordinary General Shareholders' Meeting held in 2024 to approve the financial statements for the year ending December 31, 2023.

On June 27, 2023, the shareholders approved the appointment of Ms Dominique Côté as an independent director. Her three-year term of office will expire at the end of the Ordinary General Shareholders' Meeting held in 2026 to approve the financial statements for the year ending December 31, 2025.

2023 first-half earnings

The financial statements for the first half of 2023 (January 1, 2023 – June 30, 2023), prepared in accordance with French GAAP, were approved by the Board of Directors during its meeting on October 5, 2023. The accounts have been subject to a limited review by the statutory auditors and the HY financial report will be published on October 6, 2023 after the market closing.

Corporate accounts (€)	**Jun 30, 2023** *(6 months)*	**Jun 30, 2022** *(6 months)*	**Dec 31, 2022** *(12 months)*
Net revenues	-	-	-
Total operating income	94,777	5	22
EBIT	(2,382,387)	(1,300,816)	(3,083,170)
Financial income (expense)	71,388	107,829	182,831
Non-recurring income (expense)	-	-	39,025
Corporate income tax	(200,349)	(121,632)	(417,829)
Net income	**(2,110,650)**	**(1,071,354)**	**(2,443,484)**

Shareholders' equity	1,907,772	2,216,127	843,996
Intangible assets (patents)	122,785	139,577	135,784
Liabilities	2,461,532	736,661	1,478,510
- Of which financial liabilities	72,727	85,007	83,256
- Of which operating liabilities	2,283,580	651,654	1,395,254
- Of which prepaid income	105,225		
Cash and cash equivalents	3,359,459	2,044,267	1,053,581
Balance sheet total	**5,578,281**	**3,043,765**	**2,395,484**

During the first half of 2023, NFL Biosciences recorded €94K of operating income. This amount corresponds to part of the operating grant awarded by Bpifrance (total amount of €200K). Still in the clinical trials development stage, NFL Biosciences did not record any revenues during the last two years.

In line with the resources allocated to drive progress with the programs presented above, and the Company's operations, EBIT came to €(2.4)m for the first half of 2023, compared with €(1.3)m for the same period in 2022. Payroll and social security contributions totaled €307K for four people at June 30, 2023, compared with €254K for three people at June 30, 2022.

During the first half of 2023, NFL Biosciences recorded a research tax credit (CIR) of €203K, compared with €101K for the first half of 2022, with this change reflecting the ramping up of its research programs. Over the period, NFL Biosciences received €161K of prefinancing from the research tax credit reported in 2022, which totaled €397K.

Financial income and expenses for the first half of 2023, which came to €71K, compared with €108K one year earlier, take into account the remuneration from investments of cash surpluses for €32K and the reversal of depreciation concerning the liquidity agreement for €39K. As a result, NFL Biosciences recorded €(2.1)m of net income over the period, compared with €(1.1)m at June 30, 2022.

At June 30, 2023, the Company had €1.9m of shareholders' equity and €3.4m of available cash. Cash and cash equivalents reflect the capital increase carried out at the end of January 2023 (€3.0m), as well as the advances granted by Bpifrance for the NFL-101 and NFL-301 clinical trials (€1.1m).

In the third quarter of 2023, the Company received €550K of proceeds from the exercising of the BSA and BSPCE warrants from end-June and July 2023 for a total of €550K, as well as the first installment of the grant for the PRECESTO study for €140K.

Outlook for 2023

Dr Ignacio Faus, NFL Biosciences Chairman of the Board and CEO: *"We are very satisfied with the progress made in the past few months. We carried out the PRECESTO Phase 2a clinical trial while respecting the budget and timeframes that were set. The results achieved with PRECESTO, which are presented in detail in this press release, are very promising. PRECESTO is the first placebo-controlled clinical trial for NFL-101. We have shown that NFL-101 has a greater effect than placebo on reducing smoking satisfaction. For CESTO II, we also aim to complete this clinical trial on budget and on time. After reviewing the PRECESTO results, the Board of Directors decided to modify the schedule for reporting the CESTO-II results with a view to maximizing the study's potential.*

With regard to NFL-301, our product for reducing alcohol consumption, we have made progress with developing a new product formulation. Over the next nine months our development will continue moving forward.

As we have already mentioned, NFL Biosciences has a very robust approach in place for managing fixed costs. We use the funds that are allocated to us with the greatest care and we focus them primarily on funding scientific studies. Thanks to this, the Company's cash horizon can be extended through to the end of 2024.

Given the small size of the company, we will prioritize partnerships for the development of NFL-101 beyond the studies that are underway. Discussions have been started with major American and European pharmaceutical companies and, considering the positive results achieved with PRECESTO, they could now be accelerated".

Next financial date: Shareholder and investor webinar: October 12 at 2:30pm CET. Click on this link or go to: https://www.boursedirect.fr/fr/formations#webinaires to register (you don't need to be a Bourse Direct customer to attend).

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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APPENDIX: Detailed results of the PRECESTO Phase 2a exploratory study

Recap: What is PRECESTO?

PRECESTO is a monocentric, 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, with complete independence, the modified Cigarette Evaluation Questionnaire (mCEQ) on days 4 (D4), 7 (D7), 14 (D14), 21 (D21) and 28 (D28).

The objective of PRECESTO, as mentioned in the protocol, is to "*assess the efficacy of NFL-101 to reduce the positive reinforcement of cigarettes as measured by the subscale assessing smoking satisfaction (questions 1, 2 and 12) from the mCEQ versus a placebo*". The primary criterion resulting from this objective was chosen as "the *Smoking Satisfaction subscale (items 1, 2 and 12) from the mCEQ measured on D4"*.

mCEQ, a leading international questionnaire for measuring the effects of smoking

The mCEQ is an international questionnaire that is completed independently. The study's participants, smokers who have high smoking satisfaction and do not wish to quit, answer 12 questions marking the number that best represents how smoking makes them feel (1-not at all, 2-very little, 3-a little, 4-moderately, 5-a lot, 6-quite a lot, 7-extremely). The questions are as follows:

1. Was smoking satisfying?
2. Did cigarettes taste good?
3. Did you enjoy the sensations in your throat and chest?
4. Did smoking calm you down?
5. Did smoking make you feel more awake?
6. Did smoking make you feel less irritable?
7. Did smoking help you concentrate?
8. Did smoking reduce your hunger for food?
9. Did smoking make you dizzy?
10. Did smoking make you nauseous?
11. Did smoking immediately relieve your craving for a cigarette?
12. Did you enjoy smoking?

The questionnaire uses three multi-item subscales and two single items: "*"Smoking Satisfaction*" (items 1, 2, and 12); "*Psychological Reward*" (items 4 through 8); "*Aversion*" (items 9 and 10); "*Enjoyment of Respiratory Tract Sensations*" (item 3); and "*Craving Reduction*" (item 11). Scores for each subscale are calculated as the mean of the individual item responses or the single item. Each score may therefore vary from 1 to 7. Higher scores indicate greater intensity on that scale.

The participants in the PRECESTO study completed this questionnaire themselves remotely using their computer. They were asked to refer to the cigarette that they smoked the previous day after dinner in order to standardize, insofar as possible, the change in perceptions over time for each subject.

Rationale for conducting the PRECESTO study

The PRECESTO study makes it possible to better understand the activity of NFL-101 and specifically this product's efficacy in terms of reducing smoking satisfaction.

In the fight against smoking, reducing smoking satisfaction is essential: to successfully stop smoking, it is vital to tackle both smoking satisfaction and nicotine withdrawal. In terms of withdrawal, there are nicotine replacement therapies, but to tackle satisfaction, there are no effective medicinal products that do not have side effects.

The study is important in relation to NFL BIOSCIENCES' development plan for three reasons:

1. The confirmation of the observations made during the CESTO Phase 1 study was expected, but this time with statistical calculations and comparison against a placebo. These observations described a reduction in smoking satisfaction following the administration of NFL-101.
2. Including the CESTO II study, this will take the number of controlled clinical studies measuring the effects of NFL-101 up to three. As NFL Biosciences conducts more studies corroborating the product's efficacy, this could further strengthen its appeal for pharmaceutical firms that might be likely to acquire licenses.
3. The PRECESTO results were awaited in order to further strengthen the patent application filed in the United States in October 2022 which, as mentioned in the press release from November 2, 2022, had been submitted "before the launch of dedicated clinical trials". If the patent is issued, protection would be ensured through to 2042 as a minimum. This application 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.

Results of the PRECESTO Phase 2a exploratory clinical study

It was previously verified that the statistical analysis could be carried out on all subjects and for the 2 sequences jointly. The data are processed by calculating the least squares mean taking into account the study's crossover design and in accordance with the PRECESTO protocol.

Smoking satisfaction is the average for the answers to questions 1, 2 and 12 from the questionnaire. On inclusion, the average score for smoking satisfaction was 6.12 (standard deviation 0.77).

The PRECESTO results are as follows:

- **Concerning the reduction in smoking satisfaction generated by NFL-101:** According to the observations from the CESTO Phase 1 clinical trial, a rapid effect reaching a maximum level at D4 then dissipating over 10 days was expected. The effect observed with PRECESTO is different (Figure 1): there is an effect on D4 (average reduction -0.810; confidence interval (-1.139; -0.481)) and this effect then grows stronger on a relatively linear basis through to the final measurement on D28 (average reduction -1.261; confidence interval (-1.590; -0.932)). The average level of smoking satisfaction which, on inclusion, was between quite a lot and extremely, was reduced to between moderately and a lot on D28, which represents a clinically relevant reduction.
- **Concerning the effect of NFL-101 versus placebo and the reduction in smoking satisfaction:** The placebo effect is significant, but still lower than the effect of NFL-101 throughout the observation (Figure 1 below). It increases less quickly from D7, then decreases from D21 through to D28 (average reduction -0.947; confidence interval (-1.277; -0.618)). Regarding the difference in effects between NFL-101 and the placebo (Figure 2), this did not reach significance on D4 (> 0.05) and the exploratory p-values are 0.0003 (average difference -0.188; confidence interval (-0.289; -0.087)) over the entire period monitored from D4 to D28 and 0.007 (average difference -0.314; confidence interval (-0.540; -0.088) on D28.
- Concerning the specific effect on the other mCEQ subscales and items in terms of secondary criteria: Exploratory p-values have not been calculated for these criteria. The limitations of the study, which are presented in detail below, may provide an explanation, particularly for the criterion relating to craving.

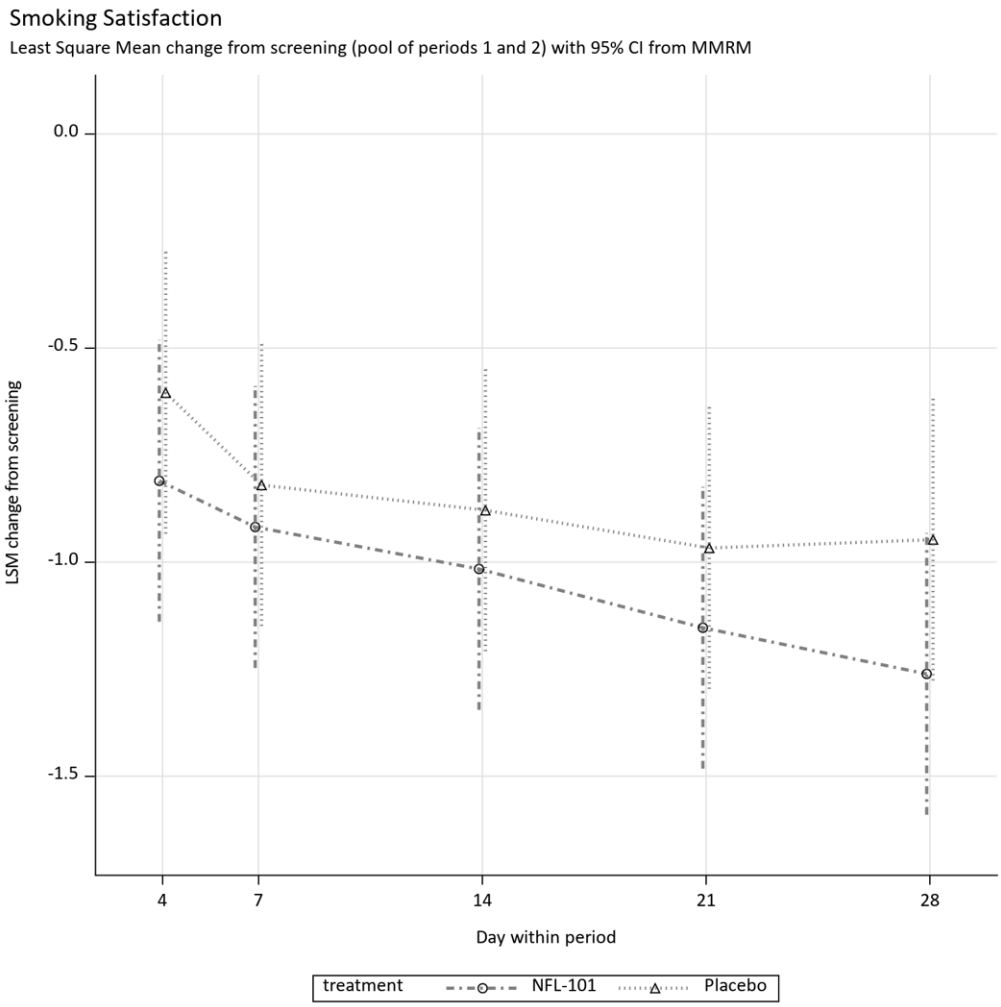

Figure 1 – Reduction in smoking satisfaction with NFL-101 and the placebo

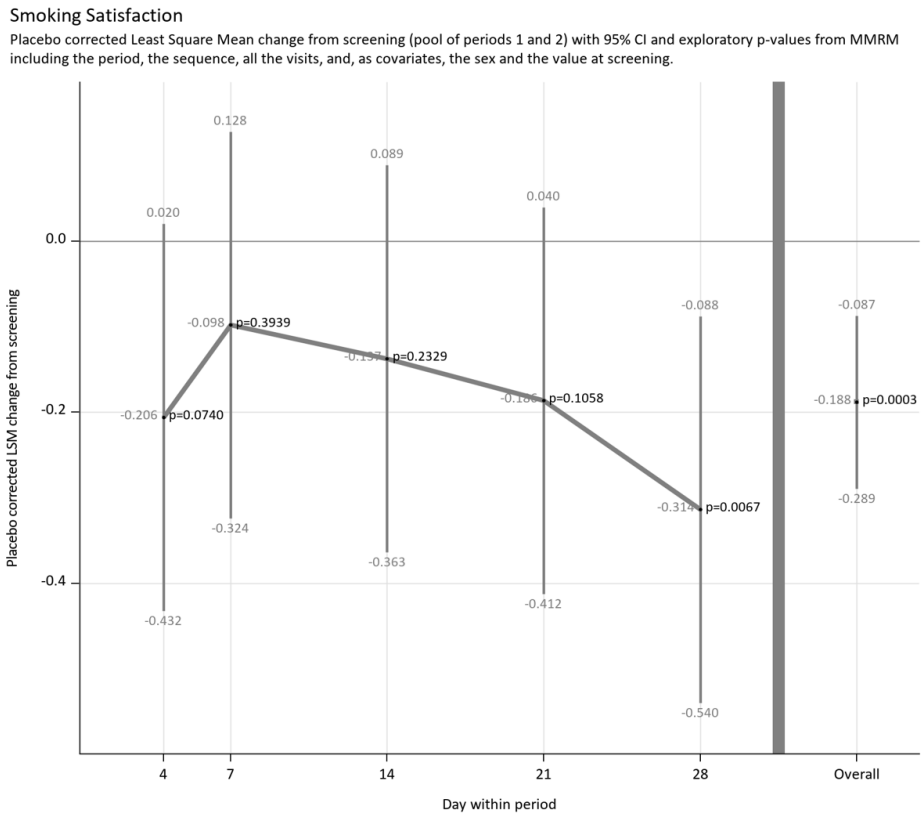

Figure 2: Difference between the reduction in smoking satisfaction with NFL-101 and the placebo, including the exploratory p-values

Clarifications concerning the p-values:

For the p-values of 0.0003 and 0.007, this means that if there were no real effects or differences in the data, there would be just a 0.03% and 0.7% chance of obtaining data that were as different as those observed.

The calculation of the exploratory p-values carried out with a post hoc analysis was limited to the study's primary objective. This approach makes it possible to reduce the risks of obtaining low p-values resulting from chance, which may be the case when p-values are calculated on a number of criteria or even by cross-referencing the criteria in relation to one another. These calculations make it possible to adapt to the observation of a more prolonged effect than expected, while respecting the spirit of the protocol and its primary objective.

Limitations of the PRECESTO study

With the PRECESTO study, the mCEQ was completed by smokers who did not want to quit and who smoked *ad libitum ("as often as desired")*. It is recognized that reducing the consumption of cigarettes or stopping smoking generates significant effects on the perceptions and the behavioral responses associated with cigarette consumption. The crossover design did not make it possible to include subjects who were going to reduce their consumption or make attempts to stop as this would have resulted in a too significant carry-over effect (persistence or continuation of an effect) from period 1 to period 2. In addition, recruiting subjects who wanted to stop smoking would have involved the risk of information loss if they stopped, because subjects who stop smoking can no longer assess their level of smoking satisfaction and therefore complete the questionnaire. By recruiting smokers who do not want to stop smoking, it was more difficult to show an effect for NFL-101 on certain criteria such as craving as this was regularly reduced by the cigarettes smoked without any constraints.

Comparison of the PRECESTO and CESTO II studies

The two clinical trials are very different.

	PRECESTO (completed)	CESTO II (underway)
Type of study	Phase 2a exploratory	Potentially Phase 2b confirmatory
Objective	Demonstrate an effect on reducing smoking satisfaction	Demonstrate efficacy for smoking cessation
Evaluation criterion	Answers to mCEQ questions	Declaration of continued abstinence confirmed by measuring exhaled CO
Subjects	Smokers who do not want to quit	Smokers who want to quit
Behavior	*Ad libitum* smoking	Make an attempt to stop
Design	Crossover (2 periods, 2 treatments: placebo, NFL-101)	Parallel arms (placebo, NFL-101 dose 1, NFL-101 dose 2)
Number of subjects	34	318
Number of administrations of NFL-101	1	2 to 4
Monitoring timeframe	2 periods of 28 days	12 months

It is also important to note that there is no clinical data available from previous research making it possible to calculate a level of efficacy for smoking cessation based on continued abstinence through a reduction in smoking satisfaction.

Conclusion: a first placebo-controlled clinical trial with promising results

This exploratory study:

- shows that a single administration of **NFL-101 reduces smoking satisfaction in a clinically relevant way and with a more prolonged effect than expected**, which confirms the therapeutic interest of NFL-101 administered on its own or in combination with nicotine replacement therapies, which reduce withdrawal symptoms;
- represents a second clinical trial after CESTO revealing **an effect on reducing smoking satisfaction, and on a placebo-controlled basis this time**, the level of proof of the effect of NFL-101 is strengthened;

- corroborates the clinical results already mentioned in the patent application filed in the United States in October 2022 and **further strengthens the solidity of the patent application and the probability of a patent being issued**, which would result in protection through to 2042 as a minimum.

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