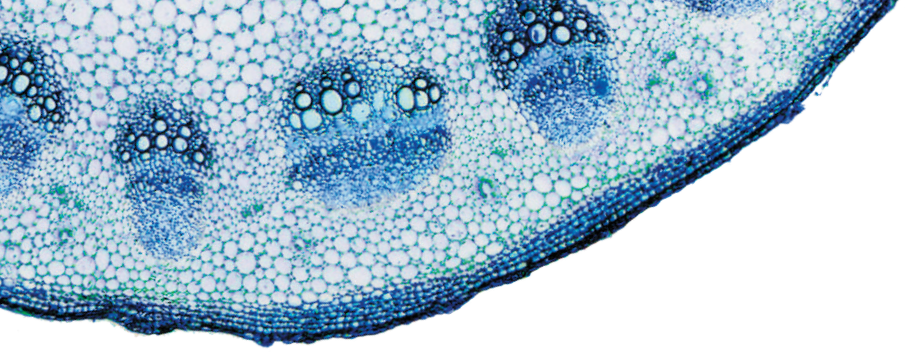

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Valbiotis announces the major success of the Phase II HEART clinical study: the patented plant-based active substance TOTUM•070 proves its efficacy against hypercholesterolemia, a cardiovascular risk factor

- This randomized, placebo-controlled Phase II clinical study with TOTUM•070 achieved its objective of reducing LDL cholesterol (primary endpoint) and confirmed the very good tolerance of this active substance.
- As early as 3 months of supplementation, the results showed a significant reduction in blood levels of LDL cholesterol (-13%) and triglycerides (-14%).
- Comprehensive data from the HEART study will be presented at international scientific conferences.
- TOTUM•070 covers the unmet need for the management of untreated mild to moderate hypercholesterolemia and addresses the expectations expressed by patients and healthcare professionals in the market studies[1] conducted by Valbiotis.
- Valbiotis sets the objective of commercialization based on these Phase II results, no later than the first half of 2024, and is intensifying its discussions with major health and nutrition players.
- Hypercholesterolemia is one of the major and most widespread cardiovascular risk factors, with a prevalence of 39% in the adult population worldwide, 48% in North America, 54% in Europe[2], and 62% in France[3], i.e., 174 million adults in the United States and the 5 major European countries alone[4].

La Rochelle, June 13, 2022 (6:30 pm CEST) - **Valbiotis** (FR0013254851 – ALVAL, PEA/SME eligible), a Research and Development company committed to scientific innovation for preventing and combating metabolic diseases, **announces the major success of the Phase II HEART clinical study, which achieved its objective of reducing blood LDL cholesterol level (primary endpoint) with TOTUM•070 and confirmed the very good tolerance of this active substance. This multicentric, randomized, placebo-controlled, double-blind study was conducted in 120 volunteers with mild to moderate untreated hypercholesterolemia and tested a daily dose of 5 g in two intakes for 6 months. As early as three months of supplementation, TOTUM•070 significantly reduced blood levels of LDL cholesterol (-13%, p<0.01), and triglycerides (-14%, p<0.05), compared to placebo. Excess of these blood lipid markers is a cardiovascular risk factor.**

Thanks to these very good clinical results, TOTUM•070, an innovative patented active substance derived from food plant extracts, without phytosterols or red yeast rice, becomes a clinically proven non-drug option for people with untreated mild to moderate LDL hypercholesterolemia, as a complement to lifestyle and dietary recommendations.

[1]Market studies conducted by IFOP and A+A institutes for Valbiotis in 2022
[2]Global Health Observatory, WHO (2018, data 2008)
[3]Wilkins E et al., European Cardiovascular Disease Statistics 2017. European Heart Network, Brussels
[4]AEC Partners, Elevated LDL cholesterol preliminary market estimation, 2020

Sébastien PELTIER, Chairman of the Board of Directors at Valbiotis, comments: *"This clinical success exceeds our expectations, as it shows a significant reduction in LDL cholesterol, our primary objective, as well as blood triglycerides, which are associated with cardiovascular risk. Given these positive results, the quality of the scientific data already obtained and the need for solutions for untreated patients, we have decided to market TOTUM•070 after these Phase II results. In this perspective, we are already engaged in the search for commercial partnerships with a commercialization horizon no later than the first half of 2024. The TOTUM•070 scientific package, combined with our market studies with patients and healthcare professionals, supports this ambition. At the same time, we will be preparing a final Phase II/III clinical step to obtain a health claim that will enhance the value of this active substance."*

Results of the Phase II HEART clinical study

The HEART clinical study was a multicentric, international, randomized, placebo-controlled, double-blind study involving 120 people with untreated mild to moderate hypercholesterolemia, with blood level of LDL cholesterol between 130 mg/dl and 190 mg/dl. The participants were divided into two equivalent arms of 60 people, supplemented for six months with a daily dose of 5 g of TOTUM•070 or a placebo, in two intakes.

After a 6-month supplementation, the study achieved its objective of significantly reducing LDL cholesterol in the blood (primary endpoint, -9% *versus* placebo, p<0,01[5]). As early as 3 months of supplementation with TOTUM•070, the results showed a significant lipid-lowering effect, with:

- a significant 13% reduction in blood LDL cholesterol level, compared to placebo (p<0.01[5]);
- a significant 14% reduction in blood triglyceride level, compared to placebo (p<0.05[5]).

In clinical practice, the reduction of LDL blood cholesterol as early as 3 months of supplementation is an expected benefit by patients and healthcare professionals[1]. The HEART study also demonstrates the persistent lipid-lowering effect at 6 months.

In addition, the study confirmed the safety and very good tolerance of TOTUM•070.

The comprehensive data from the study will be presented at international scientific conferences.

Prof. Jean-Marie BARD, professor of biochemistry and pharmacy hospital practitioner at Nantes University Hospital and at the West Institute of Cancerology (*Institut de Cancérologie de l'Ouest*), scientific advisor of the HEART study, comments: *"The results of the HEART study are very positive. They demonstrate the efficacy of TOTUM•070 on blood LDL cholesterol, a well-known cardiovascular risk factor, and a lipid-lowering effect on triglycerides, associated with cardiovascular risk. The study also confirms the very good tolerance of this active substance: this is an important issue in lipid-lowering strategies, as emphasized by international learned societies. With these data, TOTUM•070 is therefore a very good solution to address the lack of reliable options adapted to mild to moderate hypercholesterolemia, for which only lifestyle and dietary recommendations are currently proposed."*

Murielle CAZAUBIEL, Head of Development, Medical, Regulatory and Industrial Affairs, member of Valbiotis Board of Directors, adds: *"These results exceed the ambitions we had announced for TOTUM•070. It was a challenge to demonstrate the relevance of a plant-based active substance in such a demanding clinical field, in line with the preclinical data we had already published. This has been achieved. We are very proud of this achievement and would like to thank all the people involved in this study, both professionals and volunteers: thanks to them, TOTUM•070 is now a clinically proven and well-tolerated non-drug option against high cholesterol, in the context of cardiovascular risk prevention."*

[5]Intention-to-treat analysis (ITT)

The efficacy and mode of action data previously obtained for TOTUM•070

The results of the HEART clinical study are consistent with the preclinical efficacy data already obtained in dyslipidemia models and presented at the American Heart Association meeting in 2021. This work showed a significant dose-dependent reduction in LDL cholesterol and triglycerides.

In addition, clinical and preclinical studies (positive clinical results published March 29, 2022) have documented the multi-target mode of action of TOTUM•070. According to these data, the lipid-lowering effect of TOTUM•070 is based:

- at the intestinal level, on the reduction of the absorption of cholesterol;
- at the hepatic level, on the reduction of *de novo*[6] cholesterol synthesis.

In these studies, additional liver benefits were observed, with a decrease in cholesterol storage and a decrease in gene expression of inflammatory markers.

Targeting the marketing of the product by the first half of 2024 at the latest

Given the need for clinically proven non-drug options, as highlighted by market studies with patients and healthcare professionals, the Company sets the objective of commercialization no later than the first half of 2024, based on all of these Phase II results, and is intensifying its discussions with major players in the health and nutrition sectors.

Following the finalization of the industrial scale-up, TOTUM•070 will be offered in two galenic forms (capsules or powder for dilution), to be taken twice daily. It will be available over the counter in pharmacies (pharmacy stores or online) for patients and consumers. Available without a prescription, TOTUM•070 may be advised by healthcare professionals.

From a regulatory standpoint, TOTUM•070 can already be marketed in Europe, after notification to the DGCCRF in France (mutual recognition applicable for other European Union countries). Regulatory processes for North America and other areas are ongoing.

Mild to moderate hypercholesterolemia: patients and physicians awaiting solutions

Excess blood LDL cholesterol is the primary cause of atherosclerosis, a serious disease of the arteries with debilitating and potentially deadly cardiovascular complications (stroke, heart attack, arterial diseases, amongst others). Given the risk, hypercholesterolemia must be managed according to international guidelines, to reduce blood LDL cholesterol levels.

How is it managed?
Other than essential lifestyle changes, therapeutic strategies are defined for each patient following an assessment of their overall cardiovascular risk level: smoking, blood pressure, overweight, age, individual and family history, amongst others.

- For the most at-risk patients, long-term drug treatments (such as statins) are recommended and effective.
- For patients with moderate hypercholesterolemia or a lower overall risk, the initiation of these treatments is discussed between the physician and the patient depending on their benefit/risk ratio.
- For patients with a mild form and a moderate risk, the benefit/risk ratio of the treatment is unfavorable.

A real need for solutions for patients at moderate risk
Between lifestyle-dietary rules alone and long-term treatments, there is a lack of effective, well-tolerated intermediary solutions for managing cholesterolemia, preventing it from worsening, and delaying the initiation of treatment. Confronted with this need expressed by physicians and their patients, international guidelines recognize the potential benefit of non-drug products - in particular food - but highlight the lack of clinical proof so far.

[6]Cholesterol can be supplied by the diet or produced by the body itself ("*de novo* synthesis").

A world with high cholesterol

And yet the epidemiological data is worrying: according to the WHO, hypercholesterolemia affects 39% of adults in total worldwide with its prevalence reaching 54% in Europe and 48% in North America[2].
In France, 62% of adults have a total cholesterol level above 2.0 g/l[3].
Overall, it is estimated that 174 million adults in the United States and the 5 major European countries have excessive LDL cholesterol levels[4].

About Valbiotis

Valbiotis is a Research & Development company committed to scientific innovation for preventing and combating metabolic and cardiovascular diseases in response to unmet medical needs.
Valbiotis has adopted an innovative approach, aiming to revolutionize healthcare by developing a new class of health nutrition products designed to reduce the risk of major metabolic and cardiovascular diseases, relying on a multi-target strategy enabled by the use of plant-based terrestrial and marine resources.
Its products are intended to be licensed to players in the health sector.
Created at the beginning of 2014 in La Rochelle, the Company has forged numerous partnerships with leading academic centers. The Company has established three sites in France – Périgny, La Rochelle (17) and Riom (63) – and a subsidiary in Quebec City (Canada).
Valbiotis is a member of the "BPI Excellence" network and has been recognized as an "Innovative Company" by the BPI label. Valbiotis has also been awarded "Young Innovative Company" status and has received major financial support from the European Union for its research programs via the European Regional Development Fund (ERDF). Valbiotis is a PEA-SME eligible company.
For more information about Valbiotis, please visit: www.valbiotis.com

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