

VALBIOTIS presents the first market data on untreated LDL-hypercholesterolemia for TOTUM-070, and announces the initiation of the Phase II clinical study HEART

TOTUM-070 is being developed particularly for individuals with untreated hypercholesterolemia, with LDL-cholesterol levels up to 190 mg/dL associated with moderate overall cardiovascular risk. It responds to an unmet medical need for this population;

TOTUM-070 has high potential in the market for non-drug LDL-cholesterol products, which is estimated at 1.2 billion euros (USA + top 5 Europe)¹;

The clinical study HEART on TOTUM-070, a Phase II randomized placebo-controlled and double blind study, has just been initiated in accordance with the road map, the study protocol having been submitted to the French health authorities.

La Rochelle, October 27, 2020 (5:40 pm CET) VALBIOTIS (FR0013254851 - ALVAL, eligible for the PEA/SME), a Research & Development company committed to scientific innovation for preventing and combating metabolic diseases, presents the target market for its active substance TOTUM-070, for untreated mild to moderate LDL-hypercholesterolemia. The Phase II clinical study has been initiated and will begin as soon as authorizations are received from the French National Agency for the Safety of Medicines and Health Products (ANSM) and the French Committee for the Protection of Persons (CPP).

TOTUM-070 is an innovative active substance derived from food plant extracts, without phytosterols nor red yeast rice, developed to act on lipid metabolism in individuals with hypercholesterolemia.

Once development is complete, this new Health Nutrition product will be positioned mainly for people with LDL-hypercholesterolemia, at levels up to 190 mg/dL, with a moderate overall cardiovascular risk. TOTUM-070 could be advised to this large population for whom no first-line treatment is currently recommended. It aims at lowering LDL-cholesterol levels and thereby reducing overall cardiovascular risk.



Dr. Josep INFESTA, MD
Head of business
Development at VALBIOTIS²

"Excess LDL-cholesterol is a widespread cardiovascular risk factor, found in nearly 40% of the world's adult population, based on WHO data. In line with our prevention strategy, our active substance TOTUM-070 is a new solution for at-risk individuals, yet untreated according to the current guidelines. Market data supports our analysis: nearly 1.2 billion euros are spent on non-drug products for LDL-cholesterol in the USA and the 5 major European countries. TOTUM-070 is expected to show strong efficacy at the end of its clinical development, which would give it a clear advantage in the untreated hypercholesterolemia market."

The Phase II randomized, double-blind, placebo-controlled clinical study will include 120 people with untreated moderate hypercholesterolemia between 130 and 190 mg/dL. Participants will be divided into two equivalent arms of 60 people, receiving TOTUM-070 or placebo for six months. The primary endpoint of the study will be the reduction of blood LDL-cholesterol levels, with several secondary endpoints of interest. The study has just been initiated, the protocol having been submitted to the ANSM and CPP. The first subject's first visit is scheduled for the first quarter of 2021, and results are expected by the end of 2021 or early 2022.

Following VALBIOTIS' business model, the objective is to conclude a partnership and licensing agreement for the marketing of TOTUM-070, with a global health player.

Untreated hypercholesterolemia: a major market for non-drug products

In the 5 major European countries (France, Germany, Italy, Spain, United Kingdom) and the United States, an estimated 174 million adults have high LDL-cholesterol^{1,3}. The general public in these countries is very familiar with this health issue, supporting wide screening, and diagnosis rates are high, approaching 50%. The diagnosed population currently stands at 83 million people¹.

However, and in accordance with recommendations, only subjects at high overall cardiovascular risk benefit from treatment. A large proportion of those diagnosed therefore already uses non-drug products, particularly in the USA (54% of individuals diagnosed), the UK (58%), France (34%) and Germany (35%)¹. The market for such LDL-cholesterol products is currently estimated at nearly €1.2 billion in these regions, including more than €600 million in the United States¹.

	USA	France	Germany	United-Kingdom	Italy	Spain
Persons aged more than 25 years old with elevated LDL-cholesterol ³ , (millions)	64.1	23.1	30.5	22.2	19.5	14.7
Persons diagnosed with elevated LDL-cholesterol (millions)	30.6	11.9	13.5	10.6	9.3	10.6
% of persons aged more than 25 years old, diagnosed and already using non drug products against LDL-cholesterol	54%	34%	35%	58%	14%	14%

LDL-hypercholesterolemia treatment: the need for effective products from the earliest stages

According to current European and American recommendations (ESC, AAC, EAS⁴), the treatment of LDL-hypercholesterolemia is individually defined, based on LDL-cholesterol levels and overall cardiovascular risk^{5,6}. The SCORE (Systematic Coronary Risk Evaluation) index, for example, classifies patients according to five risk levels, from "low" to "very high", taking into account each individual's cardiovascular risk factors (tobacco, alcohol, overweight, high blood pressure, etc.).

The prescription of first-line lipid-lowering treatment⁷ is currently indicated for patients with high cardiovascular risk and/or high LDL-cholesterol levels^{5,6}.

The vast majority of people at lower or moderate risk are first advised to make lifestyle changes (diet and physical activity), with the prospect of treatment if blood LDL-cholesterol levels remain uncontrolled.

² External consultant

³ Blood levels of LDL-cholesterol greater than 100 or 130 mg/dL, based on available data

⁴ European Society of Cardiology, American Association of Cardiology, European Atherosclerosis Society

⁵ 2019 ESC/EAS guidelines for the management of dyslipidaemias: Lipid modification to reduce cardiovascular risk

⁶ 2018 Guideline on the Management of Blood Cholesterol, a report from the American College of Cardiology / American Heart Association, Journal Of The American College Of Cardiology, 2019

⁷ Treatment to reduce the level of lipids in the blood (e.g., cholesterol and triglycerides)



Professor Jean-Marie Bard, PharmD, PhD, University Professor and Hospital Practitioner at Nantes University Hospital, scientific advisor for the Phase II clinical study

"We now know how to treat high-risk patients with effective drugs, generally statins, which have a favorable risk/benefit ratio in such cases. Nevertheless, individual variability exists and adverse events have been identified, leading to non-compliance and treatment discontinuation. Moreover, for all other people, with no imminent cardiovascular risk, only lifestyle changes can be proposed, with variable results. For these two populations, we need additional effective and well-tolerated clinical tools that rapidly reduce LDL-cholesterol before the situation deteriorates. TOTUM-070 could very well meet this need."

LDL-CHOLESTEROL, A KEY CARDIOVASCULAR RISK FACTOR

According to international scientific societies, LDL-cholesterol is considered the number one risk factor for atherosclerosis⁶.

When present in excessive concentrations in the blood, LDL-cholesterol leads to the formation and deposition of atheromatous plaques (essentially the accumulation of fats and blood cells) on artery walls: this is atherosclerosis, a severe cardiovascular disease that causes strokes, myocardial infarction and peripheral artery disease⁵. Atherosclerosis is associated with very high morbidity and mortality: the rupture of an atheromatous plaque, for example, is the cause of 80% of sudden deaths in adults⁸.

Globally every year, excess blood LDL-cholesterol is directly responsible for 4.3 million deaths and the loss of 88.7 million years of healthy life⁹.

⁶ www.inserm.fr/information-en-sante/dossiers-information/atherosclerose

⁹ GBD 2015 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2015: A systematic analysis for the Global Burden of Disease study 2015. *Lancet*. 2016.

ABOUT VALBIOTIS

VALBIOTIS is a Research & Development company committed to scientific innovation for preventing and combating metabolic diseases in response to unmet medical needs.

VALBIOTIS has adopted an innovative approach, aiming to revolutionize healthcare by developing a new class of nutritional health solutions designed to reduce the risk of major metabolic diseases, based on a multi-target approach and made possible by the use of plant-based ingredients.

Its products are intended to be licensed to players in the health world.

VALBIOTIS was founded in La Rochelle in early 2014 and has formed numerous partnerships with top academic centers. The Company has established three sites in France – Périgny, La Rochelle (17) and Riom (63).

VALBIOTIS is a member of the “BPI Excellence” network and received the «Innovative Company» status accorded by BPI France. VALBIOTIS has also been awarded “Young Innovative Company” status and has received major financial support from the European Union for its research programs by obtaining support from the European Regional Development Fund (ERDF). VALBIOTIS is a PEA-SME eligible company.

Find out more about VALBIOTIS: www.valbiotis.com

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This press release contains forward-looking statements about VALBIOTIS’ objectives, based on rational hypotheses and the information available to the company at the present time. However, in no way does this constitute a guarantee of future performance, and these projections can be reconsidered based on changes in economic conditions and financial markets, as well as a certain number of risks and doubts, including those described in the VALBIOTIS core document, filed with the French Financial Markets Regulator (AMF) on 31 July 2020 (application number R20-018), these documents being available on the Company’s website (www.valbiotis.com).



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