Press Release

Valbiotis announces completion of recruitment for the Cardio-Liver clinical study conducted with TOTUM•448 for metabolic liver diseases (MASLD)

- **The last volunteer was included in the Cardio-Liver study ; All 70 participants have now been recruited in the randomized, double-blind, placebo-controlled Cardio-Liver study;**
- **Conducted as part of a research chair in partnership with Laval University (Quebec), this clinical study assesses the effect of TOTUM•448 on multiple risk factors involved in the early stages of metabolic liver diseases (MASLD);**
- **Results from the Cardio-Liver study will be available in the second half of 2026;**
- **TOTUM•448 will already benefit upon market launch from a fully operational commercial ramp-up in France and from resources already in place within the joint venture in Asia.**

La Rochelle, December 8, 2025 (5:40 PM CEST) – **Valbiotis** (FR0013254851 – ALVAL, PEA/PME eligible), a French laboratory specialized in the design and distribution of scientifically tested dietary supplements to support health at every stage of life **announces completion of recruitment for the Cardio-Liver clinical study, with 70 participants enrolled. The study will evaluate the effect of TOTUM•448 on multiple risk factors involved in the early stages of metabolic liver diseases (MASLD)** and in particular MASH (formerly NASH)**. The results of the Cardio-Liver study will be available in the second half of 2026.**

The Cardio-Liver clinical study is a randomized, double-blind, placebo-controlled trial enrolling 70 participants with hepatic steatosis (without significant associated fibrosis) and who are overweight or obese. Participants are divided into 2 equivalent groups of 35 people, supplemented for 4 months with **TOTUM•448** (4.28 g/day) or a placebo. The Cardio-Liver study evaluates not only the reduction of hepatic steatosis, a risk factor for metabolic liver diseases (MASLD), but also a large number of metabolic parameters linked to the development and worsening of this condition. This trial is expected to confirm the results already obtained in the bioavailability and mechanism-of-action clinical study, completed in the first quarter of 2025.

A major study in this indication

The Cardio-Liver trial stands out for the exceptional scale and depth of its clinical investigations. Conducted in partnership with a leading academic center, the study uses highly advanced measurement techniques to explore several levels of MASLD pathophysiology, a complex and multifactorial indication. Beyond the precise quantification of hepatic steatosis using advanced imaging, Cardio-Liver includes a comprehensive evaluation of cardiometabolic and inflammatory parameters, a detailed assessment of body composition, and an analysis of liver status by elastography.

The study is also noteworthy for its integration of innovative approaches, including the study of gut microbiota and the analysis of different "omic" profiles carried out on blood samples and, for some participants, on liver biopsies. This rare level of investigation in a nutritional supplementation study provides a comprehensive and integrated view of the potential effects of TOTUM•448. It will make it possible to not only assess with unprecedented accuracy its impact on the many dimensions of MASLD, but also deepen the understanding of its pathophysiology, explore mechanisms of action that are still difficult to access and, where appropriate, identify innovative biomarkers that will strengthen the characterization and clinical relevance of this nutritional solution.

"The close of recruitment for the Cardio-Liver study marks a key milestone in the clinical development of TOTUM•448. We look forward to obtaining the data from this study, which will add to the already very positive results for this highly innovative active substance. We are glad to be able to strengthen the potential of our nutritional solution for managing hepatic steatosis, a growing concern within the population. This study supports our scientific approach and our resolve to deliver innovative products focused on supporting health and quality of life for people affected."

"We are very proud to have completed recruitment for the Cardio-Liver study. This study will be conducted with great methodological rigor and features a robust experimental design with particularly sophisticated investigations. It will provide us with valuable information, particularly about the mode of action of this innovative active substance on hepatic steatosis."

TOTUM•448 already benefits from a solid level of scientific evidence, supported by several international reference publications highlighting the robustness of its efficacy and its good tolerability. Since 2022, **eight presentations at several international congresses (including the European Association for the Study of the Liver and the American Association for the Study of Liver Diseases) have also shared with the scientific community highly convincing data on the efficacy and mechanism of action of this active substance.**

The results of the Cardio-Liver study will complete the clinical validation of TOTUM•448, paving the way for the development of a high-potential new product within the Valbiotis$^{PRO®}$ range. This range currently includes three products (Valbiotis$^{PRO®}$ Cholesterol, Valbiotis$^{PRO®}$ Metabolic Health, Valbiotis$^{PRO®}$ Cardio-Circulation) already in the commercialization phase. The market launch of TOTUM•448 will address the significant market for the prevention of metabolic liver diseases.

Beyond market potential, the commercialization of this new product will lean in France on an extensive network of pharmacies and prescribers already fully engaged, as well as on a functional e-commerce platform. Internationally, the upcoming joint venture in Asia will also be a key asset for the successful commercial roll-out of TOTUM•448 in this strategic region, initially extending to several key markets (China, Hong Kong/Macau, Vietnam, Indonesia, Japan, Taiwan and Singapore). In other parts of the world, the commercial development of TOTUM•448 could benefit from future agreements with potential partners.

Metabolic liver diseases: epidemiological data

Worldwide, nearly 1 billion adults are estimated to have a metabolic dysfunction-associated steatotic liver disease (MASLD)[1]. The vast majority are affected by the first stage, simple hepatic steatosis, a risk factor for developing MASH (metabolic dysfunction-associated steatohepatitis). As with all metabolic disorders, acting at an early stage helps prevent progression to a more severe condition requiring drug intervention and difficult to reverse.

These metabolic liver disorders affect mainly individuals who are overweight or obese, often combined with an unbalanced lifestyle. A diet high in fats and sugars, sedentary habits and lack of regular physical activity all promote the accumulation of fat in the liver. Globally, an estimated 2.5 billion adults[2] (aged 18 and over) are overweight, meaning one in two adults, and around 900 million people currently live with obesity. This population is particularly at risk of developing diseases such as hepatic steatosis, making these conditions a major public health issue.

1. Guo Z., Wu D., Mao R., Yao Z., Wu Q., Lv W. Global burden of MAFLD, MAFLD-related cirrhosis and MASH-related liver cancer from 1990 to 2021. Scientific Reports. 2025.
2. World Health Organization (WHO), in 2022.

About Valbiotis

Valbiotis is a French laboratory specializing in the creation and distribution of dietary supplements scientifically tested to maintain health at every stage of life. Through an innovative approach combining scientific excellence, plant expertise and a wealth of natural ingredients, Valbiotis offers a new generation of dietary supplements to support cardio-metabolic balance and well-being, and address everyday health issues such as sleep, fatigue, mood management, immunity and vitality. Created at the beginning of 2014 in La Rochelle, France, Valbiotis has forged numerous partnerships with leading academic centers.

Valbiotis is a member of the "BPI Excellence" network and has been recognized as an "Innovative Company" by the BPI label. Valbiotis 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 on Valbiotis®, please visit: www.valbiotis.com

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