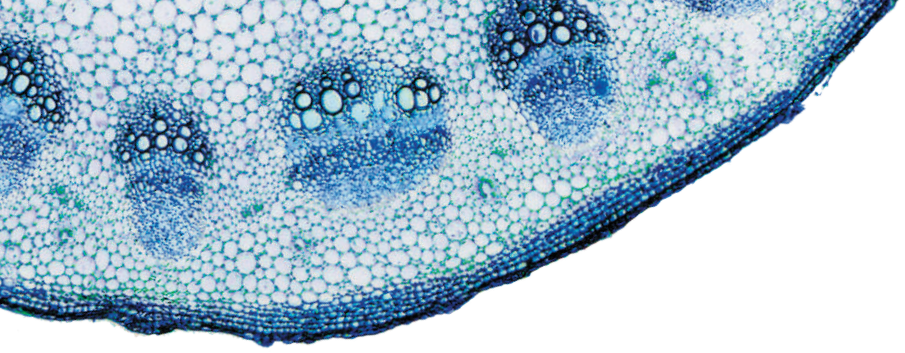

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Valbiotis announces the signature of a research partnership in intestinal microbiota with the MEDIS Unit from the Clermont Auvergne University

- The MIMETiv[1] research project, which will focus on the TOTUM•070 and TOTUM•448 active substances developed by Valbiotis, will be conducted by a joint laboratory, partly funded by the French National Research Agency (ANR) with a contribution of €363,000.
- This work will make it possible to develop the world's most complete model of the human upper digestive tract by 2024, integrating in particular the microbiota of the small intestine.
- The expected results will support the non-drug strategies against metabolic and cardiovascular diseases developed by Valbiotis, including the plant-based active substances TOTUM•070 and TOTUM•448.
- The MIMETiv project will provide proprietary data on the metabolites, bioavailability, mode of action at intestinal level and effects on the human microbiota of these two active substances.

La Rochelle, December 14, 2022 (17:40 p.m CET) - **Valbiotis** (FR0013254851 – ALVAL, PEA/SME eligible), a Research and Development company committed to scientific innovation for preventing and combating metabolic and cardiovascular diseases, **announces the signature of a research partnership in intestinal microbiota with the MEDIS[2] Unit from the Clermont Auvergne University on its active substances TOTUM•070 and TOTUM•448 against dyslipidemia and metabolic liver disease, partly financed by the French National Research Agency. Led by a laboratory shared by the two entities, the MIMETiv project will aim to develop a complete and dynamic human gastrointestinal model integrating the microbiota of the small intestine for the first time. This model will provide exclusive data on the effects and modes of action of Valbiotis' plant-based substances at the intestinal level, in the context of non-drug strategies to combat metabolic and cardiovascular diseases.**

Pascal SIRVENT, Director of Discovery, Preclinical and Translational Research, and member of the Board of Directors at Valbiotis states: *"In research and development, our public-private partnership strategy is based on collaborations with high scientific added value. The in vitro digestive model project led by the MEDIS Unit is a unique innovation in human digestion research, which we have been following for a long time and to which we are very happy to contribute within this new joint laboratory. As an industrial player, the MIMETiv project represents for us a very promising lever to approach cardiovascular and metabolic diseases from a digestive and intestinal perspective, with a particular focus on the intestinal microbiota. This is an innovative angle, in line with our research and development strategy. At the end of this project, we should obtain exclusive data for our active substances in two of our key indications: dyslipidemia and metabolic liver disease."*

[1]MIMETiv: *Microbiote intestinal et maladies métaboliques chez l'Homme* (Intestinal microbiota and metabolic diseases in humans): a unique *in vitro* digestive system to catalyze the development of innovative nutritional strategies.
LabCom Scientific document.

[2]The MEDIS Unit (*Microbiologie Environnement Digestif et Santé: Microbiology Digestive Environment and Health*) is a Joint Research Unit between INRAE (*Institut National de Recherche pour l'Agriculture, l'Alimentation et l'Environnement:* National Research Institute for Agriculture, Food and the Environment) and UCA (Clermont Auvergne University) created in January 2017.

Stéphanie BLANQUET-DIOT, Professor and Deputy Director of MEDIS, comments: *"This in vitro digestive system is unique in the number of parameters reproduced in relation to in vivo digestion in humans, such as body temperature, pH kinetics in the stomach and small intestine, gastrointestinal transit time, differential gastric emptying between liquids and solid particles, salivary, gastric, biliary and pancreatic secretions, absorption of water and digestive products, progressive anaerobics along the digestive tract and microbiota in small intestine-reproducing compartments."*

Dyslipidemia and metabolic liver disease (NAFL, NASH), the respective indications for the active substances TOTUM•070 and TOTUM•448, are highly prevalent diseases, precursors to pathologies that are life-threatening for patients (atherosclerosis, cirrhosis). Their complex pathophysiology includes, among other aspects, alterations in carbohydrate and/or lipid metabolism, digestive abnormalities and disturbances of the intestinal microbiota, all of which the MIMETiv project will be able to approach in humans in an integrated manner. Among the main innovations, MIMETiv should provide access to the microbiota of the small intestine, the major site of digestion and absorption of dietary carbohydrates and lipids in humans. To date, data linking metabolic diseases and gut microbiota have mainly been obtained from stool analysis, which partially reflects the microbiota of the colon (large intestine).

The MIMETiv project: an exclusive tool for R&D on metabolic and cardiovascular diseases

The MIMETiv project, which will benefit from the combined expertise of the MEDIS Unit and Valbiotis, will take place in two stages.

The first will lead to the design of the world's most complete model of the human digestive environment in 2024, based on the long-standing *in vitro* simulation work of the MEDIS Unit. The work will consist in optimizing the ESIN (Engineered Stomach and Small Intestine) system, developed by MEDIS, by improving its performance and integrating the human microbiota in key compartments of the digestive tract such as the small intestine.

Once validated, this model will constitute a proprietary tool for the evaluation of Valbiotis' plant-based active substances in the human digestive environment. The explorations performed will cover a complete set of R&D objectives for two active substances, TOTUM•070 and TOTUM•448:

- metabolomic analysis, to identify the metabolites of these active substances and to specify their bioavailability in the different gastrointestinal compartments;
- analysis of modes of action, to evaluate their effects on digestion and intestinal absorption of lipids and carbohydrates;
- analysis of the intestinal microbiota, to evaluate their impact on dysbiosis associated with metabolic diseases;
- analysis of hepatic metabolic pathways, thanks to the original coupling of ESINs with liver cells in culture, to assess their possible modulation by Valbiotis' active substances.

The Management Committee of the MIMETiv joint laboratory is composed of 5 members. It is co-led by Stéphanie BLANQUET-DIOT, Deputy Director of MEDIS, in charge of the digestive environment simulation platform, with strong expertise in microbiology and intestinal microbiota, *in vitro* digestion, digestive physiology and nutrition, and Pascal SIRVENT, Director of Discovery, Preclinical and Translational Research, and member of the Valbiotis Board of Directors. He is responsible for the R&D platform in Riom, with extensive expertise in metabolic diseases and the development of plant-based health products.

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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