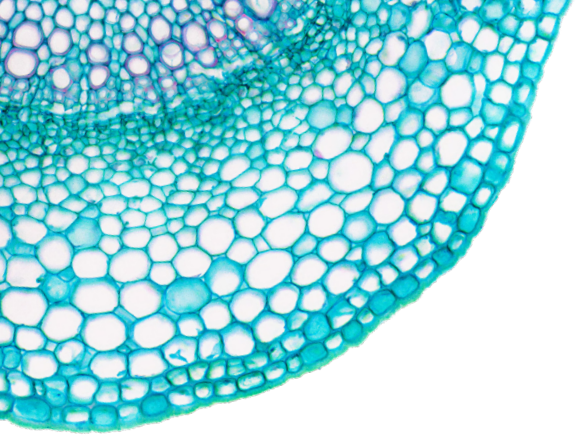

Valbiotis announces that it has submitted to the competent authorities the three clinical protocols for TOTUM•854 indicated in the reduction of blood pressure and presents its comprehensive clinical development plan

- The INSIGHT international, multicenter, randomized, placebo-controlled pivotal Phase II/III clinical study will be conducted with a 3.7 g/day dose of TOTUM•854 on 400 volunteers;
- The INSIGHT 2 international, multicenter, randomized, placebo-controlled Phase II/III clinical study will be conducted with a 2.6 g/day dose of TOTUM•854 on 400 volunteers;
- The clinical study of the bioavailability and mode of action of TOTUM•854, to characterize its metabolites and identify their effects on human cell lines, will be conducted in France on 10 volunteers.

La Rochelle, December 1, 2021 (7:35 am CET) - **Valbiotis** (FR0013254851 – ALVAL, eligible for the PEA / SME), a Research and Development company committed to scientific innovation for preventing and combating metabolic diseases, **announces that it has submitted the three clinical protocols for TOTUM•854, indicated in the reduction of blood pressure, to the competent authorities and presents its comprehensive clinical development plan, as announced at the annual meeting of the European Society of Hypertension and of the International Society of Hypertension in April 2021** (Press release dated April 12, 2021).

TOTUM•854 is the second plant-based active substance from the Valbiotis product portfolio to enter Phase II/III clinical trials and will address an unmet medical demand for non-drug prevention of arterial hypertension.

The TOTUM•854 clinical development program includes three clinical studies, whose results will be required in Europe and the United States for health claim applications in the reduction of blood pressure, which is a risk factor for cardiovascular disease. The clinical protocols for the three studies have been filed with the competent authorities.

The INSIGHT international, multicenter, randomized, placebo-controlled Phase II/III clinical study will be conducted in a population of 400 volunteers with mild to moderate blood pressure elevation (systolic blood pressure between 130 mmHg and 159 mmHg and diastolic pressure <100 mmHg). It will include two groups: a TOTUM•854 group with a dose of 3.7 g/day and a placebo group. Its main objective will be to reduce systolic blood pressure in the TOTUM•854 group after 3 months of supplementation *versus* the placebo group. 24-hour ambulatory blood pressure measurements will also be taken as a secondary study endpoint. The end of recruitment is expected at the first semester of 2023.

A second INSIGHT 2 international, multicenter, randomized, placebo-controlled study will be conducted on 400 additional subjects with the same inclusion criteria. It will include two groups: a TOTUM•854 group with a dose of 2.6 g/day and a placebo group. Its main objective will be to reduce systolic blood pressure in the TOTUM•854 group after 3 months of supplementation *versus* the placebo group. It will thus assess the effect of a reduced dose of TOTUM•854 (2.6 g/day) on blood pressure. The end of recruitment is expected at the first semester of 2023.

The clinical study of the bioavailability and mode of action of TOTUM•854, to characterize its metabolites and identify their effects on human cell lines, will be conducted in France on 10 volunteers. The results are expected at the end of 2022.

Murielle CAZAUBIEL, Member of the Board of Directors and Director of Medical, Regulatory and Industrial Affairs at Valbiotis, said: *"TOTUM•854's clinical development plan is very ambitious, but meets the health challenges of preventing arterial hypertension, which the World Health Organization considers to be the world's most prevalent chronic disease. It is a very important risk factor for cardiovascular disease. TOTUM•854 could quickly become an extremely interesting non-drug alternative for people at risk, whether or not they are already taking treatment. This innovative active substance, which contains six plant extracts, is designed to act on blood pressure regulation mechanisms. It would ultimately be produced in various dry forms, including as capsules."*

Sébastien BESSY, Member of the Board of Directors and Chief Operating Marketing and Business Officer at Valbiotis, comments: *"TOTUM•854 will open the door to a major market worth over €1.15 billion* in the United States and in the five main European countries (Germany, Spain, France, Italy and the United Kingdom), where no fewer than 124 million people suffer from mild to moderate arterial hypertension. This clinical development plan will leverage the potential of TOTUM•854 in preventing arterial hypertension, with the aim of bringing it to market as soon as the studies ends. In addition, we have registered TOTUM•854 in over 60 countries, including our key territories such as the United States, Europe, Mexico, China, Japan and already obtained in some of these territories."*

Valbiotis presented its preclinical data on the active substance TOTUM•854 at the annual meeting of the European Society of Hypertension and of the International Society of Hypertension in April 2021. The *in vivo* results obtained from two predictive models of hypertension in humans showed that TOTUM•854 effectively prevented arterial hypertension. This proof-of-concept was obtained in partnership with the Cardiovascular Pharm-Ecology Lab (LaPEC) of the University of Avignon and at the Valbiotis R&D platform. The research presented at the meeting was conducted on a model of L-NAME-induced hypertension (an NO synthase inhibitor). In this classic model of hypertension, predictive of human physiology, TOTUM•854 prevented the onset of arterial hypertension compared with the control group. Additional data, obtained from a polygenic SHR (spontaneously hypertensive rat) model of hypertension, also showed a positive effect of TOTUM•854 that delays the development of hypertension. A significant acute effect was also observed following a single dose of TOTUM•854 on the same SHR model.

*Source: AEC Partners pre-AHT preliminary market estimate 2020 data

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 health nutrition products designed to reduce the risk of major metabolic 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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