



Valbiotis reveals positive TOTUM•854 preclinical results in the prevention of hypertension at the Annual ESH-ISH Joint Meeting

An acceleration of development in order to advance the marketing horizon up to 3 years, to conquer an addressable market of over one billion euros

- Valbiotis presents preclinical data on the plant-derived active substance TOTUM•854, designed to reduce blood pressure, at the Annual Joint Meeting of the European Society of Hypertension and the International Society of Hypertension held from April 11 to 14, 2021.
- The results, obtained *in vivo* on models predictive of hypertension in humans, showed that TOTUM•854 is effective in preventing hypertension. This proof-of-concept was obtained in partnership with the Cardiovascular Pharm-Ecology Lab (LaPEC) of the University of Avignon as well as at the Valbiotis R&D platform.
- Valbiotis announces the acceleration of the development of TOTUM•854 to prevent hypertension, including the launch of a pivotal Phase II/III study to apply for a health claim.
- Commercialization would be possible as soon as the Phase II/III results are available, in partnership with a major healthcare player and up to 3 years ahead of schedule.
- Valbiotis presents market data collected by AEC Partners on mild and moderate hypertension in the United States and major European countries. The market is estimated at €1.15 billion.

La Rochelle, April 12, 2021 (7:35 am CEST) - Valbiotis (FR0013254851 - ALVAL, eligible for the PEA/SME), a Research & Development company committed to scientific innovation for preventing and combating metabolic diseases, announces the presentation of positive preclinical results of TOTUM•854 in hypertension at the joint meeting of the European Society of Hypertension (ESH) and the International Society of Hypertension (ISH) held from April 11 to 14, 2021, in virtual format.

This research, conducted on two different *in vivo* models, shows that TOTUM•854 prevents hypertension. Based on this positive data, Valbiotis is stepping up its development of TOTUM•854 and will launch three clinical studies at the end of this year, including a Phase II/III clinical study for reduction of hypertension, a risk factor for cardiovascular disease.

TOTUM•854 could be commercialized at the end of this study, up to 3 years ahead of schedule, in partnership with a major healthcare player.

Pascal SIRVENT, Member of the Board and Head of Discovery, Preclinical and Translational Research at Valbiotis, said: "We are proud of this first selection at a major international congress in the cardiovascular field, for which Valbiotis has partnered with the University of Avignon. The TOTUM•854 data collected from two different models of hypertension is remarkable, it validates our hypotheses and our approach to this condition. This very strong proof-of-concept for prevention of hypertension points to ambitious clinical development for TOTUM•854."

The work presented at the ESH-ISH Joint Meeting was conducted on a model of hypertension induced by L-NAME (a NO synthase inhibitor). In this classic model of hypertension, predictive of human physiology, TOTUM•854 prevented the onset of hypertension compared with the control group. Additional data, obtained from a polygenic model of hypertension (SHR, spontaneously hypertensive rats), also shows a positive effect of TOTUM•854 that delays the onset of hypertension. In addition, a significant acute effect was observed following a single dose of TOTUM•854 on the same SHR model.

Figure 1: Effect of TOTUM•854 supplementation on systolic (SBP) and diastolic (DBP) blood pressure after 3 weeks, in an induced hypertension model (L-NAME model). After 3 weeks, L-NAME induced a 24 mmHg-raise in SBP and a 19 mmHg- raise in DPB (grey bars). Supplementation with TOTUM•854 (blue bars) significantly reduced SBP by 16 mmHg ($p < 0.01$) and DBP by 15 mmHg ($p < 0.05$).

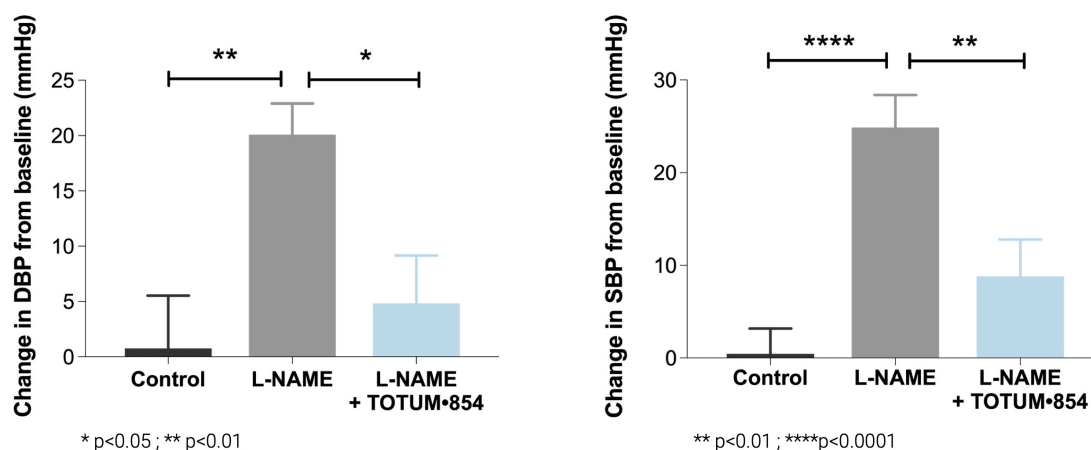


Table 1: Effect of a single oral dose of TOTUM•854 in a polygenic model of hypertension (SHR model) on systolic (SBP) and diastolic (DBP) blood pressure, during 24 hours. Starting the experiment (« baseline »), SBP (164 mmHg) and DBP (115 mmHg) were typical of an installed hypertension. Oral intake of a TOTUM•854 dose led to blood pressure reduction, resulting in a decrease of both SBP and DBP Area Under the Curve (AUC), over a 24h-record compared to the control group.

	Baseline (mmHg; mean ± SEM)	Change in area under the curve over the 24 hours following one dose of TOTUM•854 (mmHg x h, mean ± SEM)
SBP	164.4 ± 4.7	-108.0 ± 87.8
DBP	115.9 ± 3.6	-84.4 ± 69.3

These results stem in particular from a program carried out under a partnership between Valbiotis and the experimental unit of the Cardiovascular Pharm-Ecology Lab (LaPEC) of the University of Avignon, directed by Cyril REBOUL, PhD, expert in cardiovascular pharmacology.

Cyril REBOUL, PhD, head of the experimental unit of the Cardiovascular Pharm-Ecology Lab (LaPEC) of the University of Avignon, said: *“Through our work, we have shown a preventive effect of TOTUM•854 on the development of hypertension in a recognized preclinical model using the L-NAME inhibitor. Undeniably, these results constitute quite an achievement at this stage of TOTUM•854’s development. We are very pleased to have been able to contribute our expertise as part of this fruitful partnership with Valbiotis.”*

Acceleration of the development for commercialization now scheduled for 2023

Based on these results, Valbiotis has revised its clinical development program for TOTUM•854 with the launch of a Phase II/III study, the last step before a health claim application in Europe and the United States for reduction of blood pressure, a risk factor for cardiovascular disease. This international, multicenter, randomized, placebo-controlled study will be conducted in a population of 600 volunteers with mild to moderately elevated blood pressure. The study will involve three groups: a TOTUM•854 group at a dose of 3.75 g/day, a TOTUM•854 group at a dose of 2.5 g/day and a placebo group. Its primary endpoint will be the reduction of systolic blood pressure in the TOTUM•854 group (3.75 g/day) after 6 months of supplementation versus the placebo group. It will also evaluate the effect of a reduced dose of TOTUM•854 (2.5 g/day) on blood pressure. In addition, 24-hour ambulatory blood pressure measurements will be taken as a secondary endpoint of the study. The protocol is expected to be filed with the authorities in the fourth quarter of 2021, with results anticipated in the second half of 2023.

A second international, multicenter, randomized, placebo-controlled clinical study will be conducted in parallel at a dose of 3.75 g/day of TOTUM•854. This strategy will allow Valbiotis to prepare a complete health claim application.

Finally, Valbiotis will conduct a third clinical study to measure the bioavailability of TOTUM•854, characterize its metabolites and explore their mode of action.

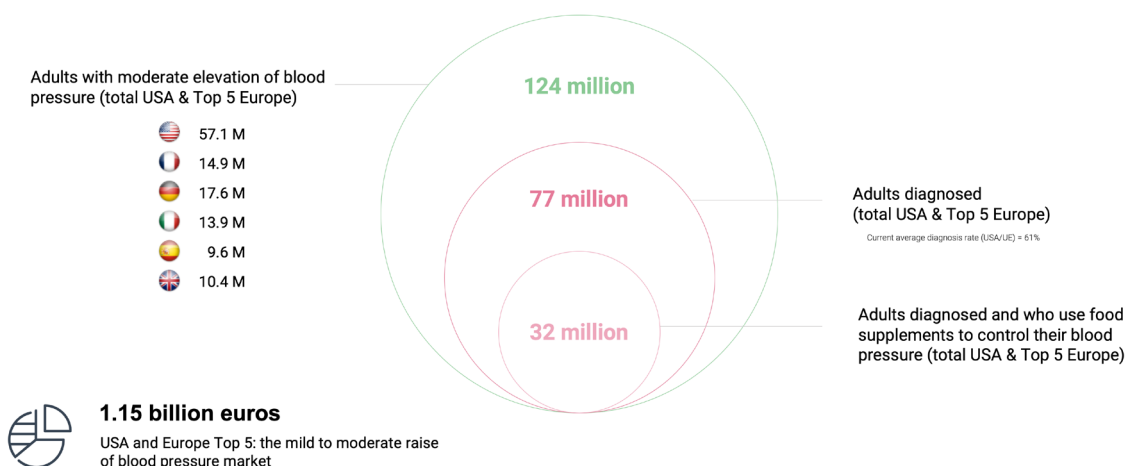
Murielle CAZAUBIEL, Member of the Board, Head of Development and Medical Affairs at Valbiotis, said: *“These preclinical results raise great hopes for the clinical development of TOTUM•854 in the prevention of hypertension. That’s why we are accelerating our strategy for this active substance. Hypertension is considered the foremost chronic disease in the world by the World Health Organization. It’s a serious risk factor for cardiovascular disease, in particular strokes. TOTUM•854 could quickly become an extremely interesting non-drug alternative for people at risk, whether or not they are already taking treatment. This plant-derived active substance would ultimately be developed in the form of capsules or powder for dilution.”*

The new strategic development plan will leverage the potential of TOTUM•854 in preventing hypertension, with the aim of bringing it to market as soon as the Phase II/III study ends, in other words by 2023.

Market data on mild to moderate hypertension: conquering an addressable market of over one billion euros

In 2020, AEC Partners conducted a mild to moderate hypertension market study in the United States and 5 main European countries (Germany, Spain, France, Italy and the United Kingdom).

It highlights the size of this market in these regions, which alone represents 124 million people with moderately elevated blood pressure.



Sébastien PELTIER, CEO and Chairman of the Board, said: *"In the US and 5 main European countries (Germany, Spain, France, Italy and the United Kingdom), our target represents 124 million people with mild to moderately high blood pressure. TOTUM•854 will give us access to a huge market worth over €1.15 billion. We are now embarking on a new cycle with the development of TOTUM•854 for prevention of hypertension. By accelerating our strategy, we will gain 3 years on our development plan, with a possible market launch on completion of the Phase II/III study. I am confident that we will achieve growth and create value for our shareholders over the long term, turning our innovations into products that can transform the lives of millions by addressing as yet unmet medical needs."*

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

↳ Contacts

Corporate communication / Valbiotis

Carole ROCHER / Marc DELAUNAY

+33 5 46 28 62 58

media@valbiotis.com

Financial communication / Actifin

Stéphane RUIZ

+33 1 56 88 11 14

sruiz@actifin.fr



Name: Valbiotis
ISIN code: FR0013254851
Mnemonic code: ALVAL
EnterNext© PEA-PME 150

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).

This press release, as well as the information contained herein, does not constitute an offer to sell or subscribe to, or a solicitation to purchase or subscribe to, Valbiotis' shares or securities in any country.