VALBIOTIS

PRESS RELEASE

VALBIOTIS announces additional positive results from the Phase IIA clinical study of VALEDIA®, the first product proven effective in people with prediabetes, in lipid metabolism and arterial hypertension

- **VALEDIA® significantly reduced blood glucose levels, and body weight compared to placebo (topline data, published on 3 July 2019[1]).**

- **VALEDIA® also significantly reduced, compared to placebo :**
  - **Blood triglyceride levels by 32.2% ;**
  - **Fatty liver index (accumulation of fat in the liver) by 18.7% ;**
  - **Arterial hypertension by 10.6 mmHg, and 18.9 mmHg in hypertensive people ;**
  - **Blood LDL cholesterol levels by 11.7%.**

- **The results of Phase IIA study have exceeded all set objectives and the overall efficacy of VALEDIA® in subjects at risk of metabolic diseases has been proven.**

La Rochelle, 2 September 2019 (5:40 PM CEST) – **VALBIOTIS** (FR0013254851 - ALVAL / PEA/SME eligible), a Research & Development company committed to scientific innovation for preventing and combating metabolic diseases, **today announced additional positive results from its Phase IIA clinical study[2] of VALEDIA® on four parameters which were among the secondary endpoints of the study: blood triglyceride levels, Fatty Liver Index (fat accumulation in the liver), blood LDL cholesterol levels, and arterial hypertension.**

Topline data from the study were published on 3 July 2019[1], which showed a significant reduction in hyperglycemia, body weight and waist size compared to placebo. The entire Phase IIA clinical study has therefore demonstrated the efficacy of VALEDIA® on various abnormalities in carbohydrate and lipid metabolism.

[1] VALBIOTIS published the methodology and «Topline» results for the Phase IIA study in a press release on 3 July 2019 : https://www.valbiotis.com/app/uploads/2019/07/2019-06-21-PR_VALBIOTIS_PHASEIIA-VALEDIA.pdf

[2] ID-RCB Number: 2016-A00484-47

"The full results clearly demonstrate a positive effect on the entire clinical profile: hyperglycemia, hypertriglyceridemia, hepatic steatosis, overweight and abdominal obesity, hypercholesterolemia and arterial hypertension. These risk factors, contribute to an increased risk of type 2 diabetes, cardiovascular disease and liver diseases such as NASH."

Pr Jean-Marie BARD
Hospital Practitionner and Professor of Fundamental and Clinical Biochemistry at the University of Nantes, scientific expert for the study

" Today, we are presenting very compelling data which demonstrates the global efficacy of TOTUM-63, active substance of VALEDIA® and its action on the metabolic profile as a whole. This is excellent news for our priority to reduce the risk of type 2 diabetes in prediabetic patients.
We will soon be launching two concurrent Phase IIB studies in prediabetic patients (last studies), as announced previously. Our medium-term strategy is also clear: the significant lipid-lowering effect of VALEDIA® bodes extremely well for the reduction of non-alcoholic fatty liver, a risk condition for developing NASH. This will be the main focus of another Phase IIB clinical study. These results have opened up new opportunities for TOTUM-63 in the future, in the field of hypertension, for example."

Murielle CAZAUBIEL
Member of Executive Board
Director of Development and Medical Affairs of VALBIOTIS

Additional results from the Phase IIA clinical study of VALEDIA® in lipid metabolism and arterial hypertension

The international Phase IIA clinical study evaluated the efficacy of VALEDIA® on carbohydrate and lipid metabolism. The subjects included presented with prediabetes, abdominal obesity and hypertriglyceridemia, which were not treated according to current guidelines, as well as a high fatty liver index and high blood pressure. Hypoglycemic, lipid-lowering or hypotensive treatments were excluded. Lipid and hypertension parameters were secondary criteria in the study.

Methodology

This was a multicenter, randomized, placebo-controlled, double-blind study. Subjects received a daily dose of 5 grams of VALEDIA®, compared to 5 grams of placebo for subjects in the control group, over a 6-month period. Diet and physical activity levels remained the same throughout the study in both groups. Analyses were based on 51 subjects, 13 in the placebo group and 38 in the VALEDIA® group.

Characteristics of participants at the beginning of the study

35 women, 16 men; average age: 57.1 years.

	Average value of participants at the beginning of the study (baseline)	**Maximum values recommended for adults**
Body Mass Index (BMI)	31.3 kg/m²	25 kg/m² (overweight threshold)
Glycemic parameters		
- Fasting blood glucose	1.26 g/L	1.00 g/L (prediabetes threshold*)
- Blood glucose level at 2 hours (OGTT)	1.85 g/L	1.40 g/L (prediabetes threshold)
Lipid parameters		
- Fasting triglycerides	1.78 g/L	1.50 g/L (men) and 1.20 g/L (women)
- Fatty Liver Index	73.34	60 (threshold for very high probability of steatosis)
Systolic blood pressure	131 mmHg	130 mmHg (in the case of metabolic syndrome) or 140 mmHg

*According to the American Diabetes Association (1.10 g/L according to the WHO)

Results in lipid metabolism:

VALEDIA® significantly reduced two metabolic parameters for lipids, compared to placebo: triglyceridemia ($p < 0.01$) and Fatty Liver Index ($p<0.001$).

Triglycerides

	Variation at 6 months (g/L)	**Variation of VALEDIA® *vs* placebo**[3]
Placebo (n=13 subjects)	+ 0.15 (± 0.15)	**- 32.2%**
VALEDIA® (n=38 subjects)	- 0.31 (± 0.10)	

Average values (± SEM)

Fatty liver index

	Variation at 6 months	**Variation of VALEDIA® *vs* placebo**[3]
Placebo (n=13 subjects)	+ 5.64 (± 3.06)	**- 18.7%**
VALEDIA® (n=38 subjects)	- 4.66 (± 1.51)	

Average values (± SEM)

Compared to placebo, VALEDIA® also significantly reduced blood LDL cholesterol levels ($p<0.05$).

LDL cholesterol

	Variation at 6 months	**Variation of VALEDIA® *vs* placebo**[3]
Placebo (n=13 subjects)	+ 0.08 (± 0.07)	**- 11.7%**
VALEDIA® (n=38 subjects)	- 0.07 (± 0.04)	

Average values (± SEM)

[3] Difference between averages of individual variations expressed in %

Results in arterial hypertension:

Compared to placebo, VALEDIA® significantly reduced systolic blood pressure ($p<0.01$) in the total study population.

Systolic blood pressure

	Variation at 6 months (mmHg)	Variation of VALEDIA® *vs* placebo[4]
Placebo (n=13 subjects)	+ 7.54 (± 3.29)	**- 10.57 mmHg**
VALEDIA® (n=38 subjects)	- 3.03 (± 1.23)	

Average values (± SEM)

Additional analyses were conducted on a subgroup, involving all subjects at the beginning of the study with systolic blood pressure levels higher than 130 mmHg, the threshold for hypertension in cases of metabolic syndrome. The difference in the changes measured at the end of the study was significant ($p <0.001$) and reached 18.9 mmHg in favor of the VALEDIA® group (n = 18) compared to placebo (n = 8).

Systolic blood pressure

	Variation at 6 months (mmHg)	Variation of VALEDIA® *vs* placebo[4]
Placebo (n=8 subjects)	+ 10.75 (± 4.31)	**- 18.86 mmHg**
VALEDIA® (n=18 subjects)	- 8.11 (± 2.62)	

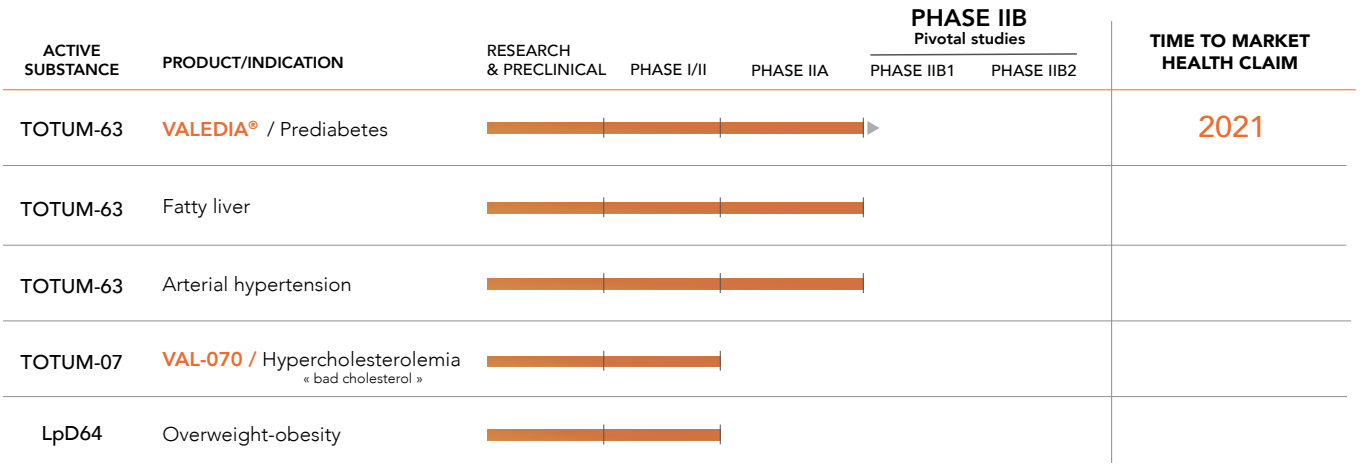
Average values (± SEM)

Sébastien PELTIER
CEO of VALBIOTIS

"The additional results from this Phase IIA clinical study have far exceeded our expectations. This data demonstrates the efficacy of VALEDIA® for its primary indication, the reduction of risk of developing type 2 diabetes in people with prediabetes. What's more, this study demonstrates the comprehensive action of VALEDIA® on metabolic syndrome. This is a major asset for VALBIOTIS, opening up new prospects in promising markets, such as in the field of non-alcoholic fatty liver or arterial hypertension, which will be a major focus point for future developments. In terms of our commercial strategy, these excellent results will naturally give new impetus to our negotiations with potential partners".

[4] Difference between averages of individual variations

VALBIOTIS pipeline



TOTUM-63

About TOTUM-63, the active ingredient of VALEDIA®

Prediabetes is a growing public health problem worldwide, which is recognized by international organizations such as the WHO, the American Diabetes Association and the International Diabetes Federation, among others. Without effective treatment, 70% to 90% of prediabetic patients will develop type 2 diabetes.

VALEDIA® is the first clinically validated product specifically designed to help prediabetics reduce their risk of developing type 2 diabetes. VALEDIA® is the only product that contains the active ingredient TOTUM-63, a unique and patented combination of 5 plant extracts that act in synergy to target the physiopathological mechanisms of type 2 diabetes.

TOTUM-63 has already shown perfect tolerance and safety during a Phase I/II clinical study conducted in healthy volunteers. The results of the first international randomized, placebo-controlled study showed that in patients with prediabetes, TOTUM-63 reduces fasting blood glucose and blood glucose at 2 hours, two risk factors of type 2 diabetes. In these subjects, who also presented with hypertriglyceridemia and abdominal obesity, TOTUM-63 significantly reduced body weight, waist circumference, blood triglycerides, Fatty Liver Index, blood cholesterol levels, and arterial hypertension.

The published Phase IIA study results and all key information about the Company are presented in an updated corporate presentation, available at the following link:

www.valbiotis.com/en/documents/

ABOUT VALBIOTIS

VALBIOTIS is a Research & Development company committed to scientific innovation for preventing and combating metabolic diseases. Its products are made for major players in the health care sector. VALBIOTIS particularly focuses on solutions to prevent type 2 diabetes, NASH (nonalcoholic steatohepatitis), obesity and cardiovascular diseases.
VALBIOTIS was founded in La Rochelle in early 2014 and has formed numerous partnerships with top academic centers in France and abroad, including La Rochelle University, the CNRS and Clermont Auvergne University located in Clermont-Ferrand. These partnerships have enabled VALBIOTIS to benefit from strong financial leverage, particularly thanks to experts and technical partners who support its projects. The Company has established three sites in France - Périgny, La Rochelle (17) and Riom (63) - and an American office in Boston (MA).
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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Name: VALBIOTIS - ISIN Code: FR0013254851 - Mnemonic code: ALVAL

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