VALBIOTIS

PRESS RELEASE

VALBIOTIS announces positive results from first pilot Phase I/II clinical study of VAL-070 in hypercholesterolemia

- VAL-070 is safe and well-tolerated
- The results obtained support the Phase II clinical development of VAL-070 with blood LDL-cholesterol as the primary endpoint
- VALBIOTIS plans to accelerate the development of VAL-070 as a potential new first-line option to reduce LDL-cholesterol in subjects with mild to moderate hypercholesterolemia
- Clinical development aims at applying for a proprietary health claim related to the reduction of LDL cholesterol, of which elevated levels are a risk factor for cardiovascular diseases, in North America and Europe

La Rochelle, 10 July 2018 (5:35 pm CET) – VALBIOTIS (FR0013254851 – ALVAL / PEA/SME eligible), a French Research & Development company committed to scientific innovation for preventing and combating metabolic diseases, today announced positive results from a Phase I/II pilot study on VAL 070, demonstrating that the product was safe and well-tolerated in subjects with untreated mild to moderate dyslipidemia. These results obtained on blood LDL-cholesterol support usage of this parameter as the primary endpoint of the Phase II clinical development.

VAL-070 is a combination of four food plant extracts that acts on lipid metabolism without the use of phytosterols or red yeast rice, with a patent pending in 60 countries.

The randomized, placebo-controlled, double-blind Phase I/II clinical study was conducted in France in accordance with Good Clinical Practices. It was conducted on 40 male and female volunteers aged 18 to 70 years with mild to moderate hypertriglyceridemia and hypercholesterolemia, who are not currently undergoing any treatment with hypolipidemic drugs. Volunteers were divided into three groups, receiving supplements over the course of 12 weeks, without any modifications to diet or physical activity:

- One group of 10 volunteers receiving a placebo;
- One group of 15 volunteers, receiving VAL-070 (3.5 g/day);
- One group of 15 volunteers, receiving VAL-070 (3.5 g/day) and a daily 1.5 g dose of phytosterols, nearly double the effective dose defined by the EFSA* (0.8 g/day).

The objectives of this study were to validate safety and tolerance, to establish the primary endpoint for the Phase II studies and to evaluate the benefit of VAL-070 compared to phytosterols.

Hemodynamic, hepatic and renal parameters demonstrated that VAL-070 has a favorable safety profile, and no adverse events were observed. In volunteers receiving VAL-070, alone or in combination with phytosterols, an average reduction of nearly 7% was observed in blood LDL-cholesterol levels from baseline to the end of the study in the two groups. This study was not designed to achieve statistical significance. These results support future Phase II clinical studies of VAL 070, in which blood LDL-cholesterol will be the primary endpoint.

These results represent a key milestone in the clinical development of VAL-070 and its potential to address hypercholesterolemia, a public health issue that represents a major risk factor for cardiovascular diseases," commented Sébastien Peltier, CEO of VALBIOTIS. "VAL-070 has the potential to become a first line option that differentiates from currently marketed dietary supplements: plant sterols and stanols or red yeast rice. We continue to bolster and diversify our pipeline of products to prevent cardio-metabolic diseases, and look forward to providing updates on continued development of VAL-070."

Sébastien PELTIER

CEO of VALBIOTIS

VALBIOTIS plans to initiate a Phase II registration study during the first half of 2019, as soon as the regulatory authorizations are received. This will be an international, randomized and controlled study on a target population with mild to moderate hypercholesterolemia. It will be statistically powered to demonstrate a significant reduction in blood LDL-cholesterol levels.

VAL-070 is being developed for subjects with mild to moderate hypercholesterolemia, with the aim of establishing a proprietary health claim related to the reduction of blood LDL-cholesterol, of which elevated levels are a risk factor for developing cardiovascular diseases. VALBIOTIS plans to seek regulatory approval in the United States, Europe and Canada (FDA**, EFSA and Health Canada).

For healthcare professionals, VAL-070 would offer an innovative first line treatment solution and clinical benefit to subjects with moderate cardiovascular risk, with a favorable efficacy and safety profile. For agri-food and pharmaceutical companies, VAL-070 could provide a means of differentiating from existing dietary supplements, being free of phytosterols and red yeast rice and with a proprietary LDL-cholesterol lowering health claim.

Professor Jean-Marie Bard, University professor, Hospital practitioner at CHU Nantes commented, «*This pilot study demonstrates the clinical benefit of VAL 070 to reduce LDL-cholesterol. These results should be confirmed in later clinical development on the final target population. This product has the potential to provide a new option to subjects at moderate risk for cardiovascular diseases, for whom a first-line medication is not systematically prescribed.*»

MODERATE HYPERCHOLESTEROLEMIA: A NEED FOR CLINICALLY-PROVEN, NON- PHARMACEUTICAL PRODUCTS

Hypercholesterolemia affects almost 30% of the adult French[2] and American[3] populations, and constitutes one of the major risk factors for atherosclerosis and cardiovascular diseases. The beneficial effects of reducing LDL cholesterol in the blood on cardiovascular risk have been well established[4] : a reduction in blood cholesterol levels of 10% leads to a 50% reduction in the risk of heart diseases at 5 years[5]. In subjects with hypercholesterolemia, treatment involves a lifestyle change and possibly a medicinal prescription[3]. In France and the United States, statin treatment from the onset is recommended for subjects at high risk for cardiovascular diseases, according to the latest guidelines[4,6].

According to the European Society of Cardiology and the European Atherosclerosis Society, dietary supplements can be incorporated into prevention strategies, if they have a proven positive effect on blood lipid levels demonstrated in randomized, controlled clinical studies[7]. Included among these dietary supplements, products developed to reduce LDL-cholesterol in patients not eligible for treatments are today mainly based on phytosterols, which carry a generic health claim[1]. The market for these products is expected to reach a billion dollars by 2024[8]. Red yeast rice is also considered to be an effective agent but contains a natural statin, monacolin K. Its status as a dietary supplement has thus been called into question by authorities. For example, the marketing of this ingredient is prohibited in the United States[9], Belgium and Switzerland and is subject to restrictions in some European Union countries[10].

[1]Commission Regulation (EU) no. 432/2012 of 16 May 2012 establishing a list of permitted health claims made on foods, other than those referring to the reduction of disease risk and to children's development [2]De Peretti C, Perel C, Chin F, Tuppin P, Iliou MC, Vernay M, et al. Cholestérol LDL moyen et prévalence de l'hypercholestérolémie LDL chez les adultes de 18 à 74 ans, étude nationale nutrition santé (ENNS) 2006-2007, France métropolitaine. BEH 2013;(31):378-85
[3]Center for disease control, 2018, www.cdc.gov/cholesterol/index.htm, Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das SR, Deo R, et al. Heart disease and stroke statistics—2017 update: a report from the American Heart Association. Circulation. 2017;135:e1–e458.
[4]ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults, 2013
[5]http://www.who.int/gho/ncd/risk_factors/cholesterol_text/en/
[6]US Preventive Services Task Force, Final Recommendation Statement, Statin Use for the Primary Prevention of Cardiovascular Disease in Adults: Preventive Medication, JAMA, Novembre 2016
[7]Reiner Z, Catapano AL, De Backer G et al (2011) ESC/EAS Guidelines for the management of dyslipidaemias: the Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS). Eur Heart J 32(14):1769–1818
[8]https://www.gminsights.com/pressrelease/phytosterols-market-size
[9]National Center for Complementary and Integrative Health,https://nccih.nih.gov/health/redyeastrice
[10]Levure de riz rouge : déconseillée dans le cholestérol, Prescrire, 1er Oct. 2016, http://www.prescrire.org/fr/3/31/52215/0/NewsDetails.aspx

* European Food Safety Authority
** Food and Drug Administration

ABOUT VALBIOTIS

VALBIOTIS is a French Research & Development company committed to scientific innovation, for preventing and combating metabolic diseases. Its products are made for manufacturers in the agri-food and pharmaceutical industries. 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 the La Rochelle University, the CNRS and the Clermont Auvergne University located in Clermont-Ferrand, where the company opened a second office. These partnerships have enabled VALBIOTIS to benefit from strong financial leverage, particularly thanks to experts and technical partners who support its projects. 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).

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