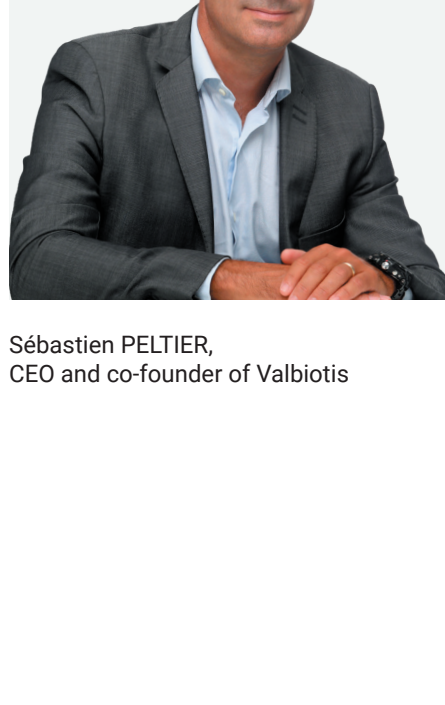


# Letter to Shareholders No.6

February 2023



**Sébastien PELTIER,**  
CEO and co-founder of Valbiotis

"Dear Shareholders,

Committed for nearly a decade to the prevention and fight against metabolic and cardiovascular diseases, Valbiotis has managed to build a portfolio of four plant-based active substances with a high level of scientific evidence composed of TOTUM-63 (prediabetes), TOTUM-070 (high LDL cholesterol), TOTUM-448 (NAFL/NASH) and TOTUM-854 (raised blood pressure). This promising portfolio is the result of years spent on R&D and the clinical advancement of our products.

Today, we are beginning a new phase of development intended to promote our TOTUM products as much as possible and to rapidly generate sales. This ambition is based on a two-pronged strategy: a local one with income earned from direct marketing in France, and an international one with global income generated by licensing and/or distribution partnerships.

In 2023, we expect to make the first steps of this strategic acceleration a reality with the signing of one or more licensing agreements for TOTUM-070, while continuing to structure the Company and ramp up industrial operations in order to prepare for the first marketing operations in the first half of 2024; the launch of TOTUM-070 in France by Valbiotis and the delivery of the first commercial batches of TOTUM-63 to our partner Nestlé Health Science.

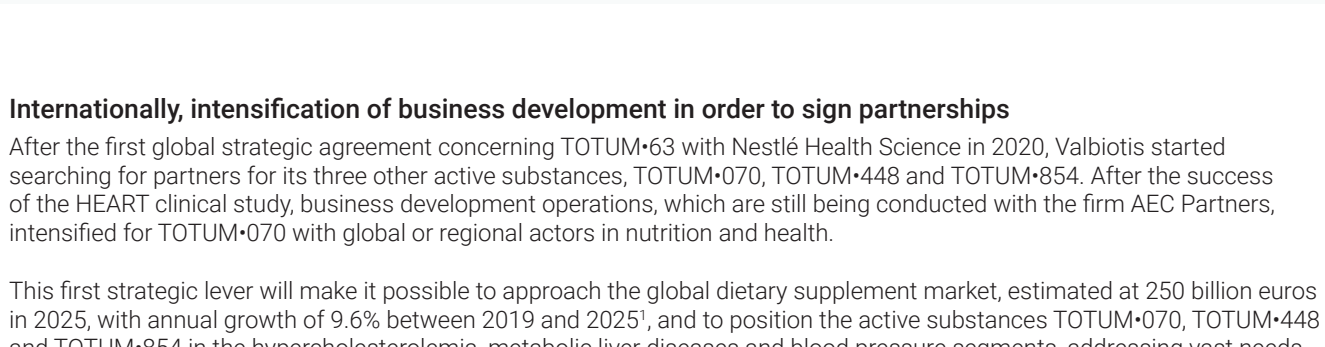
The fiscal year will also bring us major clinical results for TOTUM-63, particularly on Phase II/III REVERSE-IT, the last step before marketing and the health claim request.

Valbiotis is approaching this pivotal year with a strong financial footing thanks to the raising of 9.7 million euros in funds at the end of 2022. We are very pleased with the participation of hundreds of individual shareholders via the PrimaryBid platform (Bourse Direct, Boursorama, Easybourse) and the confidence that institutional investors showed us on this occasion. This increase in funds gives Valbiotis the means to pursue its ambitions in the dietary supplement market, which is enjoying strong growth in France and abroad and will have an estimated worth of 250 billion euros in 2025.

On behalf of all the Valbiotis teams, which are fully mobilized during this promising period of strategic acceleration, I would like to warmly thank our shareholders. Their support is as precious as it is decisive at the dawn of this key step in the marketing of the TOTUM products, which should enable Valbiotis to meet the challenge of preventing metabolic and cardiovascular diseases."

## Focus on marketing of active substances in the portfolio

After years dedicated to Research and Development, Valbiotis is approaching a decisive step with the upcoming marketing of these 4 active substances in the markets for the prevention of metabolic and cardiovascular diseases. Valbiotis is continuing its historic strategy of signing licensing and/or distribution partnerships with global or regional players in health and nutrition. Furthermore, Valbiotis has set itself the additional objective of marketing three of its active substances in its own name on the French market. This double lever will make it possible to accelerate Valbiotis' growth and boost its innovative abilities.

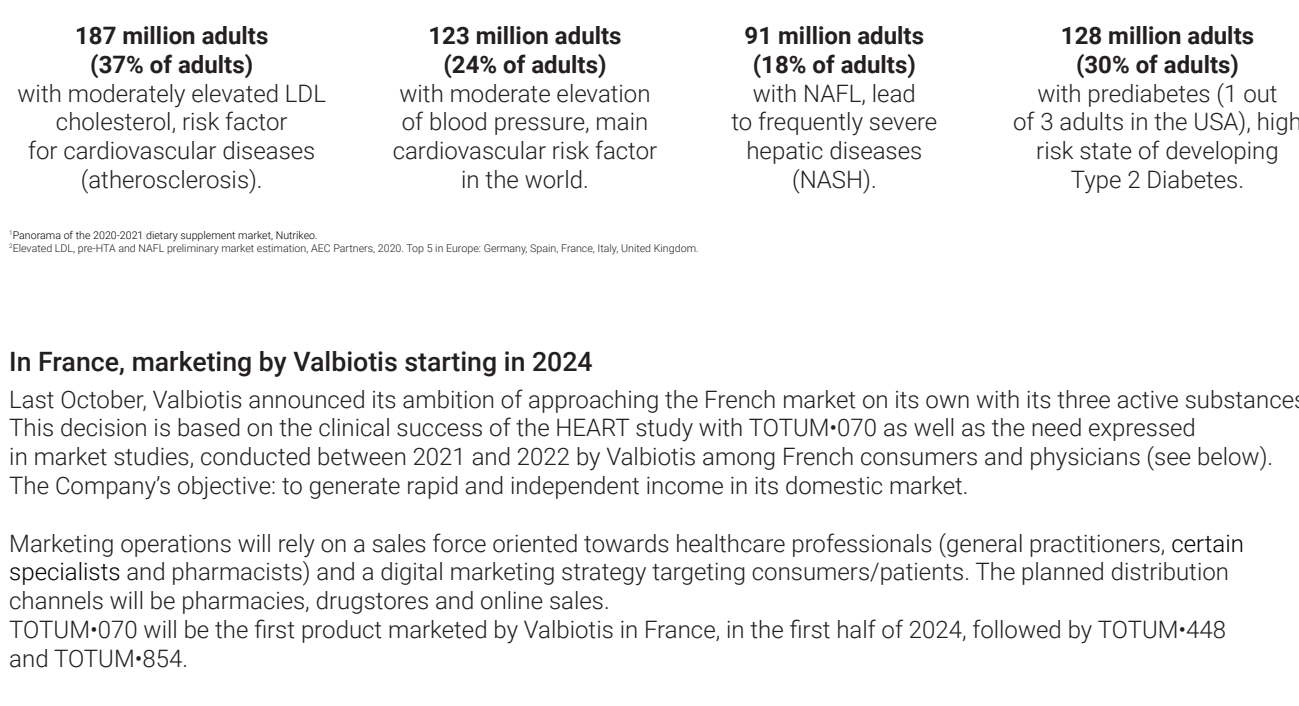


## Internationally, intensification of business development in order to sign partnerships

After the first global strategic agreement concerning TOTUM-63 with Nestlé Health Science in 2020, Valbiotis started searching for partners for its three other active substances, TOTUM-070, TOTUM-448 and TOTUM-854. After the success of the HEART clinical study, business development operations, which are still being conducted with the firm AEC Partners, intensified for TOTUM-070 with global or regional actors in nutrition and health.

This first strategic lever will make it possible to approach the global dietary supplement market, estimated at 250 billion euros in 2025, with annual growth of 9.6% between 2019 and 2025<sup>1</sup>, and to position the active substances TOTUM-070, TOTUM-448 and TOTUM-854 in the hypercholesterolemia, metabolic liver diseases and blood pressure segments, addressing vast needs on a global scale.

The target populations for TOTUM-070, TOTUM-854, TOTUM-448 and TOTUM-63 in the United States and in Europe (top 5):



<sup>1</sup>Source: Statista (2022) Dietary supplement market, Nutrition. <sup>2</sup>Statista (2022) Dietary supplement market, Nutrition. <sup>3</sup>Statista (2022) Dietary supplement market, Nutrition. <sup>4</sup>Statista (2022) Dietary supplement market, Nutrition. <sup>5</sup>Statista (2022) Dietary supplement market, Nutrition.

## In France, marketing by Valbiotis starting in 2024

Last October, Valbiotis announced its ambition of approaching the French market on its own with its three active substances. This decision is based on the clinical success of the HEART study with TOTUM-070 as well as the need expressed in market studies, conducted between 2021 and 2022 by Valbiotis among French consumers and physicians (see below). The Company's objective: to generate rapid and independent income in its domestic market.

Marketing operations will rely on a sales force oriented towards healthcare professionals (general practitioners, certain specialists and pharmacists) and a digital marketing strategy targeting consumers/patients. The planned distribution channels will be pharmacies, drugstores and online sales. TOTUM-070 will be the first product marketed by Valbiotis in France, in the first half of 2024, followed by TOTUM-448 and TOTUM-854.

**A promising French market for Valbiotis' active substances**

The French dietary supplement market will reach 3.2 billion euros in 2025, with annual growth of 7.3% between 2019 and 2025, primarily bolstered by natural products<sup>1</sup>.

The potential is considerable for Valbiotis: 34% of French people with moderately high blood pressure or LDL cholesterol use dietary supplements to regulate their blood pressure and cholesterol<sup>2</sup>.

**Metabolic and cardiovascular risk factors widely spread**

Mild to moderate hypercholesterolemia  
**49%** of adults<sup>3</sup>

Mild to moderate raise in blood pressure  
**29%** of adults<sup>4</sup>

Metabolic liver disease (NAFLD)  
**16%** of adults<sup>5</sup>

<sup>1</sup>Statista (2022) Dietary supplement market, Nutrition. <sup>2</sup>Statista (2022) Dietary supplement market, Nutrition. <sup>3</sup>Statista (2022) Dietary supplement market, Nutrition. <sup>4</sup>Statista (2022) Dietary supplement market, Nutrition. <sup>5</sup>Statista (2022) Dietary supplement market, Nutrition.

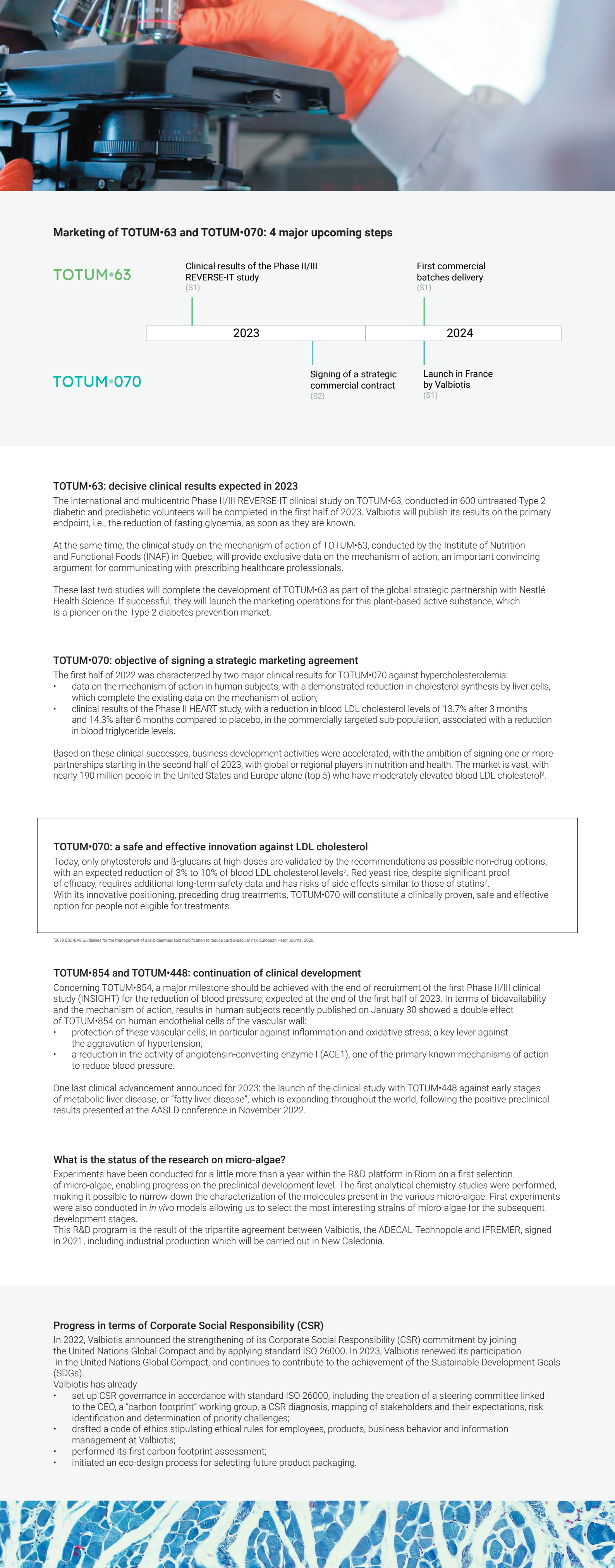
The market studies conducted by Valbiotis revealed that physicians and consumers viewed its three active substances very favorably. According to these studies, 46% to 56% of French consumers questioned and concerned expressed a very strong intent to buy for TOTUM-070, TOTUM-448 and TOTUM-854 in their indications (see below).

**Effective, natural and safe (no side effects):** the main points of interest towards the concepts for French consumers (top 5) for Valbiotis in 508 French consumers (2022)

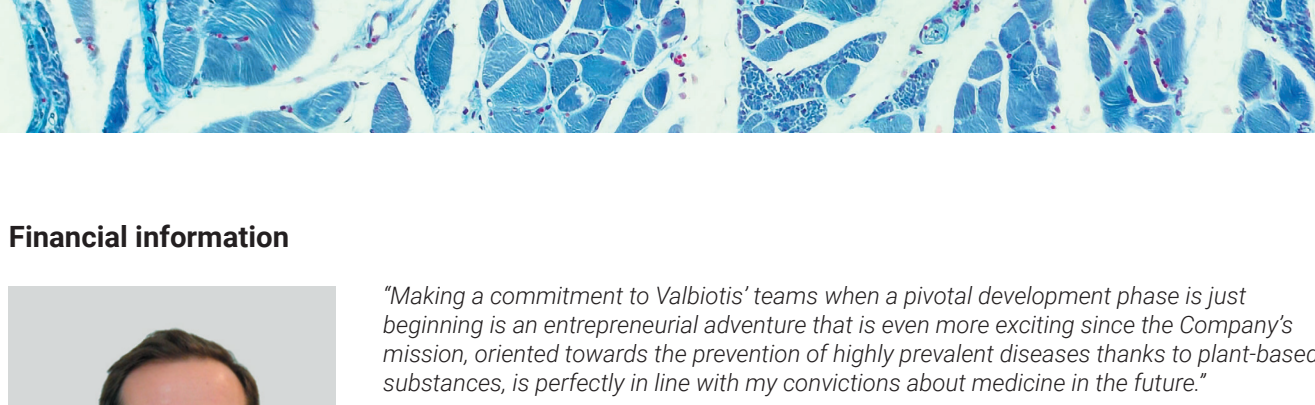
	Overall interest in the product (mean score /10)	% of concerned consumers reporting very high likelihood to purchase
<b>TOTUM-070</b>	<b>7.9</b>	<b>52%</b>
<b>TOTUM-854</b>	<b>7.7</b>	<b>46%</b>
<b>TOTUM-448</b>	<b>8.0</b>	<b>56%</b>

As far as physicians were concerned, they considered these three concepts to be relevant (assessed at 7/10), unique (assessed at 8/10) and suited to medical needs (assessed at 7/10)<sup>1</sup>.

<sup>1</sup>©2022 Valbiotis. All rights reserved. <sup>2</sup>Statista (2022) Dietary supplement market, Nutrition. <sup>3</sup>Statista (2022) Dietary supplement market, Nutrition. <sup>4</sup>Statista (2022) Dietary supplement market, Nutrition. <sup>5</sup>Statista (2022) Dietary supplement market, Nutrition.



## Marketing of TOTUM-63 and TOTUM-070: 4 major upcoming steps



## TOTUM-63: decisive clinical results expected in 2023

The international and multicentric Phase II/III REVERSE-IT clinical study on TOTUM-63, conducted in 600 untreated Type 2 diabetic and prediabetic volunteers will be completed in the first half of 2023. Valbiotis will publish its results on the primary endpoint, i.e., the reduction of fasting glycemia, as soon as they are known.

At the same time, the clinical study on the mechanism of action of TOTUM-63, conducted by the Institute of Nutrition and Functional Foods (INAF) in Quebec, will provide exclusive data on the mechanism of action, an important convincing argument for communicating with prescribing healthcare professionals.

These last two studies will complete the development of TOTUM-63 as part of the global strategic partnership with Nestlé Health Science. If successful, they will launch the marketing operations for this plant-based active substance, which is a pioneer on the Type 2 diabetes prevention market.

## TOTUM-070: objective of signing a strategic marketing agreement

- The first half of 2023 was characterized by two major clinical results for TOTUM-070 against hypercholesterolemia:
  - data on the mechanism of action in human subjects, with a demonstrated reduction in cholesterol synthesis by liver cells, which complete the existing data on the mechanism of action;
  - clinical results of the Phase II HEART study, with a reduction in blood LDL cholesterol levels of 13.7% after 3 months and 14.3% after 6 months compared to placebo, in the commercially targeted sub-population, associated with a reduction in blood triglyceride levels.

Based on these clinical successes, business development activities were accelerated, with the ambition of signing one or more partnerships starting in the second half of 2023, with global or regional players in nutrition and health. The market is vast, with nearly 190 million people in the United States and Europe alone (top 5) who have moderately elevated blood LDL cholesterol<sup>1</sup>.

## TOTUM-854 and TOTUM-448: continuation of clinical development

Concerning TOTUM-854, a major milestone should be expected with the end of recruitment of the first Phase II/III clinical study (INSIGHT) for the reduction of blood pressure, achieved at the end of the first half of 2023. In terms of bioavailability and the mechanism of action, results in human subjects recently published on January 30 showed a double effect of TOTUM-854 on human endothelial cells of the vascular wall:

- protection of these vascular cells, in particular against inflammation and oxidative stress, a key lever against the aggravation of hypertension;
- a reduction in the activity of angiotensin-converting enzyme I (ACE1), one of the primary known mechanisms of action to reduce blood pressure.

One last clinical advancement announced for 2023: the launch of the clinical study with TOTUM-448 against early stages of metabolic liver disease, or "fatty liver disease", which is expanding throughout the world, following the positive preclinical results presented at the AASLD conference in November 2022.

## What is the status of the research on micro-algae?

Experiments have been conducted for a little more than a year within the R&D platform in Riom on a first selection of micro-algae, narrowing down on the preclinical development level. The first analytical chemistry studies were performed, making it possible to embark on the characterization of the molecules present in the various micro-algae. First experiments were also conducted in *in vivo* models allowing us to select the most interesting strains of micro-algae for the subsequent development stages. This R&D program is the result of the tripartite agreement between Valbiotis, ADECAL-Technopole and IFREMER, signed in 2021, including industrial production which will be carried out in New Caledonia.

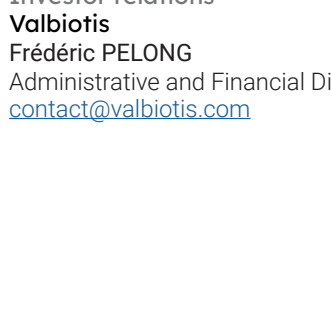
## Progress in terms of Corporate Social Responsibility (CSR)

In 2022, Valbiotis announced the strengthening of its Corporate Social Responsibility (CSR) commitment by joining the United Nations Global Compact, and by applying standard ISO 26000. In 2023, Valbiotis renewed its participation in the United Nations Global Compact, and continues to contribute to the achievement of the Sustainable Development Goals (SDGs).

Valbiotis has already:

- set up CSR governance in accordance with standard ISO 26000, including the creation of a steering committee linked to the CEO, a "carbon footprint" working group, a CSR diagnosis, mapping of stakeholders and their expectations, risk identification and determination of priority challenges;
- drafted a code of ethics stipulating ethical rules for employees, products, business behavior and information management at Valbiotis;
- performed its first carbon footprint assessment;
- initiated an eco-design process for selecting future product packaging.

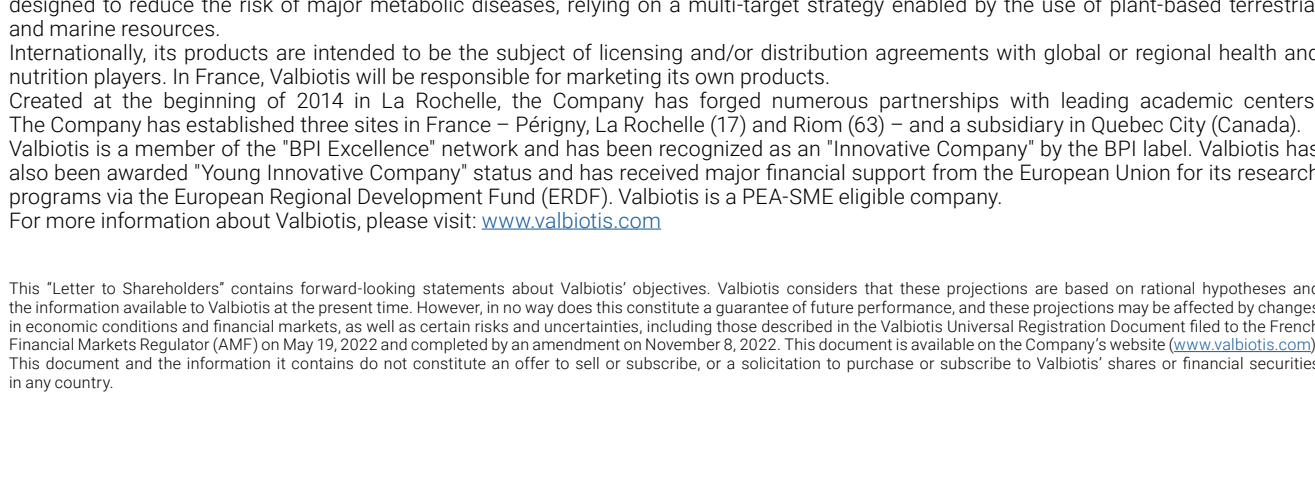
## Financial information



"Making a commitment to Valbiotis' teams when a pivotal development phase is just beginning is an entrepreneurial adventure that is even more exciting since the Company's mission, oriented towards the prevention of highly prevalent diseases thanks to plant-based substances, is perfectly in line with my convictions about medicine in the future."

**Frédéric PELONG,** Administrative and Financial Director and member of the Executive Committee, joined Valbiotis on June 1, 2022.

## Share Price trend: over three years, Valbiotis shares have clearly outperformed their benchmark index



## Shareholders breakdown

November 2022



- Market capitalization: €48 M at Feb. 22, 2023 (price €3.87)
- Number of shares: 12,424,918
- Cash position: € 15.4M at June 30, 2022.
- Excluding the proceeds of the fundraising achieved Nov. 8, 2022 (€ 9.7M).

Identity card Listed on Euronext Growth Paris  
Mnemonic code: ALVAL  
ISIN code: FR0013254851  
Eligibility: PEA / PEA-SME  
Indices: EnterNext® PEA-PME 150

## 2023 financial calendar



## Analysts coverage

<b>Portzamparc</b> Mohamed KAABOUNI Target price: 12.90 EUR (Jan. 2023)	<b>Invest Securities</b> Thibaut VOGLIMACCI-STEPHANOPOLI Target price: 10.60 EUR (Nov. 2022)	<b>Oddo BHF</b> Martal DESCOUTURES Target price: 10.00 EUR (Nov. 2022)	<b>Midcount Partners</b> Coréintin MARTY Target price: 10.40 EUR (Nov. 2022)
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<sup>1</sup>©2022 Valbiotis. All rights reserved. <sup>2</sup>Statista (2022) Dietary supplement market, Nutrition. <sup>3</sup>Statista (2022) Dietary supplement market, Nutrition. <sup>4</sup>Statista (2022) Dietary supplement market, Nutrition. <sup>5</sup>Statista (2022) Dietary supplement market, Nutrition.

## Contacts

<b>Investor relations</b> <b>Valbiotis</b> Administrative and Financial Director <a href="mailto:contact@valbiotis.com">contact@valbiotis.com</a>	<b>Corporate Communication</b> <b>Valbiotis</b> Carole ROCHER Communications and Public Affairs Director	<b>Financial Communication</b> <b>Seitosei Actifin</b> Marianne PY Senior Consultant <a href="mailto:valbiotis@actifin.fr">valbiotis@actifin.fr</a>
	<b>Marc DELAUNAY</b> Communication Manager <a href="mailto:media@valbiotis.com">media@valbiotis.com</a>	

## About Valbiotis

Valbiotis is a commercially oriented 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 diseases, relying on a multi-target strategy enabled by the use of plant-based terrestrial and marine resources. Internationally, its products are intended to be the subject of licensing and/or distribution agreements with global or regional health and nutrition players. In France, Valbiotis will be responsible for marketing its own products. 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 Québec 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](http://www.valbiotis.com).

This "Letter to Shareholders" contains forward-looking statements about Valbiotis' activities. Valbiotis considers that these projections are based on rational hypotheses and the information available to Valbiotis at the present time. However, in no way does this constitute a guarantee of future performance, and these projections may be affected by changes in economic conditions and financial markets, as well as certain risks and uncertainties, including those described in the Valbiotis Universal Registration Document filed to the French Financial Markets Regulator (AMF) on May 19, 2022 and completed by an amendment on November 8, 2022. This document is available on the Company's website ([www.valbiotis.com](http://www.valbiotis.com)). This document and the information it contains do not constitute an offer to sell or subscribe, or a solicitation to purchase or subscribe to Valbiotis' shares or financial securities in any country.

Due to environmental considerations, as part of our commitments, our "Letter to Shareholders" will now be offered in digital format only.



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