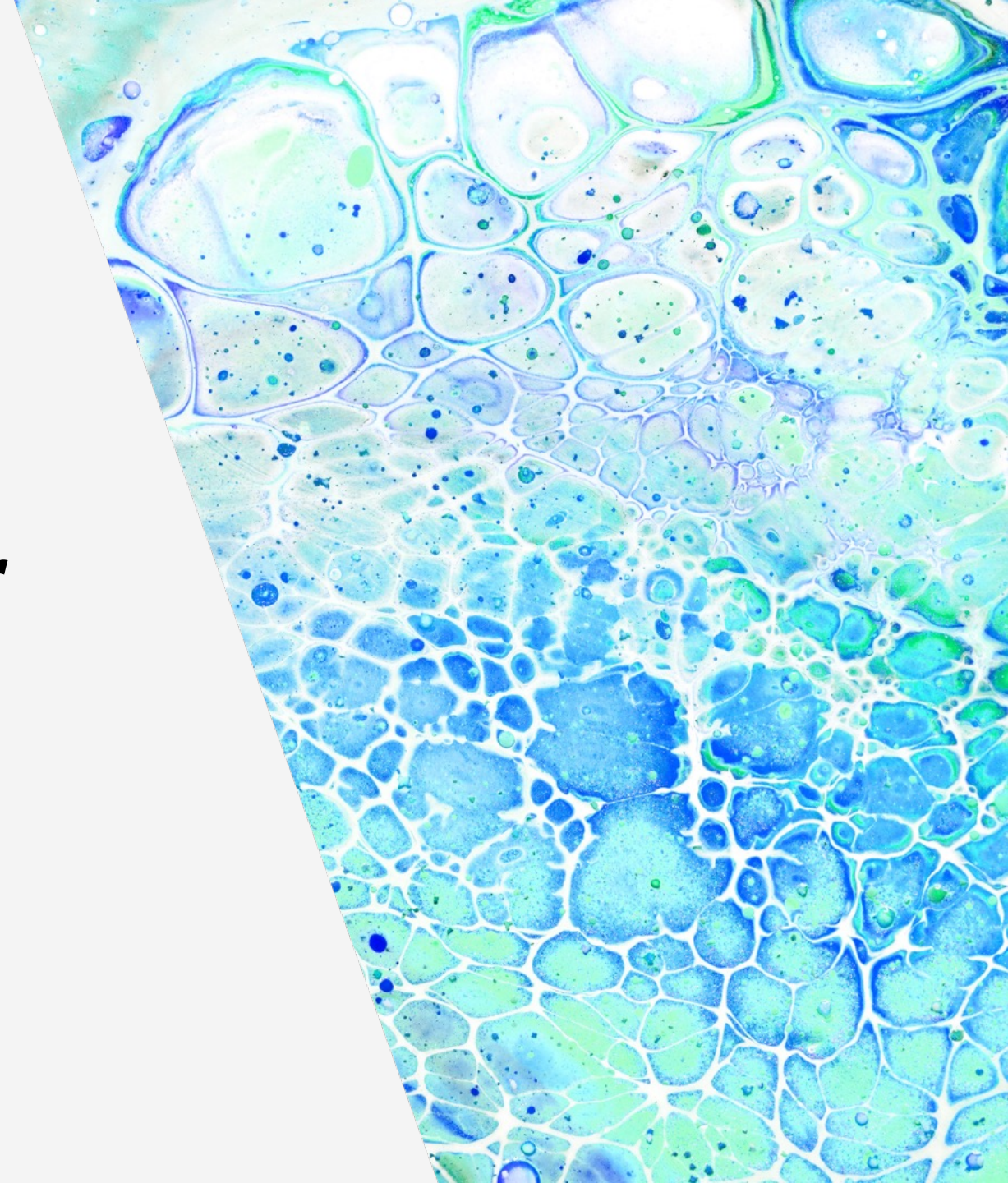


valbiotis®

**A future European leader
in 100% plant-based
dietary supplements**

April 2024



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Summary

Valbiotis

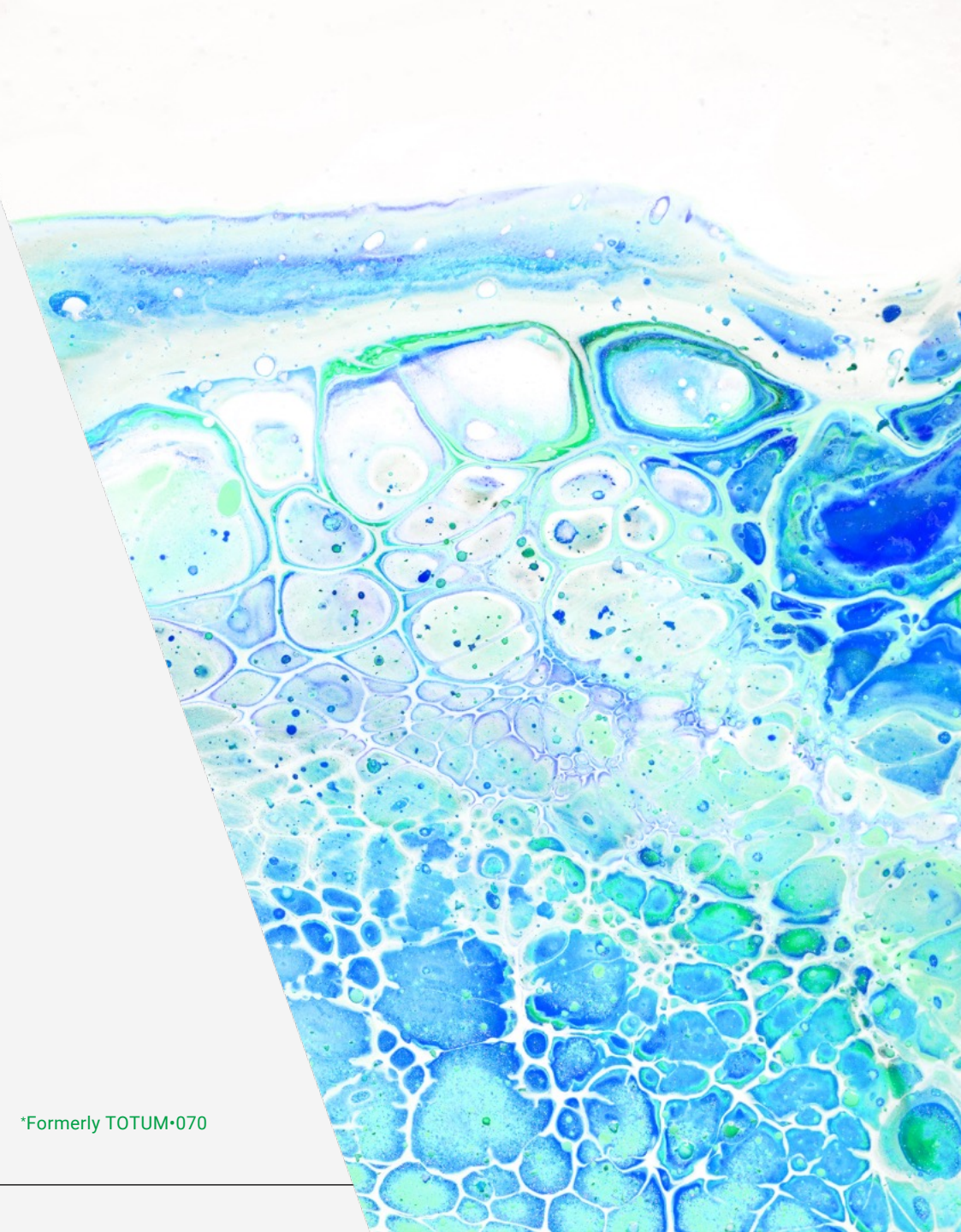
- Preventing metabolic and cardiovascular diseases: our job
- An expert management
- An efficient business model
- R&D, the core of our development

Development

- **TOTUM-63**: to reduce the risk of type 2 diabetes
- **Lipidrive^{®*}**: to reduce hypercholesterolemia
- **TOTUM-854**: to reduce blood pressure
- **TOTUM-448**: to reduce hepatic steatosis
- **Microalgae**: an exclusive agreement in New Caledonia

Financial information & CSR

*Formerly TOTUM-070



Profile

**Foundation of the Company
in 2014**

Listed on Euronext Growth

65 employees

3 sites in France

Périgny (17),
La Rochelle (17),
Riom (63)
+ a subsidiary
at Québec City (Canada)

**A diversified portfolio with 4 food supplements
addressing major cardio-metabolic conditions**

Type 2 diabetes, LDL-cholesterol, hypertension,
metabolic liver diseases (MASLD, formerly NAFLD)

Active substances
protected by
3 patent families

**At least 61
countries**

An innovative
approach based on
**100% natural
products, based
on plant extracts**

Products supported
by a **high level of
scientific evidence**

**Own marketing
in France (excluding
TOTUM•63)**

**A global strategic
partnership with
Nestlé Health Science
(TOTUM•63, Type 2 diabetes)**

**Cash position:
€ 13.7M**
at June 30, 2023

Our mission

Valbiotis is a French scientific research laboratory, specialized in the development and marketing of food supplements for the prevention and fight against metabolic disorders causing cardiovascular diseases.

Our goal: reduce the impact these diseases may have on millions of early stage diagnosed patients in the world, to avoid them from developing a pathology.

Valbiotis has adopted an innovative approach, aiming to revolutionize healthcare by developing a new class of health nutrition products, inspired by evidence-based medicine, designed to reduce the risk of major metabolic and cardiovascular diseases, based 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 agreements with global and regional health and nutrition players. In France, marketing is carried out directly by Valbiotis.



Metabolic and cardiovascular health: considerable markets to conquer

Concerned populations in the USA and in the top 5 European countries

Prediabetes

30% of adults

148 million

38% adults with prediabetes in the USA

TOTUM-63

High risk state of developing Type 2 Diabetes

LDL cholesterol

37% of adults

187 million

adults with moderately elevated LDL cholesterol

Lipidrive®

Formerly TOTUM-070

Risk factor of cardiovascular diseases (atherosclerosis)

Raised blood pressure

25% of adults

123 million

adults with moderate elevation of blood pressure

TOTUM-854

Main cardiovascular risk factor in the world

Metabolic liver diseases without fibrosis (MASLD*)

18% of adults

91 million

adults with MASLD without fibrosis

TOTUM-448

Leads to frequently severe liver damage (MASH*)

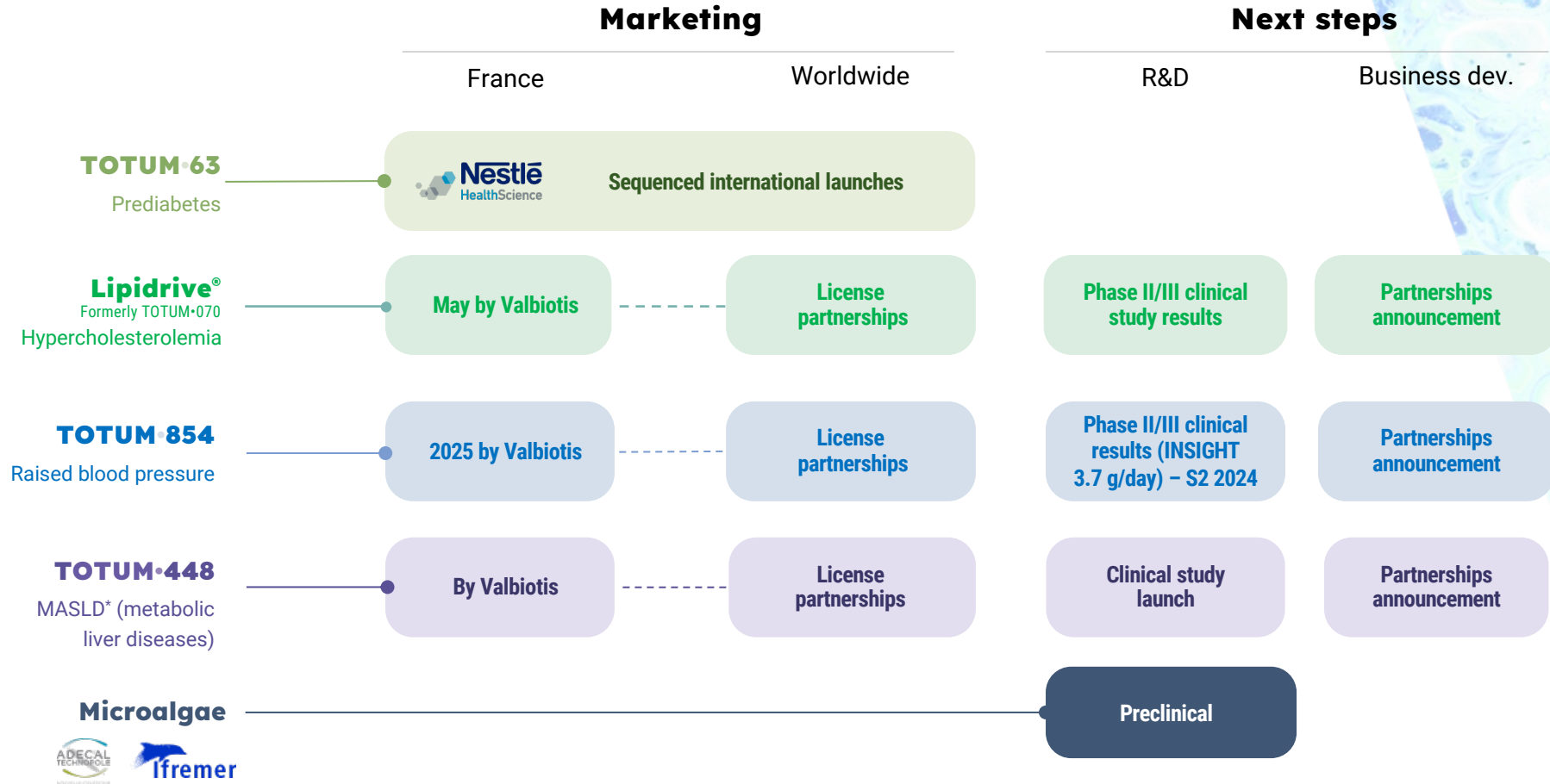
AEC Partners data, 2022.

*Metabolic-dysfunction-associated steatotic Liver Disease (MASLD) and metabolic-dysfunction-associated steatohepatitis (MASH), new designation of liver metabolic diseases (NAFLD and NASH) since June 2023.

A mature portfolio, for rapid marketing

Clinical evidence for our non-drug active substances

Development of 4 patented active substances, dedicated to reduce the risk of developing chronic complex metabolic and cardiovascular diseases.



*Metabolic-dysfunction-associated steatotic Liver Disease (MASLD) et metabolic-dysfunction-associated steatohepatitis (MASH), nouvelles dénominations des maladies métaboliques du foie (NAFLD et NASH) depuis juin 2023.

An expert management team for healthcare innovation

Executive Committee



**Sébastien
PELTIER**

Chief Executive Officer,
co-founder
PhD, HDR



**Pascal
SIRVENT**

CSO – Head of discovery,
preclinical and translational
research | PhD, HDR



**Murielle
CAZAUBIEL**

CMO – Head of medical,
regulatory and industrial
affairs (M.Sc.)



**Sébastien
BESSY**

COO – Head
of commercial and
marketing operations



**Stanislas
SORDET**

CFO – Head of
administration and
finance



**Charlotte
JEZEQUEL**

CPO – Head
of human relations

Supervisory board



**Laurent
LÉVY**

PhD – Chairman of the Supervisory Board
Remuneration Committee
CEO, co-founder, NANOBLOTIX



**Agnès
TIXIER**

Audit Committee
Investment Director then
Executive Director at Crédit Mutuel
Equity for 30 years.



**Dr Jean
ZETLAOUI**

MD, MBA
Audit Committee
Medical Affairs and Clinical
Development Consultant

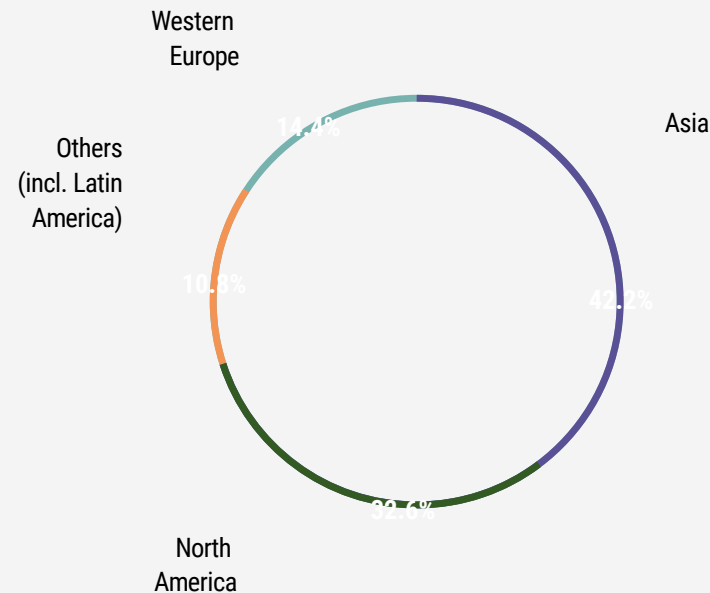
Food supplements: a strong growth global market

A €250 billion TO expected in 2025¹

A 9,6%¹, annual growth rate in TO supported by:

- A growing focus on health and prevention;
- The raising costs related to healthcare, the seek of alternatives for several problems;
- A segmentation of the offer depending on the specific needs of each population category;
- The popularity of plant-based products, as a complement to modern medicine².

A global market dominated by North America, Asia, Western Europe



Nutriform Business Days, 2019

A high turn over potential³

Brand	Company	TO (M€)
USA		
Nature Made	Otsuka	598
Nature's Bounty	The Bountiful Company (NHS)	435
Oilly	Otsuka	260
EUROPE		
Centrum	Haleon	106
Doppelherz	Queisser	105
Magne B6	Sanofi	104
ASIA		
Lipovitan	Taisho	387
Dong-e E-jiao	Dong-e E-jiao Group	365
Caltrate	Haleon	327

¹ Overview of the food supplements market – 2020-2021, Nutrikeo

² Vitamins & Dietary Supplements Market trends Overview , PwC Analysis, Technavio 2019, Press

³ Nicholas Hall , Viatmins/Minerals/Food Supplements market (2020)

A multiplier business model combining licensing partnerships and direct marketing in France

TOTUM•63
Prediabetes



Global strategic partnership



Exclusive global partnership since 2020



Global or regional strategic partnerships



Commercialization in France by
valbiotis®

Lipidrive®
Hypercholesterolemia

TOTUM•854
Raised blood pressure

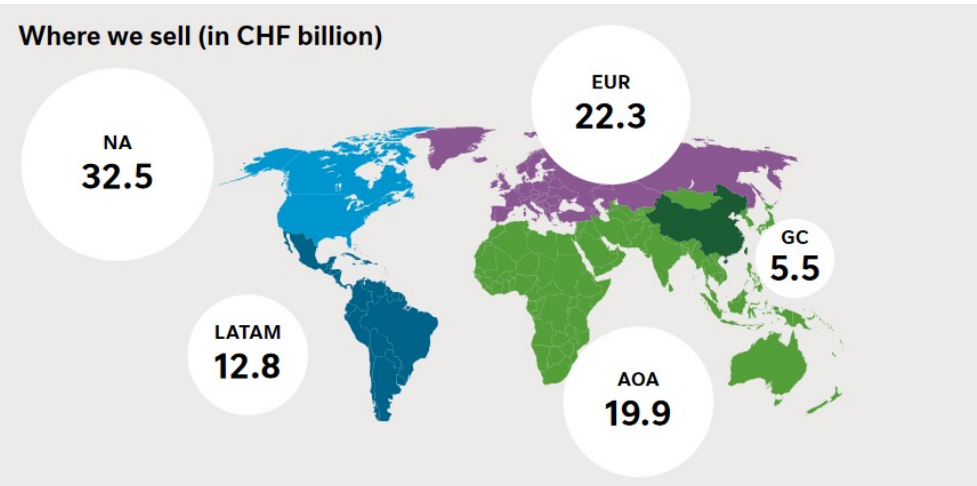
TOTUM•448
MASLD* (metabolic liver diseases)

Nestlé Health Science: “empowering healthier lives through nutrition”



A global agri-food giant

Operating in 188 countries.
2023 TO : 93 billion CHF.



EMENA: Europe, Middle-East and North Africa; AMS: Americas; AOA: Africa, Oceania, Asia



At the heart of Nestlé’s organic and external growth

The power of a player recognized by the medical community

- A global leader in the field of nutrition therapies.
- A turnover more than doubled since 2017 (CHF 6.5 billion in 2023), supported by an external growth strategy.
- Fields: healthy aging, healthy growing, gut health, metabolic health focusing on obesity.

A wide range of consumer health brands, medical nutrition and food supplements

Science-based to address unmet and emerging needs.



The partnership with NHS on TOTUM-63

A long-term strategic partnership for the development and worldwide commercialization of TOTUM-63, signed in February 2020, after the Phase II positive clinical results.

- **An exclusive license agreement worldwide** in prediabetes, type 2 diabetes, overweight and obesity
- **Deal structure:** a 3-pillar contract providing multiple sources of revenue



Lump sum payments

Up to CHF 71M

To receive

Up to
CHF 58,5 M



**Already
received**
CHF 12.5M

Royalties

Royalties on net sales

Supply revenue

An exclusive supply agreement
worldwide

First TOTUM-63 order
planned at S1 2024

- **A Joint Advisory Committee** to manage alliance

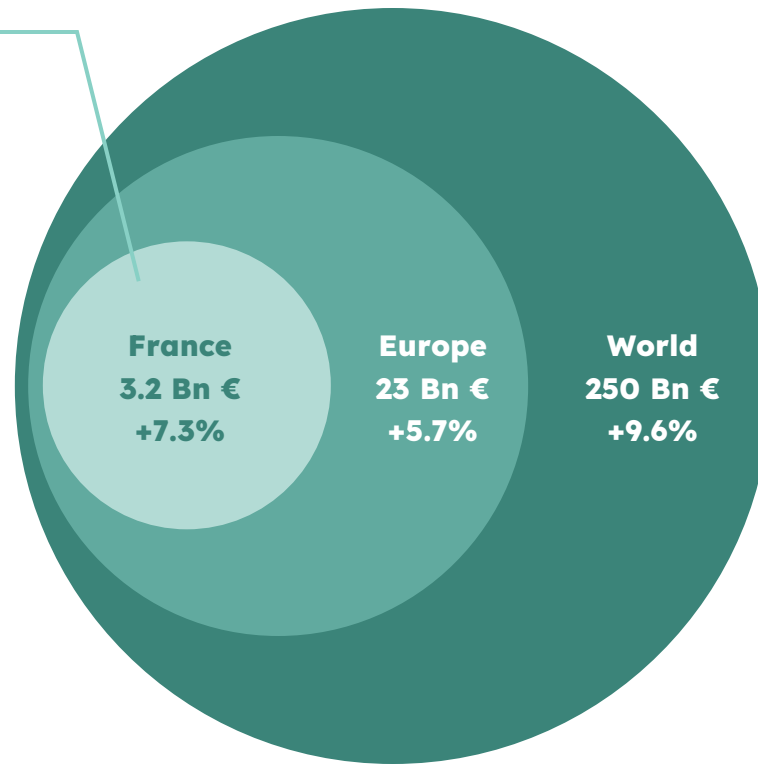
The French market: a strong demand of natural products and a large need for prevention

French food supplements market forecasted to grow faster than Europe¹

French market supported by natural products

88%
of drugstores with a shelf dedicated to natural health products¹.

93%
of the global revenue growth supported by plant-based products².



Forecasted market size in 2025 and annual growth rate in turn over 2019-2025

Metabolic and cardiovascular risk factors widely spread

Mild to moderate hypercholesterolemia

49% of adults³

Mild to moderate raise in blood pressure

29% of adults⁴

Metabolic liver disease (MASLD*)

16% of adults⁵

¹ Overview of the food supplements market – 2020-2021, Nutrikeo

² IQVIA, Food supplements in France, 2019

³ Cholesterol LDL \geq 1.0 g/L & Total cholesterol \geq 1.93 g/L, Elevated LDL, pre-HTA and NAFL preliminary market estimation, AEC Partners, 2020.

⁴ Ibid, SBP from 120 to 139 mmHg, DBP from 80 to 89 mmHg.

⁵ Vallet-Pichard A, et al. Épidémiologie de la stéato-hépatite non alcoolique, Étendue du problème et son impact sur la santé publique, Presse Med. 2019.

*Metabolic-dysfunction-associated steatotic Liver Disease (MASLD) and metabolic-dysfunction-associated steatohepatitis (MASH), new designation of liver metabolic diseases (NAFLD and NASH) since June 2023.

Plant-based products for prevention and early-management are valued by physicians



IFOP survey among French and German general practitioners and gastro-enterologists (2021/2022)¹

Physicians unanimously agree on prevention

"Prevention is the heart of medicine. Cardiovascular diseases, obesity, high cholesterol: prevention is always the most important!"

A clear interest in natural products

"It helps to avoid immediate therapeutic escalation. The main advantage is the low risk of side effects. There is a high demand from patients, it's trendy."

Multi-target modes of action considered relevant

"Products that have a synergistic and complementary action on several physiological targets are very interesting."

A strong expectation of clinical data

"Most of these natural products have no proven efficacy. I need to see data. My opinion? If the effectiveness is proven, I am absolutely in favor of these products. It must be effective, otherwise patients will be disappointed."

"It's great to have plant-based alternatives: patients increasingly want natural solutions that are effective, safe and relatively affordable."¹

¹METABOLIC DISEASE PREVENTION - Exploratory research & concept test , IFOP HealthCare
Methodology: individual interviews of 24 GPs and 12 gastroenterologists (France, Germany; 17 Nov. to 4 Dec. 2021), online community of 15 GPs (France, Germany; 24 to 31 Jan. 2022)

Natural health products: a very strong consumer trend



Focus on France 🇫🇷

Consumers are seeking for natural health

- **40%** of French people take food supplements to avoid taking medication when it is not necessary¹.
- The natural origin of products is the **2nd purchase** after effectiveness².

Distributors in tune with their customers

88% of pharmacies have a section dedicated to natural health products³.



A structuring effect on the evolution of the market

93% of the growth of food supplement market is accounted by plant-based products⁴.

- *"I would like to support my efforts to change my lifestyle with a solution that is effective on my liver and yet natural"*⁵
- *"I would like to be able to postpone taking blood pressure medications"*⁵
- *"I would like to be able to treat my cholesterol seriously and effectively with natural products and thus reduce the side effects of the chemical molecules"*⁵

¹Opinionway : les français et les compléments alimentaires, 2019

²Phytolia, les compléments alimentaires à base de plantes, janvier 20217

³Panorama du Marché des compléments alimentaires – 2020-2021, Nutrikeo

⁴QVIA, Marché des compléments alimentaires en France, 2019

⁵ Patients' insights, Valbiotis concept research

A commercial strategy in France targeted at healthcare professionals (general practitioners and pharmacists) and patients/consumers



Targeting of High potential GPs



Targeting of key pharmacies in the GPs perimeter



Targeting of patients/consumers with appropriate online marketing strategy



Sizing of commercial field force (16 APM recruited in 2024, 1 Area Director, 1 Medical Expert, Customer Relations department)



Mapping of commercial geographic areas

**Product ranges:
a complete offer accessible
to as many people as possible**

Valbiotis^{PRO}

- **Range of food supplements clinically proven** to prevent cardio-metabolic diseases (early stages) (TOTUM).
- **Recommended by prescription** by the general practitioner following a patient's blood test.
- **Presence in pharmacies in pharmacy drawers** and **over the counter** on the advice of the pharmacist and **on the e-commerce site**.

In support

Valbiotis^{PLUS}

- **Range of natural food supplements** to address disorders commonly associated with cardio-metabolic diseases and meeting the needs of patient-consumers.
- **Disponibles exclusivement sur le site e-commerce.**



R&D supported by experts, results acknowledged by international learned societies

Scientific and medical board

Over 900 scientific publications, including prestigious journals:
The Lancet, Nature, Diabetes Care.



Pr Samy HADJADJ

MD, PhD, PU-PH
Nantes University Hospital



Pr Jean-Marie BARD

PharmD, PhD, PUPH
Nantes University Hospital
(Emeritus Prof.)



André MARETTE

PhD - PU
Laval University Hospital INAF (Canada)



Bruno GUIGAS

PhD – Associate Prof.
Leiden University
Medical Center
(Netherlands)



Thierry MAUGARD

PhD, PU
La Rochelle University



Nathalie BOISSEAU

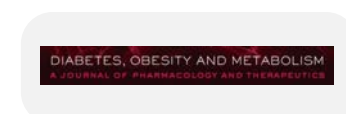
PhD, PU
Clermont Auvergne University

Scientific results validated by learned societies

More than 40 communications during
scientific congresses since 2016, including:



10 scientific papers published by international
journals since 2021



TOTUM•63

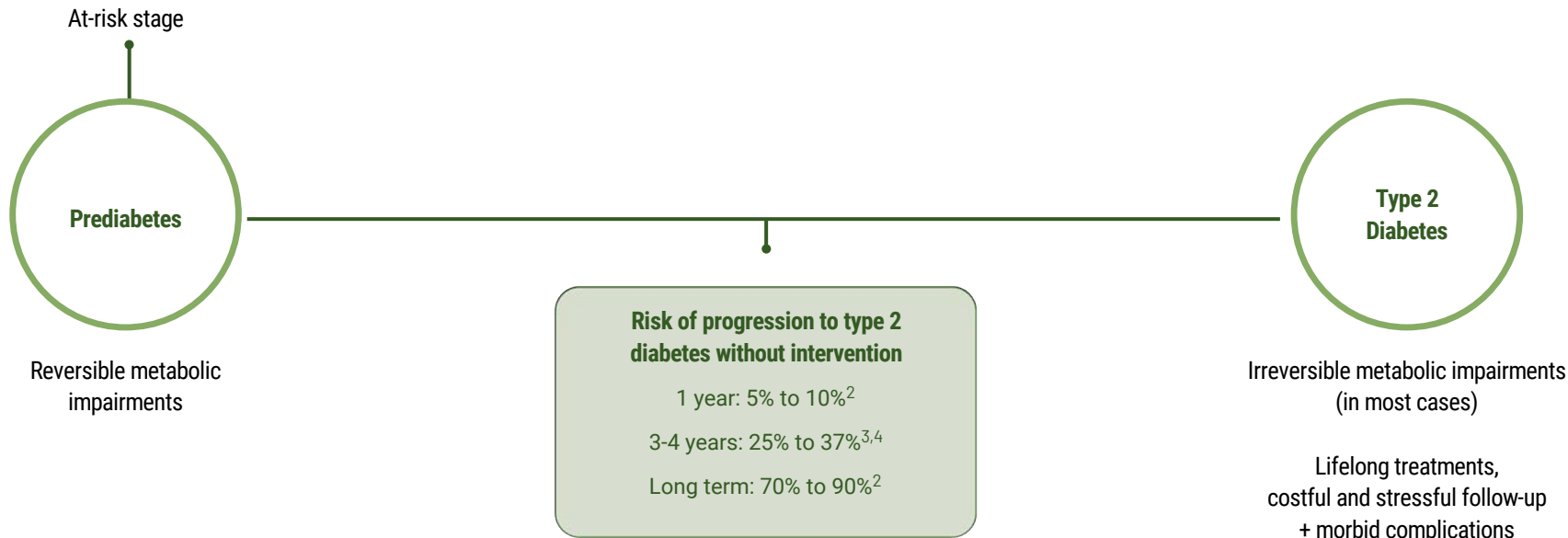
For early glycemc disorders, from prediabetes to early stage untreated type 2 diabetes.



TOTUM-63: prediabetes, an opportunity for type 2 diabetes prevention



“Prediabetes should not be considered as a disease but as a high-risk stage of developing Type 2 diabetes”¹



¹ Standards of care in Diabetes, ADA 2017 ;
² Tabak A.J. et al., Lancet, 2012 ;
³ Nathan D.M. et al., Diabetes Care, 2007 ;
⁴ Knowler W.C. et al., N Engl J Med, 2002

TOTUM-63: prediabetes market data



900 million
prediabetics in the world

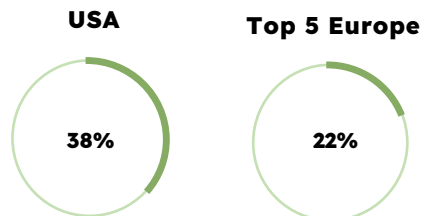


148 million
adults with prediabetes in the USA
and the Top 5 European countries



1 out of 3
adults with prediabetes in the USA
and the Top 5 European countries

Incidence of prediabetes

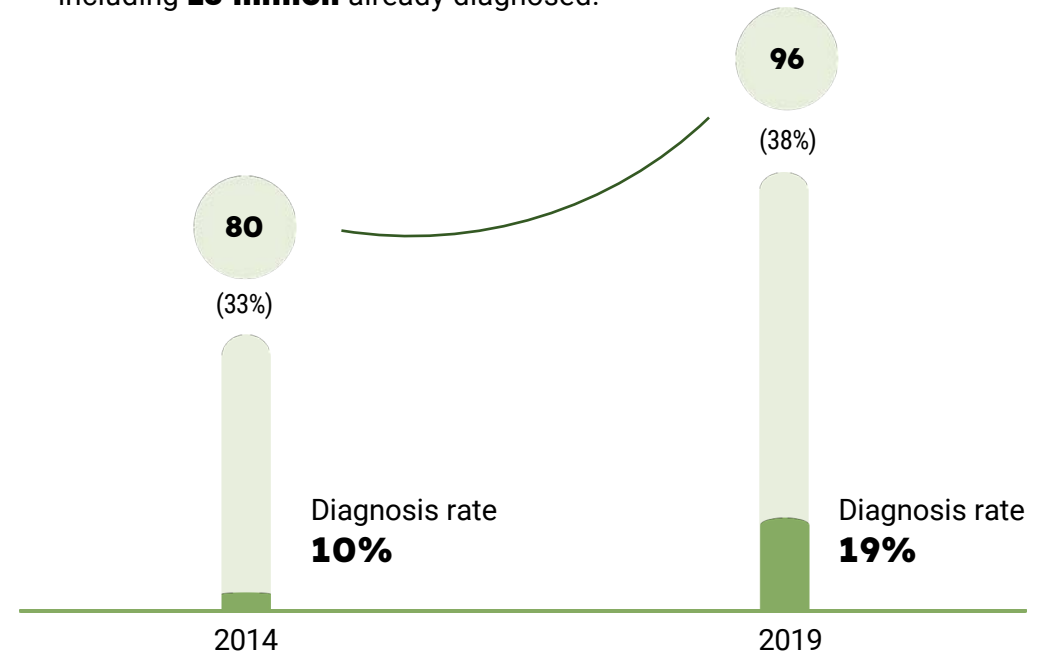


Data AEC Partners, 2019 et 2022.



**In the USA, a continuous growth
in the number of cases and in the diagnosis rate**

In 2019, **96 million** of adults with prediabetes,
including **18 million** already diagnosed.



www.cdc.gov/diabetes/data/statistics-report/prevalence-of-prediabetes.html
Center for Disease Control, accessed Oct. 3rd, 2023

TOTUM-63: prediabetes, a favourable environment for new products



**An easy diagnosis in primary care,
based on routine blood tests**



Moderate fasting hyperglycemia

Fasting glycemia
between:

1.00 and 1.25 g/L

HbA1c :

≥ 5.7% and < 6.5%

and/or

Fasting glycemia
between:

1.10 and 1.25 g/L

Impaired glucose tolerance

Fasting glycemia between:

1.4 and 2 g/L

2 hours after a 75 g oral glucose intake

**A recognition by international scientific societies
and health authorities**

- Awareness campaigns
- Encouragement of prediabetes testing
- Recommendations for prediabetes management

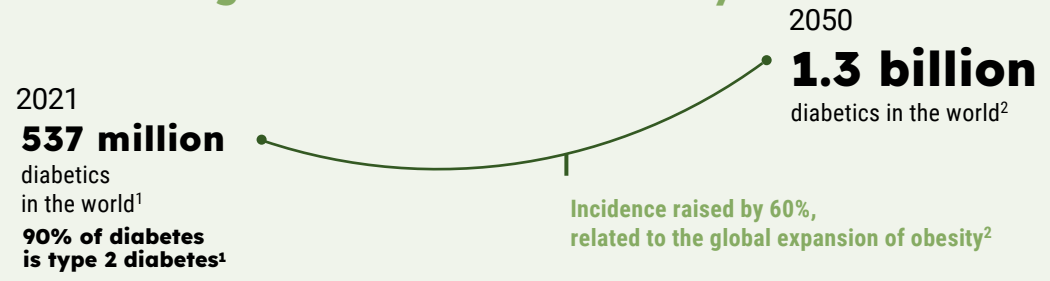
KNOW WHERE YOU STAND
DoIHavePrediabetes.org

American Diabetes Association | AMA | CDC

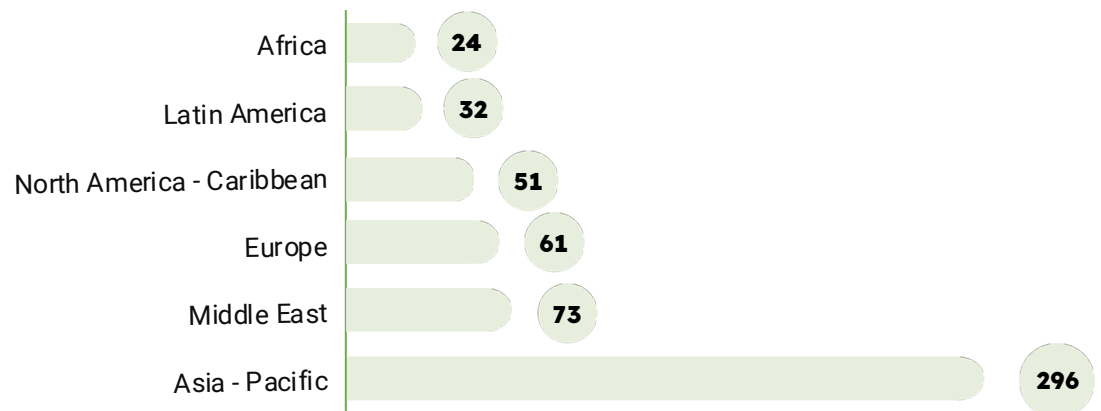
TOTUM-63: the constantly growing type 2 diabetes market



“Diabetes is one of the fastest growing global health emergencies of the 21st century”¹



People with diabetes in 2021 (million adults)¹



Including China and India (respect. 141 and 74 million people diabetes)

First stages of Type 2 diabetes: a large part of the market

Management of diagnosed patients (France and USA^{3,4,5,6})

No treatment



12 to 15%

First line therapy: one oral antidiabetic drug



34 to 46%

Therapeutic escalation: polymedication ± insulin



39 to 54%

¹ IDF Diabetes Atlas, 10th edition, International Diabetes Federation, 2021 ;
² Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050 a systematic analysis for the Global Burden of Disease Study 2021, The Lancet, 2023 ;
³ Bringer J et al. Prevalence of diagnosed type 2 diabetes mellitus in the French general population: The INSTANT study. Diabetes Metab 2008 ;
⁴ Prévalence et incidence du diabète, et mortalité liée au diabète en France, Anne Fagot-Campagna, InVS, 2010. ;
⁵ Diabetes in America, 3rd edition (chiffres 2007-2010) Cowie CC, et al., NIDDK, 2018, chap. 39 ;
⁶ Turner L. et al., Ambulatory Treatment of Type 2 Diabetes in the U.S., 1997–2012, Diabetes Care, 2014

TOTUM-63: the highest evidence-based active substance against prediabetes and untreated Type 2 diabetes (early stage)

An innovation in partnership with Nestlé Health Science.



An exclusive combination of 5 plant extracts

For early glycemc disorders, from prediabetes to early stage untreated type 2 diabetes



4 positive clinical studies
(2 RCTs), 720 people



Patents: France and international
(58 countries)



15 communications in international congresses



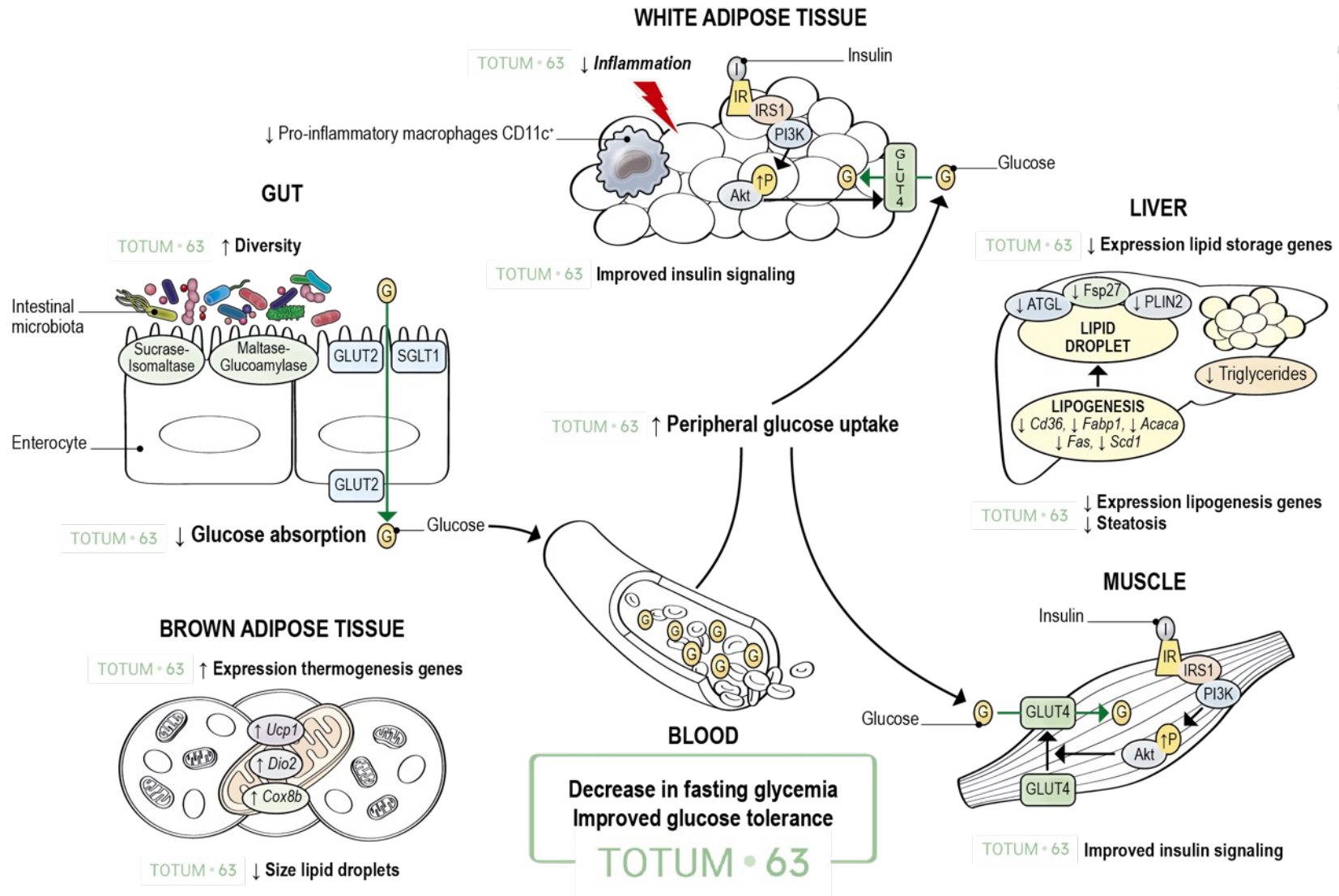
7 publications in international scientific journals



An unparalleled scientific and clinical package for a non-drug active substance

- ✓ **Multitarget mode of action with clinical evidence**
(glycated hemoglobin, inflammation, gastrointestinal hormones, post-prandial metabolic response).
- ✓ **Proven efficacy in all the clinical studies: Phase I/II, Phase II, Phase II/III**
(reduction of glycemc parameters and insulin resistance).
- ✓ **Favourable tolerance and safety profile, validated in all studies, compliance over 97%.**

TOTUM-63: a multitarget action on several tissues involved in metabolic regulation



TOTUM-63 / REVERSE-IT, the international Phase II/III pivotal study in prediabetics and untreated Type 2 diabetics



Study design

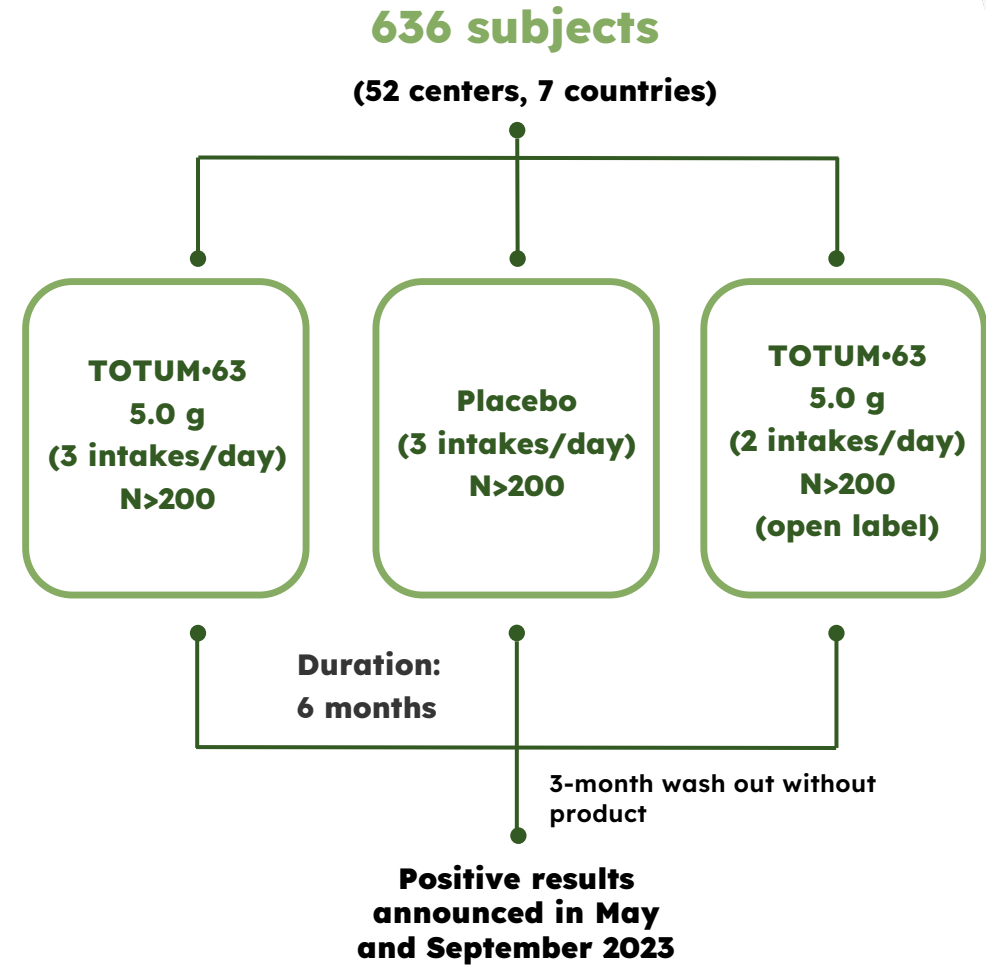
An international multicentric, randomized, placebo-controlled, double blind study.
Dose: 5g/day
Lifestyle advice to all participants
2 regimens: 2 and 3 intakes/day
A 3-month follow-up period, post-supplementation

Extended target population

Prediabetics + early stage untreated type 2 diabetics
• Elevated fasting glycemia (≥ 1.10 g/L and ≥ 1.26 g/L)
Abdominal obesity: waist circumference ≥ 102 cm (men) and > 88 cm (women)

Endpoints

Primary endpoint: reduction in fasting glycemia, a risk factor for type 2 diabetes, with TOTUM-63, 3 intakes/day, *versus* placebo
Other criteria: 2h glycemia (Oral Glucose Tolerance Test, OGTT), HbA1c, insulin-resistance score, low grade inflammation.
+ other metabolic parameters of interest



TOTUM-63 / REVERSE-IT: very good data regarding safety and tolerance, with a very high compliance rate



✓ **No safety problem reported during the study**

A very favourable tolerance profile

- No reported hypoglycemias
- Good gastro-intestinal tolerance

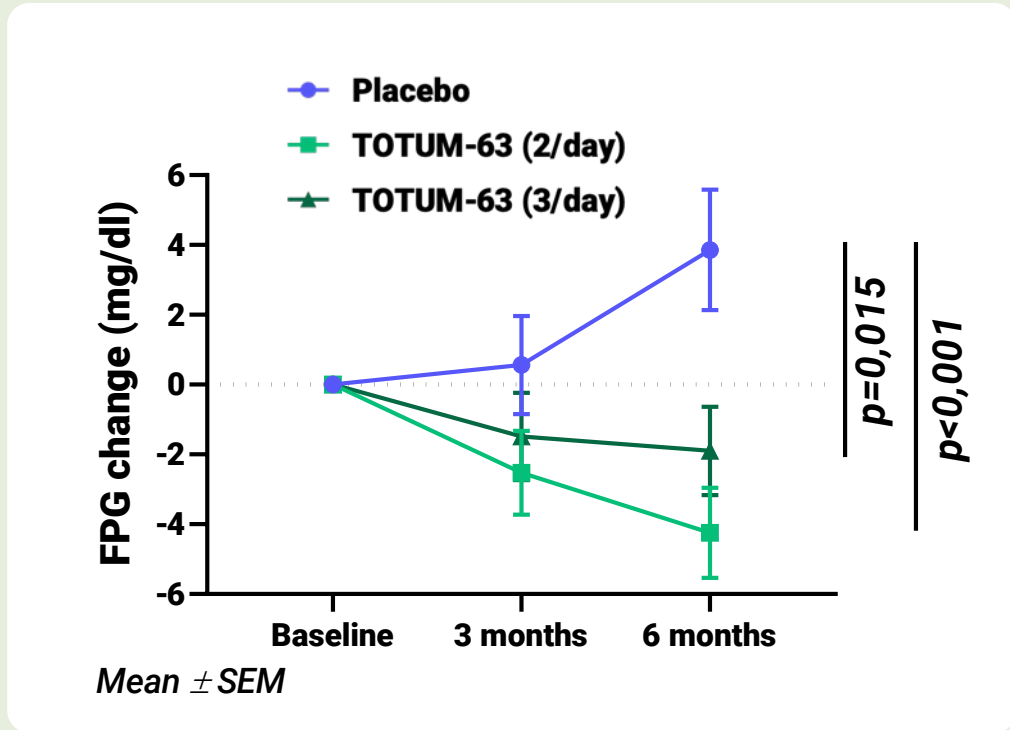
✓ **Excellent compliance**

> 97% compliance in the 3 groups throughout the study.

TOTUM-63 / REVERSE-IT: proven efficacy on fasting glycemia vs placebo in 2 and 3 intakes per day (study primary endpoint)



TOTUM-63, significantly reduces fasting glycemia after 6 months, vs placebo



Primary endpoint met (3 intakes/day)
High statistical significance (ITT and *per protocol*)



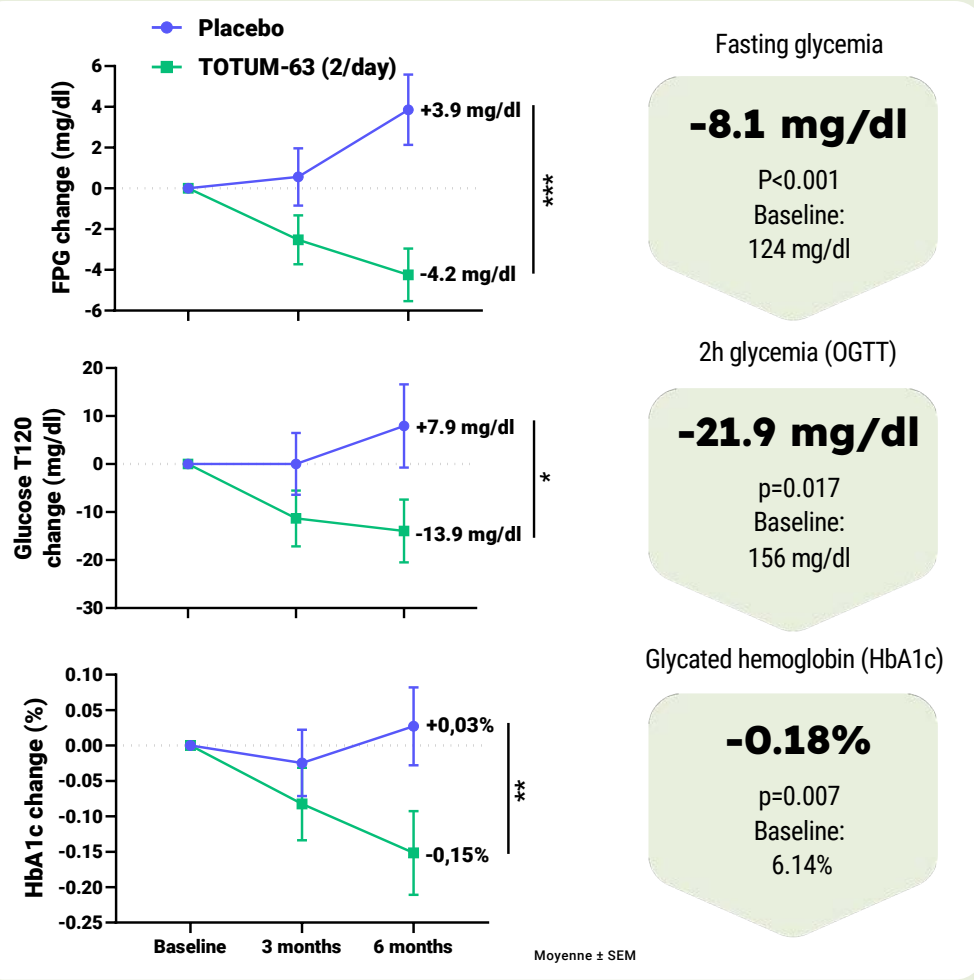
Validation of the 2 intakes/day regimen, the optimal regimen for patients and compliance in real life
No statistical difference between the two regimen

TOTUM-63 / REVERSE-IT: proven efficacy on the main glycemc markers



TOTUM-63,

2 intakes/day, after 6 months vs placebo



Significant reduction of glycemia, without reported hypoglycemia



Significant improvement in glucose tolerance



Significant reduction of HbA1c, marker of the microvascular risk, used for monitoring type 2 diabetes

TOTUM-63 / REVERSE-IT: efficacy levels to be compared to certain antidiabetic drugs in a similar population

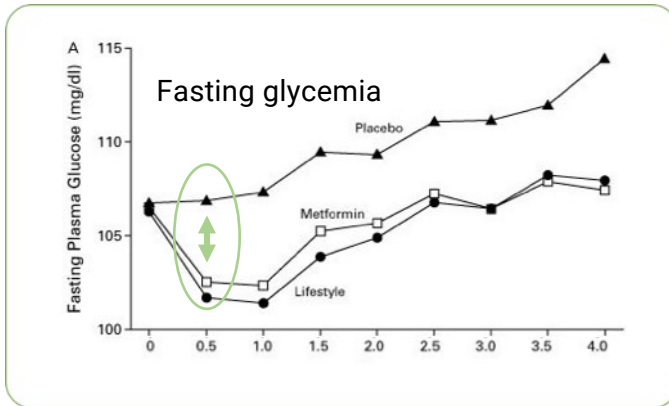
Efficacy of metformin (off label), a first line antidiabetic, in a prediabetic population



US Diabetes Prevention Program, USA: 3,041 prediabetes patients¹



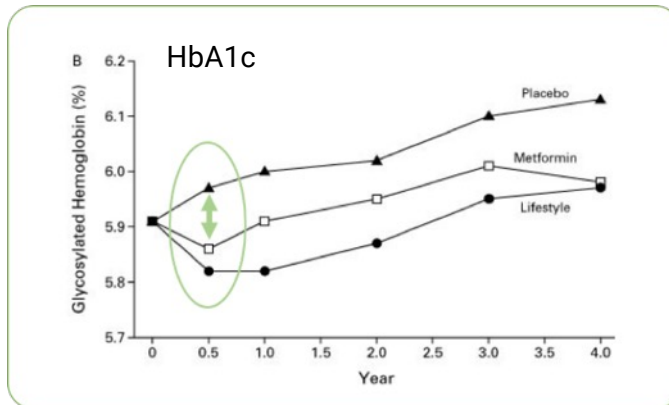
T-63



Metformin
- 3 mg/dl
vs
placebo

Fasting glycemia
After 6 months

- 8.1 mg/dl
vs
placebo



- 0.1%
vs
placebo

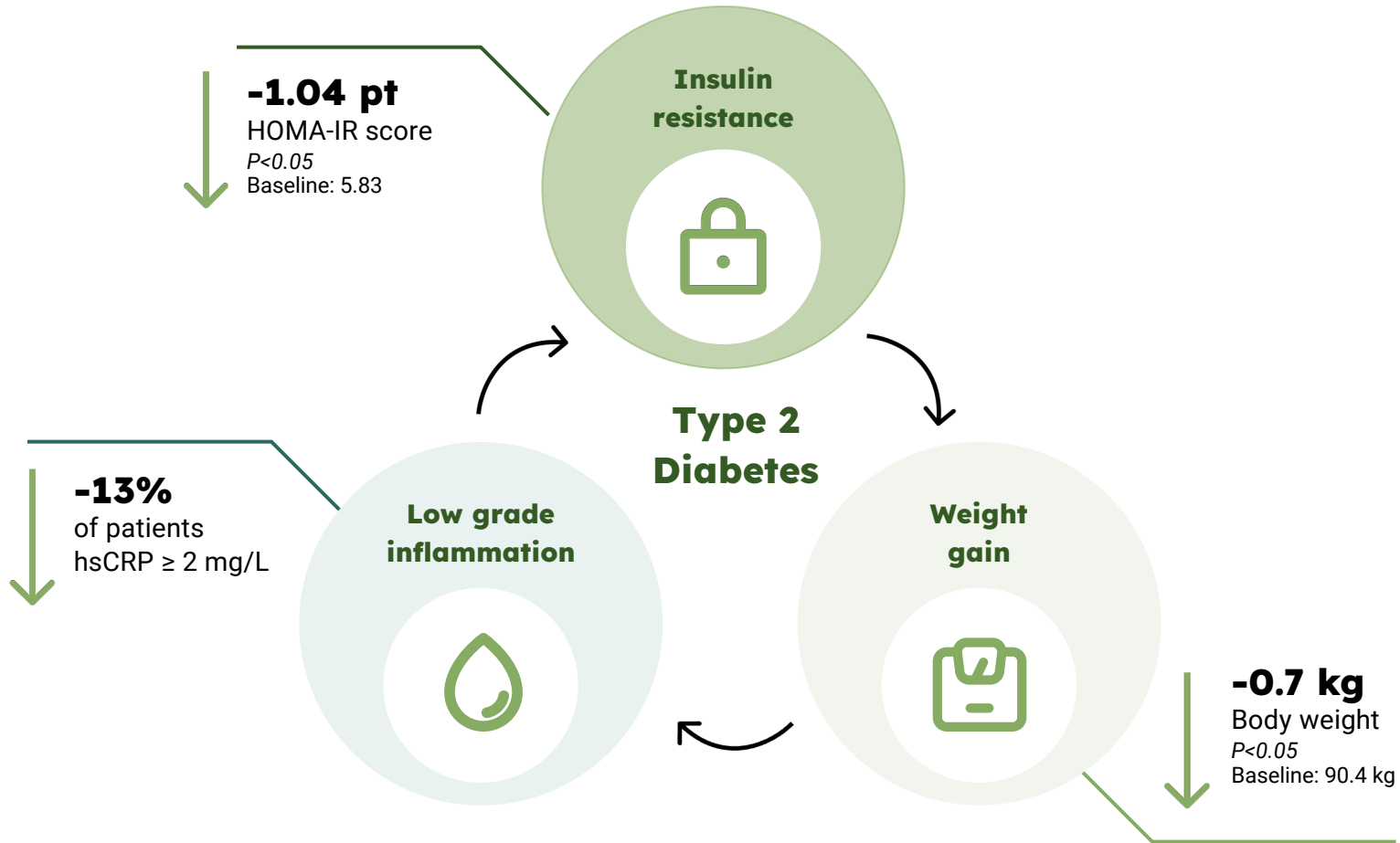
HbA1c
After 6 months

- 0.18%
vs
placebo

¹Reduction in the Incidence of Type 2 Diabetes with Lifestyle Intervention or Metformin, N Engl J Med 2002

TOTUM-63 / REVERSE-IT: efficacy on the pathogenesis of type 2 diabetes

TOTUM-63, 2 intakes/day, after 6 months vs placebo



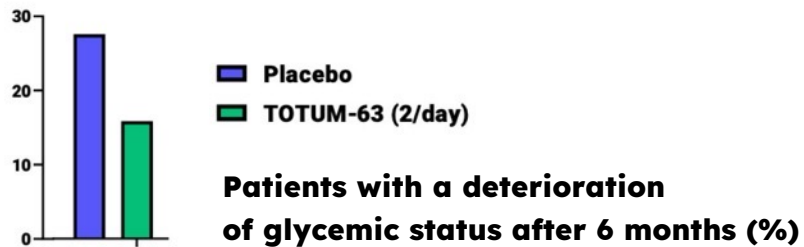
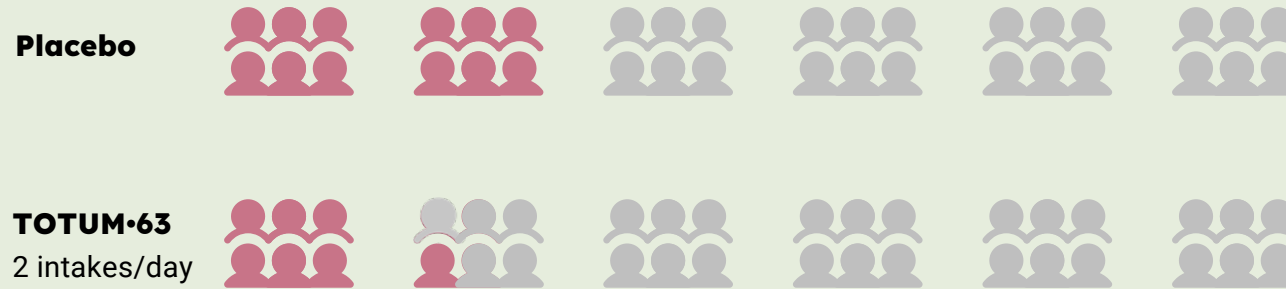
TOTUM-63 / REVERSE-IT: progression to type 2 diabetes significantly reduced



Prediabetics at baseline, having developed type 2 diabetes after 6 months

TOTUM-63
2 intakes/day
-40%

In new cases of diabetes after 6 months vs placebo.



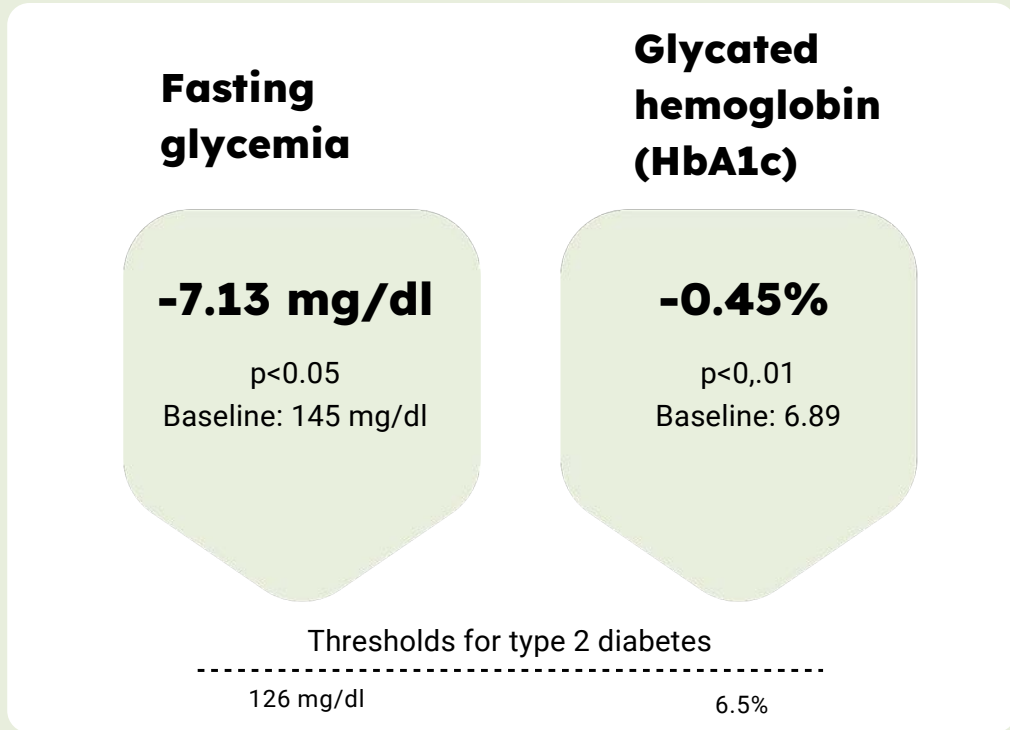
Proven preventive effect in prediabetics

TOTUM-63 / REVERSE-IT: beyond prediabetes, a proven efficacy in patients with early stage type 2 diabetes



TOTUM-63

2 intakes/day after 6 months compared to baseline



Results in the sub-population of patients with early stage, untreated type 2 diabetes



Clinical use validated in untreated early stage type 2 diabetics



Remarkable efficacy on HbA1c

Lipidrive®

For people with mild to moderate LDL hypercholesterolemia,
ahead of treatments.

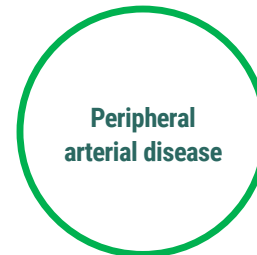
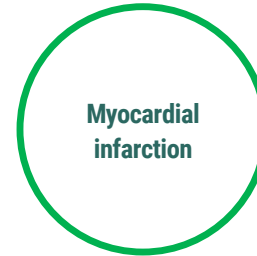
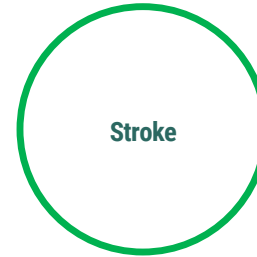
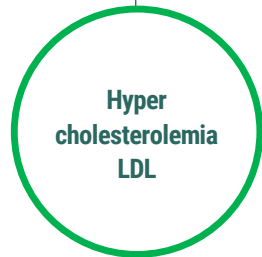


Lipidrive®*: LDL hypercholesterolemia, a risk factor for cardiovascular diseases

*Formerly TOTUM-070

“LDL-cholesterol is the primary cause of atherosclerosis.”¹

Alone or associated with other cardiovascular risk factors (arterial hypertension, diabetes, obesity, etc.)



Risk ++ of cardiovascular mortality

Atheroma plate breakage is the cause of 80% of sudden deaths.²



¹2018 Guideline on the Management of Blood Cholesterol, a report from the American College of Cardiology/American Heart Association, Journal Of The American College Of Cardiology, 2019

²<http://www.inserm.fr/information-en-sante/dossiers-information/atherosclerose>, accessed April 2, 2022

Lipidrive®*: mild to moderate LDL hypercholesterolemia: the market data (USA + Europe Top 5)

*Formerly TOTUM-070

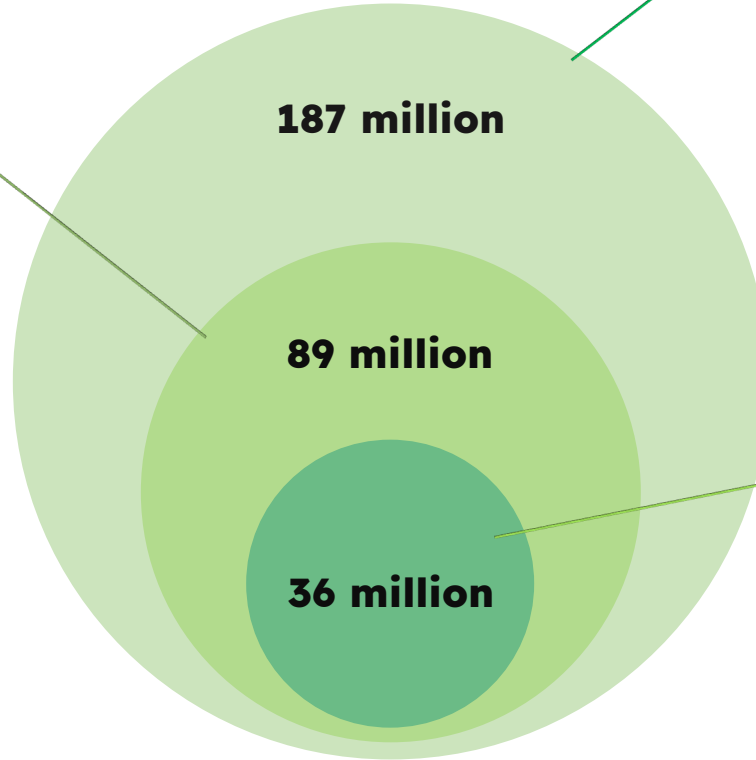
Prevalence: 37%

Adults diagnosed
Taux de diagnostic
moyen actuel : **48%**



1,2 billion euros

USA and Europe Top 5:
a large and well-established market



Adults with moderately elevated LDL cholesterol

 69.8 M	 20.8 M
 24.9 M	 15.5 M
 32.4 M	 23.7 M

Adults diagnosed and who use
food supplements to control
their cholesterol levels

Data AEC Partners, 2022.

Lipidrive®*: hypercholesterolemia in France

*Formerly TOTUM-070



Hypercholesterolemia (high concentration of LDL cholesterol) is one of the main causes of morbidity and healthcare consumption in France¹.

- **2nd cause of death** after cancer²
- **1st of death among women**, all ages combined²
- **20% of French adults** suffer from excess LDL cholesterol (> 1.6 g/l)

1 in 2 French adults have mild to moderate hypercholesterolemia

- **9%** of adults take lipid-lowering treatment
- **7%** of adults are on statins
- **Only 1 in 2 French people** are aware of their hypercholesterolemia

Sources: Santé publique France
Ministère de la Santé et de la Prévention

Lipidrive®*: both patients and physicians plebiscite non-drug options to reduce LDL cholesterol

*Formerly TOTUM-070

37% of adults worldwide aged 20 years or over have hypercholesterolemia

Natural products address medical needs:

- **Lack of efficient non-drug options** for early/borderline stages, and only moderate satisfaction with current treatments ;
- Need to **delay initiation** of pharmacological treatment and associated side effects ;
- Patients **do not always accept medical treatment** (notably statins).

2/3 of primary care physicians believe in a “pre-stage” to dyslipidaemia (caused by increased LDL cholesterol), that could concern 1 in 5 patients.

International scientific societies approve non-drug approaches, **if supported by clinical evidence.**



“I know that high cholesterol is a disease that should not be ignored because it is progressive. I know that there are effective medications, but I have also been told that they can have significant side effects, such as cramps and muscle pain. I would like to be able to treat my cholesterol seriously and effectively with natural products and thus reduce the side effects of the chemical molecules contained in usual medicines.”



“We have the need for an additional non-drug option in our clinical toolbox, efficient and well-tolerated, that reduces LDL-cholesterol before the situation worsens.”

Pr. Jean-Marie BARD

PharmD, PhD, PUPH CHU Nantes (Professor Emeritus)
Scientific advisor of the HEART study

Sources: Metabolic disease prevention – Exploratory research & concept test – Reporting interviews, Enquête IFOP pour Valbiotis, France, 2021 – US Qualitative Market Research 2022 - Valbiotis concept research

Lipidrive®*: an innovative and clinically tested non-drug response

*Formerly TOTUM-070



Produit commercialisé en France sous la marque Valbiotis®PRO Cholestérol

Lipidrive® was developed for people with mild to moderate hypercholesterolemia associated with a low to intermediate overall cardiovascular risk, before treatments and as a support to health and diet measures.

Reduce the blood level of LDL cholesterol, and through it the overall cardiovascular risk, without waiting for the situation to deteriorate

Lipidrive®, an innovative non-medicinal active substance:

- 100% natural, based on a patented combination of 5 plant extracts (artichoke leaf, olive leaf, golden chamomile, goji berry, black pepper);
- Without red yeast rice;
- No coloring, gluten-free, allergen-free, preservative-free;
- Designed and developed in France.



Artichoke leaf



Olive leaf



Golden Chamomile



Goji bath



Black pepper

Lipidrive®*: a demonstrated multitarget mechanism of action

*Formerly TOTUM-070

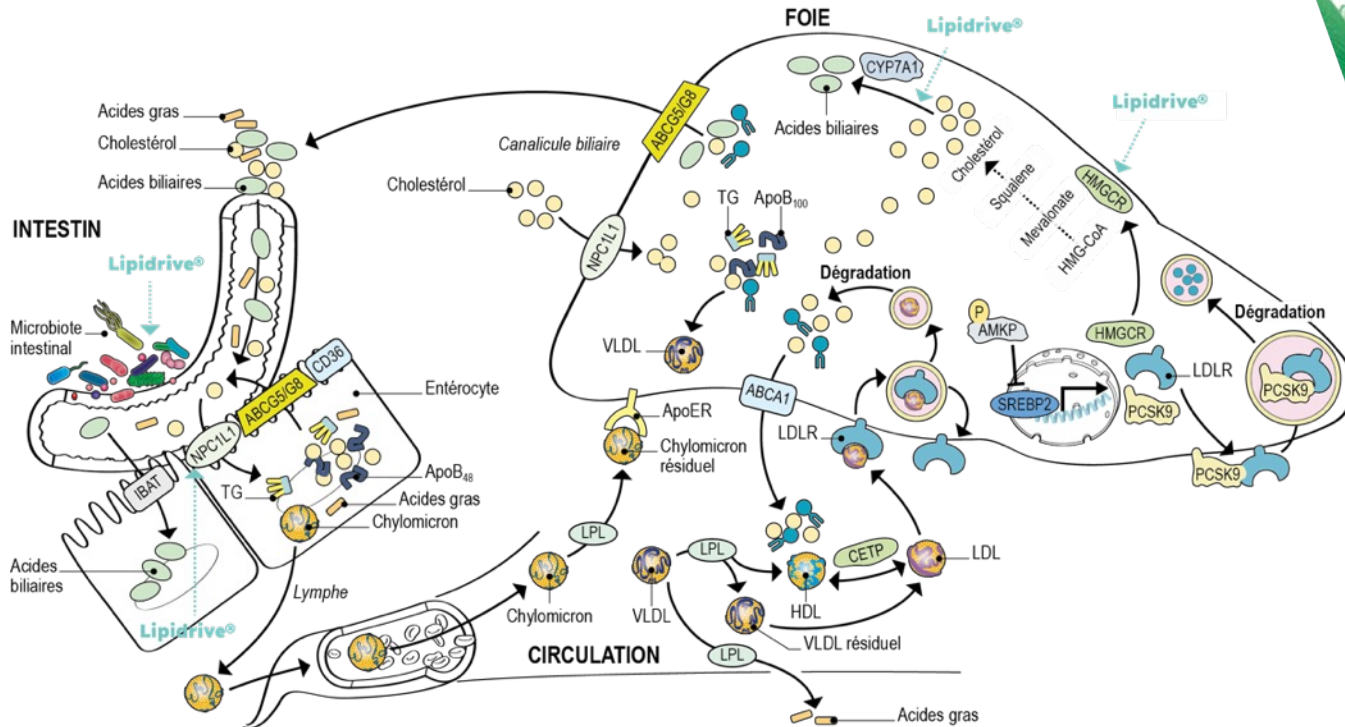
Intestine

- Reduced cholesterol absorption by enterocytes

Liver

- Reduction in cholesterol production by hepatocytes ;
- Reduction of cholesterol storage in hepatocytes.

In humans, Lipidrive® specifically reduces the abundance of bacteria of the Dorea genus, associated with hypercholesterolemia, while preserving the intestinal microbiota.



Sources :
 Wauquier et al. Nutrients, 2023 : <https://www.mdpi.com/2072-6643/15/8/1903>
 Langhi et al. Nutrients, 2023 : <https://www.valbiotis.com/wp-content/uploads/2023/12/nutrients-15-05056.pdf>
 Langhi et al. Frontiers in Cardio Med, 2024 :
https://www.frontiersin.org/articles/10.3389/fcvm.2024.1342388/full?utm_source=Email_to_authors&utm_medium=Email&utm_content=T1_11.5e1_author&utm_campaign=Email_publication&field=&journalName=Frontiers_in_Cardiovascular_Medicine&id=1342388

Lipidrive®*: two clinical efficacy studies (HEART and OLALIP), carried out on more than 150 subjects

*Formerly TOTUM-070

Increased effectiveness on the targeted population from 6 weeks

Cholesterol LDL > 1.3 g/L



Cholesterol LDL > 1.6 g/L



Efficative for 93% of patients, positive results were observed in volunteers with mild to moderate excess cholesterol, and not following lipid-lowering treatment.

Both studies demonstrated:

- excellent tolerance revealing no major side effects
- excellent compliance of 97% (average for the two clinical studies)

A Phase II/III study is underway on 180 patients

15 communications in congresses

3 scientific publications

valbiotis®

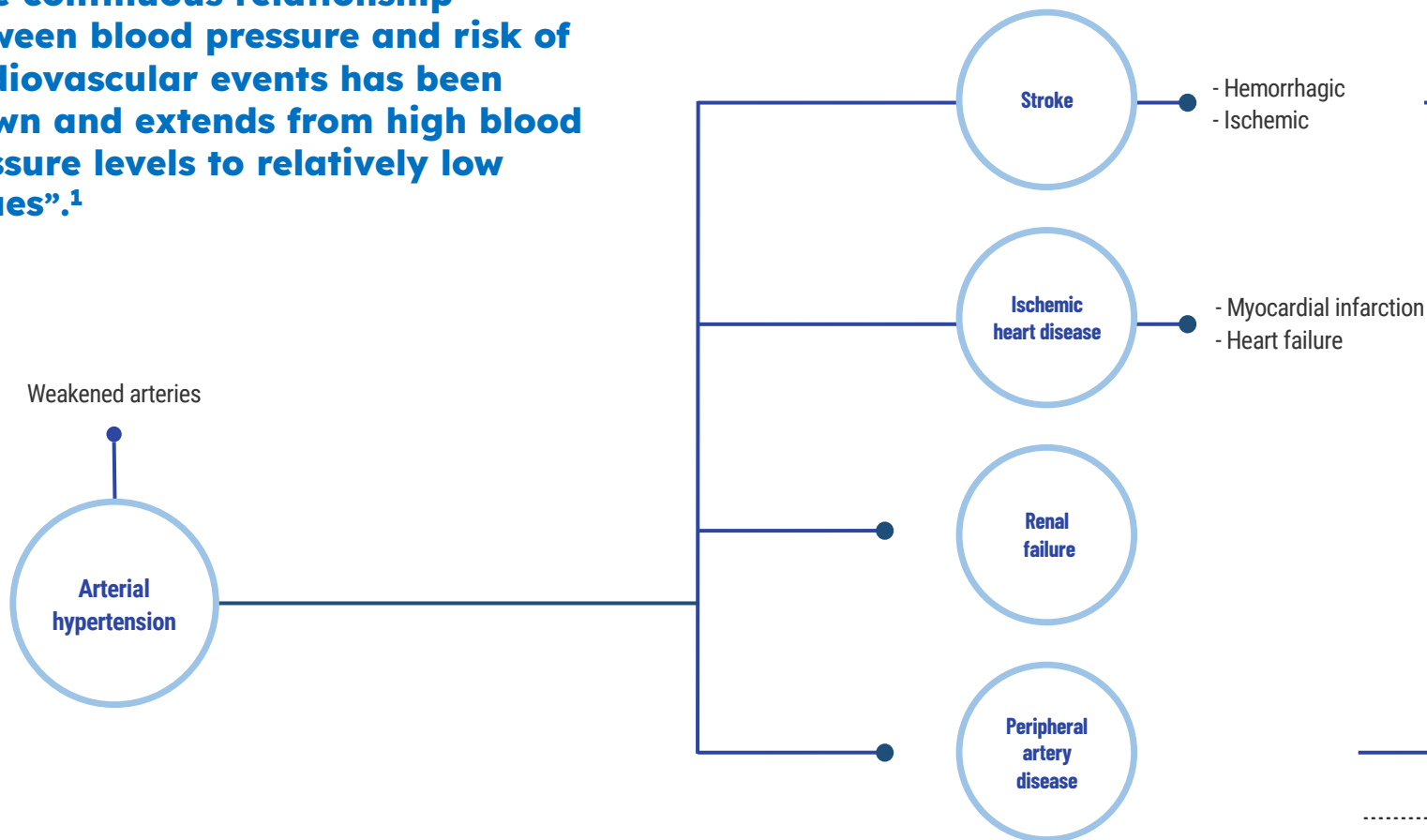
TOTUM•854

For mild to moderate raise in blood pressure,
ahead of treatments.



TOTUM 854: raised blood pressure, the leading cardiovascular risk factor in the world

“The continuous relationship between blood pressure and risk of cardiovascular events has been shown and extends from high blood pressure levels to relatively low values”.¹



Major risk of mortality and disability
First cause of premature death in the world: 10 million in 2015.¹
Up to 76 million deaths by 2050 according to WHO









¹ ESC/ESH Guidelines for the management of arterial hypertension, European Heart Journal, 2018

TOTUM-854: mild to moderate elevation of blood pressure, the market data (USA + Europe Top 5)

Prevalence: 25%

Adults diagnosed
Current average
diagnosis rate: **62%**

Adults with moderate elevation of blood pressure

-  56.5 M
-  14.9 M
-  17.7 M
-  13.9 M
-  9.6 M
-  10.4 M

123 million

76 million

32 million

Adults diagnosed and who use food supplements to control their blood pressure



1,15 billion euros

USA and Europe Top 5:
the mild to moderate raise
of blood pressure market

Données AEC Partners, 2022.

TOTUM-854: non-drug options are needed to control arterial blood pressure, to postpone pharmacological treatment and avoid associated side effects

1.3 billion people suffering from arterial hypertension worldwide¹
→ **world 1st chronic disease**

The majority of doctors and learned societies have accepted the existence of an early stage of hypertension, affecting approximately **15%** of patients, and characterized by slightly elevated blood pressure values.²

Medical needs remain for early-stage patients:

- Lack of **options for patient with a mild raise in blood pressure and/or associated risk** (incl. Stage 1);
- Lack of efficient products to **delay initiation of pharmacological treatment**;
- **No natural products recommended** so far, mainly because unproven.



*“My doctor feels that my blood pressure is becoming too high and is considering taking blood pressure medication in the next few months. I would like to be able to **postpone taking such medication**.”*



*“With high blood pressure affecting so many people, prescription blood pressure medication is being used more than ever. While medication is effective, there are **negative side effects** that some people may not be able to tolerate”*



*“In patients at risk of cardiovascular and metabolic diseases, it is important to act as soon as blood pressure starts to raise. These persons, non-eligible to treatments, should be provided **with a non-drug option, clinically proven and well-tolerated**, to control blood pressure.”*

Murielle CAZAUBIEL

Head of Medical, Regulatory and Industrial Affairs, Valbiotis

Arterial hypertension thresholds

- Europe: arterial blood pressure $\geq 140/90$ mmHg* persisting over time², or $\geq 130/85$ mmHg in subjects with metabolic syndrome
- USA: arterial blood pressure $\geq 130/90$ mmHg

Sources:

¹ <https://www.who.int/fr/news/item/19-09-2023-first-who-report-details-devastating-impact-of-hypertension-and-ways-to-stop-it>

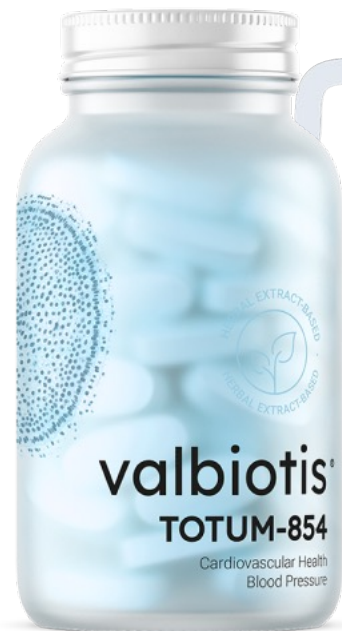
² ESH 2023 guidelines

Metabolic disease prevention – Exploratory research & concept test – Reporting interviews, Enquête IFOP pour Valbiotis, France, 2021 – US Qualitative Market Research 2022 - Valbiotis concept research – Dr Andrew Weil Youtube Channel

TOTUM-854: an active substance for early stage arterial hypertension

An exclusive combination of 6 plant extracts

For mild to moderate raise in blood pressure, ahead of treatments.



Patents: France and international
7 communications in congresses since 2021



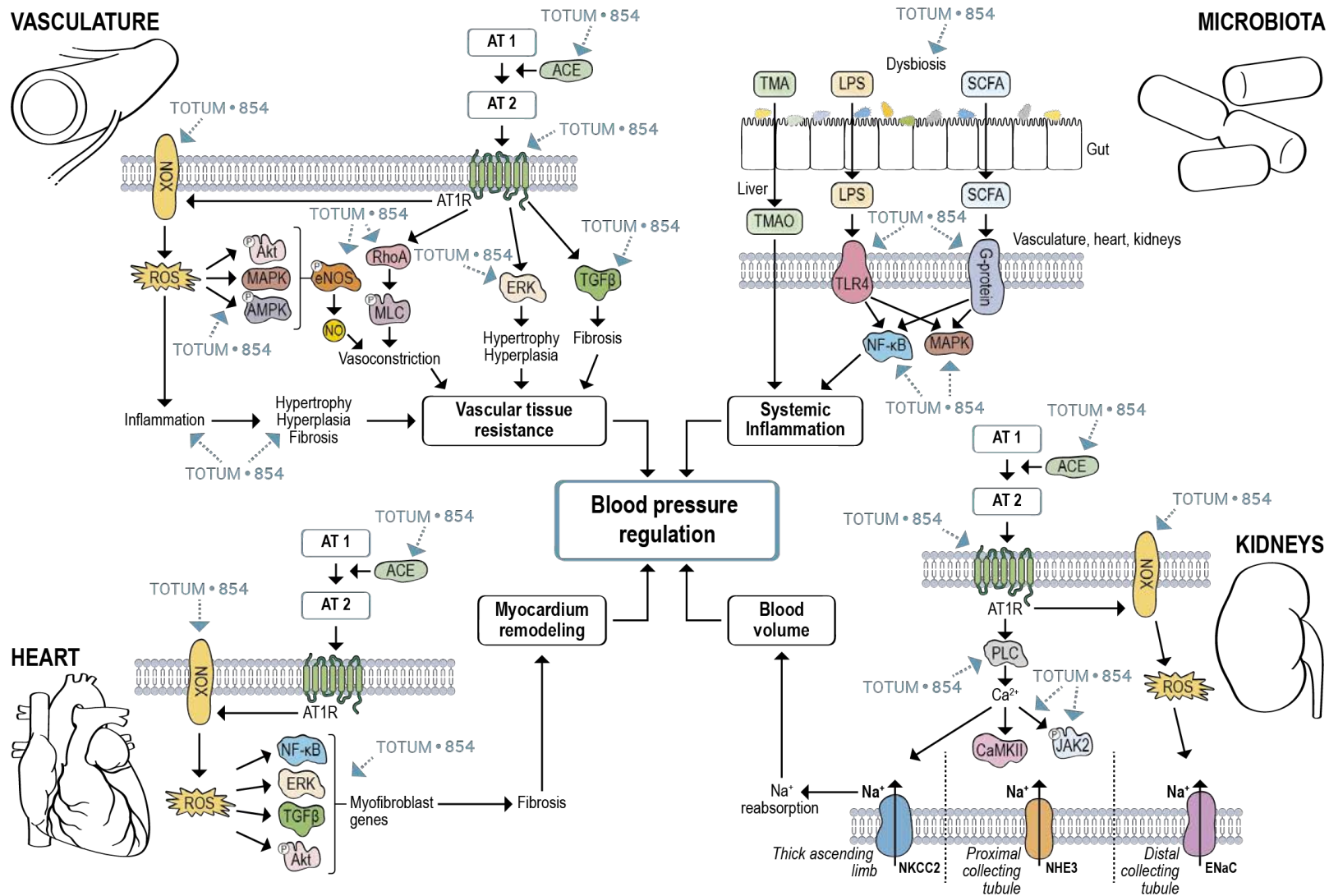
Scientific and clinical package

Already obtained:

- ✓ **Bioavailability and characterization of circulating metabolites in human**
- ✓ **Mode of action targeting different biological and tissue mechanisms, demonstrated in humans and preclinically:**
 - Reduction in ACE I activity;
 - Protection of vascular cells against inflammation and oxidative stress;
 - Preservation of the vascular structure;
 - Modification of the intestinal microbiota.
- ✓ **Proven efficacy in preclinical studies**
(L-NAME and SHR models)

Ongoing: two Phase II/III clinical studies, each led in 400 volunteers, INSIGHT 1 (recruitment completed) and INSIGHT 2 (end of recruitment at a later date).

TOTUM-854: hypothesis currently studied, for a multitarget mode of action on blood pressure regulation



TOTUM-854: preclinical evidence for the prevention of arterial hypertension

A broad preventive effect on systolic blood pressure (SBP) and diastolic blood pressure (DBP)

In vivo models renowned in arterial hypertension

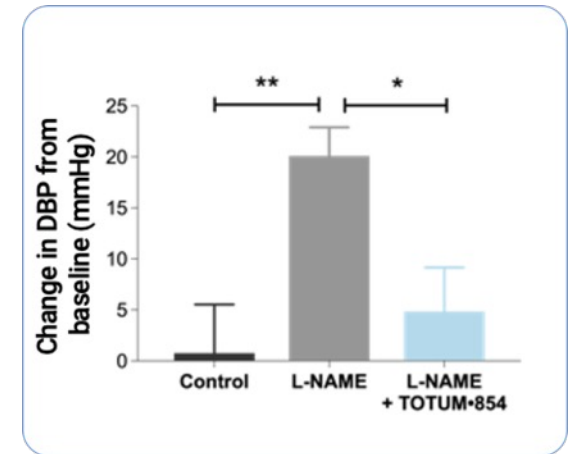
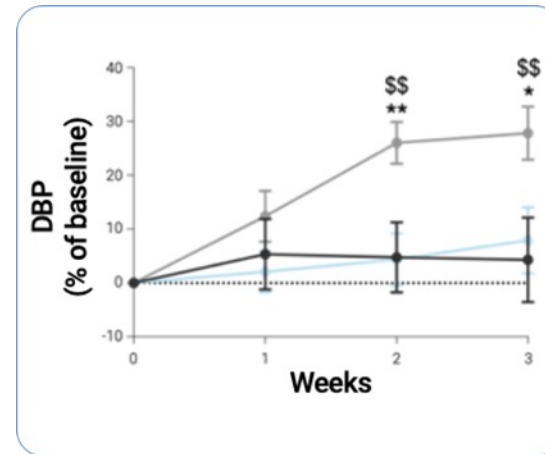
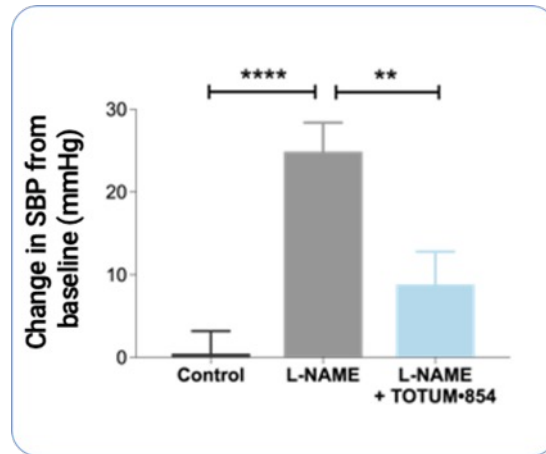
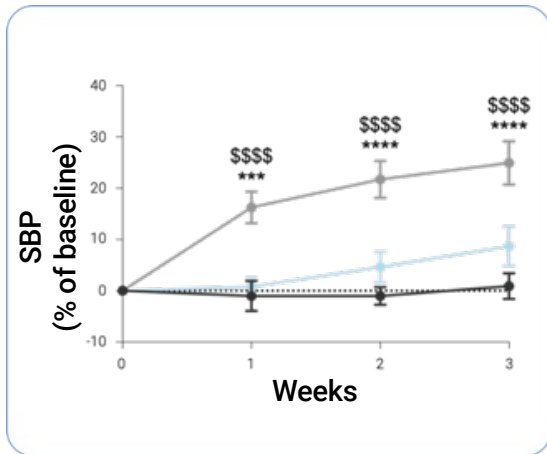
Induced AHT model (L-NAME)

- Control
- L-Name
- L-Name + TOTUM-854

Selection in scientific congresses



TOTUM-854 lowers Blood Pressure in L-NAME-Induced Arterial Hypertension in Mice and in Spontaneous Hypertensive Rat Mode ESH/ISH annual congress, poster presentation, 2021 & AHA annual congress, poster presentation, 2021



TOTUM•854: INSIGHT 1 and 2, a large clinical Phase II/III against early arterial hypertension

INSIGHT 1 (Phase II/III)

Study design

A randomized, placebo-controlled, double-blind study

Population : **400 subjects**

Dose: **3.7 g/day**

Duration: **3 months**

Target population

People with mild to moderate elevation of blood pressure, untreated

• **Systolic blood pressure between 130 mmHg and 159 mmHg and diastolic blood pressure < 100 mmHg**

Objectives

Primary endpoint: reduction in systolic blood pressure, with TOTUM•854 versus placebo (measurement in clinical investigation center).

Other endpoints: blood pressure ambulatory measurement over 24h.

INSIGHT 2 (Phase II/III) Dose reduction

Same design, duration of supplementation and population

Tested dose: **2.6 g/day**

No blood pressure ambulatory measurement over 24h.

valbiotis®

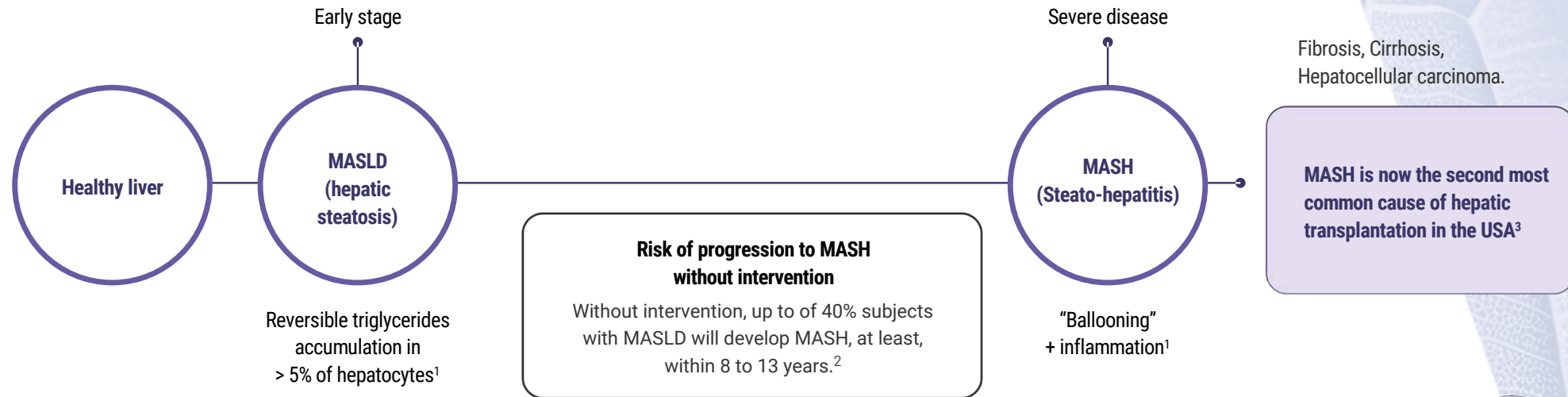
TOTUM•448

For people with a MASLD or an early stage of MASH.



TOTUM-448: metabolic liver damage, fat accumulation leading to frequently severe hepatic diseases

“The progression from MASLD* (hepatic steatosis) to MASH* (steato-hepatitis) dramatically increases the risks of cirrhosis, liver failure, and hepatocellular carcinoma.”¹



*Metabolic-dysfunction-associated steatotic Liver Disease (MASLD) and metabolic-dysfunction-associated steatohepatitis (MASH), new designation of liver metabolic diseases (NAFLD and NASH) since June 2023.

¹Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis; World Gastroenterology Organization, 2012.

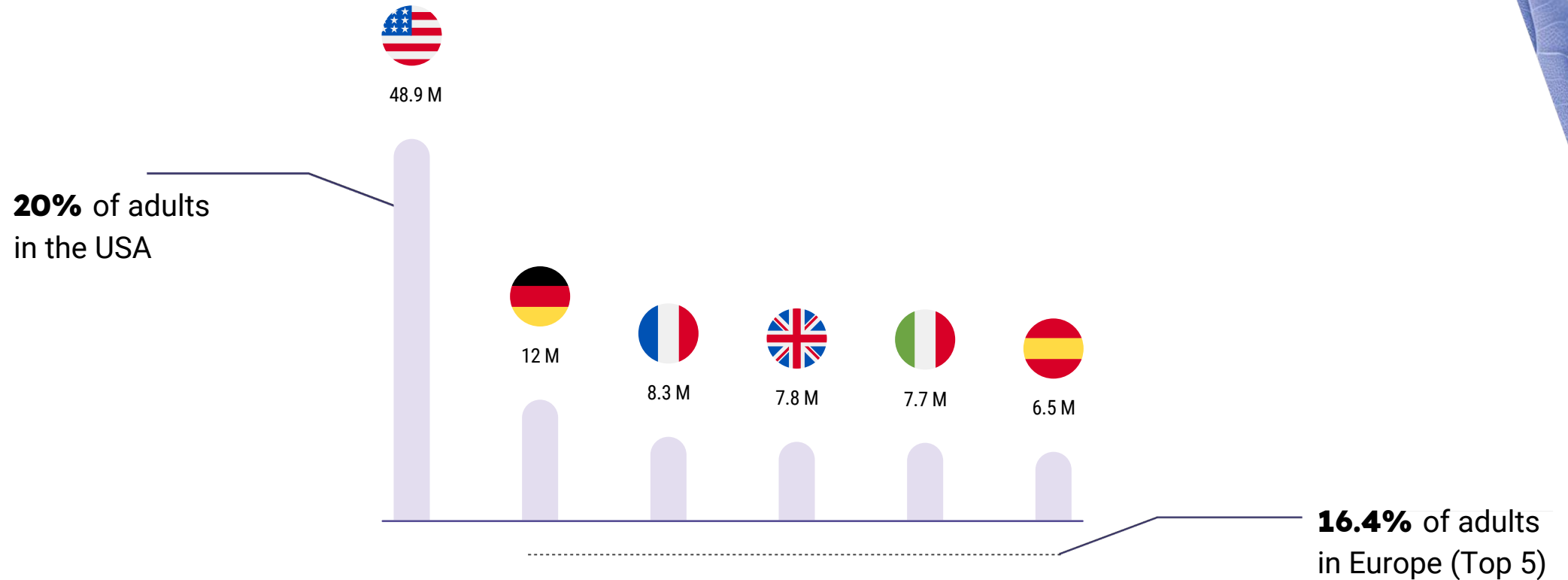
²EASL–EASD–EASO 2016 Clinical Practice Guidelines on the management of non-alcoholic fatty liver disease. J Hepatol 2016.

³Cholankeril G, et al. Liver Transplantation for Nonalcoholic Steatohepatitis in the US: Temporal Trends and Outcomes. Dig Dis Sci. 2017.



TOTUM-448: metabolic liver diseases (MASLD): the market data (USA + Europe Top 5)

18% of adults have a MASLD without fibrosis
i.e. **91 million** adults



Données AEC Partners, 2022.

TOTUM-448: there is a lack of natural products for the management of patients with early-stage metabolic liver disease

Prevalence of metabolic fatty liver diseases **doubled** in the last 20 years

MASLD is a **clear pre-stage to MASH**

Medical needs remain:

- **No preventive or therapeutic option**, evidence-based, is yet available, while patients struggle to change their lifestyle ;
- Strong physicians' expectations for **efficient products at early-stages**, against hepatic steatosis and inflammation.



*"My doctor told me that I have "fatty liver" disease and that it must be treated. He also told me that there are few medications available, except for a drastic change in my diet and physical activity. I would like to support my efforts to change my lifestyle with **a solution that is effective on my liver and yet natural.**"*



*"There is some evidence that several [natural] ingredients or nutrients help get fat out of the liver, increase the liver function, or stop the liver inflammation. This is really an interesting topic. There is **more than weigh loss** in this story."*



*"Metabolic liver diseases have raised rapidly in the population, in the wake of diabetes, obesity or dyslipidemias. But their management remains to be consolidated, and both preventive and therapeutic strategies suffer from **a lack of dedicated products, with proven efficacy, at the earliest stages.**"*

Pascal SIRVENT

Head of Discovery, Preclinical and Translational Research, Valbiotis

Sources: Metabolic disease prevention – Exploratory research & concept test – Reporting interviews, Enquête IFOP pour Valbiotis, France, 2021 – US Qualitative Market Research 2022 - Valbiotis concept research
*Metabolic-dysfunction-associated steatotic Liver Disease (MASLD) and metabolic-dysfunction-associated steatohepatitis (MASH), new designation of liver metabolic diseases (NAFLD and NASH) since June 2023.

TOTUM-448: high expectations for solutions against MASLD and MASH



General practitioners and gastro- enterologists currently preoccupied¹

- MASLD and MASH : recent and rising diseases.
- No specific treatment available.
- Limited solutions: interventions aiming at weight loss and blood lipid reduction (lifestyle and treatments).
- A need to act at the earliest stage, on hepatic steatosis.

A diagnosis to amplify, at the earliest stages (MASLD)

Recommendations for screening²

+

Validated diagnosis exams (Fatty Liver Index³, liver ultrasonography^{2,4})

¹ METABOLIC DISEASE PREVENTION - Exploratory research & concept test , IFOP HealthCare
Methodologie : entretiens individuels de 24 médecins généralistes et 12 gastro-entérologues (France, Allemagne ; 17 nov.au 4 déc. 2021),
Communauté en ligne de 15 médecins généralistes (France, Allemagne ; 24 au 31 janv. 2022)

² EASL-EASD-EASO 2016 Clinical Practice Guidelines on the management of non-alcoholic fatty liver disease. J Hepatol 2016

³ Bedogni, G. et al., BMC Gastroenterology; 2006 ; Hernaez R et al. Hepatology. 2011

⁴ Global Guidelines Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis, World Gastroenterology Organisation, 2012

TOTUM-448: a plant-based active substance, to act on early stages of liver metabolic diseases

An exclusive combination, based on 5 plant extracts

For people with a MASLD or an early stage of MASH.



Patents: France and international
9 communications in international scientific congresses since 2022



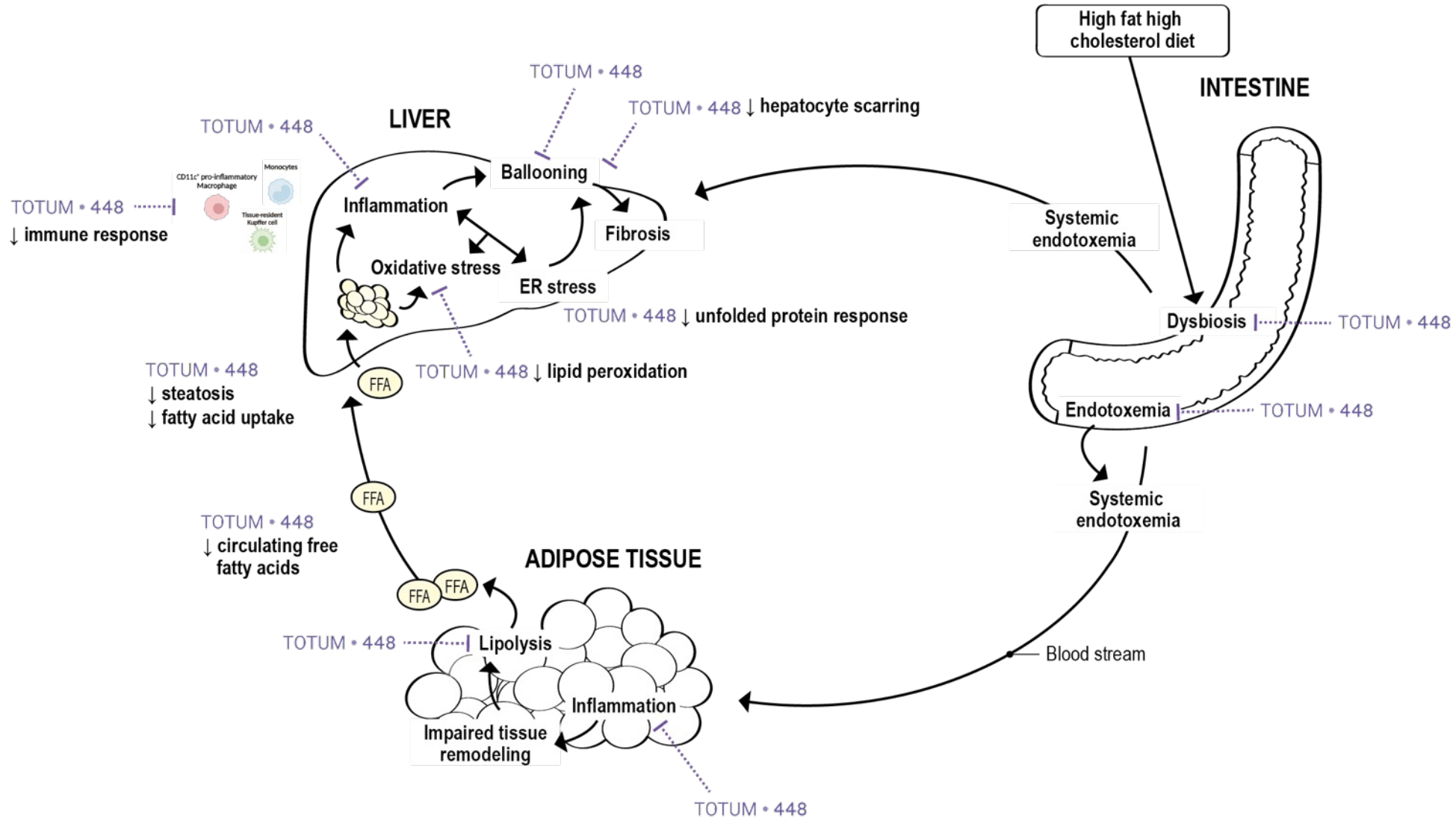
Scientific and clinical package

Already obtained:

- ✓ **A preclinical program in collaboration with Leiden University (Netherlands) and Hospices Civils de Lyon (France)**
- ✓ **Positive results on the main markers of disease progression:**
 - Reduction of triglycerides storage in the liver (steatosis)
 - Reduction of inflammation
 - Improvement in some markers of fibrosis

Ongoing: final clinical strategy and academic partnerships unveiled in the upcoming months.

TOTUM-448: hypotheses under study for a multitarget mode of action



TOTUM•448: a plant-based active substance, to act on early stages of liver metabolic diseases

TOTUM•448 efficacy on the main markers of MASLD and MASH:

- Hepatic steatosis;
- Blood lipids;
- Related metabolic parameters;
- Several markers of inflammation and fibrosis.

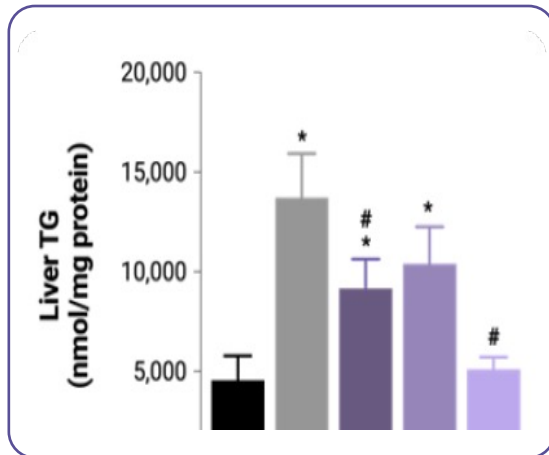
- Control
- High-fat diet
- HFD + TOTUM•448 (1.5%)
- HFD + TOTUM•448 (2%)
- HFD + TOTUM•448 (2.5%)

Selection in scientific congresses

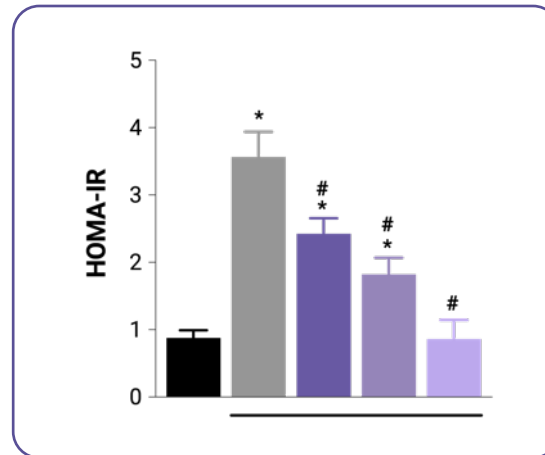


The novel plant-based active principle TOTUM•448 decreases hepatic steatosis and inflammation in diet-induced NAFLD mice
 Lambooj J et al., Poster #2483, The liver meeting, AASLD, 2022.

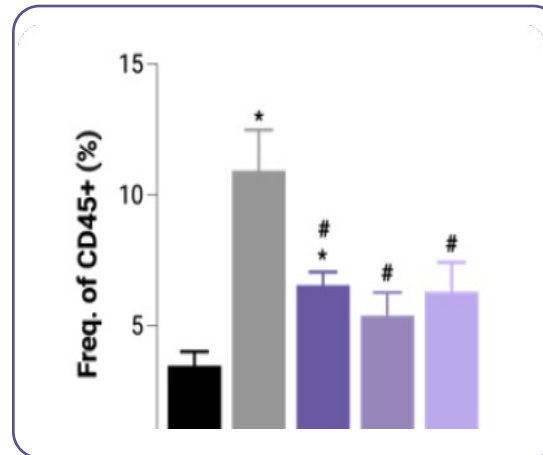
Hepatic steatosis



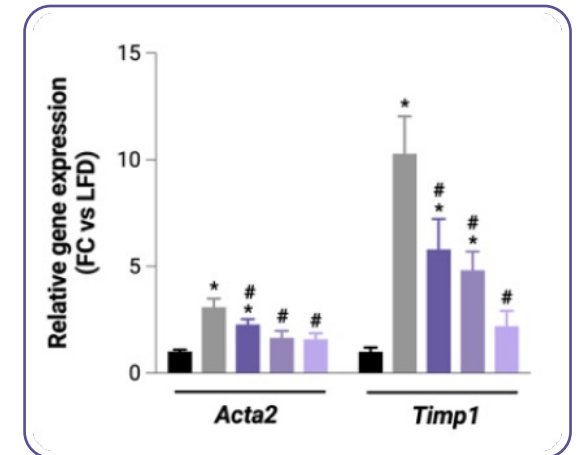
Insulin-resistance



Inflammation (immune signature)



Fibrosis (molecular markers)



MICRO-ALGUES

An exclusive program to develop innovative healthcare solutions
in New Caledonia.



Microalgae: an exclusive program to develop innovative healthcare solutions in New Caledonia



Microalgae

A \$ 3.8 billions global market in 2024, 3.5% annual growth¹

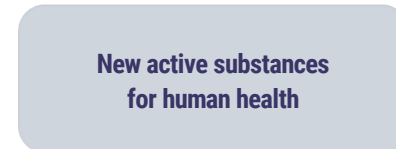
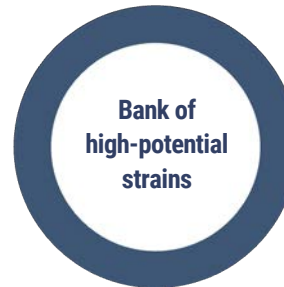
- Marine plant microorganisms, with a size < 1µm
- A fast production of biomass
- A remarkable molecular richness for health applications



Prospection and selection since 2013

valbiotis®

Expertise in plant R&D



- New international patents, exclusive and worldwide exploitation rights for Valbiotis²
- Regulatory status: "GRAS" / "Novel Food"
- Scale-up and industrial production in New Caledonia, with private operators
- Compliant with the Nagoya Protocol

¹Global Microalgae Market Growth 2019-2024, Fior Markets, 2019 ; <https://www.fiormarkets.com/report/global-microalgae-market-growth-2019-2024-372987.html>

²Le domaine d'exploitation est défini comme suit : «Nutraceutique, médicaments et dispositifs médicaux en santé humaine et animale dans le cadre strict de la prévention et du traitement des maladies métaboliques suivantes : diabète, dyslipidémie, hypertension artérielle, surpoids, obésité, NAFLD (Non-alcoholic fatty liver disease)».

FINANCIAL INFORMATION & CSR



Corporate Social Responsibilities (CSR)

Valbiotis positions itself as a company firmly committed to promoting a more responsible, ethical, and sustainable future. This commitment goes beyond our initial mission focused on reducing the impact of metabolic and cardiovascular diseases on millions of at-risk individuals worldwide.

Key commitments for the development of Valbiotis



Structuring a comprehensive CSR approach following ISO 26000 standards

Under the direction of a specific steering committee reporting to the CEO

This approach commits us to contribute to sustainable development challenges and to integrate risk management related to social, environmental, and economic issues into all our activities. We commit to initially address these deemed essential issues:

- **Respecting the rights of individuals and promoting responsible relationships and working conditions**
- **Reducing the impact of our activities on the environment**
- **Developing ethics in our business relationships**
- **Focusing on local development and the common good**

[Manifesto for a sustainable future \(in French\)](#)



Valbiotis joined the Coq Vert community in 2023

Community of leaders convinced of the need to act and already engaged in the ecological and energy transition. Launched by Bpifrance, in partnership with ADEME and the Ministry of Ecological Transition, this community advocates to promote the sharing of expertise

2024: a provided newsflow

Commercial

TOTUM•63

(prediabetes)

1st order from Nestlé Health Science

Lipidrive®

(formerly TOTUM•070)

(hypercholesterolemia)

On the market - France

Business development

Lipidrive®

(formerly TOTUM•070)

(hypercholesterolemia)

Deal

Clinical

Lipidrive®

(formerly TOTUM•070)

(hypercholesterolemia)

End of recruitment Phase II/III

TOTUM•854

(raised blood pressure)

Phase II/III results(INSIGHT)

TOTUM•448

(metabolic liver diseases)

Clinical strategy

Analysts coverage and shareholders breakdown

€ 11.40

Target price (data December 2023)
Portzamparc*
Mohamed KAABOUNI

+ 214%**

€ 10.10

Target price (data December 2023)
Invest Securities*
Thibaut VOGLIMACCI-STEPHANOPOLI

+ 179%**

€ 9.20

Target price (data January 2024)
ODDO BHF*
Martial DESCOUTURES

+ 154%**

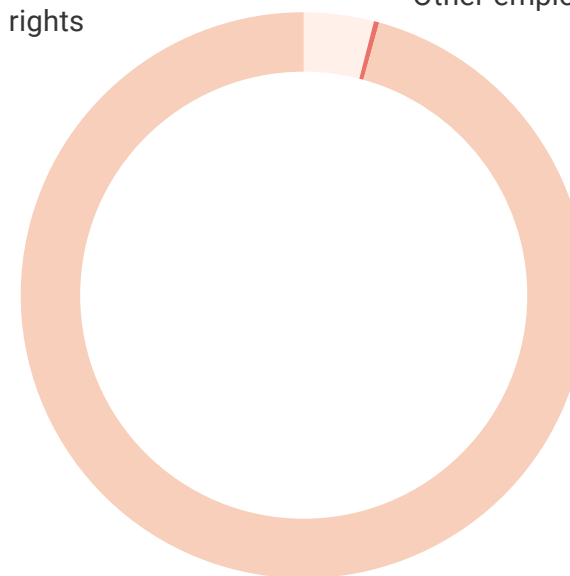
€ 9.20

Target price (data December 2023)
TP ICAP MIDCAP*
Corentin MARTY

+ 154%**

4.0%
Sébastien PELTIER, CEO and co-founder of Valbiotis
+ DJANKA Investissement, controlled by S. PELTIER
i.e. 7,49% of voting rights

0.4%
Other employees



95.7%
Free float



IStock market indices

NEXT BIOTECH · EnterNext® PEA-PME 150

Sponsored research; **Versus closing value at April 2, 2024 (€ 3.62)

Capital breakdown updated as of December, 22, 2023
32.2% of capital held by individual investors (Source: TPI, September, 25, 2023)

Cash and R&D expenses

Cash position: € 13.7M

(at June 30, 2023)

End of cash is estimated Q4 2024 including the CHF 4M (NHS milestone), but without any potential revenue from a partnership on TOTUM•070.

IFRS in K€, at June 30	2023	2022	31 Dec. 2022 <small>(annual results)</small>
Operating income , including	5 236	1 541	2 814
• Turn over	4 241	635	785
• Grants	24	101	137
• Research Tax Credit	816	778	1 692
• R&D expenses	-5 006	-4 055	-9 102
• Sales and marketing expenses	-873	-911	-1 703
• Overhead costs	-923	-768	-1 651
Operating profit for the period	-1 820	-4 929	-12 026
Operating profit	-1 820	-4 929	-12 026
Earnings before tax	-1 920	-5 096	-12 314
Net profit	-1 927	-5 097	-12 312



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