PRESENTATION OF THE INDUSTRIAL IMPLEMENTATION ACTION PLAN OF THE "ITALIAN MICROBIOME INITIATIVE FOR IMPROVED HUMAN HEALTH AND AGRO-FOOD PRODUCTION"

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The view of the industry

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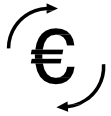
ALFASIGMA

Pharmaceuticals with passion

A privately owned Italy based multinational
company founded in 1948



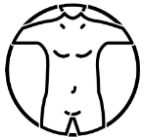
A turnover of € 1,05 billion in 2019
Equally split between Italy and RoW

2nd largest Italian company in the Italian retail market
118th WW corporation in the Global Pharma market

A workforce of 3.000+ in 17 countries
45% sales force

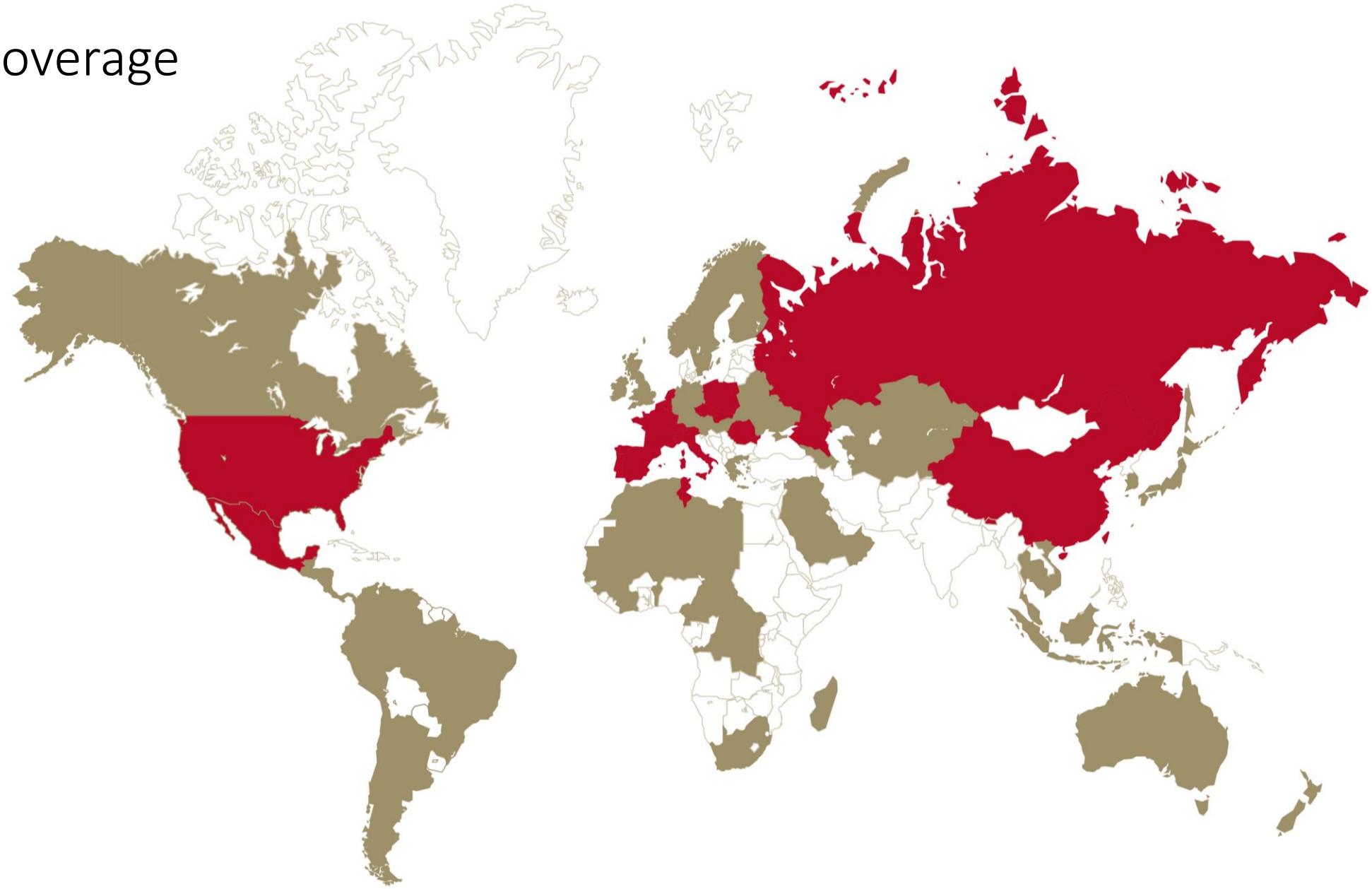
Internal R&D labs and 5 production sites
In Italy, Spain and in US

1 blockbuster product fully developed internally
Rifaximin, with € 1,8 bn WW revenues



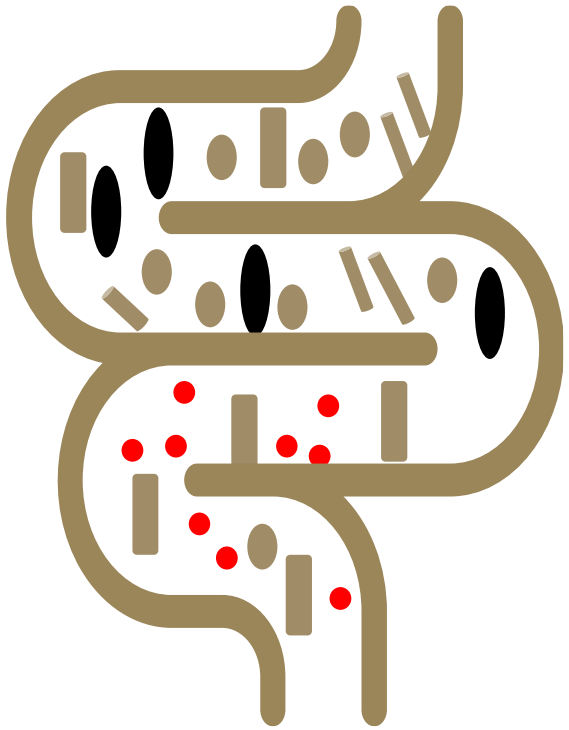
2 main therapeutic areas
Gastroenterology
Vascular

Geographic coverage



- **Subsidiaries**
- **Distributors**

Alfasigma Microbiome-based Products
The R&D Innovation Engine



RIFAXIMIN

(one of the most effective microbiome modifier on the market)

Irritable Bowel Syndrome (IBS)

Hepatic Encephalopathy

BRILACIDIN

Distal Colitis (UP/UPS) Clinical Development

The Microbiome Platform

Novel Microbiome Products under exploration

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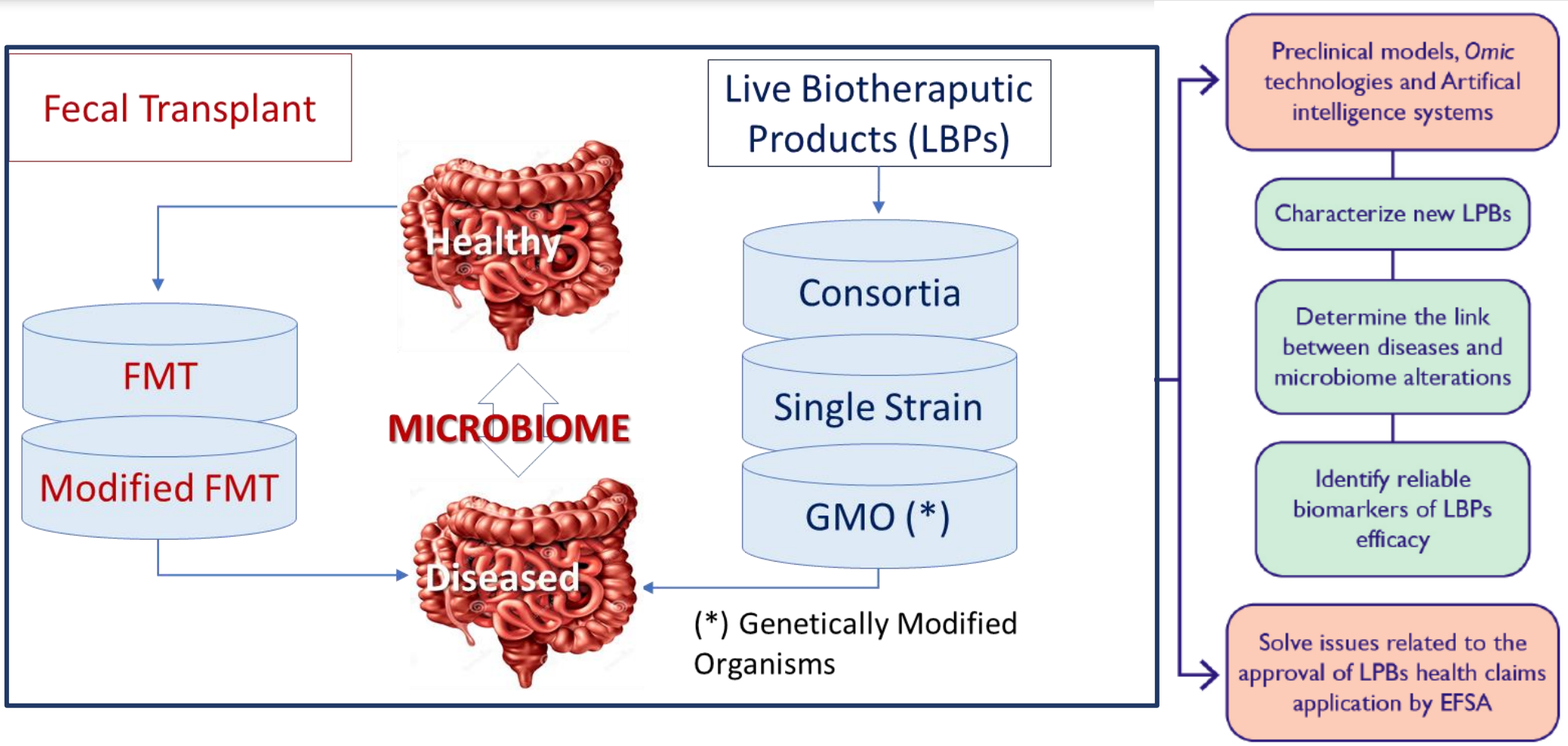
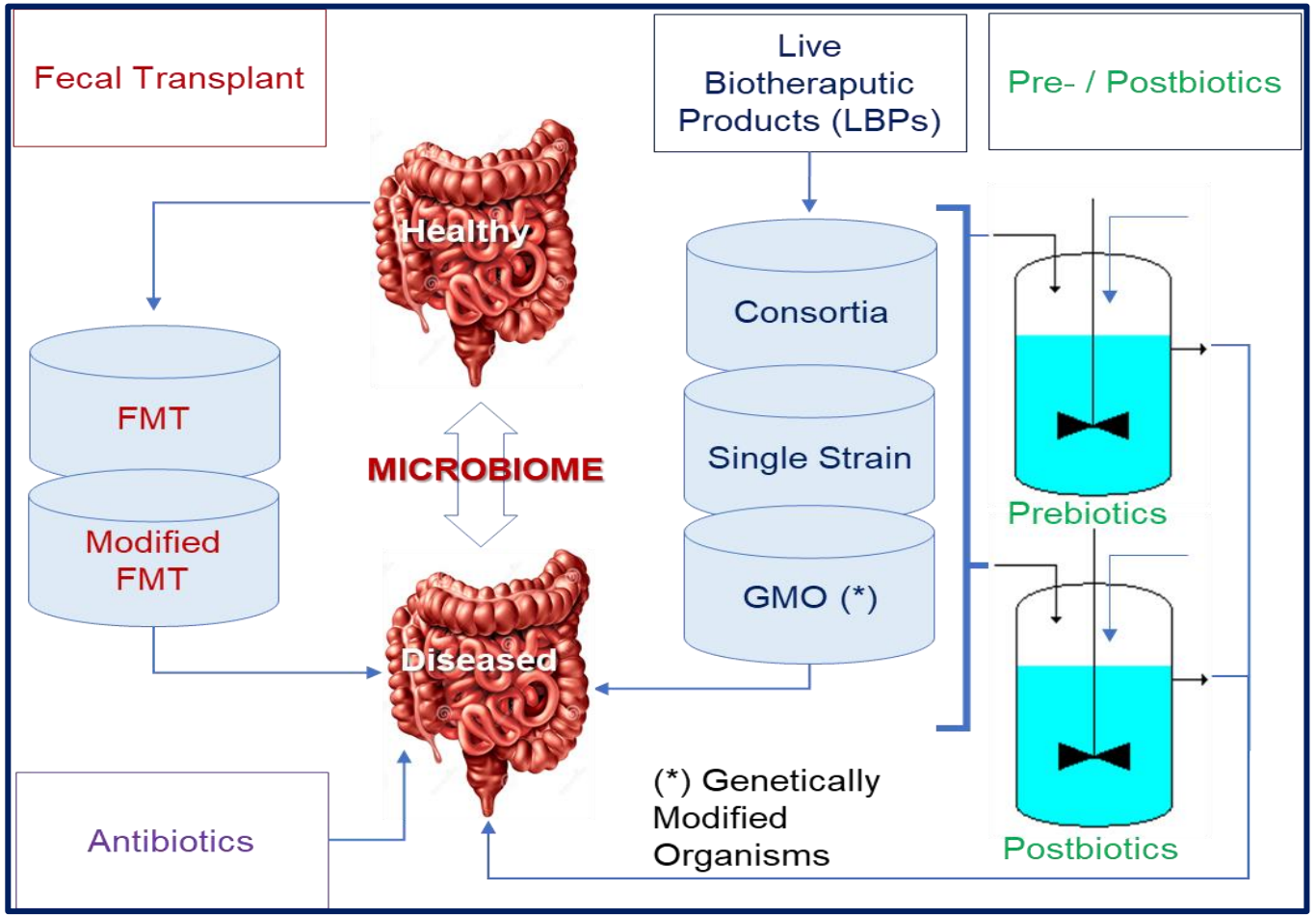
IAP - Planned Pilot Industrial Actions in The Microbiome Pharma System

1. **Production of Next Generation Probiotics**.
2. Probiotic formulation for human gut microbiota eubiosis and host health
3. **Exploit knowledge on microbiome and drug metabolism**
4. Exploit the knowledge on microbiome and metabolism of nutraceuticals and xenobiotics
5. **Exploit knowledge on microbiome and prevention and progression of some pathologies**
6. Exploit the nexus microbiome, enteral nutrition and special nutrition

Production of Next Generation Probiotics



Exploit Knowledge on Microbiome and Drug Metabolism



Collection of microbiome samples (gut, oral, vagina, skin) from human clinical trials, including longitudinal and cross-sectional studies throughout the drug development phases, including the post marketing studies

- In vitro screening of APIs and formulated drugs using fecal samples or selected bacterial strains for the study of microbiome-drug interactions.

- Analysis of efficacy and ADMET data, along with multi-omics and microbiological results, to detect potential correlations with the microbiome fingerprint;

Exploit Knowledge on Microbiome and Prevention and Progression of Some Pathologies

Systematic collection and analysis of clinical data, microbiome samples and metabolites over the time (including long-term measurements), at different stages of disease progression and in patients under treatment.

Setting of specific models, including in silico and in vivo approaches, to study the microbiome changes during disease progression.

Development of new microbiome-based products either as novel foods, to be used as ingredients for innovative food supplements and foods for special medical purposes, or drugs, following the guidelines and the recommendations of the competent regulatory bodies for nutraceuticals and pharmaceuticals (EFSA, EMA).

To fully realize the potential of microbiome-based products to prevent or cure disease in humans, the effort of nutritional and pharmaceutical developers must evolve into translational work leading to product development and commercialization. To this purpose, the main requirements are:

- **well-characterized product candidates,**
- **well-designed development plans**, including clinical studies with relevant end-points,
- **well-defined target product profiles.**

Areas of Innovation : Postbiotics and Psychobiotics

Postbiotics

- Microorganisms that reside in the outer mucous layer can rarely reach the epithelium and underlying immune cells. Instead, postbiotics (cell components and metabolites derived from probiotic strains) can pass the intestinal barrier and interact with intestinal epithelial cells and macrophages.
- The therapeutic activity of these products is carried out via interactions with specific targets, within the microbiota and the intestinal mucosa, and, through the gut-liver, gut-brain axis, with the main functions of the organism.

Psychobiotics

- The microbiota-gut-brain axis is a potential new therapeutic target for effective treatment of central nervous system disorders, in addition to being a potential cause of drug side effects.
- Altered gut microbial profiles have been described in several psychiatric and neurological disorders.
- Psychobiotics, live biotherapeutics or substances whose beneficial effects on the brain are bacterially mediated, are currently being investigated as direct and/or adjunctive therapies for psychiatric and neurodevelopmental disorders and possibly for neurodegenerative disease, and they may emerge as new therapeutic options in the clinical management of brain disorders.

Priorities and Recommended Actions

- Launch **information campaigns** to disseminate the awareness of the importance of the microbiome for the human health and QOL.
- Implement **pre-competitive initiatives** to sustain microbiome research and accelerate the development of innovative solutions by start-up and SMEs.
- Facilitate scientific collaborations between industrial and academic players to exploit **translational capabilities** and select best development candidates as innovative microbiome products.
- Harmonize the **EU regulatory framework** for the development of new microbiome nutraceutical and drug products.
- Increase **EU financial support** to microbiome research programs to pave the way to technology transfer and industrial partnerships.


Thank You!