

**Financial perspectives on the emergence of a
microbiome based industry :
sorting out the hype from the hope ?**

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8 April 2016



How did microbiome interest start at Seventure ?



Health For Life Capital: a visionary approach to venture capital

Our venture capital job is to identify segments where

- ✓ Breakthrough innovation push
- ✓ Meets large unmet needs
- ✓ At the same timing

For that, we scrutinize in various countries:

- ✓ Scientific and academic publications
- ✓ Consumer and societal evolution
- ✓ Medical trends
- ✓ Prevalence and incidence evolution
- ✓ Politics and reimbursements scheme



In 2006, we identified « gut flora » and « pharma/nutrition/food convergence »

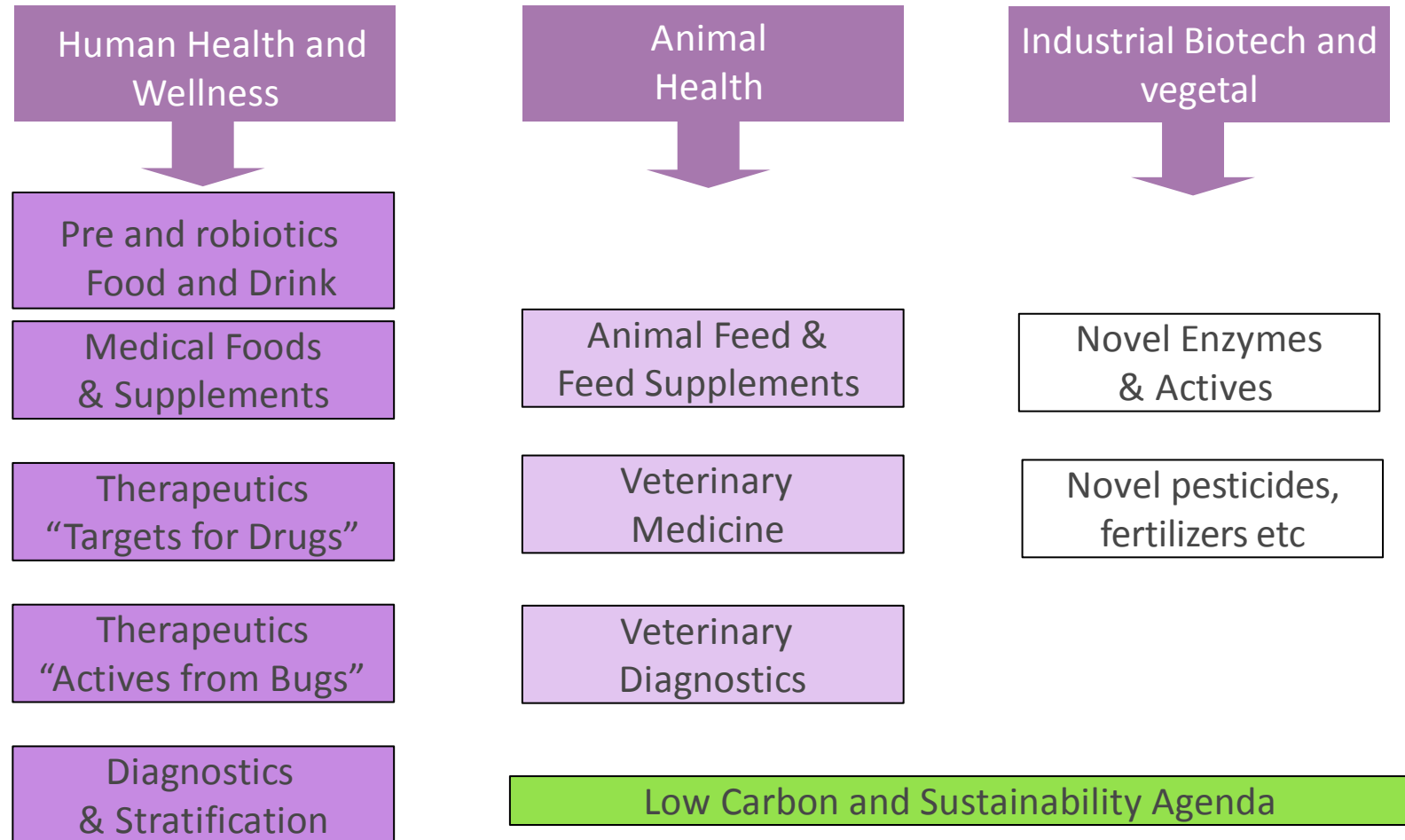
In 2008, we started to invest in these fields which soon renamed to microbiome

In 2013, we raised a Euro 160M dedicated fund: Health For Life Capital, from financial institutional investors, as well as strategic prestigious partners such as Danone, tereos, Lesaffre, Bel and Novartis pharma. (Seventure currently manages 630M).

What will future microbiome industry look like ?



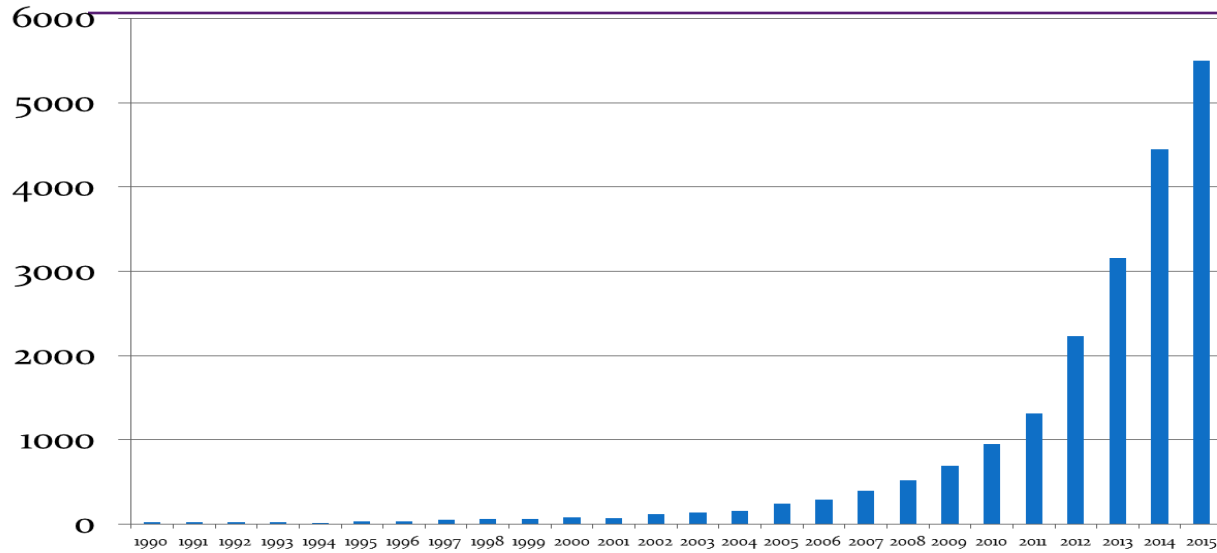
Potential Microbiome Market Opportunities – Overview



What are the current trends on microbiome ?



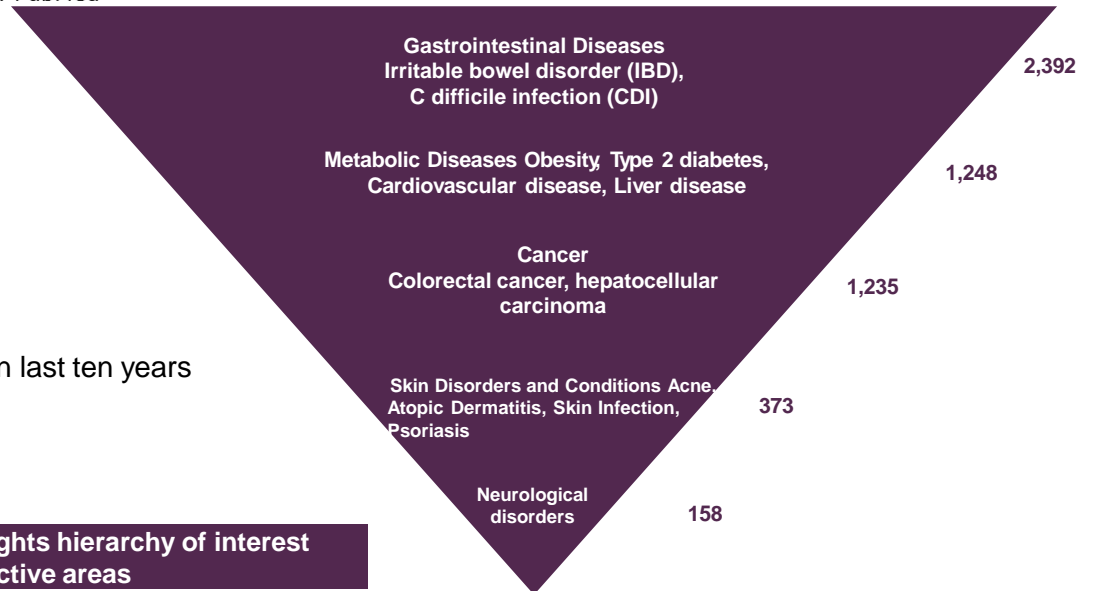
Microbiome : Scientific literature skyrocketing *Seventure*



LITTÉRATURE « Microbiota » 1990 – 31 décembre 2015 (articles / year). Source : PubMed

of publications in last ten years

Publication record highlights hierarchy of interest – identification of most active areas



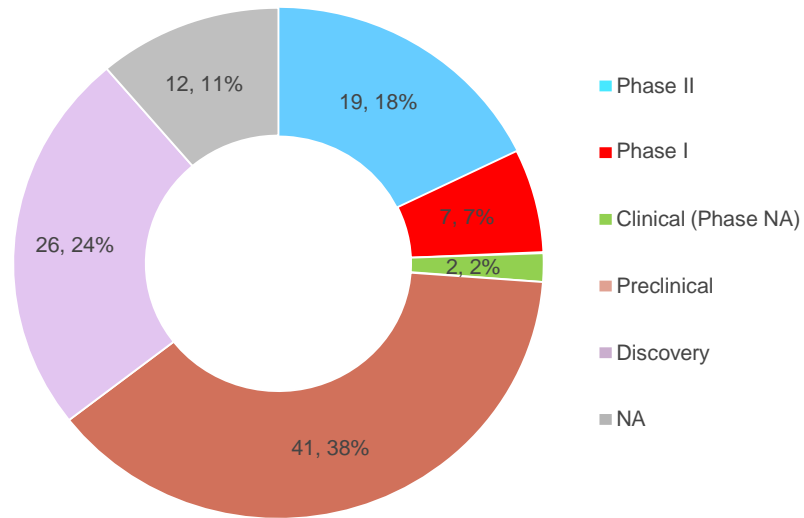
- ✓ This area continues to benefit from the **exponential growth of its academic research** (by number of publications). The translation of those scientific discoveries in the **general press** happens unusually rapidly.
- ✓ **'Taxonomic'** studies of the correlations between disease states and microbiota composition are still carried out and are useful to **generate hypotheses**. However, the main spotlight now falls on translational and diagnostic microbiome research.
- ✓ Alongside the **'usual suspect' therapy areas** for microbiota therapeutic research (narrow-focus antibiotics, immunology, metabolism, gastro-intestinal), the number of **CNS and dermatology** studies is experiencing fast growth. **Oncology** has also appeared as a highly promising area for the application of microbiome-based therapeutics and diagnostics.
- ✓ The molecular modalities used to intervene therapeutically on the microbiome cover the **whole range** of the pharmacopeia. The largest group of study uses live biotherapeutics (bacteria, sometimes viruses), but small molecules are growing fast, showing that this pioneer area is getting more mature.

How far away are we from science to products ?



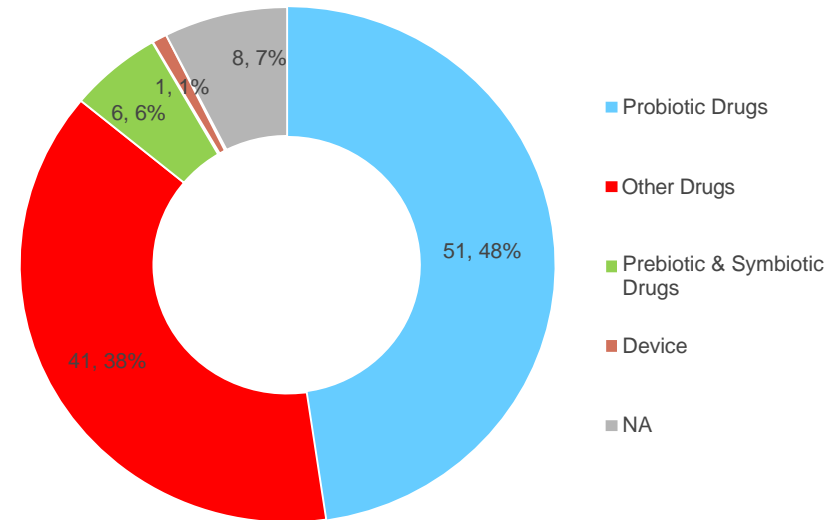
Increasing number of microbiome therapeutic products under development

Distribution by Phase of Development



- The market is characterised by the presence of over 100 products in development; molecules in phase II account for 18% of the pipeline.
- A large proportion of the pipeline (62%) is captured by molecules in preclinical and discovery stage

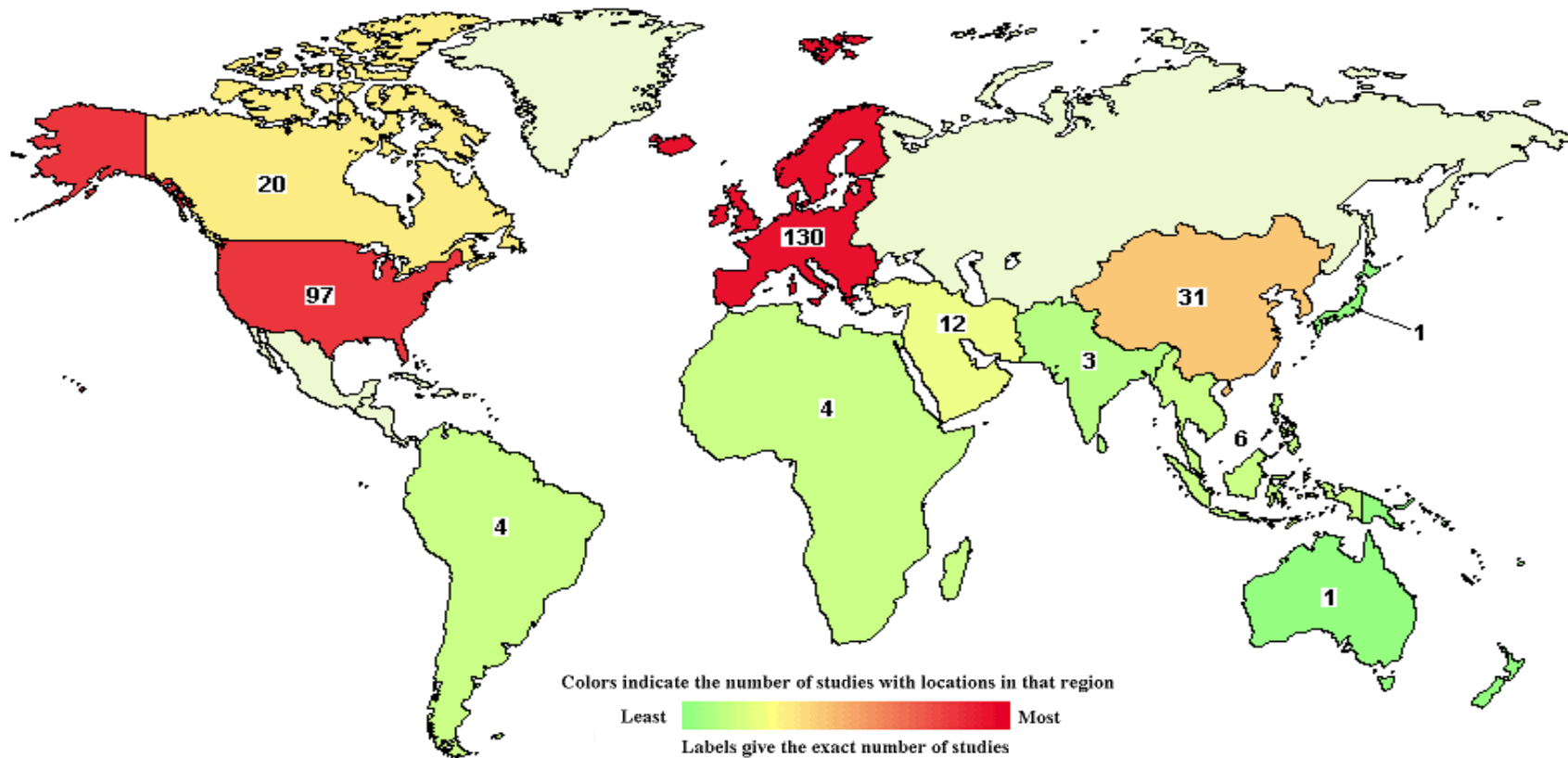
Distribution by Type of Product



- With a share of approximately 48%, probiotic drugs are the most popular. Other drugs capture 38% of the pipeline.
- Only a few microbiome products fall in the category of prebiotic drugs, symbiotic drugs and devices

Increasing number of microbiome related trials under development

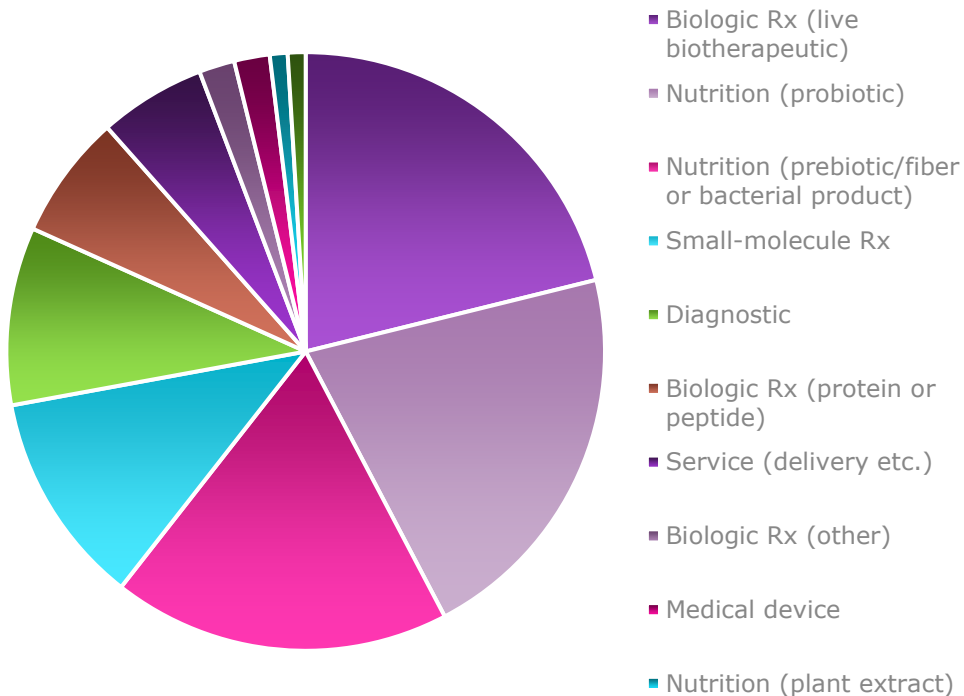
- Over 300 microbiome related **trials**
(Source: Open studies. Image downloaded from www.clinicaltrials.gov on December 3rd, 2015)
- Over 13 diseases for which microbiome-related therapies are being investigated



Source: Guggenheim securities – report 3/2016

More and more microbiome companies contact seventure to raise funds : over 140 in the last 2 years

% of companies in Seventure deal flow
(by type of compound)

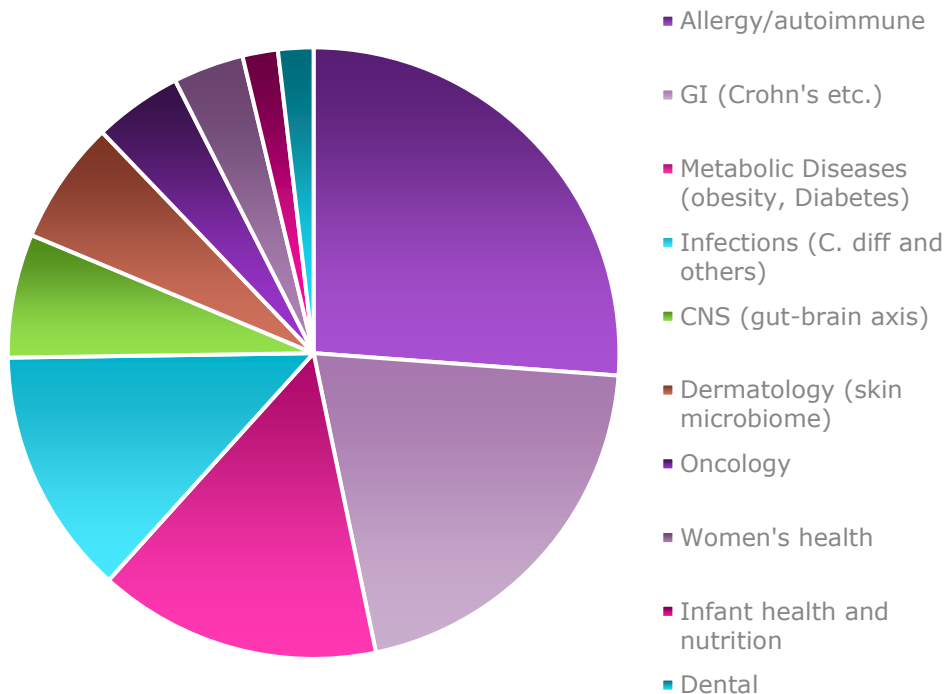


✓ **High proportion of living organisms (Rx or nutrition)**

✓ **Small molecule (Rx) or prebiotic are not far behind**

More and more microbiome companies contact seventure to raise funds : over 140 in the last 2 years

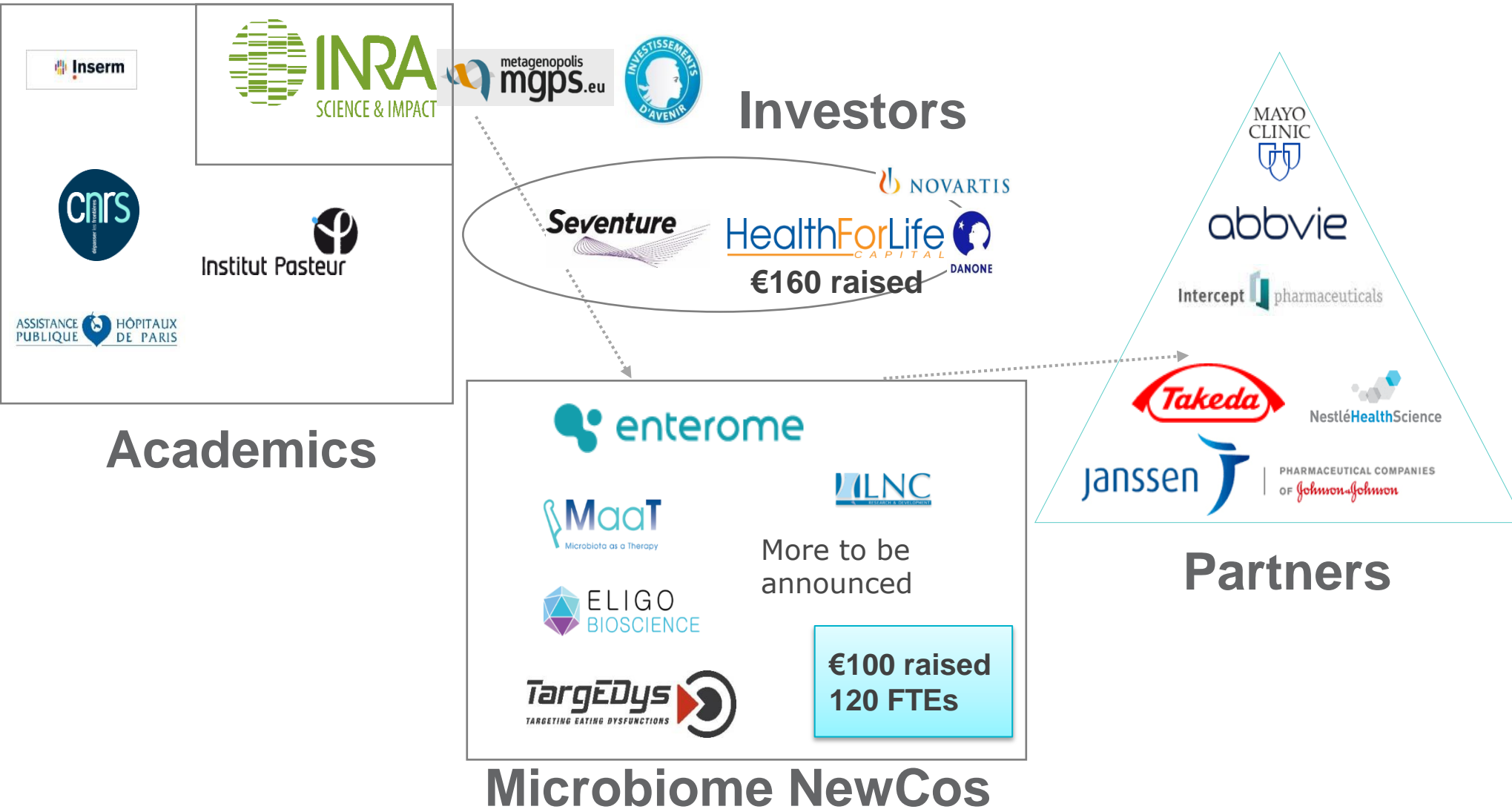
% of companies in Seventure deal flow (by therapy area)



✓ **Immunology, GI, metabolic & infections are leading the way**

✓ **High proportion and strong growth of SNC & dermatology**

Example of an industrial Ecosystem grown in 4 years from French Science



Microbiome Therapeutics in small companies- the landscape

« Bugs as Drugs »

Broad activity

« Drugs from Bugs »

Targeted activity



Undefined consortia
Faecal microbiome transfer

Defined consortia

Single strain native

Single strain modified
Synthetic biology

Molecule



**How far away are we from
product to sales ?**

Microbiome : Who finance up to now ?

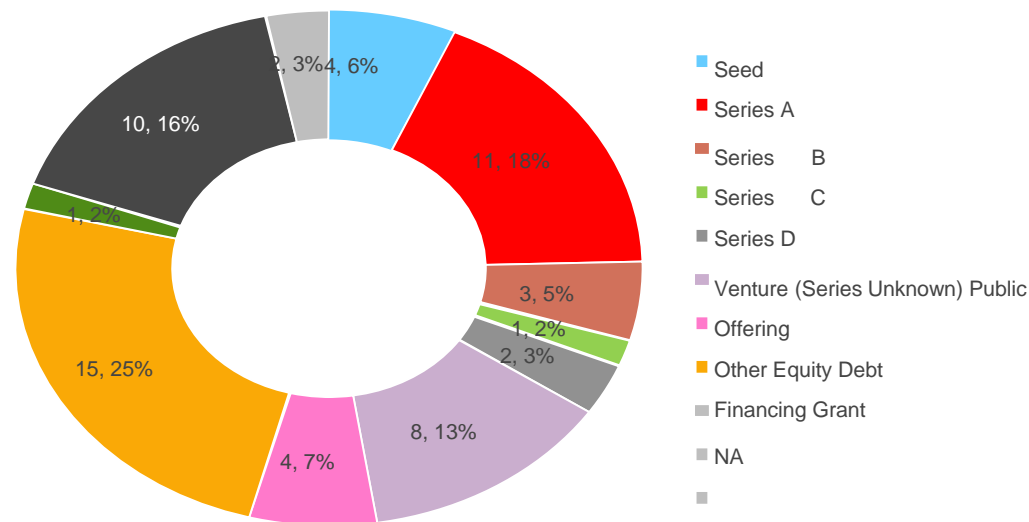
**Most countries initiated ambitious governmental programs in the last 4 years
And are competing in a world wide race**

- Ireland == > 50M€ announced in June 2013
- Canada == > announced in February 2014
- USA:
 - == > 173M\$ were committed in 2008-2014 for HMP.
 - == > 922M\$ were committed in the last 3 years in 2784 research projects reported NSTC in Nov 2015.
 - == > additionnal 500M\$ over next 10 years announced in October 2015
 - == > white house calls for projects in january 2016
- UK: == > 100M£ (in preparation)
- France == > bioaster, metagenopolis.... More to come?
- etc.

Microbiome : Who finance up to besides governments ?

Microbiome Therapeutics
Funding Instances, 2005-2015

Venture capitalists and strategic investors have been the most popular investment vehicle In the last 10 years



And this was before April 5th 2016 when Human longevity announced a \$220M series B including Illumina, Celgene, GE ventures after a VC series A in 2014. The firm is developing a genome and phenotype database.

Source : Roots Analysis 2016 report

The MicroBiome is no longer ignored by key Healthcare players...



And many more....

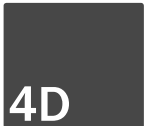
The MicroBiome is no longer ignored by the financial community



2 venture capital funds are very active:



2 public markets have been very active:



Microbiome : financial trends in private market

- ✓ No significant acquisitions yet
- ✓ The number of industrial partnerships and collaborations is rising, though financials were not disclosed until very recently.....



news

- ✓ 2015 janv , J & J partnered with Vedanta on their lead product VE-202 in IBD at pre-clinical stage in a \$ 241 million milestone deal
- ✓ 2016, March 23, Nestlé NHS partnered with Seres to acquire commercialization rights outside the US&Canada to 4 gastrointestinal product candidate. Ser-109, an oral composition of 50 species of bacteria in spore form for multi recurrent C diff infections, SER-262 for primary CDI, SER-287 in UC and IBD and SER-301 for crohn disease.
The deal is announced as a \$1.9Bn milestones & royalties deal including a \$120M upfront payment

What financial perspectives for microbiome can we expect ?



Microbiome : a few market reports have been published



Scottish enterprise published a report in **July 2013** and wrote :

Pre- and probiotic ingredients and foods, and related supplements, are already big business with a global market of \$19 billion (2009) growing at 7.6% CAGR (2010-2015)
== > in reality they tripled in China and doubled in the US in the last 5 years and are E32Bn in 2015 and Euromonitor predicts E44Bn in 2020.

Medical foods and drinks are worth around \$9 billion globally (2009 figures) with a US market of around \$2 billion. We think US and EU markets could be worth ~\$15 billion by 2015.

Diagnostics

The era of stratified medicine has arrived, and molecular diagnostics can be used to differentiate and treat patients on the basis of their disease. The current market for diagnostics is ~\$4.2 billion and is predicted to grow at 13% CAGR (to 2015).³

1. BCC Research The Probiotics Market
2. 2010 IMS Health data 2012
3. HRI International 2011 Global Market for Medical Devices and Diagnostics

Microbiome : a few market reports have been published



Scottish enterprise published a report in **July 2013** which continues :

Therapeutics

The market for therapeutics was ~\$956 billion in 2011 and is expected to rise to ~\$1.2 trillion by 2016, representing 3-6% CAGR. If the association between microbe/s and specific disease states is conclusive, this could generate a suite of exciting new targets for drug developers (or indeed vaccine manufacturers).

Equally, microbes are a rich source of novel actives and enzymes that themselves might find therapeutic application in, for example, the hunt for novel antibiotics to treat drug-resistant strains.

The size of each market which could be addressed by microbiome-based drugs are:

- **Irritable Bowel Disease: ~\$5 billion (2009)**
- **Type 2 Diabetes: \$21 billion (2010) with 7% CAGR predicted till 2017**
- **Obesity: ~\$1 billion globally, albeit restrained by the limited number of approved therapies**
- **High Blood Cholesterol: Statins alone generate over \$25 billion in revenue globally.**
- **Antibiotics: The identification of novel bioactives from microbiota could also address the urgent need for new antibiotics.**

We think that microbiome therapies could take at last 20% of these markets ie \$10 billion within the next 15 years

Microbiome : a few market reports have been published



Roots analysis published in **2016** a report « microbiome therapeutics market 2015-2030 » where they write:

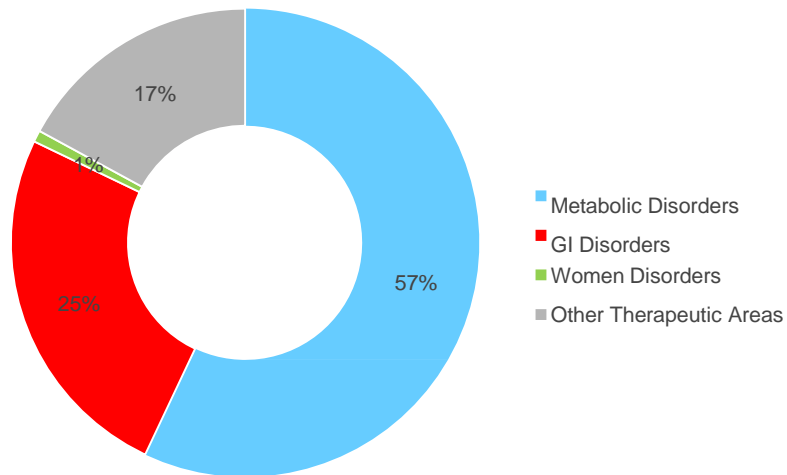
- market will grow 73% per annum between 2015 and 2030
- metabolic and GI disorders are the key therapeutic areas
- using microbiome has unique advantages over traditional small molecules and biologics. It can be used to identify individual therapeutic microorganisms and help in designing the therapies customized to the patient's microbiome.
- Unlike the adverse effects posed by the prolonged use of drugs (eg antibiotics) microbiome therapeutics have a lower risk of toxicity associated with them. In addition microbiome therapies provide a rich source of new biomarkers helping the classification of the patients into relatively homogeneous subpopulations.

Note : These reports focus on therapeutic&diagnostic . Mainly gut microbiome. They do not include prevention ie nutrition & food. They do not include vegetal or animal applications of microbiome. They do not include skin microbiome and cosmetic.

Microbiome therapeutic Market in the future

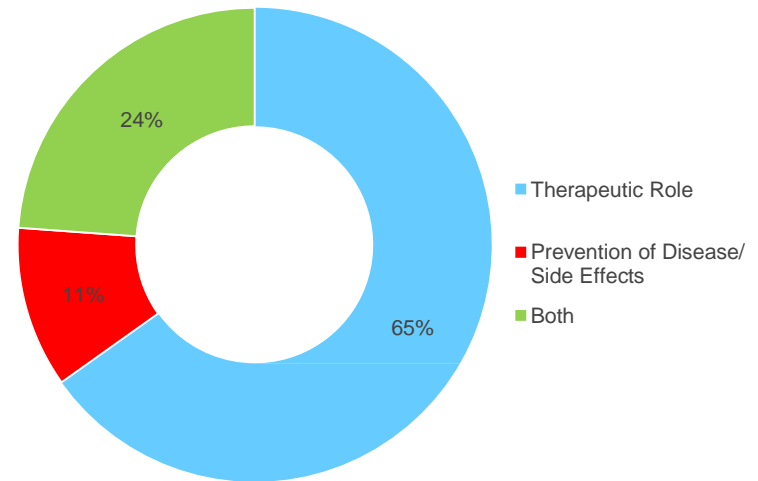
Roots analysis 2016 report continues:

Microbiome Therapeutics Market, 2030
Distribution by Therapeutic Area (%)



- Owing to the huge type 2 diabetes market and a high target patient population, therapies for metabolic disorders are likely to become highly popular

Microbiome Therapeutics Market, 2030
Distribution by Application (%)

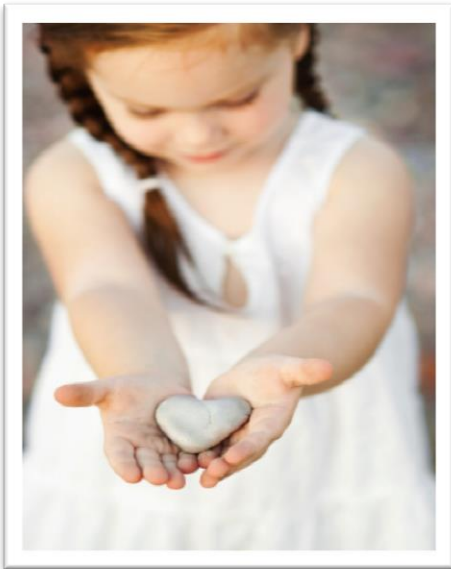


- Pipeline products are expected to reduce adverse side effects of current treatment medications as well as have a high curative potential

Will the microbiome industry be as big as **Seventure** the biotechnology industry?



It took only 15 years for biotech industry to grow from 5000 pubmed publications to what it is today.



In 15 years, will the microbiome industry in 2030 be as big as the biotechnology industry is today?

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