

BIOSEARCH

**From PON to a Newco proposal
The first Italian biotech in search for innovative drugs
from marine organisms**



Stazione Zoologica Anton
Dohrn (SZN)



Institute of Biomolecular
Chemistry, CNR-ICB

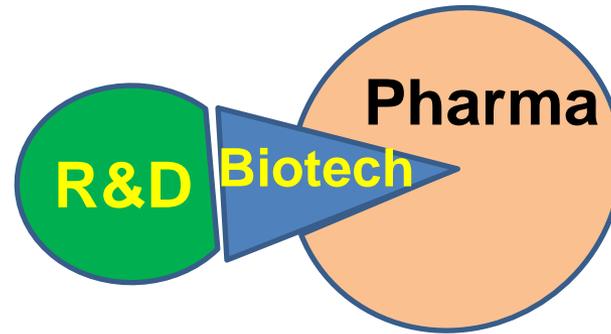
**A NewCo looking at new natural marine products
to treat immune disorders and cancer**

Why the Pharmaceutical Sector?

Global pharmaceutical market being worth nearly one trillion U.S. dollars.

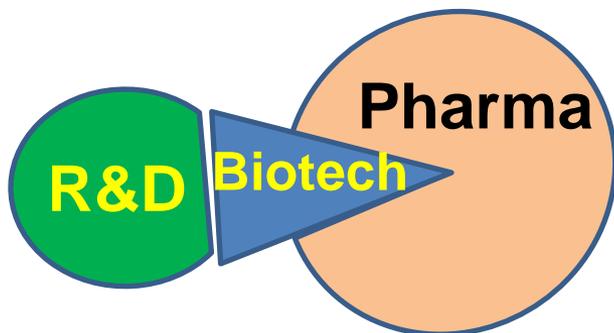
- ❑ **5,000 new medicines** are in development in the world with approximately 3,400 compounds currently being studied in the United States.
- ❑ In the last decade the search for new therapeutic compounds has tremendously changed. The drastic decrease in development of **synthetic small molecule** is accompanied by slow introduction of **complex molecules of biological origin**.
- ❑ **This trend will rapidly increase** in the coming years, due to the progressive knowledge in **molecular biology** and the constant improvement in the technological know-how, particularly **nanotechnology**. It is reasonable to expect that new techniques will overcome the major limitations of this type of compounds, i.e. poor bioavailability, degradation, failure to reach of the target.

Why the Pharmaceutical Sector?



- ❑ **Biotechs** are focused on risky innovative R&D projects (early phases - discovery and pre-clinical). They have **novel intellectual properties** and/or **some new technologies** to be developed into a commercially viable products, but they haven't usually the scale in sales and marketing.
- ❑ **Pharma** companies have the **strategic and economical power** to bring a pipeline to fruition and to engage the sales and marketing forces for new products commercialization.
- ❑ **Big Pharma** need to replace drugs with expiring patents and they need to improve their portfolio. They rely more on external research performed by Universities, SMEs and innovative Biotechs.

CURRENT PHARMACEUTICAL PLAYERS



- Key market indicators show that the pharmaceuticals industry appears to be at the tipping point in its adoption of outsourced solutions (51 over 114 NDA are outsourced in 2014).
- There are 1,466 biotech firms in the United States with about 200,000 employees. This is still a vibrant industrial sector where investors are most likely to put their money.
- In Europe leading countries for Biotech companies are Fr, D, UK and CH but there is an increasing presence also in Spain, Portugal and Greece (<http://biopharmguy.com/links/company-by-location-europe.php>);
- Universities, mainly in USA, UK and Canada, are developing centers and incubators.
- **In Italy biotechs have difficult in attracting venture capitals**

From PON to a NewCo proposal.

Line 2 – search of new products: screening of marine and soil microorganisms for their ability to produce secondary metabolites with potential therapeutic applications in the fields of anti-infective, cancer and chronic-degenerative diseases.



Why marine molecules?

The ocean covers 71% of the Earth's surface and contains 97% of the planet's water. Most of this world remains unexplored

Marine environment is a rich source of new microbial diversity for the discovery of new natural bioactive products.

Nature has been a source of medicinal products for millennia. Natural products represent an invaluable source of new complex, high functionalized molecules and this **chemical diversity is unreproducible in the laboratory**

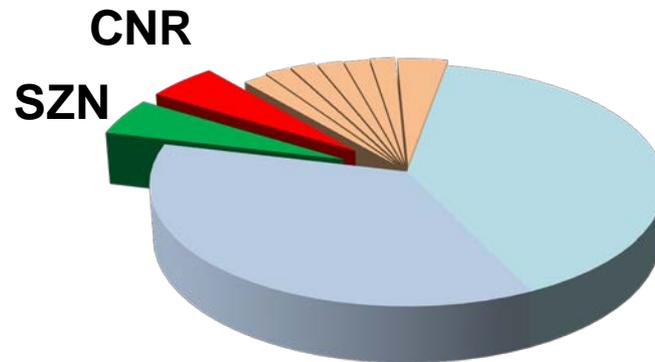
Newco name: **BIOSEARCH**

Mission

- ❑ **BIOSEARCH** will be an original hub of public and private research institutions with complementary and synergic activities. It will **develop pharmaceutical, nutraceutical and cosmetic products of natural origin.**
- ❑ **BIOSEARCH** will implement and coordinate a platform of discovery based on **marine protists** which represent a renewable source of biomass.
- ❑ **BIOSEARCH** will develop newly discovered molecules up to the proof of concept (POC) in translational pharmacological models. High quality candidates will be characterized at preclinical levels and could be objects of specific collaborations with private partners or *offered to our pharma network.*



BIOSEARCH will be registered as **innovative start up** with the following distribution of shares :



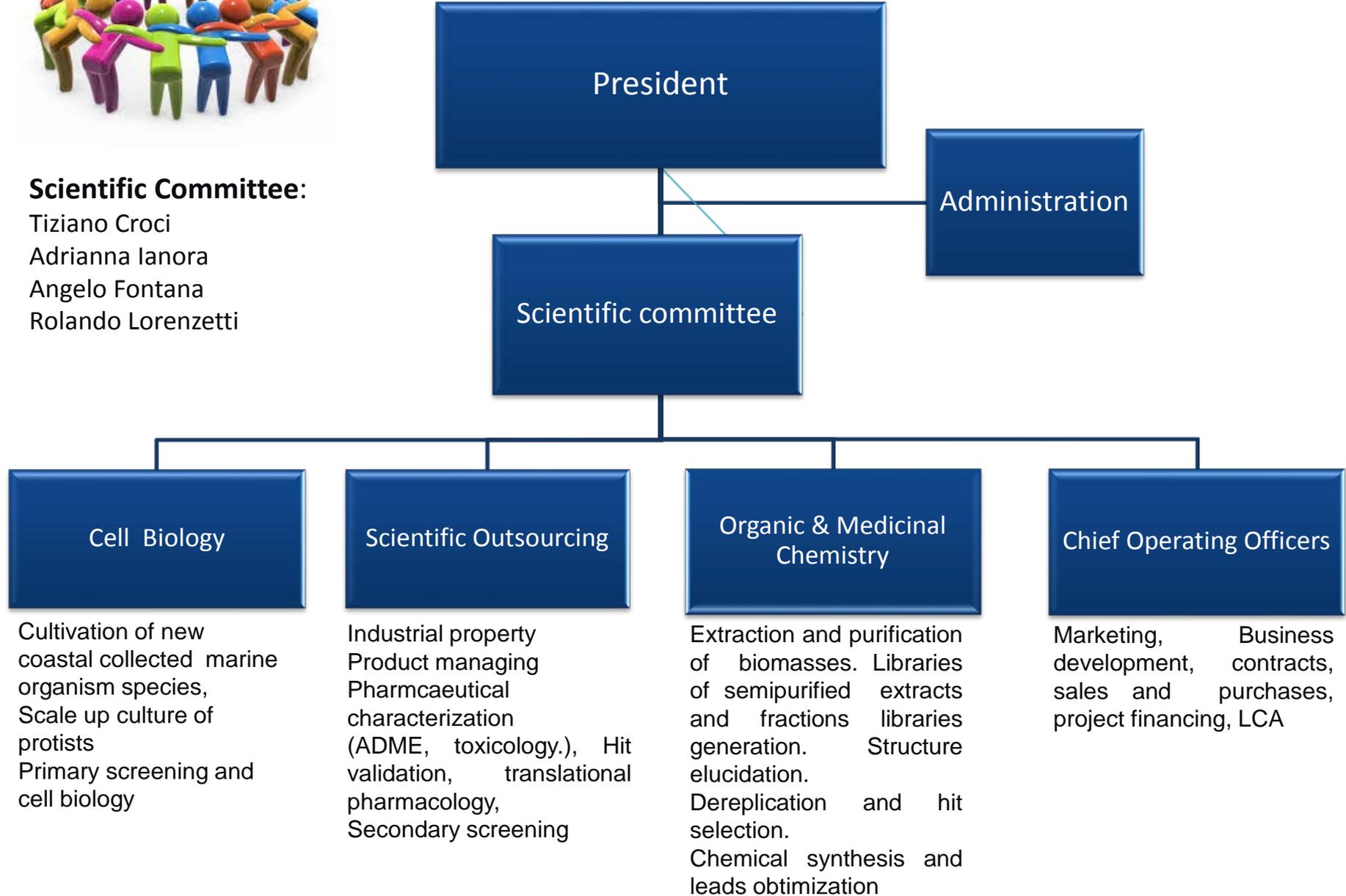
- **66%** is held by **four founders**. Part of these options (between 18 and 36%) could be transferred to support the development of the NewCo.
- **CNR and SZN hold 20%** of shares.
- **14%** is hold by **scientists** directly involved in its activity. The experience of this people will be the added-value of our company.

Organization chart



Scientific Committee:

Tiziano Croci
Adrianna Ianora
Angelo Fontana
Rolando Lorenzetti



Core Organization



❑ **Stazione Zoologica Anton Dohrn (A. Ianora's group), Naples**

Sampling and maintenance of marine organisms, biomass production through improved methods of cultivation, molecular biology, primary screening on cancer cell lines. A well genetically characterized collection of 70 species of marine microorganisms available for screening.



❑ **Laboratory of Bio-organic Chemistry (A. Fontana's group) Istituto di Chimica Biomolecolare, CNR-ICB Naples**

Scientific and technical support for chromatographic isolation of biologically active compounds, high-field NMR spectroscopy, mass spectrometry and related techniques, organic synthesis of low molecular-weight metabolites, spectroscopic analysis. Purification and identification of bioactive metabolites, organic synthesis of natural products and chemical analogs.

Therapeutic areas of interest

We search for new **antitumor (autophagy) compounds**, **immunomodulators** and **vaccine adjuvants**, as well as anti-inflammatory and anti-infective molecules against clinically relevant pathogens

present

IMMUNOMODULATORS
(targeting DCs, NKT,
macrophages)

ONCOLOGY
(colon, pancreas, thyroid,
ovary)

**VACCINE
ADJUVANTS**
(prophylactic and
therapeutic)

future

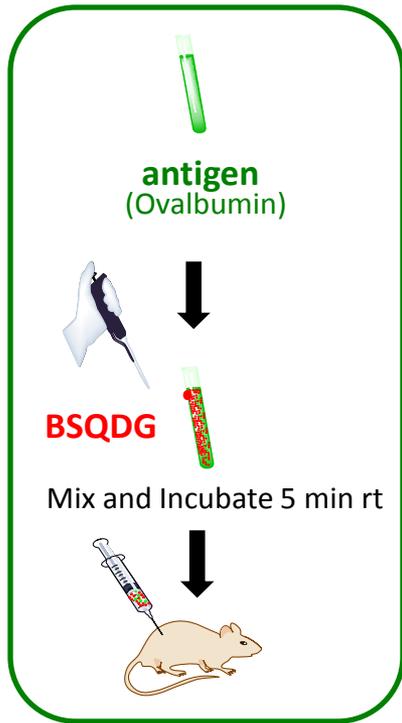
INFLAMMATION

**INFECTIOUS
DISEASES**

AGING
drugs and supplements

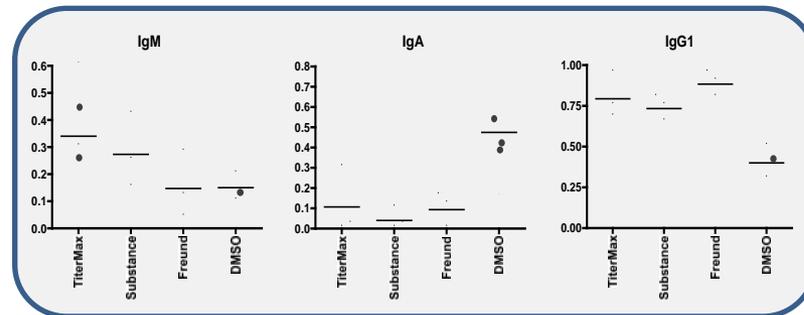
Projects for Newco portfolio creation (1)

❑ BSQDG-16/2 - A novel vaccine adjuvant



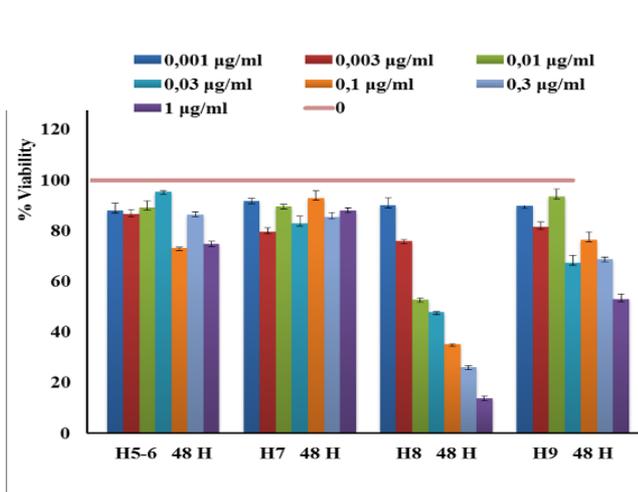
The lead is a small molecule of synthesis tested in vitro and in vivo for immunostimulant activity in comparison to standard reference compounds, TiterMax and Freund's adjuvants (PCT/IB2014/062098). BSQDG mechanism of action is currently object of investigation.

Market: the need for adjuvants as a component of vaccines is still an important need despite of the stringent regulatory environment. The global market is estimated at \$32 billion in 2013 and is expected to reach \$84 billion by 2022.

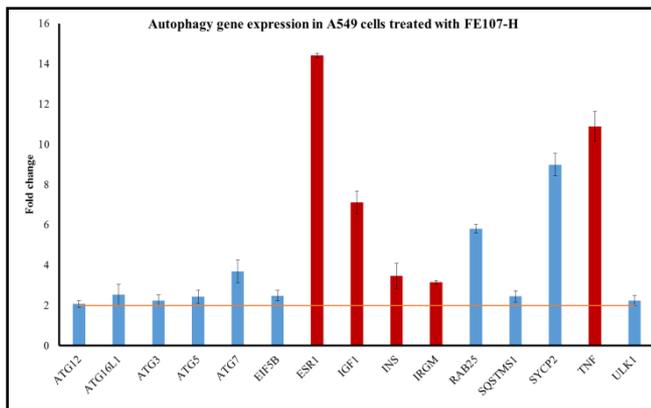


Projects for Newco portfolio creation (2)

- Marine microalgae contains potent cytotoxic and antiproliferative molecules



One pure compound and two purified extracts displayed potent antiproliferative activity against several cancer cell lines with different degrees of chemotherapy- and malignancy- resistance. Autophagic and mitophagic responses have been observed. Cytotoxic activity was low or absent in normal cells.



Market: The global market for oncology drugs reached \$91 billion in 2013. Cancer is still a leading area of healthcare. Investment has shifted toward biologics that will have a very significant impact in the near future. Competition is high.

Projects for Newco portfolio creation (3)

□ DHG – A new antiinflammatory molecule for psoriasis treatment by systemic or topical applications

This new molecule, derived from a marine sponge, reduced the proliferative response and the viability of phytohemagglutinin (PHA) stimulated by PBMC. In CD4+T cells, these effects were accompanied by up-regulation of IL-4 production. IFN- γ was not affected. It down-regulated the expression of both Cox-2 and NF-kB. Topic application significantly reduced mouse ear oedema and PGE2 production. Preliminary results on human keratinocytes suggest that it exerts anti-inflammatory effects favoring a Th2 switching.

Therapy: DHG and its derivatives found a clinical potential application in autoimmune diseases.

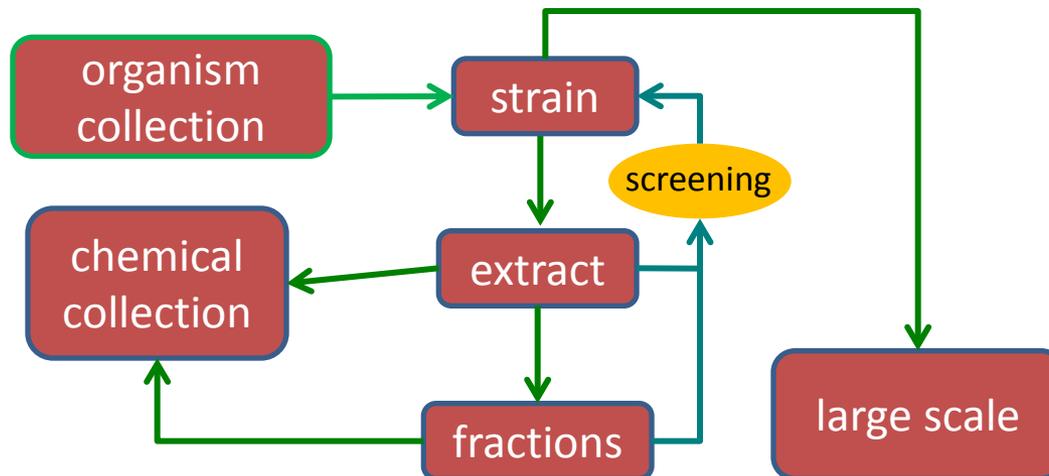
Market: topical treatments are usually the first line of defense in treating psoriasis but they have low long term efficacy. Prescription therapies will increase from \$4.1 billion in 2010 to nearly \$8.1 billion in 2020.

Projects for Newco portfolio creation (4)

❑ Private collection of organisms and extracts

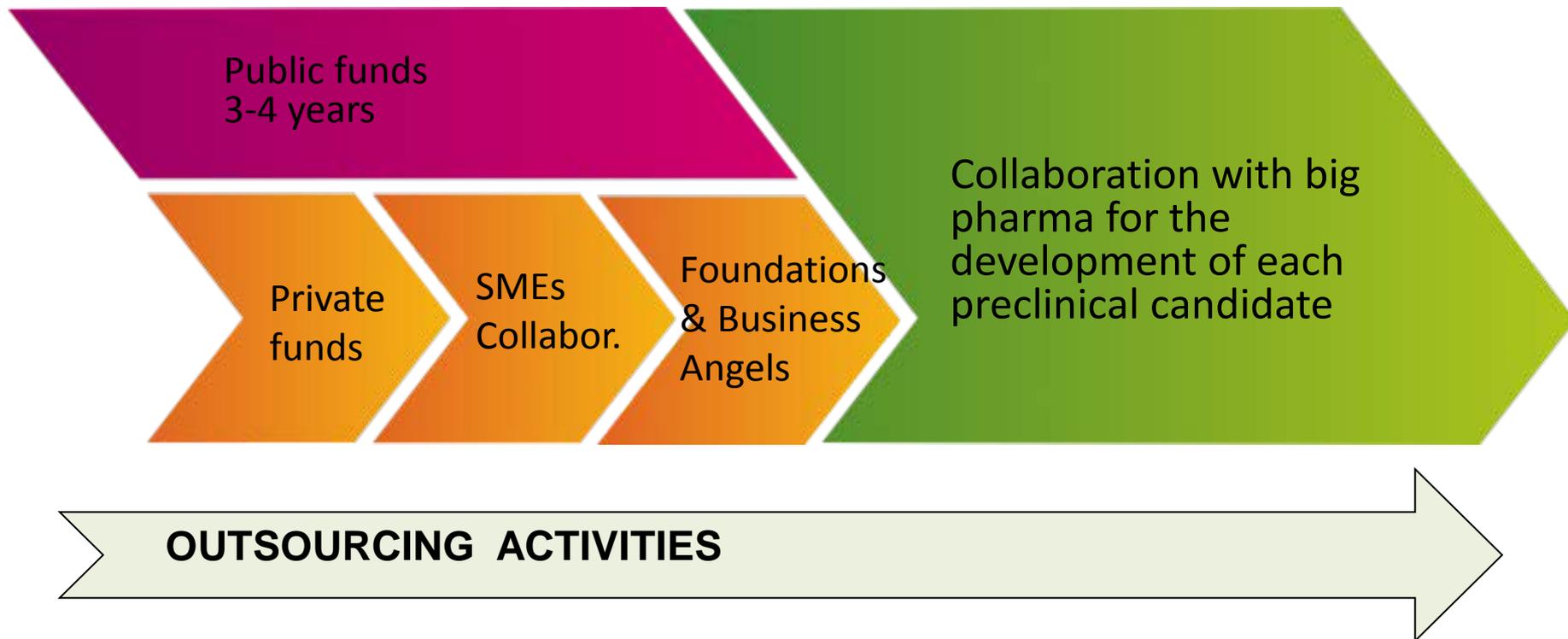
BIOSEARCH implements the CNR and SZN collection of marine protists to produce biomasses and spiked library of extracts for screening purposes. **BIOSEARCH** will make available to private and public customers its collection of organisms, biomasses and extracts.

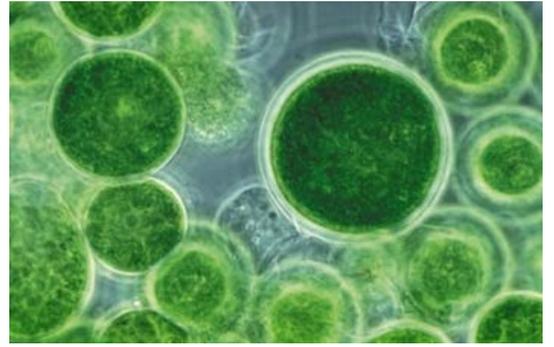
These contracts will be ruled by confidential agreement and exploitation of the results will be shared between the customer and the NewCo. This strategy will allow to achieve funds for the development of **BIOSEARCH** and to strength the relationship with private and public players.



Business Development

Our strategy is to grow through external outsourcing and alliance with academia and private companies





SWOT ANALYSIS

Strengths

- The Newco will be the first biotech working on cultivable marine microorganisms for drug-discovery
- It will contribute to create efficient collaborations and synergies among partners
- Partners' work will focus on deliverable products with industrial applications.
- A preliminary portfolio of interesting molecules and well-characterized marine microorganisms has already been developed
- Institutions will support the spinoff for 3-4 years

Opportunities

- We want to create in four years a real independent company with its labs and scientists.
- We develop interesting projects on important therapeutic applications
- We have identified public funds for supporting the Newco up to the breakeven.
- Partners have a good international network

Weaknesses

- We should have a proper financial support to outsource a few activities.
- Competition is high.
- Time to reach the objectives is long
- Bureaucracy of public institutions could slow the Newco development
- The low number of people involved in such initiative in relation to the ambitious goals is a limit.
- People working in public institutions lack an industrial approach

Threats

- After 3-4 years the Newco will need to implement collaboration with industrial partners or getting the support of venture capitals to develop further its leads.