

Marine Resources & Medicine

Yondelis[®] : A successful, high-value
application of marine resources





1. PharmaMar

A Spanish biopharmaceutical company: leader in developing anticancer compounds of marine origin

2. Blue Biotechnology

The potential of marine resources for fighting disease.

3. A success story: Yondelis

A successful, high-value application of marine resources



Biotechnology Discovery & Development of new medicines

Chemistry Manufacture & sale of consumer chemicals



Founded: 1986
HQ: Madrid (Spain)



PharmaMar: the first company in the world to develop and market a drug of marine origin to fight cancer (Yondelis®).

- ✓ **Unique bio-pharmaceutical company** (€450 M, 20 years).
- ✓ **Unique library** of marine organisms (> 120.000 samples).
- ✓ **Five marine-derived** compounds in clinical development

110
Patent families

450
M € invested in
R&D






120.000
Marine
samples

700
New chemical
entities

>70
Countries where
Yondelis is sold

300
Employees

5
Compounds
in clinical trials

THERAPEUTIC AREA	INDICATION	CLINICAL DEVELOPMENT				
		PHASE I	PHASE II	PHASE III	REGULATORY	MARKET
ONCOLOGY						
Yondelis® <i>Trabectedin</i>	Soft Tissue Sarcoma(STS) – 2nd/3rd line					
	Relapsed Ovarian cancer (Yondelis+Doxil)- 2nd/3rd line					
	STS with Translocations – 1st line					
Aplidin® <i>Plitidepsin</i>	Multiple Myeloma				 <i>Aplidium abicans</i>	
	T-cell lymphoma - non cutaneous					
Zalypsis®	Multiple Myeloma				 <i>Joruna funebris</i>	
	Ewing Sarcoma					
PM01183	Pancreatic cancer				 Synthetic	
	Ovarian Cancer (Resistant)					
	Breast cancer					
	Leukemia					
	Combination Studies					
PM060184	Solid tumours				 <i>Lithoplocamia lithooides</i>	

Life originated from the sea

34 of 37 phyla of life in sea
(compared to only 17 on land)

Macro-organisms
(invertebrates)



Micro-organisms
(bacteria)



Environmental DNA
(metagenomics)



Sea has higher biodiversity than land

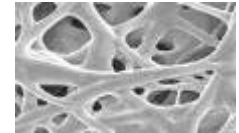
- ⇒ Higher chemical diversity
- ⇒ Many potential applications



Medicines &
Research Tools



Personal care
& Nutrition



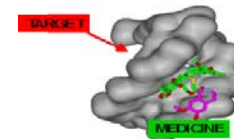
Biomaterials

“One of most exciting technology sectors”.

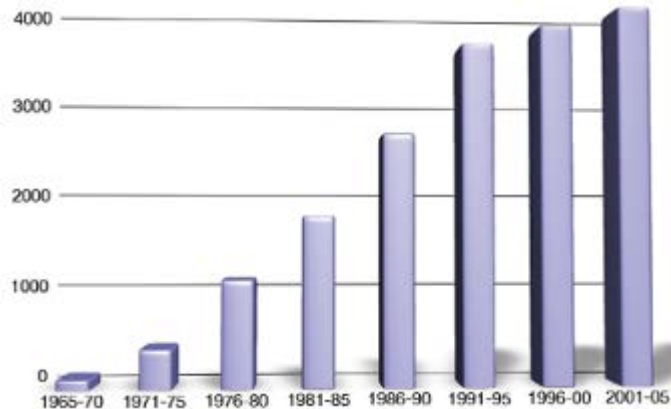
Blue Biotechnology = Marine and aquatic applications of biotechnology.



Nature: > 50% of the 1355 new chemical entities that have reached the market over the last 30 years have origins in nature.



Number of marine natural products reported (last 40 years)



Increasing numbers of “**exciting leads**”.... but marine drug discovery remains largely an academic pursuit.



- ✓ **Structural Diversity**
- ✓ **Potency** (inherent activity)
- ✓ **Largely** unexplored
- ✓ **Evolution** against challenges

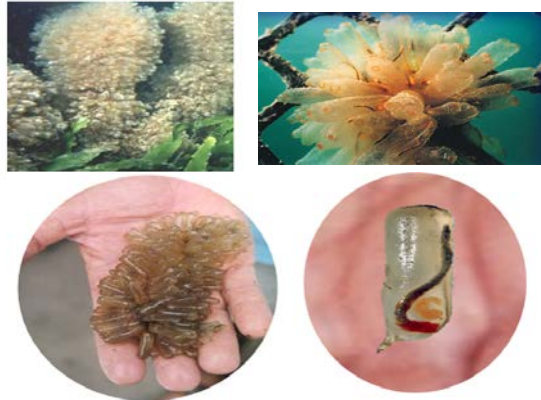


- x **Sourcing** (political hurdles)
- x **Legal uncertainty** (patents)
- x **Technological & Scientific**



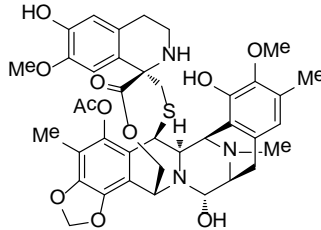
BioDiversity

Ecteinascidia turbinata:
small soft bodied marine
animal (**sea squirt**).



Lives in shallow coastal waters (0-15m)
in the **Caribbean** & temperate regions of
the **Atlantic** & **Mediterranean**.

Bioactive Molecule



Yondelis

Oncology
Medicine

Approved for ST
Sarcoma (July 2007)
& platinum-sensitive
ovarian cancer
(September 2009).



2001: Co-development Agreement **CENTOCOR**
ORTHO BIOTECH (J&J) outside Europe.

2009: Licence **TAIHO PHARMACEUTICAL** Japan.

Advantages: Only method at start of development !!

Sea farms



Artificial facilities (tanks containing sea-water)



Limitations

Seasonal (May – Oct)
Cost & security of supply
Low yield & variable quality
Complex extraction & purification
Logistics (transport of frozen organism)

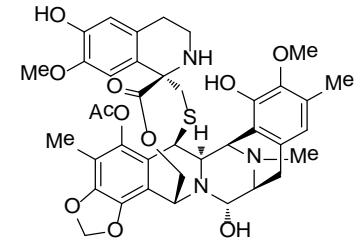
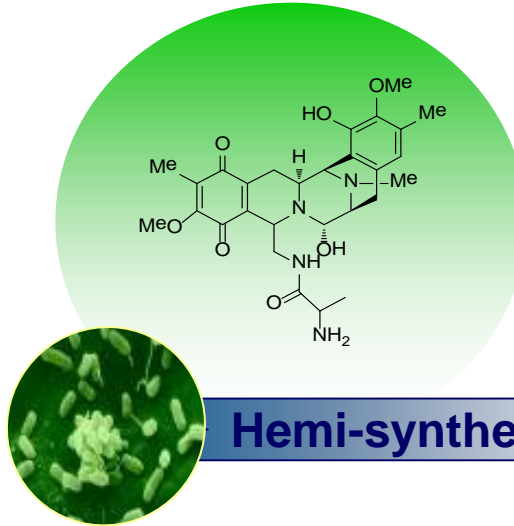
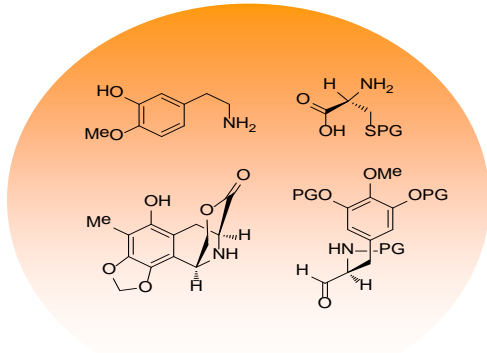
1 Tonne = 1g ET-743
Low yielding !!

The Supply Problem – Solved !

Total Synthesis (1996), > 50 steps



0.1-1g



Pseudomonas fluorescens



Hemi-synthesis



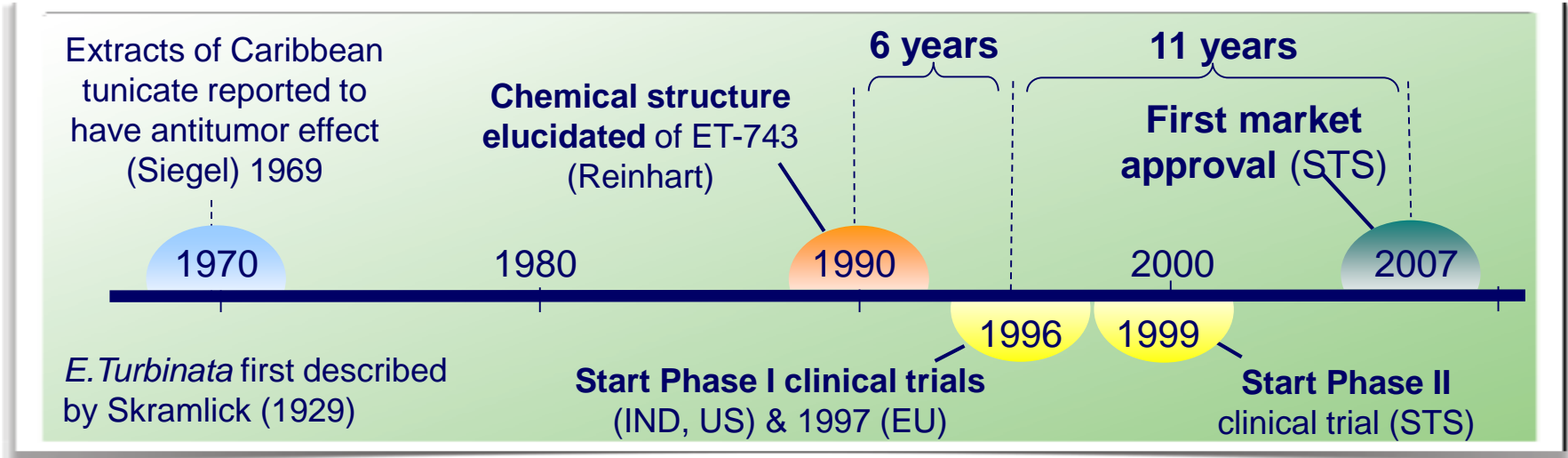
> 100g

- 2000 - First large-scale fermentation
- 2001 - Commercial route defined (laboratory scale)
- 2002 - First synthetic batch [2003 – end of *mariculture*]
- 2005 - Synthetic material used for first time in clinical study

Current Industrial
Process for GMP Yondelis[®]
manufacture *

* Cuevas & Francesch. *Nat. Prod. Rep.* 2009

Yondelis® Development Timeline



2005 - Synthetic material used for first time in clinical study.

- ❑ **Source:** access to marine samples & freedom to conduct Marine Research.
- ❑ **Legal Certainty:** CBD/UNCLOS and IP protection
- ❑ **Science:** knowledge generation requires excellent science (& scientists !)
- ❑ **Screening:** technical problems, “isolate & then test” or “test & then isolate”
- ❑ **The Supply Problem:** Key limitation, new technologies required
- ❑ **Technology Transfer:** Strengthen Academia- Industry partnerships:
- ❑ **Multidisciplinary research centres:** for Marine Drug Discovery
- ❑ **Ecology:** to understand the natural function of marine metabolites
- ❑ **Awareness & Visibility:** strong biotechnology identity

Marine Biodiversity has enormous potential !!

