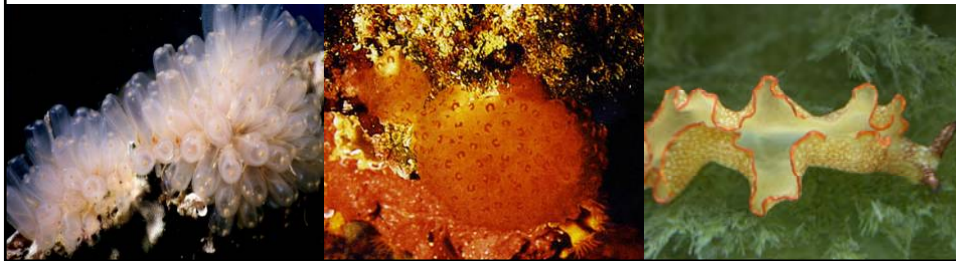




From Marine Expeditions to New Drugs in Oncology

26 June, 2007



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PharmaMar : Facts & Figures



- **Bio-pharmaceutical company** (20 years; Investment € 400 M)
- **Unique library** (> 42.000 marine samples)
- **Broad network of collaborations** (> 50 international centers)
- **Over 110 inventions** (660 patents granted; 700 on prosecution)
- **Five compounds from marine sources in clinical development.**

Goals

- **Launch Yondelis®** in STS in 2007 and in Ovarian by 2008/09
- **Increase pipeline:** one new compound in the clinic every 24 months
- **New strategic alliances** for drug development & commercialization
- **Become a profitable biopharmaceutical** company.



BioDiversity: The Business Case



PharmaMar

A Biopharmaceutical Company

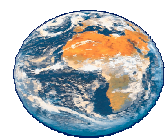
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Sources of Bioactive Molecules



BioDiversity

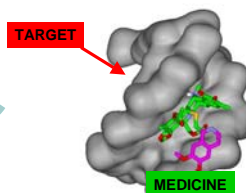


Literature & Patents

Bio-Active
Molecule



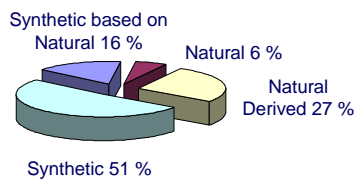
Combinatorial Chemistry
(High Throughput Screening)



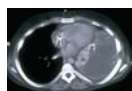
Target-based Design

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BioDiversity: Strong Track Record as Drugs



> 60 % of the 877 new chemical entities
that reached the market over the last 20
years **have origins in nature** *



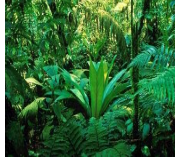
Advantages	Difficulties
Structural Diversity	Sourcing (political hurdles)
Potency (inherent activity)	Legal uncertainty (patents)
<i>Evolution</i> against challenges	Scientific (isolation, synthesis.)

Successes in Cancer	
Paclitaxel (TAXOL)	Roots of bush <i>Taxus brevifolia</i>
Irinotecan (CAMPTOSAR)	Leaf of plant <i>Camptoteca acuminata</i>
Etoposido (VEPESID)	Roots of plant <i>Podophyllum peltatum</i>
Doxorubicina (ADRIAMICINA)	Bacterium <i>Streptomyces peucetius</i>

* DJ Newman et al. 2003 . Journal of Natural Products 66, 1022-1067

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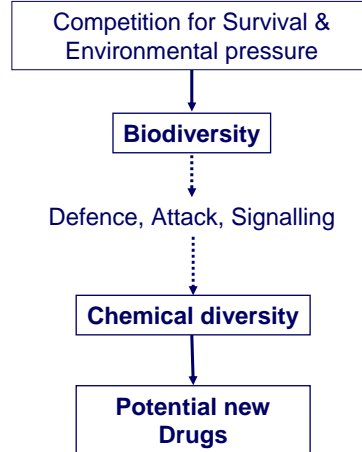
Advantages of Marine Biodiversity



Sea has higher biodiversity than land
High Biodiversity = High chemical diversity

Opportunity: Marine exploration for pharmaceutical purposes < 20 years old.

0.01% of terrestrial samples show anti-tumor potential vs **1% of marine samples***



* US National Cancer Institute (NCI) Estimates

Value Creation: The R&D Process



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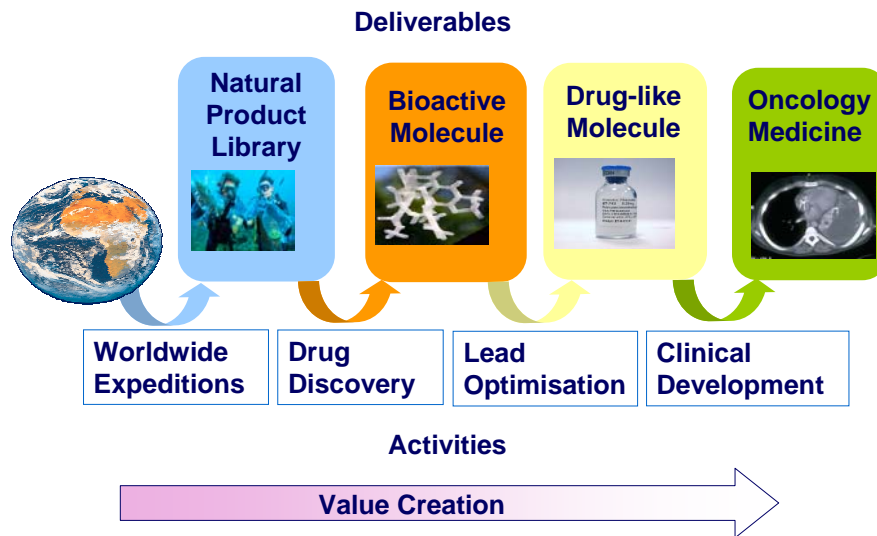
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The R&D Process: Value Creation



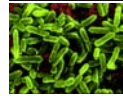
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Expeditions (Access & Benefit Sharing)

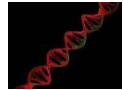


Macro-Organisms (mainly invertebrates)

Taxonomic classification, limited material, no control of metabolites present.



Micro-Organisms Associated with macros, possible to change metabolites, potential for fermentation



Environmental DNA Obtained from non-cultivable organisms

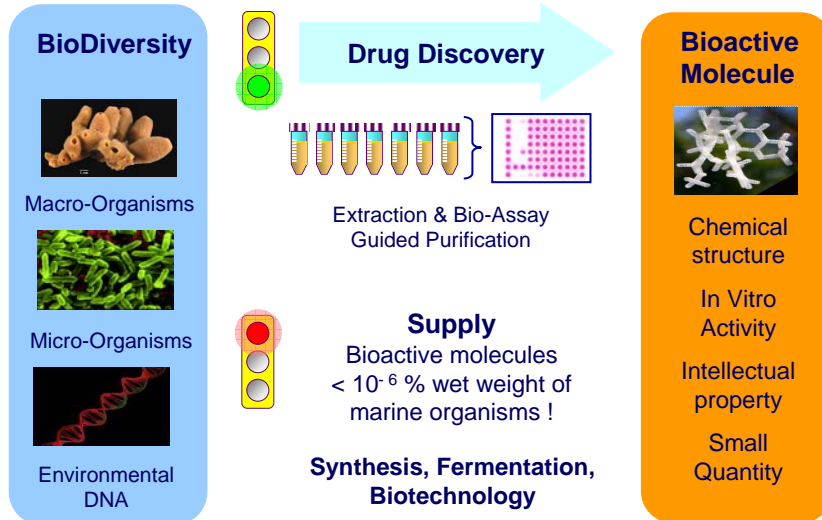
Natural Product Library



Monetary Benefits	Non-Monetary Benefits
Access Fees, Fee per sample	Sharing of Research results
Milestone payments	Collaboration in Education & Training
Royalties & Licensing Fees	Collaborative R&D Projects
Special Fees to support conservation & sustainable use of biodiversity	Transfer of technology & expertise for conservation or study of biological resources
Research funding for local initiatives	Resources to protect biodiversity
Joint ventures	Joint ownership of intellectual property

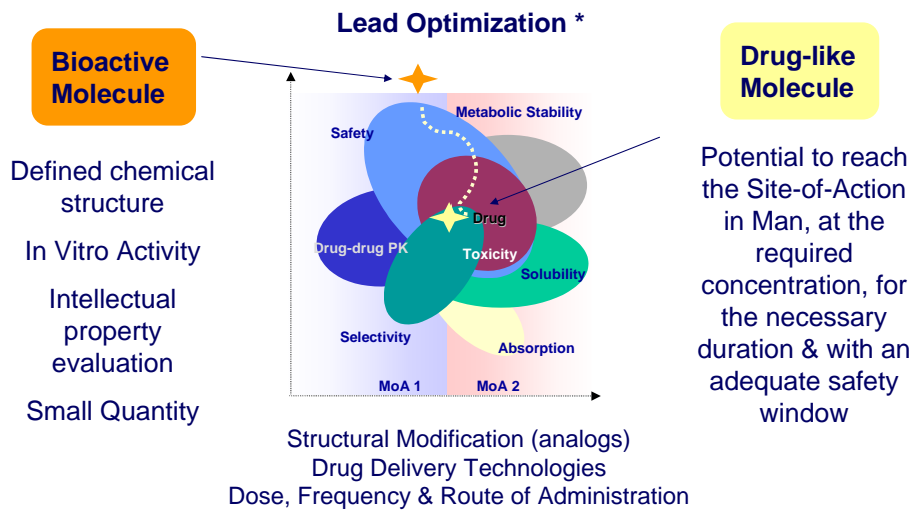
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Drug Discovery



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Lead Optimisation



* Fundamental to minimize risk of downstream failure.

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Clinical Development



Drug-like Molecule

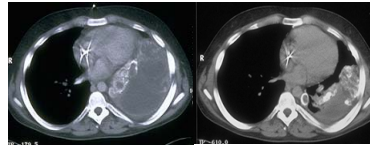
Ready for Clinical Trials

Clinical Development & Regulatory Approval



Oncology Medicine

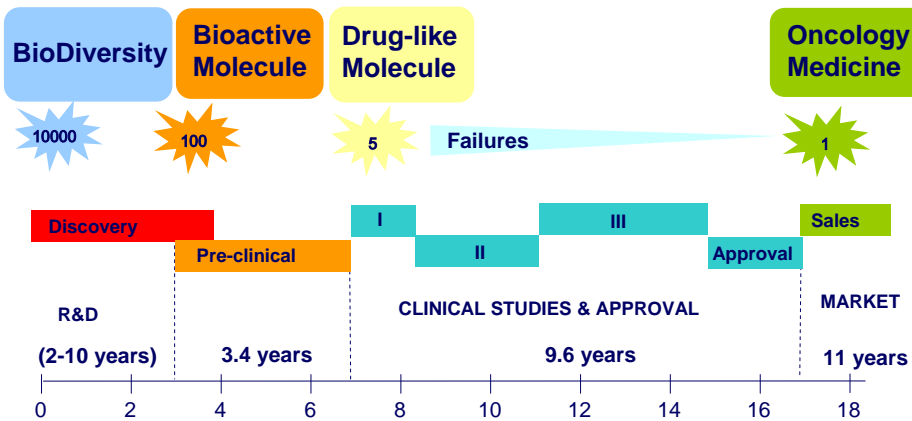
Demonstrated Quality, Safety & Efficacy



Phase I, Safety, Dose, Pharmacokinetics
Phase II, Efficacy, Tumour Type
Phase III, Large-scale, Comparative studies

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The Drug Development Process







Paclitael (TAXOL) : > 20 years from Structural Determination (Bioactive molecule) to FDA approval

Cost ~ \$ 802 mill.* Only 2 in 5 Marketed Drugs recover costs

* Di Massi 2003 16

New Medicines from BioDiversity



	Multiple Myeloma Leukaemia Melanoma	Aplidin® > 565 patients
	Solid & Haematological Tumours Solid Tumours Severe Psoriasis	Kahalide F > 265 patients
	Solid Tumours Haematological	Zalypsis® > 38 patients
	Solid Tumours	PM02734 > 20 patients

- “Orphan Drug” for Soft Tissue Sarcoma & Ovarian Cancer
- More than 3500 patients treated
- Novel MOA; Manageable toxicity
- Ovary, Breast, Prostate Cancers (plus paediatric & combination).
- Licenced to Johnson & Johnson outside EU
- Dossier submitted (July, 2006) to the European EMEA for STS Registration

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Conclusions



BioDiversity offers enormous potential for discovery and yields very interesting, highly potent **BioActive Molecules**.

Conversion of BioActive Molecules to Medicines requires a long-term commitment (10-15 years), **significant financial (800 M \$) & human resources & expertise** (multi-disciplinary). **Success is not guaranteed**.

Without research investment, there will be no **benefits or commercial rewards** to share.

Legal certainty is required to protect research investment.

Access and Benefit-Sharing are equally important if benefits of nature to be shared by all.

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Thank You



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