



Bio-mining the microbial treasures of the ocean

Early drug discovery and models for
entering pharmaceutical pipelines

Dr. Antje Labes



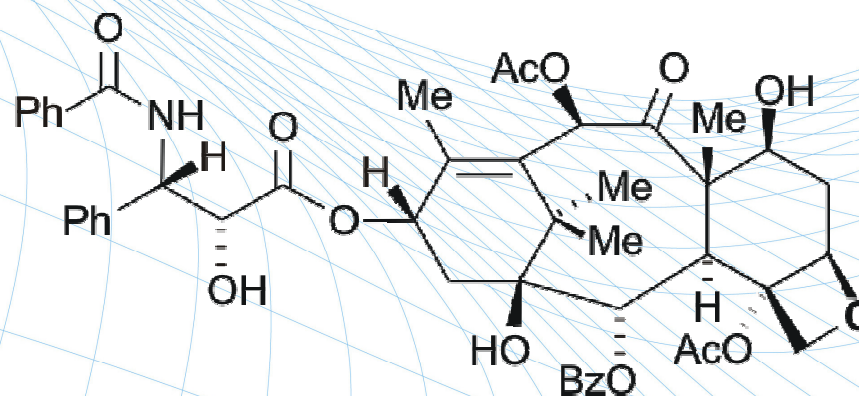
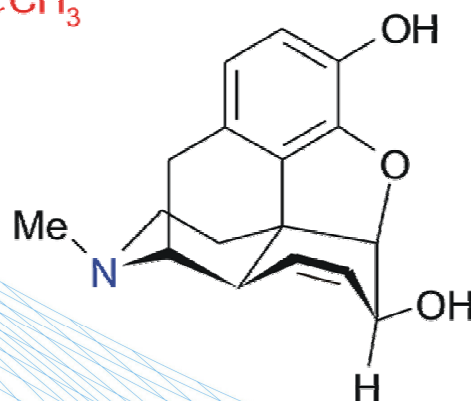
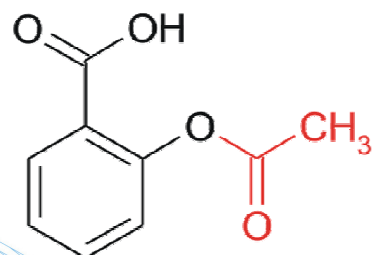
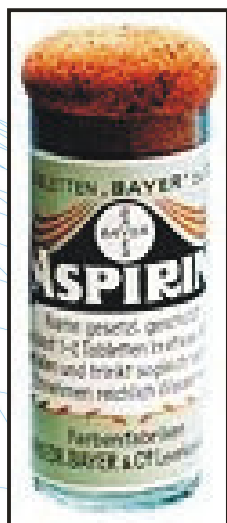
**Helmholtz Center for
Ocean Research Kiel**

Marine microbial compounds: from habitat to product



Kieler Wirkstoff-Zentrum

Natural compounds – highly potential molecules



Newman & Cragg, *J. Nat. Prod.* **2007**, *70*, 461-77.

„high potentials“ of the ocean



**70% of earth's surface
Less than 1% of microbial diversity known**

**New compounds
New enzymes**

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- In 1967, a small symposium was held in Rhode Island, USA, with the ambitious title “Drugs from the Sea”. The catchphrase of the symposium title has endured over the decades as a metaphor for drug development from marine natural products, though the first genuine drug from the sea was a long time coming (Molinski et al., 2009). The need for novel substances for the treatment of severe human diseases such as cancer, microbial infections and inflammatory processes, combined with the recognition that marine organisms provide a rich potential source of such substances support the intensive search for new substances from marine organisms. In the past, often algae and marine invertebrates have been investigated.

High added value products from marine organisms

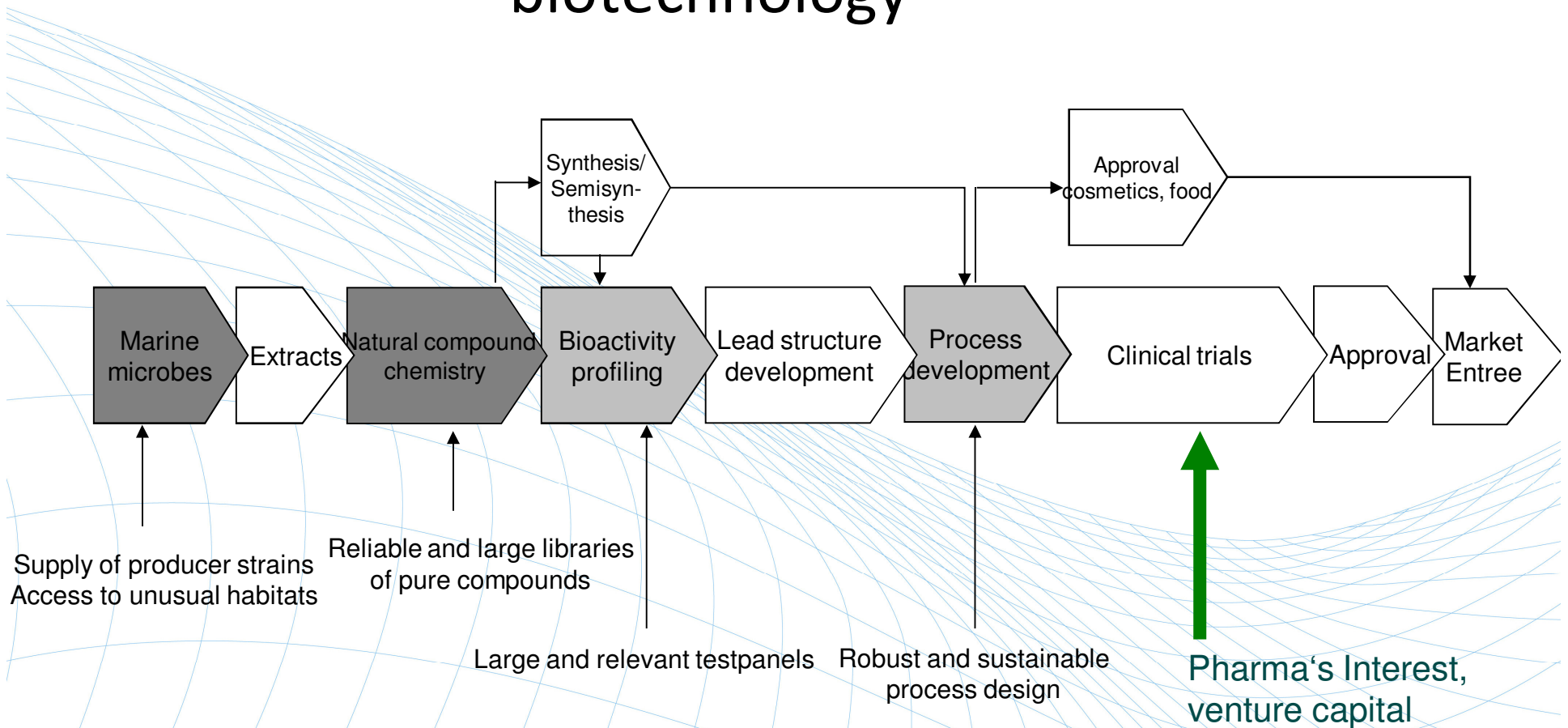


„Much of nature's treasure trove of small molecules remains to be explored, particularly from the marine and microbial environments.“
(Newman & Cragg, 2007)



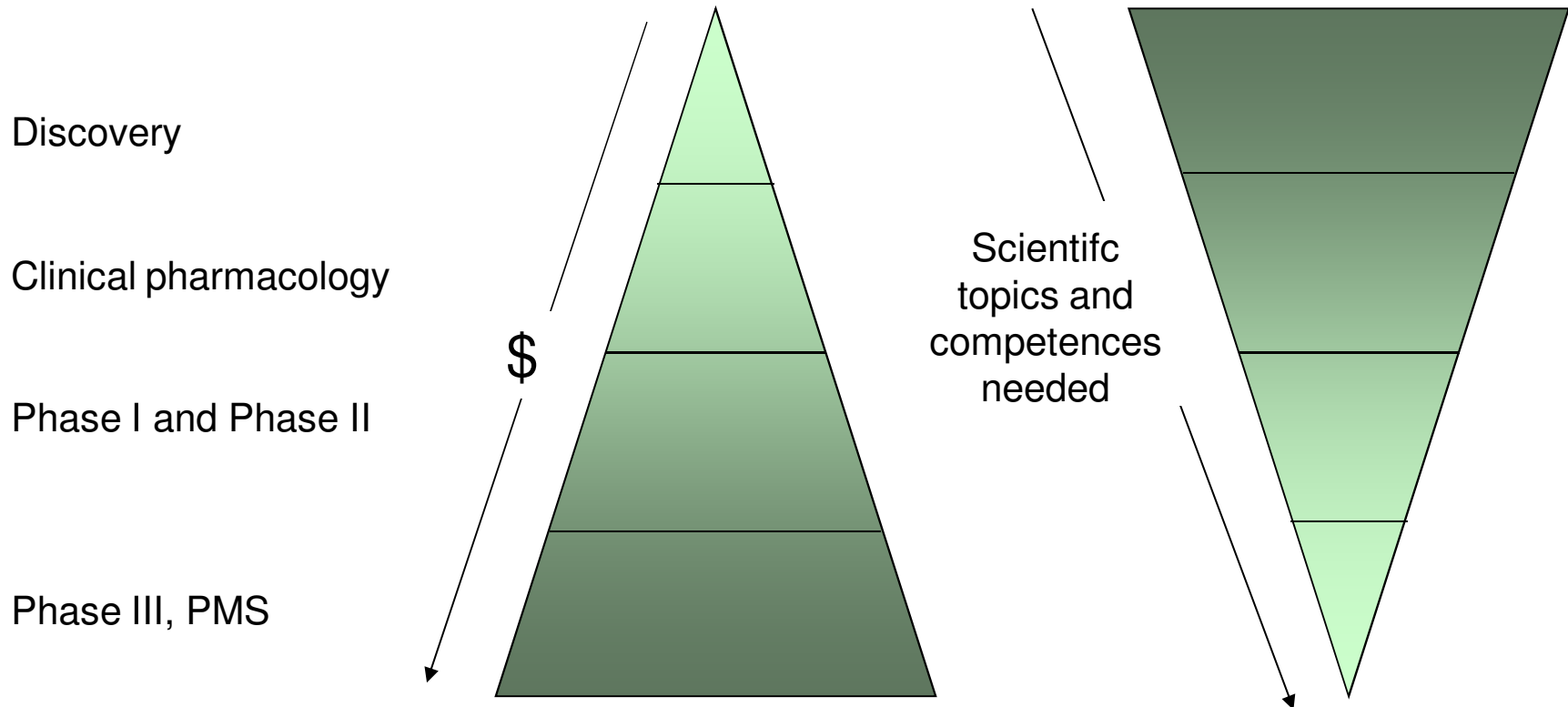
**Pharmacy, Medical technology and hygiene, Cosmetics
Industrial biotechnology, Food, Plant protection**

High added value chain from habitat to biotechnological product in marine biotechnology



► Classical value/risk problem?

Value/risk/scientific topics



Acc. to Douglas et al. 2010

Number of big pharma deals is decreasing

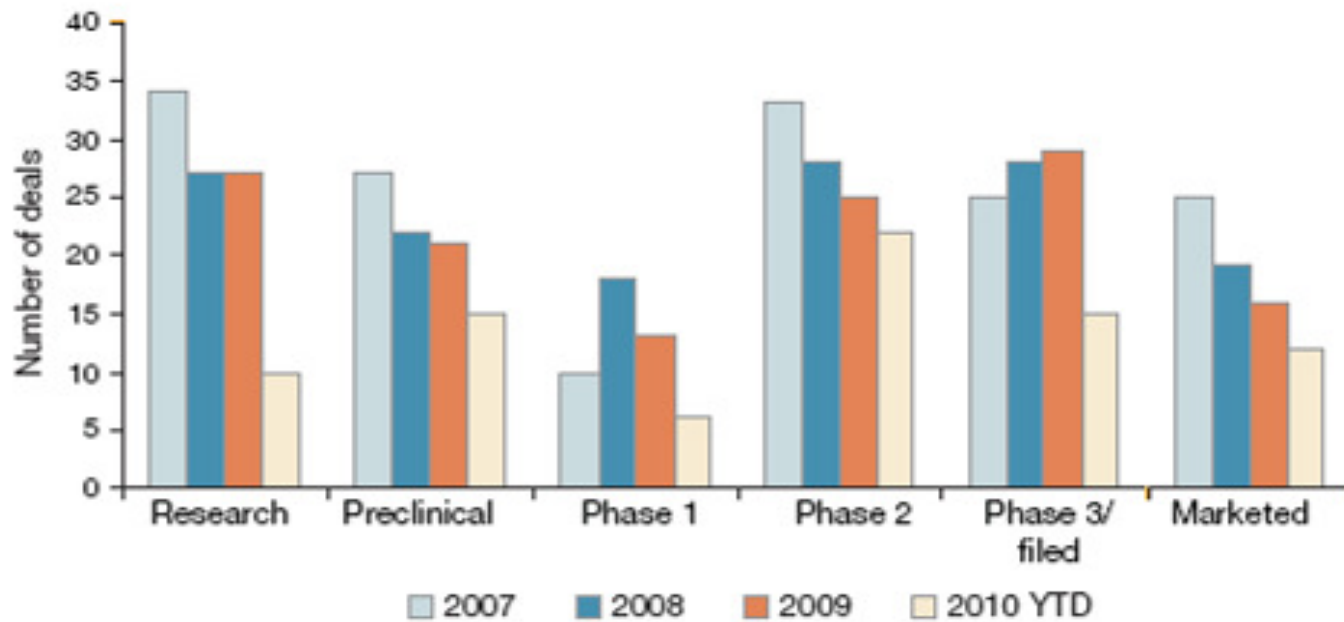
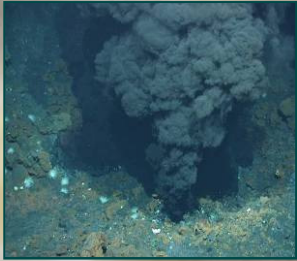
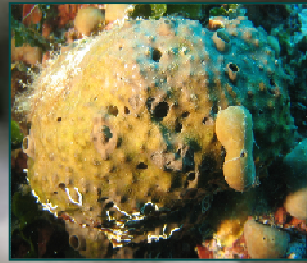


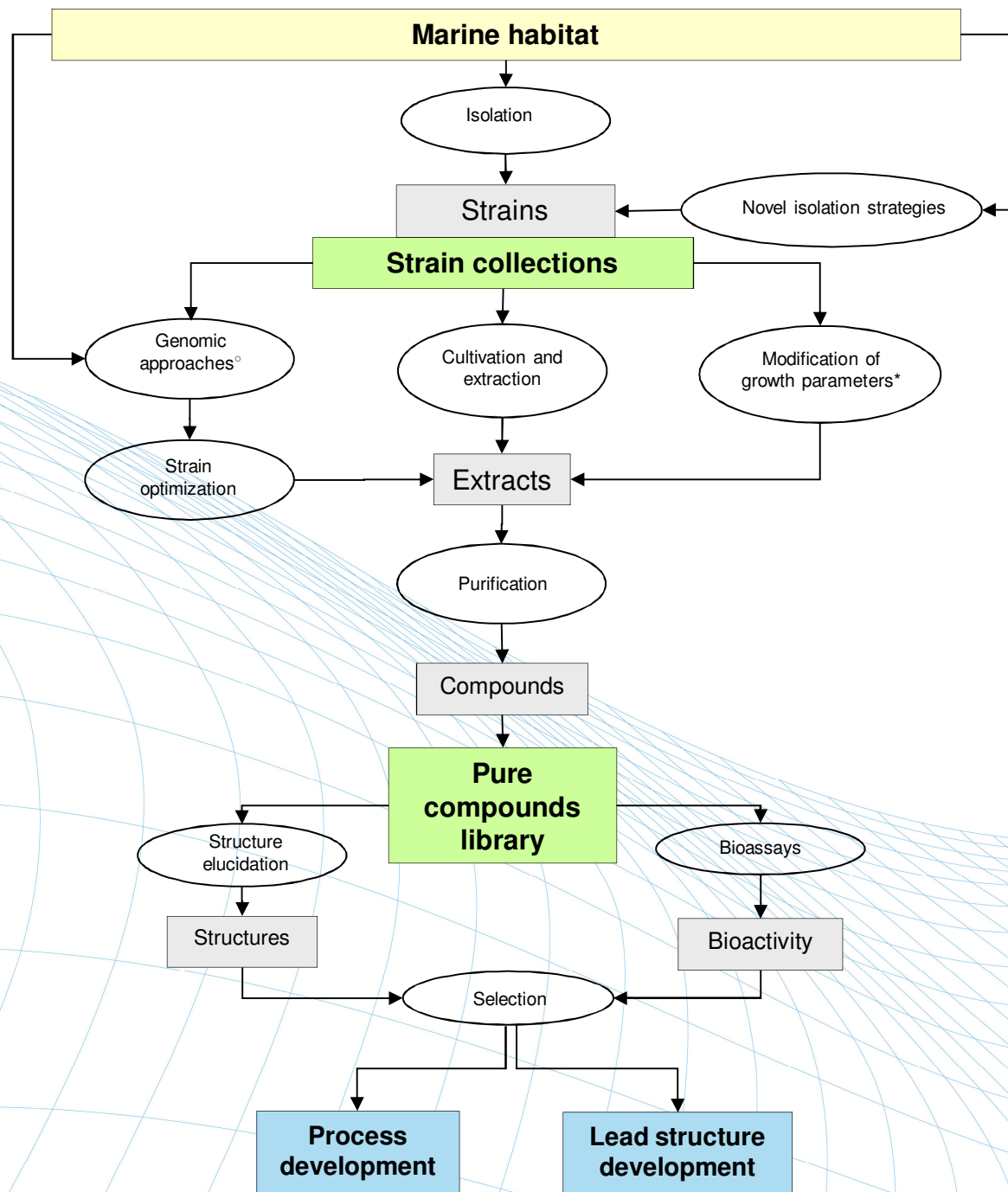
Figure 1 The number of big pharma deals with biotech have fallen in all stages. Source: Burrill & Co. (San Francisco); 2010 year to date (YTD) is through September 30.

“Post-mega-merger pharmaceutical landscape“

Adapted from Kessel, 2011



Example: Culture collections
ca. 15.000 marine bacteria
ca. 10.000 marine fungi
Access to diverse marine habitats



(aus: Imhoff et al., 2011)

WP1: Project Management and Coordination



Molecular based approach

Selected fungal strains

WP2

Genome analysis, identification of biosynthetic genes and regulators



FP7, 265926



Culture based approach

Selected marine macrobes from geographically distinct habitats

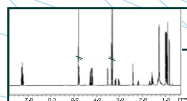
WP3

Isolation and identification of new fungal strains and optimisation of secondary metabolite production



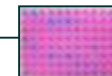
WP4

Chemical identification and biochemical characterisation of active metabolites and substance purification



WP6

In vitro bioassays for cancer targets, rational lead structure selection and *in vivo* efficacy determination in xenograft models



WP5

Strain improvement



WP7

Robust and sustainable process development



WP8: Intellectual Property protection & and dissemination activities



11 partners within MARINE FUNGI



Success?



Table 1 | New drugs approved by the FDA CDER from 1998 to 2007 by type and discovering organization*

Drug classification	Pharmaceutical company [†]	Biotechnology company	University; first transfer to a pharmaceutical company [§]	University; first transfer to a biotechnology company	Total
<i>Original CDER classification</i>					
sNMEs	87.7 (75%, 60%)	8.8 (7%, 20%)	9.2 (8%, 43%)	11.4 (10%, 29%)	117 (46%)
pNMEs [¶]	55.4 (57%, 38%)	15.4 (16%, 35%)	9.1 (9%, 43%)	18.0 (18%, 46%)	98 (39%)
NTBs	4.0 (11%, 3%)	19.9 (54%, 45%)	3.1 (8%, 14%)	10.0 (27%, 25%)	37 (15%)
<i>After reclassifying 21 polypeptide and two polynucleotide NMEs as NTBs</i>					
sNMEs	83.7 (79%, 57%)	6.4 (6%, 14%)	7.2 (7%, 34%)	8.7 (8%, 22%)	106 (42%)
pNMEs [¶]	52.2 (61%, 35%)	9.3 (11%, 21%)	8.6 (10%, 40%)	15.9 (18%, 40%)	86 (34%)
NTBs (expanded)	11.2 (19%, 8%)	28.4 (47%, 64%)	5.6 (9%, 26%)	14.7 (25%, 37%)	60 (24%)
<i>All drugs (including NTBs) classified according to review priority</i>					
Standard	90.5 (70%, 62%)	15.2 (12%, 35%)	10.2 (8%, 48%)	13.0 (10%, 33%)	129 (51%)
Priority [¶]	56.6 (46%, 38%)	29.0 (23%, 65%)	11.2 (9%, 52%)	26.3 (21%, 67%)	123 (49%)
<i>All drugs classified according to scientific novelty</i>					
Follow-ons	95.6 (71%, 65%)	14.2 (11%, 32%)	12.0 (9%, 56%)	12.2 (9%, 31%)	134 (53%)
Scientifically novel	51.5 (44%, 35%)	29.9 (25%, 68%)	9.4 (8%, 44%)	27.2 (23%, 69%)	118 (47%)
<i>Overall</i>					
Orphan drugs	15.6 (29%, 11%)	12.0 (22%, 27%)	6.7 (12%, 33%)	19.6 (36%, 49%)	54 (21%)
Total	147.2 (58%)	44.1 (18%)	20.4 (8%)	40.3 (16%)	252



Kellner 2010

From scientific rationale to capital flow?

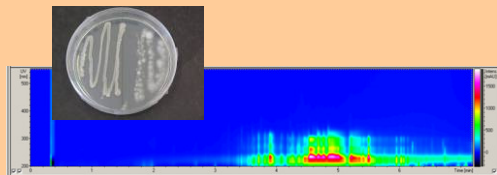


Biology of marine fungi

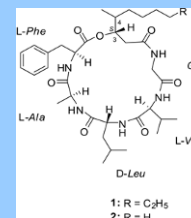
Understanding the complexity of a neglected group with diverse functions



Microbial interaction Understanding communication at the μm -level



Marine natural products Linking ecology and biotechnology



Transfer models for early drug discovery



- Early – proof of concept
 - Broad research possibilities, public funding for basic tasks
 - Enhance academic value
 - Early onset of SME
 - Public-private partnerships
- Middle – proof of relevance
 - Focussing on few tasks – transition
 - Funding cycle oriented with exit-strategy
- Question of IP models

Beyond venture capital

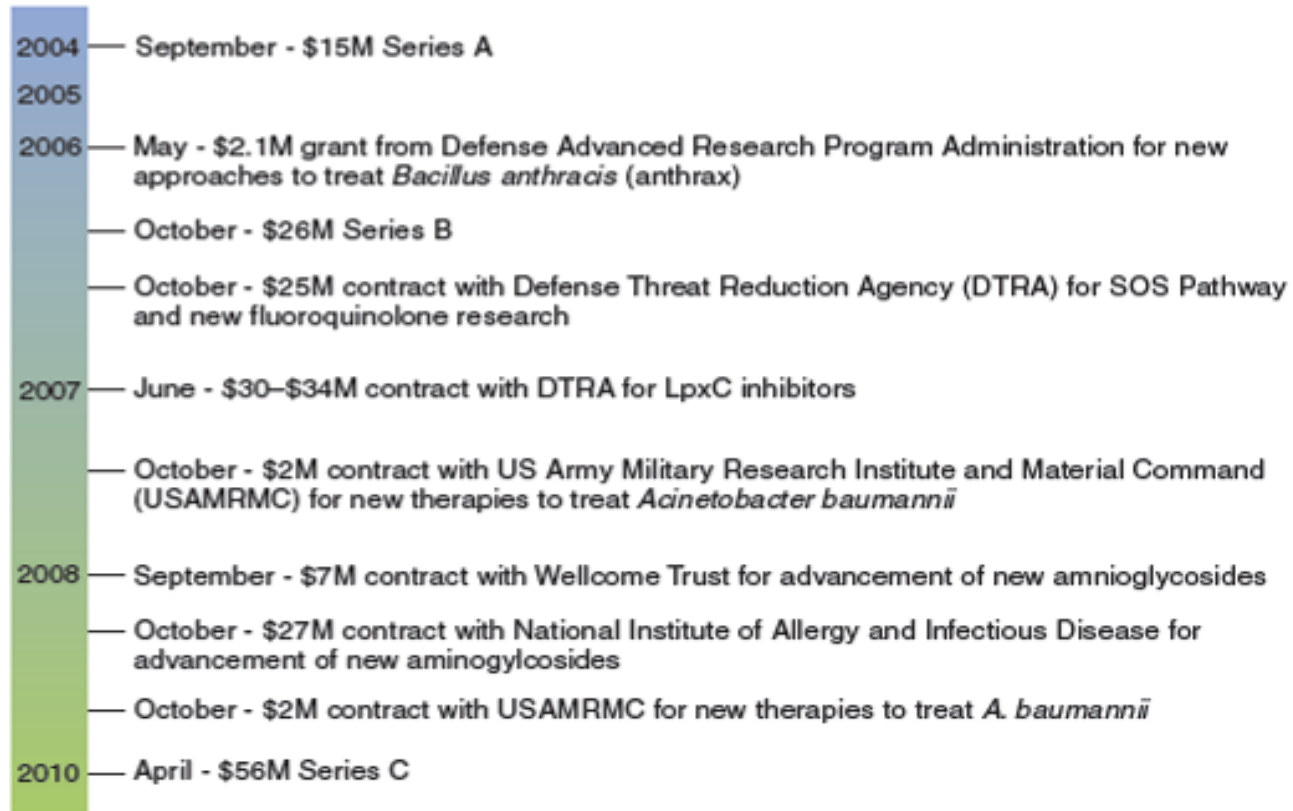


Figure 1 Achaogen's funding timeline

European Approach?

Hollway 2010



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