



**entrechem**  
b i o t e c h n o l o g y

*Francisco Morís, Director General*

**Foro del Emprendedor**

*Oviedo, 23 de Setiembre 2009*

# Who is EntreChem?

- Spin-off from **the University of Oviedo (Spain)**
  - ▶ Started operations in 2006
- **Cofounders:**
  - ▶ Francisco Morís, Ph.D. (entrepreneur, 11 years in USA)
  - ▶ Prof. José A. Salas (Microbiology, Genetic Engineering)
  - ▶ Prof. Vicente Gotor (Organic Chemistry, Biocatalysis)
- **Seed Capital from 3 spanish institutions (total €0.8M):**



SRP

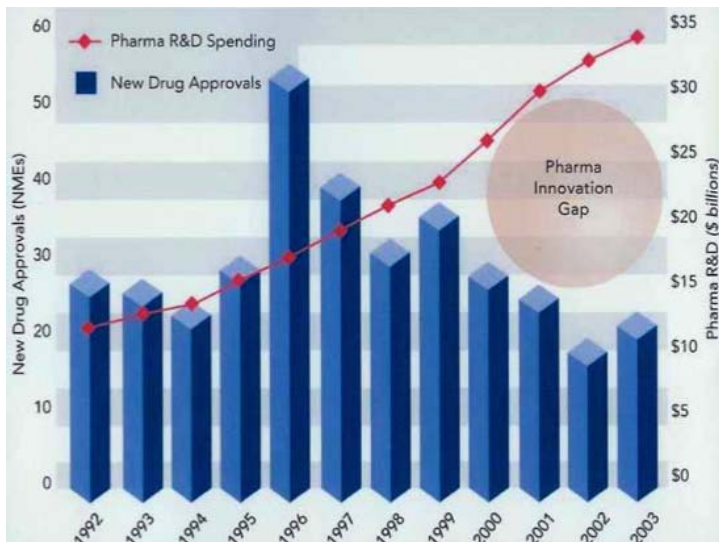


# Drugs from Natural Products

- "45% of today's best-selling drugs originate from natural products or their derivatives"

- L. Muller-Kuhrt (CEO, Analyticon): "Putting Nature Back into Drug Discovery" Nat. Biotechnology 2003, 602.

- Bacteria is the main natural source of leads
- Annual drug sales in 2003: \$20B (only *actinomycetes*)

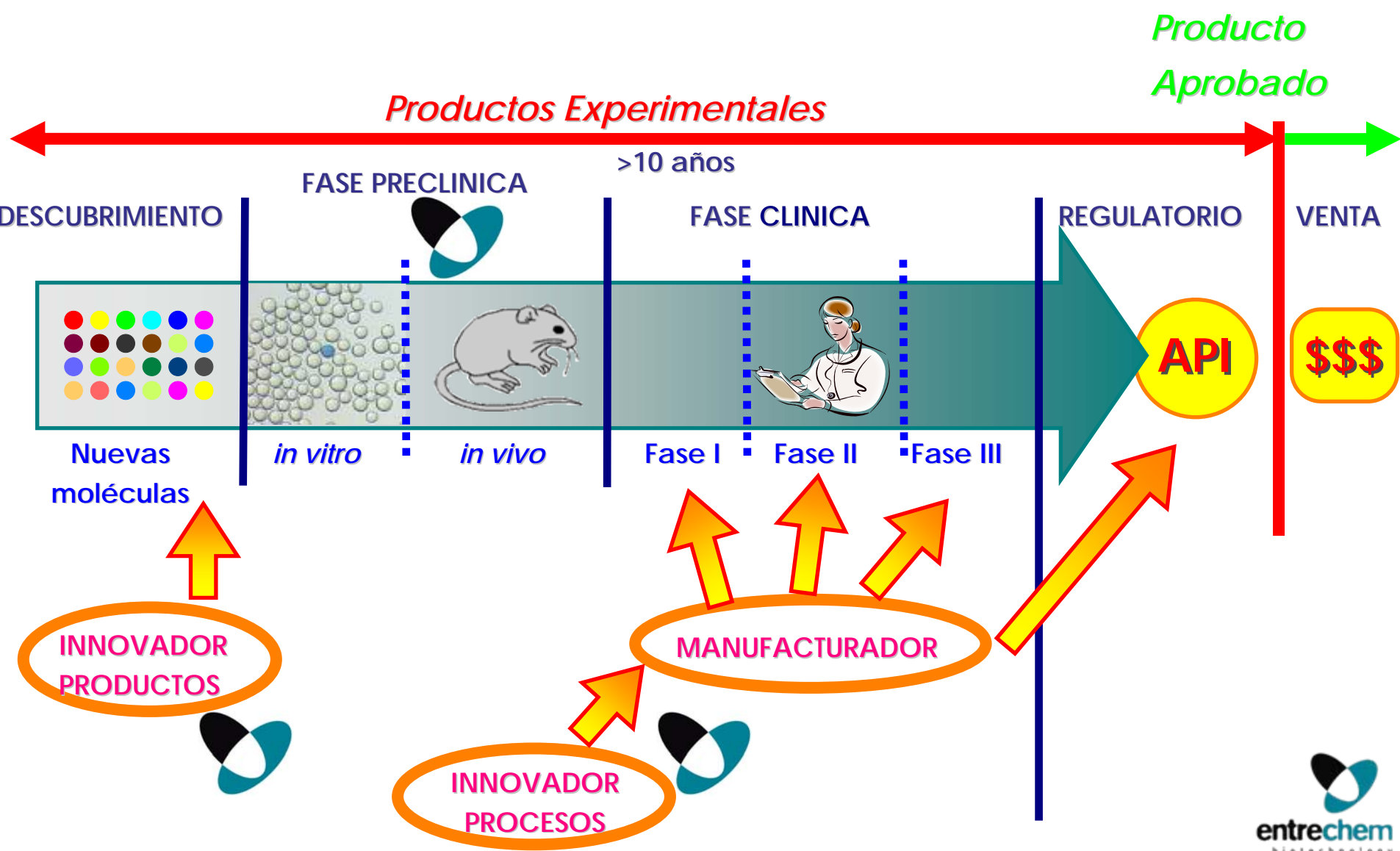


Nola Mastersons, Science Futures, Inc. (BioHouston, May 2004)

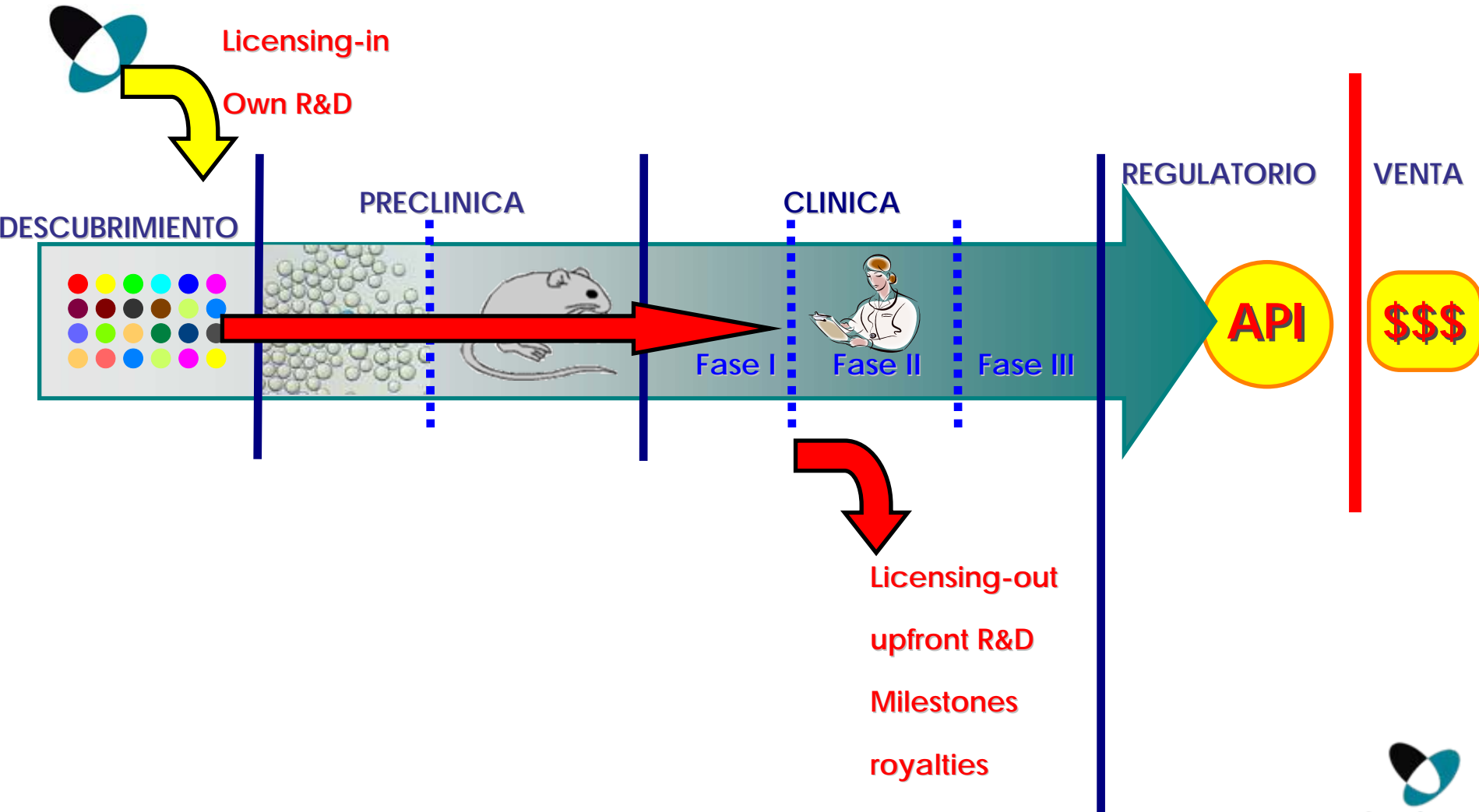
- Big Pharma NCEs productivity is decreasing
- Coming back to Nature to expand the Chemical Space

**Technology Gap filled by  
spin-offs & VCs**

# EntreChem en la Cadena de Valor de Nuevos Fármacos



# EntreChem en la Cadena de Valor de Nuevos Fármacos



# Pipeline

EntreChem's Technology enables development of a product pipeline

	Genetic tractability	Diversity Generation / <i>in vitro</i> assays	<i>in vivo</i> Proof of concept	Formal Preclinical Devlpmt.
<i>cancer (solid tumors, lymphomas)</i>				
Sp1-binding inhibitor	→			
multi-kinase inhibitor	→			
target to be determined	→			
<i>other programs</i>				
RNA pol. inhibitor	→			
Topo-II inhibitors	→			

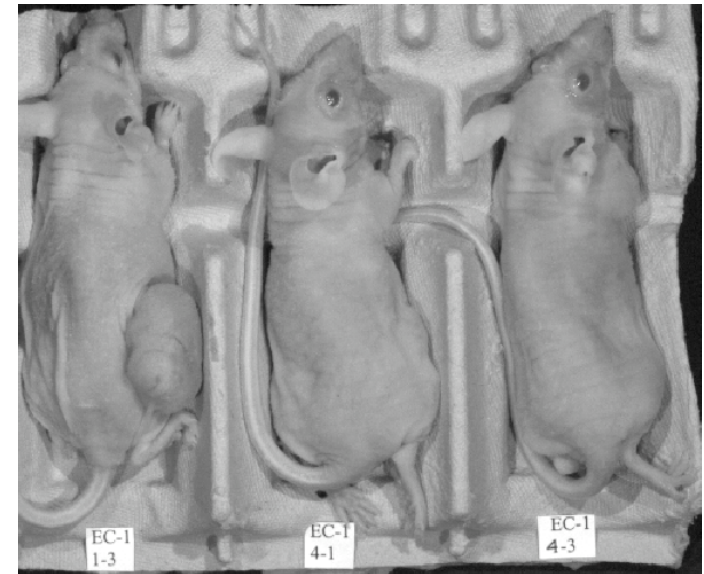
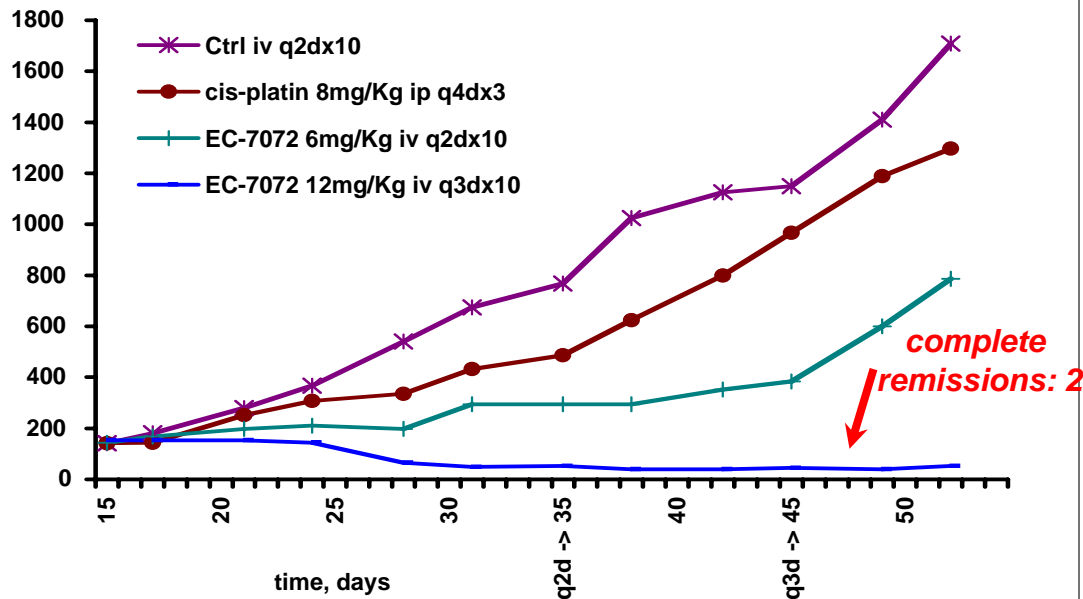
# IP Summary

PROGRAM / App. ID	Ownership / Licensing status	REGION
Sp1 inhibitors (1st gen.) <i>US2005/0192432</i>	Licensed from UniOvi / UK	US
Sp1 inhibitors (2nd gen.) <i>PCT/ES2008/070015</i> <i>ES P200700378</i>	Licensed from UniOvi / UK	worldwide
Sp1 inhibitors (3rd gen.) <i>to be filed in May 2009</i>	100% owned by EntreChem	worldwide
Kinase inhibitors <i>ES P200801077</i>	Co-property of UniOvi and EntreChem	worldwide
Angucyclines <i>ES P200800982</i>	Licensed from UniOvi	worldwide

# Proof of Concept

- Human colon cancer mouse xenograft model
- Regression at high dose, remission and 2/8 cures
- No toxicity signs at the tested doses

COLO-205 (NCr nu/nu mice, n=8)



# Novel Potent, Selective Ikkb and JAK2 inhibitors

- ▶ <30pM IKKb inhibitor: IKKb prevents activation of NF- $\kappa$ B pathway
  - 📖 potential application on inflammation and cancer
- ▶ selective subnanomolar Jak2 inhibitor
  - 📖 potential application on myeloproliferative disorders

Data in nM	EC70119	EC70120	EC70123	EC70124	EC70127	EC70128
AurA	-	>10	5.0	>10	>10	6.7
AurB	-	-	6.8	-	-	4.5
Chk1	2.4	1.0	-	4.9	>10	-
Dyrk1a	-	4.0	-	-	>100	>10
Ftl3	0.59	0.57	0.54	0.56	-	0.43
FGFR1	-	8.9	>10	-	>100	>10
HGK	-	0.78	-	-	>10	>10
Ikkb	-	0.17	-	<0.03	>100	>10
Jak2	0.43	0.50	0.57	0.74	0.53	1.2
KDR	-	3.7	-	0.55	>10	>10
SYK	-	1.0	-	1.1	>10	2.3

# Development Plan

**Goal: complete preclinical development of one candidate and be ready to start Phase I clinical trials in 2 years**

- **Lead program (SP1)**
  - ▶ First year: complete pharmacology
  - ▶ Second year: IND-enabling preclinical development
- **Kinase program**
  - ▶ First year: complete in vitro profiling of compounds
  - ▶ Second year: determine a candidate for development

# Financiación

- **Etapa inicial: Financiación Pública**
  - ▶ Fundación Genoma España
  - ▶ Programa I+D+i Principado Asturias: SRP, IDEPA, FICYT
  - ▶ Programa NEOTEC
  - ▶ Programa Marco de la UE: FP6
- **Etapa de desarrollo: Mix Público Privado**
  - ▶ Programa NEOTEC-2 (plan de desarrollo ambicioso)
  - ▶ Business Angels
  - ▶ Fondos de inversión nacionales

# NEOTEC-2

- **Unica empresa de Asturias con NEOTEC aprobado**
  - ▶ Demuestra proyecto genuino de I+D, necesario para acceder a créditos blandos y ventajas fiscales
- **EntreChem elegible para €0.6M**
  - ▶ Préstamo a interés cero
  - ▶ Sin calendario de amortizaciones
  - ▶ Devolución al obtener cash-flow positivo
- **Aprobado en el consejo del CDTI en Mayo**
- **Sujeto a incremento de fondos propios (300k)**

# Tipos inversor

- **Business Angels**
  - ▶ Proximidad, due diligence basada en “gut feeling”
  - ▶ Pactos de socios relativamente simples
  - ▶ Aportaciones limitadas
- **Fondos especializados**
  - ▶ Aportaciones sustanciales
  - ▶ Due diligence eminentemente técnica
  - ▶ Pacto de socios complejo
- **Fondos regionales**
  - ▶ Buscan implantar operaciones de manufactura en sus CCAA

# Algunos puntos clave

- **Comunicación**

- ▶ Transparente
- ▶ Preservar confidencialidad
- ▶ Muy importante transmitir el valor intangible

📖 El gestor de la SGCR también “vende” su estrategia a los inversores

- **Preparación para la negociación**

- ▶ Documentación lista (y actualizada) en todo momento  
Licencias y solicitudes de patente, escrituras, auditorías, etc
- ▶ Negociación transparente con sindicatos de ángeles
- ▶ Apoyo legal para Pacto de socios complejo (ratchets antidilución)