Programa Cooperación Farma-Biotech

Jornada IIb: **Oncología**

Novel derivatives of polyunsaturated fatty acids for the treatment of lung and pancreatic cancer

Madrid, 12 de mayo de 2011

CataloniaBIO
Associació catalana d'empreses de biotecnologia

MEDICAMENTOS INNOVADORES
Plataforma Tecnológica Española

GOBIERNO DE ESPAÑA
MINISTERIO DE CIENCIA E INNOVACIÓN

farmaindustria

Content

1. **The Company**
2. **The Product**
   a) **Therapeutic focus**
   b) **Innovative mechanisms of action**
   c) **Differential features facing the market**
   d) **Current status of development**
   e) **IPR protection**
   f) **Pitfalls & Risks to be considered**
3. **Availability for cooperation**

Programa Cooperación Farma-Biotech

Jornada IIb: **Oncología**

THE COMPANY

Eureka Building – Research Park
Autonomous University of Barcelona

Pharma-Biotech Company

New Therapeutic Approach:

MEMBRANE LIPID THERAPY

For: **LUNG & PANCREATIC CANCER**

Founded in November 2009

Shareholders & Founders: Carles Domènech, PhD,

Jordi Espadaler, PhD and AB-Biotics, SA

One Drug in Phase I in 1Q 2012 (GLPtox and GMP manufacturing ongoing)

A second drug candidate to start preclinical development in 2Q2011.

Patent Protection (2030)

Expected Income over **15 Million € in 2014**

Experienced Management & Qualified Team of Advisors

MANAGEMENT

Carles Domènech, PhD - Chief Executive Officer - Co-founder

- PhD in Cell Biology & Business Training.
- 13 yrs in BDL at Almirall & Lacer.
- 2.5 yrs in biotech venture capital (Barcelona Emprèn and CIDEM).
- 8 yrs in science research, incl.2 yrs at Memorial Sloan-Kettering Cancer Center (New York).

Jordi Espadaler, PhD - VP Discovery - Co-founder

- 4 yrs Chief Research Officer at AB-Biotics, SA .
- PhD in molecular biology. Research at Rockefeller University (New York), University of California - San Francisco and UAB.

José Alfón, PhD - VP Drug Development.

- 4 yrs. Team leader drug development (pre-clinical and clinical) at the biotech Palau Pharma, SA
- 8 yrs, team leader drug discovery at the pharmaceutical company Uriach, SA
- PhD in Pharmacology , Research at Hebrew Univ. of Jerusalem and Universitat de Barcelona.

BOARD OF DIRECTORS

Miquel Àngel Bonachera, CEO and Co-founder of AB-Biotics, SA *
Sergi Audivert, CEO and Co-founder of AB-Biotics, SA *
Luis Sánchez-Lafuente, former CEO and owner of Laboratorios Gelos, SA.
Carles Domènech, PhD.
Undisclosed, CEO, UK biotech company

* **AB- Biotics, SA - (Co-founder)** is the first Catalan biotech publically traded at the alternative stock market of Spain (MAB).

ABTherapeutics
real medicine for real life

Programa Cooperación Farma-Biotech

Jornada IIb: **Oncología**

ADVISORY BOARD

Jesús Llenas, PhD. EU Preclinical Development Interim Manager. GLPTox, formulation and regulatory affairs. More than 25 years experience as Director of several functions in preclinical development at Almirall, SA. Experience with FDA and EMEA. 3 drugs approved internationally, including FDA.

Toni Pérez, MD. Clinical Development Interim Manager and Advisor. More than 25 years experience as medical director in several pharmaceutical companies (Almirall, Novartis Headquarters in Basel, Basilea Pharmaceuticals and Esteve). Currently advisor and consultant for Novartis and biotech companies. Experience with FDA and EMEA. 2 drugs approved internationally. Several products in phase III.

Peter Wyld, MD. Clinical Development Interim Manager and Advisor. More than 20 years experience as medical director in several pharmaceutical companies (Amgen, Biogene, Johnson & Johnson Oncology). Currently advisor and consultant for pharmaand biotech companies. Experience with FDA and EMEA.

Non-disclosed. Regulatory Affairs Advisor. 30+ ys. Experience as Chief Regulatory Officer at a leading mid-size pharmaceutical company. Successful experience with FDA and EMEA (several approvals).

José Luís Fábregas, PhD. Pharmaceutical Development Advisor. 40 ys. experience as Director, Pharmaceutical Development at Almirall. Several drugs approved internationally, including FDA.

Pablo Escribá, PhD. Opinion leader in Membrane Lipid Therapy. Professor at Universitat de les Illes Balears.

25+ years experience, each, in senior positions in multinational pharmaceutical companies (Novartis), mid-size (Almirall, Esteve) and biotechs (Basilea Pharmaceuticals). Experience with EMEA and FDA: 3 DRUGS APPROVED

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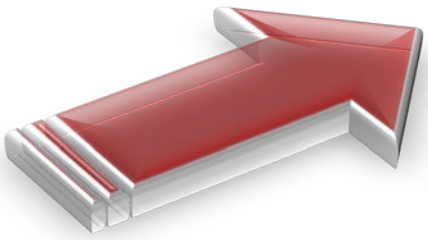
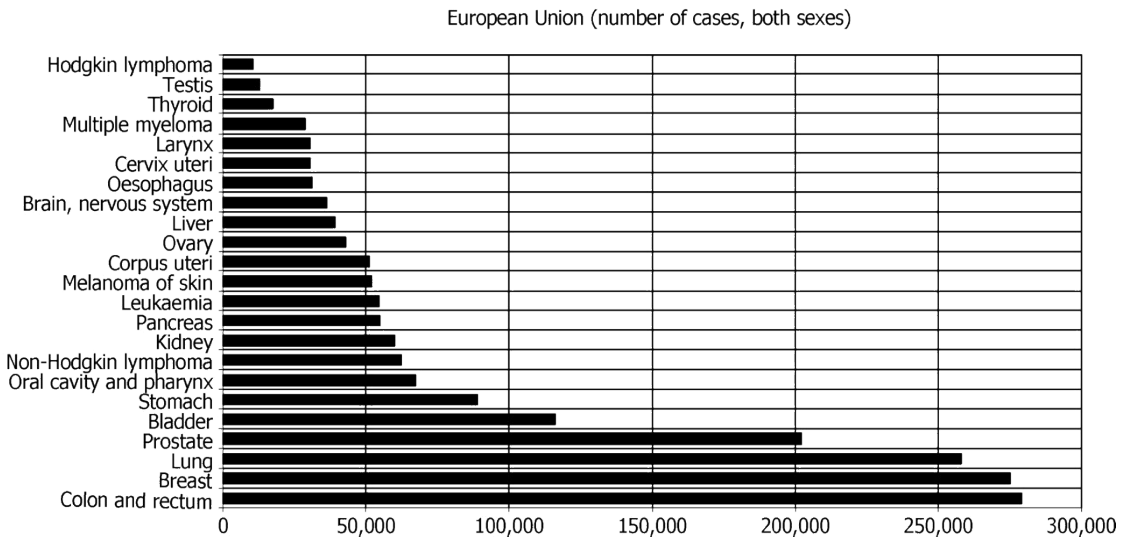
- **Lung cancer** causes 30% of all cancer deaths.
  - 42% of patients survive after one year, but only a the 15% survive after 5 years.
  - Non-Small Cell Lung Carcinoma (NSCLC) accounts for the 25% of all drugs sales for cancer treatment.
- **Pancreatic cancer** has a very low survival (**less than 5% after 2 years**).



UNMET MEDICAL NEEDS

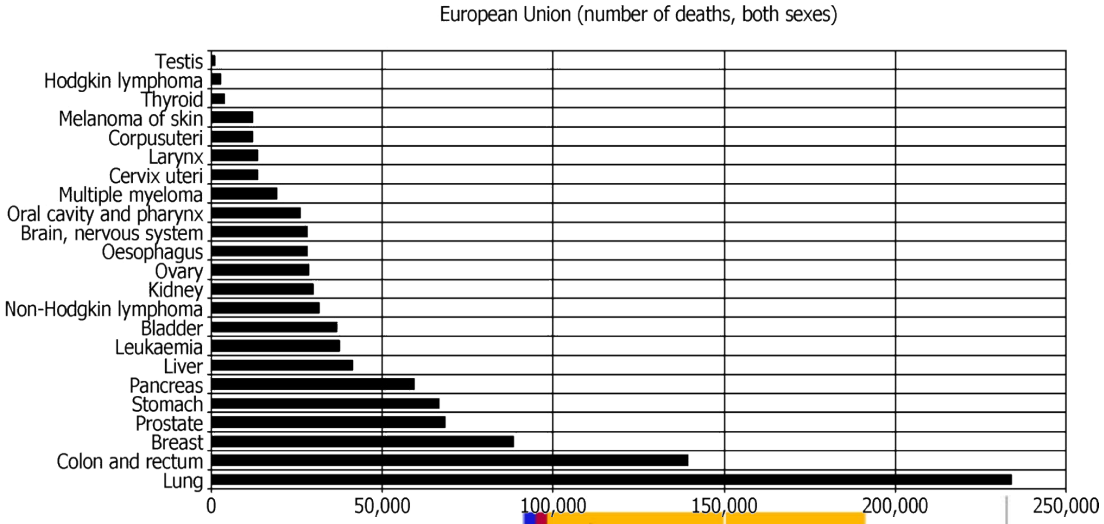
OPPORTUNITY TO IMPROVE HUMAN HEALTH

MARKET OPPORTUNITY (sales > 1.5 B €)



Incidence and Mortality of Cancer

Colon, breast, lung and prostate cancer are by far the most common types of cancer. **Lung cancer accounts for 12% of all cancers.**



However, lung cancer mortality is much higher than others. Actually, **lung cancer causes 30% of all cancer deaths.**

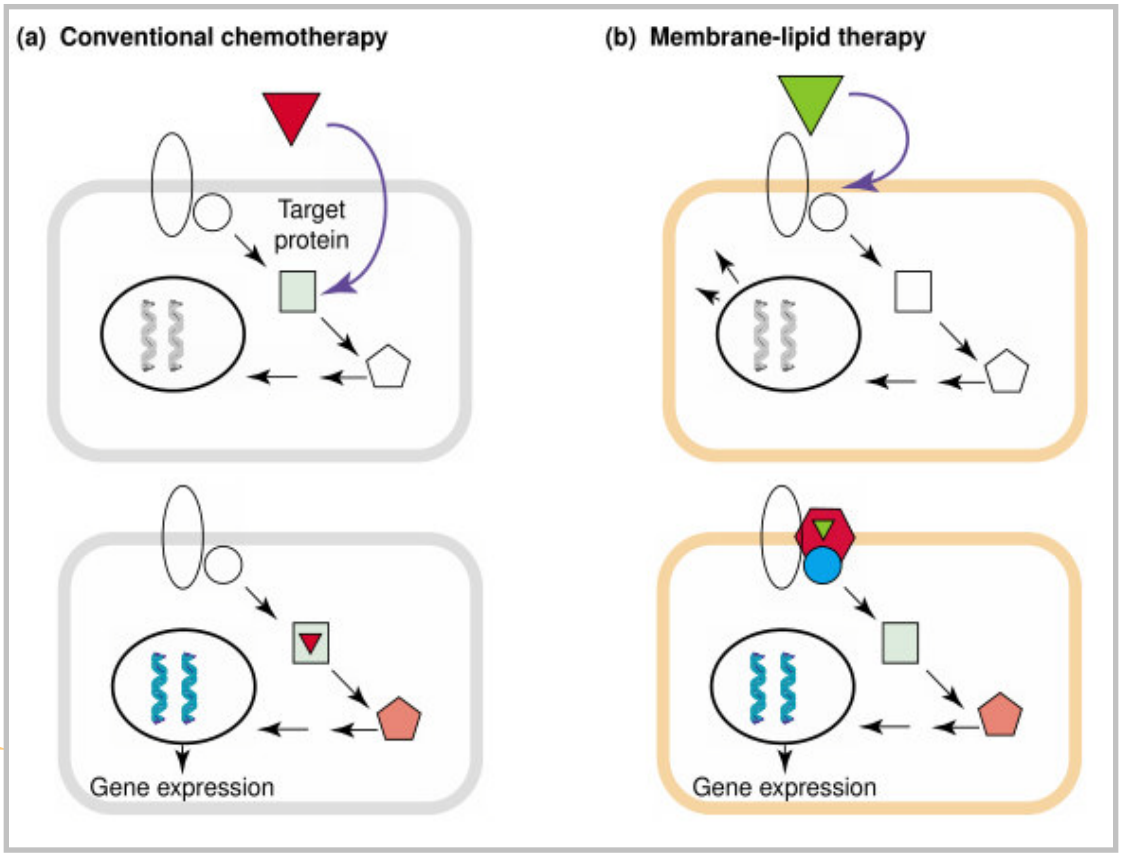
Pancreatic cancer, although it is the 10th type of cancer, it has an extremely high mortality, holding the **6th position as cause of death.**

Membrane Lipid Therapy: Concept

In **conventional chemotherapy** a drug binds specifically to a **protein target**, altering its function.

Tumors may respond by increasing the amount of the target protein, mutating that protein or reducing the permeability of the membrane.

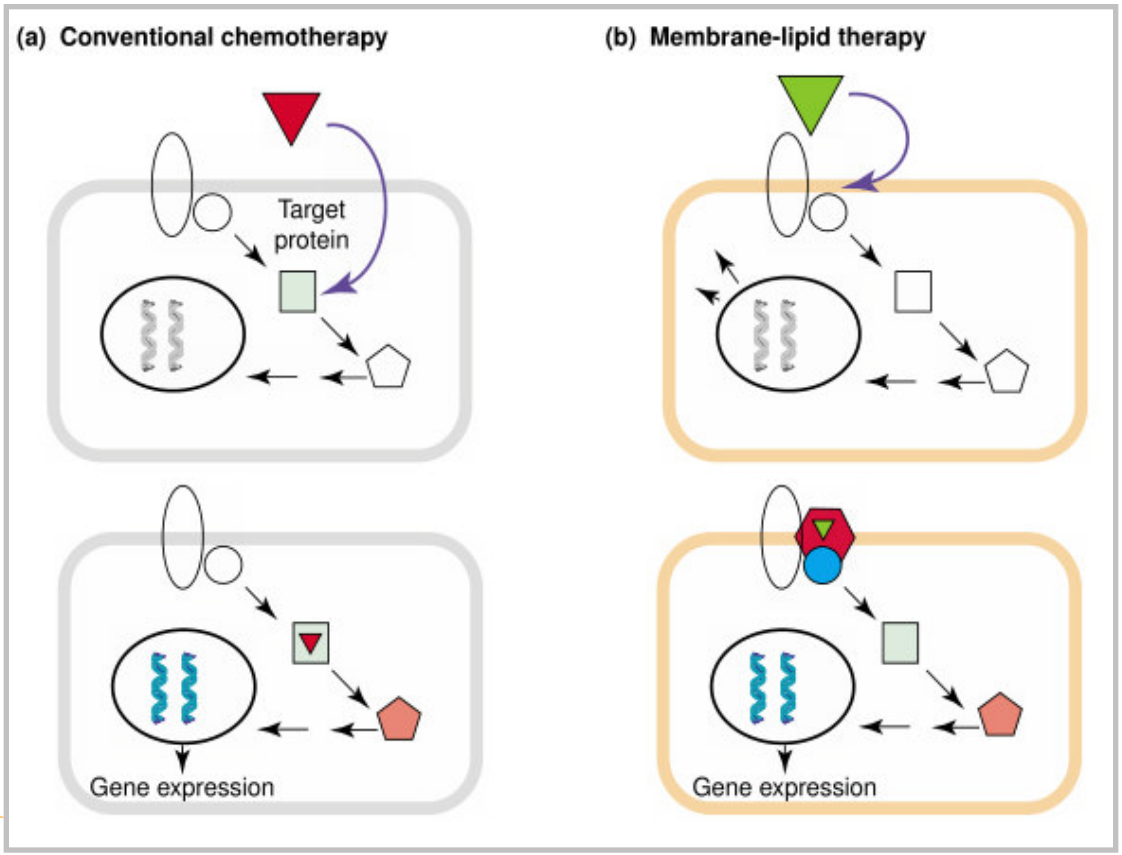
This leads to a **partial or total decrease of the efficacy** of the drug.



Membrane Lipid Therapy: Concept

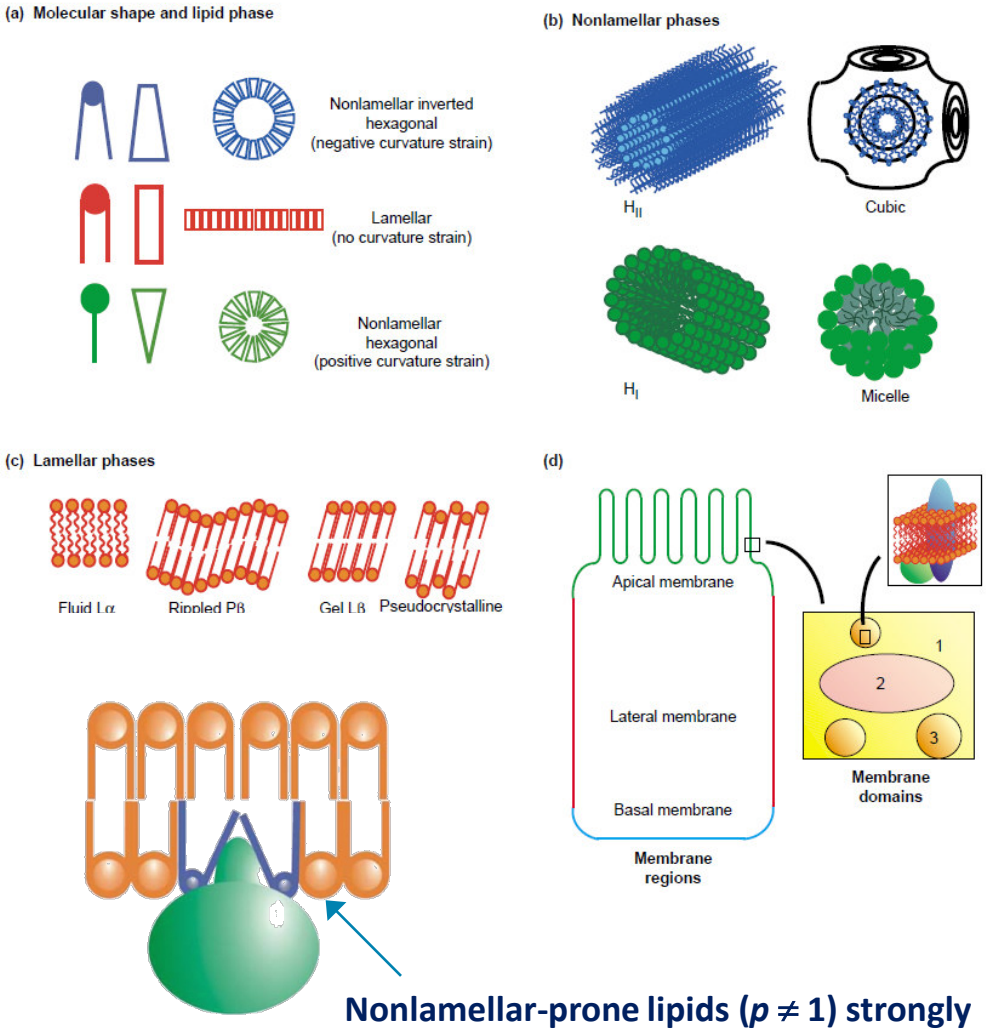
- In **membrane-lipid therapy**, a drug modifies the composition of the cell membrane, modifying the activity of **multiple membrane proteins**.
- Changes in the permeability of the membrane have little effect on the efficacy.
- Risk of appearance of mutations leading to resistance is lower due to multi-target approach.

It is more difficult for the tumor to become resistant.



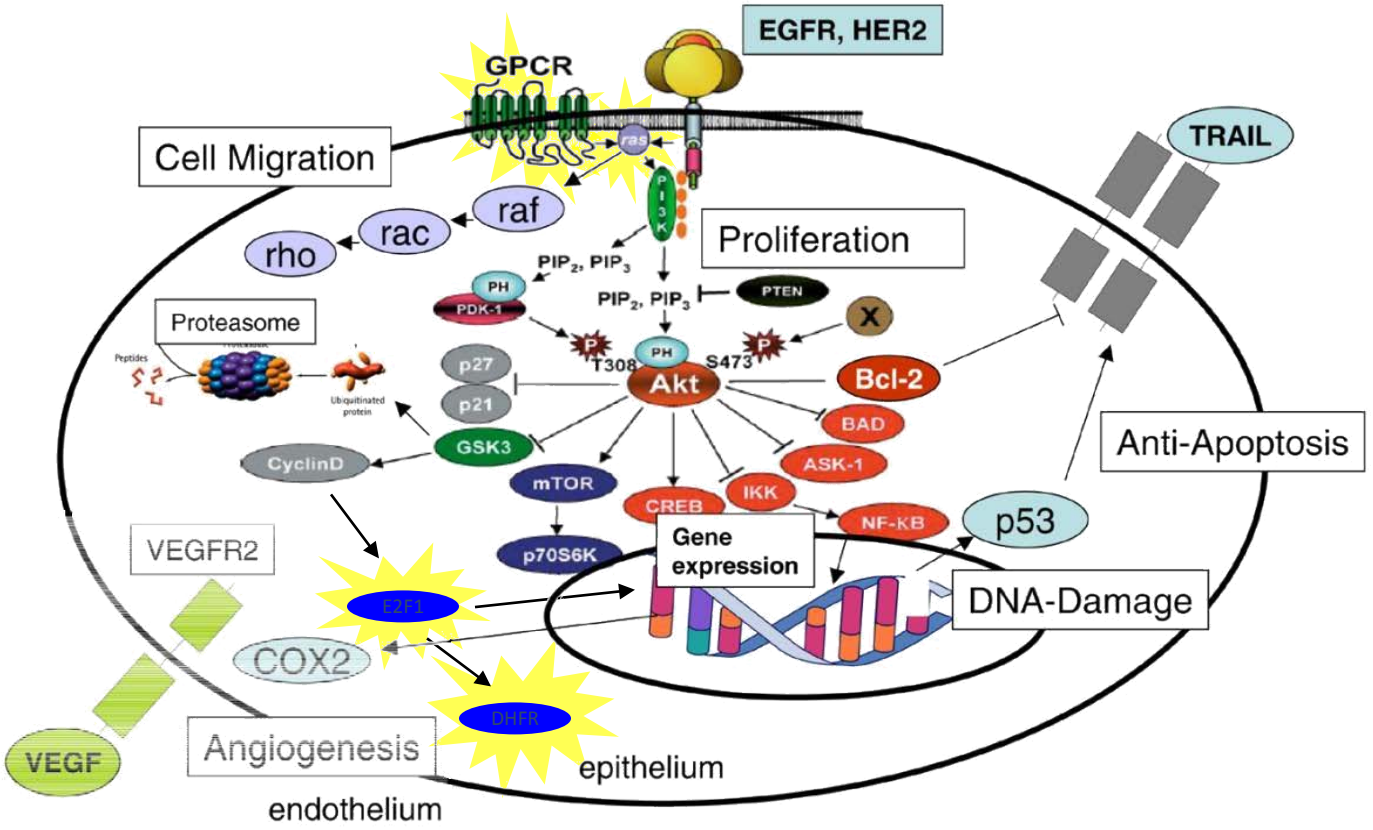
Membrane Lipid Therapy: Concept

- Fluid lamellar phase (Lα or liquid crystalline) is the structure found in most membrane regions and domains.
- Under different conditions, lipids can organize into more-ordered bilayers, such as Lβ (gel), Lc (pseudo-crystalline) or Pβ (rippled) membranes.
- Lε (frustrated) membranes contain high levels of nonlamellar-prone lipids, allowing acyl chains to interact with non-integral proteins.



Nonlamellar-prone lipids ($p \neq 1$) strongly influences protein binding to the cell membrane

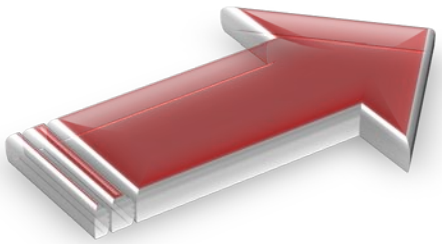
Membrane Lipid Therapy: Mechanism



Membrane Lipid Therapy has been shown to modulate the activity of **G-protein coupled receptors** (*e.g. Ras*) and **Protein Kinase-C**, causing to ***E2F1*** (gene expression) and ***DHFR*** (DNA synthesis) knockdown. This has both anti-proliferative and cell-differentiation effects.

MEMBRANE LIPID THERAPY

- **The drug modifies the lipid composition of the cell membrane, modifying the activity of multiple membrane proteins**
- **Multitarget strategy: alters the signaling of several targets.**
- **Low risk of appearance of mutations causing resistance to the treatment**



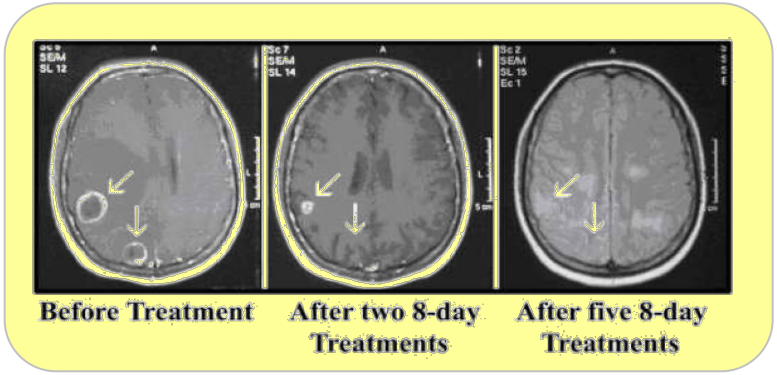
HIGH EFFICACY (animal models)

VERY LOW TOXICITY

MEMBRANE LIPID THERAPY:

FIRST GENERATION COMPOUND*: PROOF OF CONCEPT OF IN HUMANS

(compassionate use in terminal patients)



Patient	Type of cancer	Toxicity	Effect
1	Lung	No	Yes
2	Lung	No	Yes
3	Breast	No	No
4	Lung	No	Yes
5	Brain	No	Yes
6	Brain	No	Yes
7	Neck	No	Yes

- **No toxic effects observed in humans (N=7)**
- **Efficacy in lung tumors and glioma (N=5)**

*** The first generation compound is in pre-clinical development. AB-Therapeutics does not have rights this compound**

MEMBRANE LIPID THERAPY:

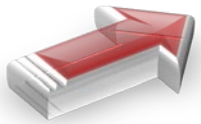
SECOND GENERATION COMPOUNDS - LICENSED & DEVELOPED BY AB-THERAPEUTICS

CANDIDATE SELECTION

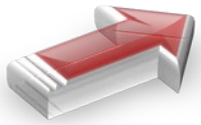
ABTL0812
ABTL0813
ABTL0823
ABTL1014
ABTL1015
ABTL1216

ABTL0812
ABTL0813
ABTL1014

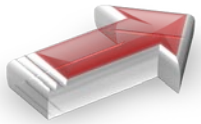
ABTL0812
ABTL1014



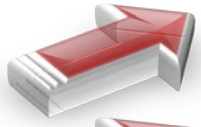
Higher activity on lung cancer and pancreatic cancer in vitro (cell culture)



Selective induction of apoptosis in tumor cells (vs. fibroblasts)



High efficacy in human cancer models in immunosupressed mice (nu-nu & SCID)



Low toxicity

Oral & parenteral

CANDIDATE SELECTION

Antiproliferative activity in vitro*

Compound	Pancreatic	Lung	Glioma	Breast
1st Generation	+	+/++	++	+
Compound A	+++	+++	+++	++
Compound B	+++	++++	+++	++
Compound C	++	++	++	++
Compound D	++++	++++	++++	++
Compound E	++	++	+	++
Compound F	++++	++++	+++	+++

*Additional antiploiferative activity shown in lymphoma, hepatoma and melanoma

Induction of apoptosis (programmed cell death) in vitro

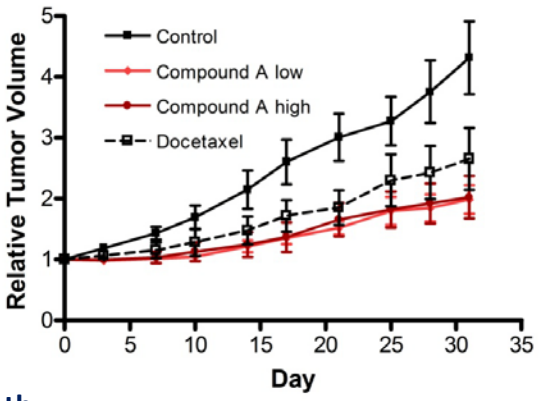
Compound	Pancreatic	Lung	Glioma	Fibroblasts
1st Generation	+	-	++	-
Compound A	++++	++	+++	-
Compound B	++	++	++	+
Compound D	+++	++	++++	-
Compound F	+	+	+++	++

CANDIDATE SELECTION

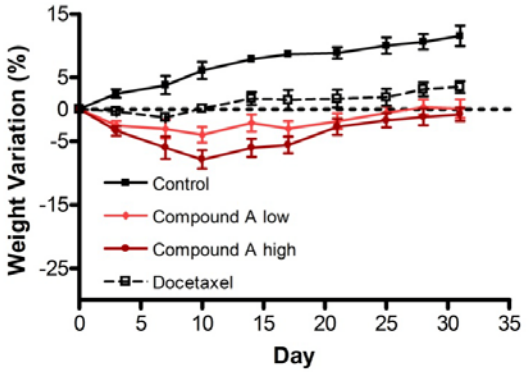
Efficacy experiments in vivo - Lung cancer (NSCLC)

Compound A

Effect of Compound A administered orally on Tumor Growth



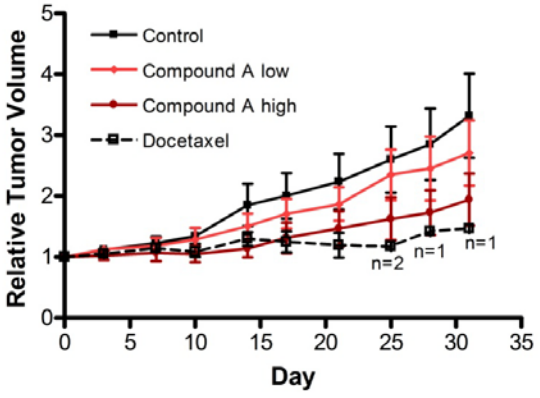
Effect of Compound A administered orally on Body Weight



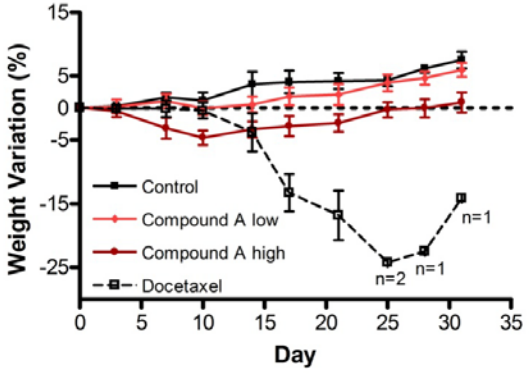
Inhibition of tumor growth

Weight loss

Effect of Compound A administered ip on Tumor Growth



Effect of Compound A administered ip on Body Weight

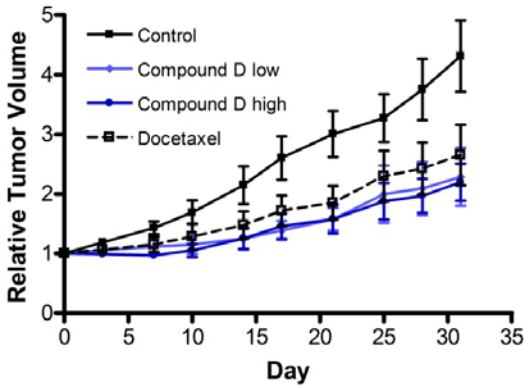


CANDIDATE SELECTION

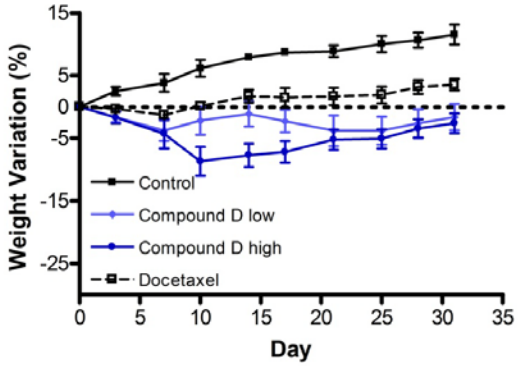
Efficacy experiments in vivo - Lung cancer (NSCLC)

Compound D

Effect of Compound D administered orally on Tumor Growth



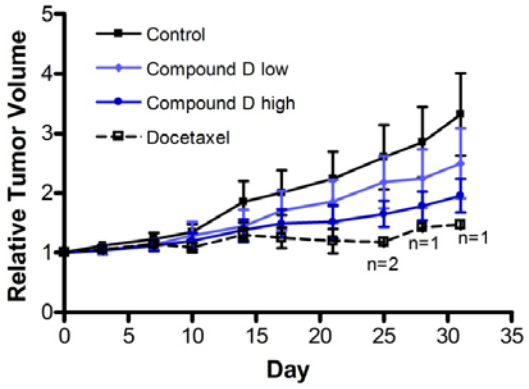
Effect of Compound D administered orally on Body Weight



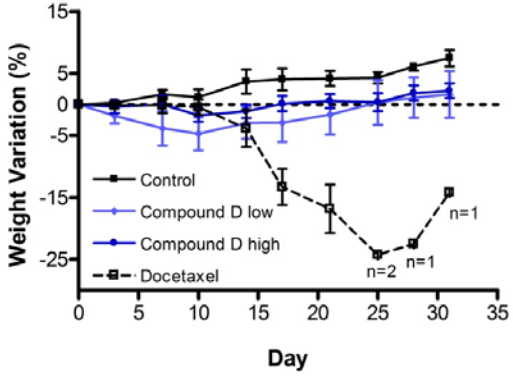
Inhibition of tumor growth

Weight loss

Effect of Compound D administered ip on Tumor Growth



Effect of Compound D administered ip on Body Weight

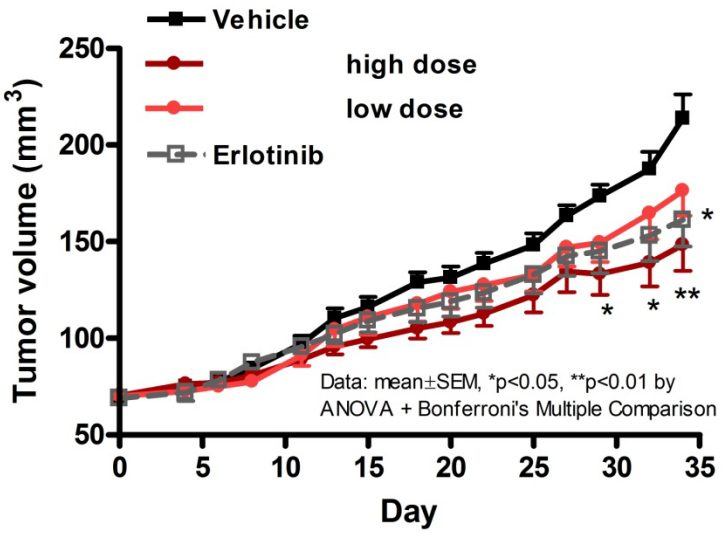


CANDIDATE SELECTION

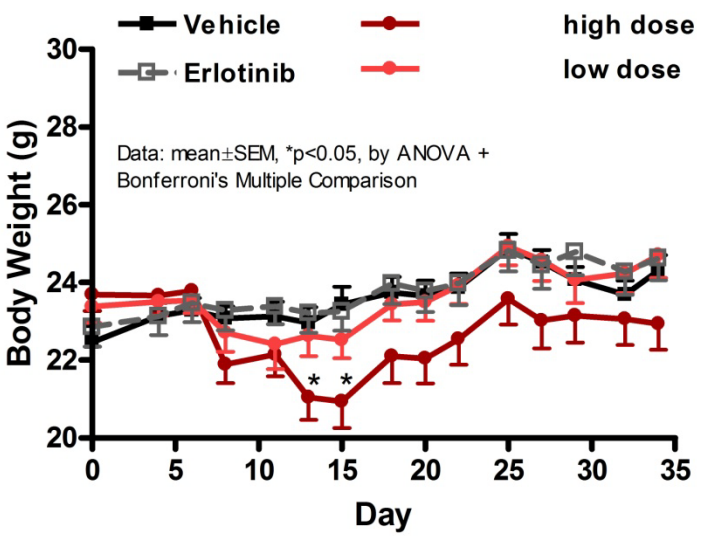
Efficacy experiments in vivo - Lung cancer (NSCLC)

Compound A – vs. erlotinib (Tarceva)

Effect of Compound A administered orally on Tumor Growth

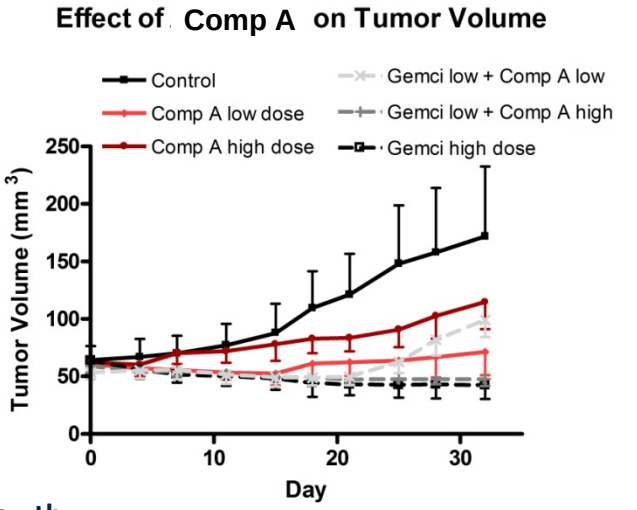


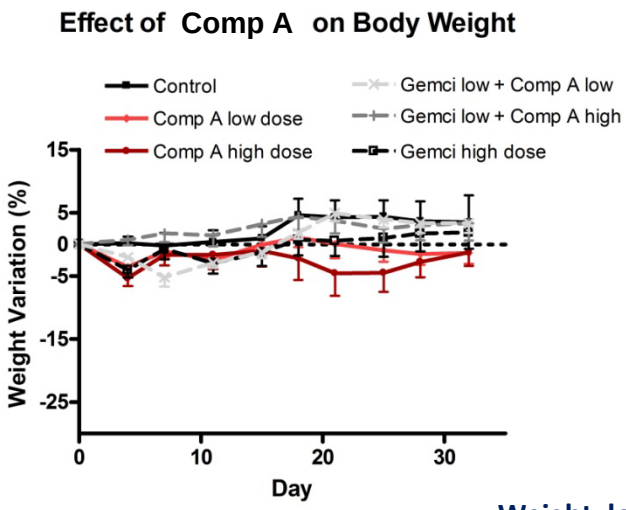
Effect of Compound A administered orally on Body Weight



CANDIDATE SELECTION

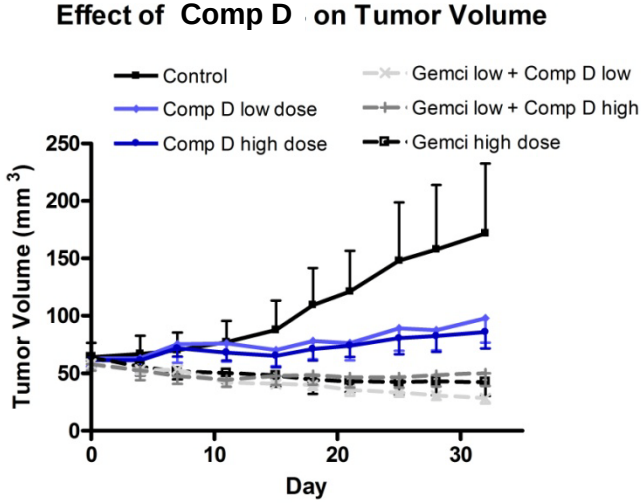
Efficacy experiments in vivo – Pancreatic cancer

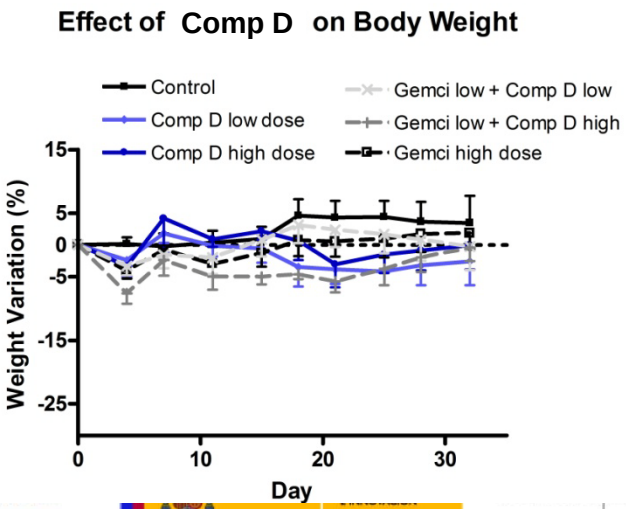




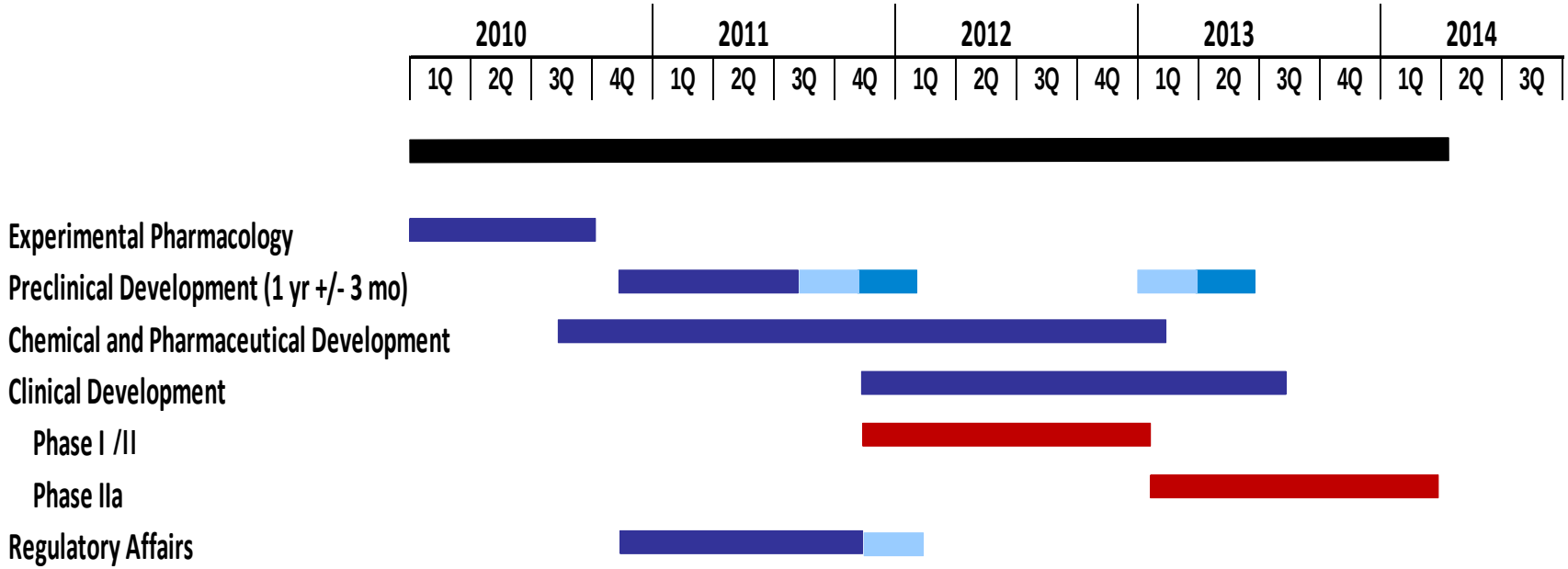
Inhibition of tumor growth
IP administration

Weight loss





DEVELOPMENT PLAN



PRECLINICAL DEVELOPMENT COMPOUND A
Accomplished Tasks

Study	Description	CRO
009/2010	CNS Safety Study: Irwin test Study	Spain
011/2010	Toxicity evaluation of one compound administered by oral route	USA
012/2011	Oral and ip route administration schedules	USA
013/2011	Acute toxicity study in rat, oral route	Spain
014/2011	Pharmacokinetic profile in rat, oral single	France
015/2011	Plasma protein binding in 4sp	UK
016/2011	Metabolic profile in 4 sp	France
Manufacturing	GMP Manufacturing (1 Kg)	Spain

INTELLECTUAL PROPERTY

- Patent application at the Spanish Office of Patents and Trademark.
  - Patent number: P200900725.
  - Title: Use of 2-Hydroxy derivatives of poly-unsaturated fatty acids as medicinal products.
  - Filing date: March 16, 2009.
  - The application includes the protection of use of the compounds in the treatment of cancer.
  - Exclusivity protection until 2029.
- PCT process was initiated in March 2010
  - Patent Number (PCT/ES2010/070153).
  - Patent has already been published (as WO/2010/106211)
- The patent will be extended to the main pharmaceutical markets.

COMPETITION

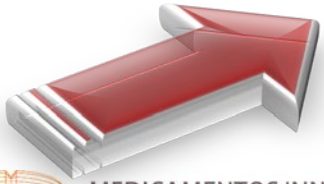
> 300 DRUGS IN DEVELOPMENT FOR LUNG CANCER (NSCLC)

Monoclonal Antibodies	**Small Molecules**
Kinase inhibitors	**Vaccines (11 in pII , 5 en pIII)**

Pipeline View for Non-Small-Cell Lung Cancer

CompanyName	Total Trials	PC	I	II	III	M	A	PA	D	F
Eli Lilly & Co	26	0	0	20	6	4	0	1	4	1
F. Hoffmann-La Roche Ltd	21	0	0	14	7	2	1	0	7	0
Genentech, Inc.	20	0	1	13	6	2	1	0	3	0
Bristol-Myers Squibb Company	11	0	1	8	2	1	0	1	7	0
Pfizer Inc	9	0	0	4	5	0	0	0	9	1
Sanofi-aventis	9	0	0	6	3	2	0	0	1	0
ImClone Systems	7	0	0	5	2	0	0	1	1	0
Boehringer Ingelheim GmbH	6	0	2	1	3	0	0	0	0	0
Merck & Co Inc	6	0	1	5	0	0	0	0	3	0
Amgen Inc	5	0	0	4	1	0	0	0	1	0
AstraZeneca Plc	5	0	0	4	1	1	0	0	8	0
Bayer Ag	5	0	0	3	2	0	0	0	1	1
Fox Chase Cancer Center	5	0	1	4	0	0	0	0	0	0
GlaxoSmithKline plc	5	0	1	2	2	0	0	0	5	0
Novartis AG	5	0	0	3	2	0	0	0	2	0
OSI Pharmaceuticals Inc	5	0	0	2	3	1	1	0	0	1
Agennix AG	4	0	0	2	2	0	0	0	1	0
Onyx Pharmaceuticals Inc	4	0	0	2	2	0	0	0	0	1
PharmaMar (Irvalec, Elipsidin)	1	0	0	1	0	0	0	0	1	0
Pique Therapeutics, Inc.	1	0	0	1	0	0	0	0	0	0
University of Chicago	1	0	0	1	0	0	0	0	0	0
University of Pittsburgh	1	0	0	1	0	0	0	0	0	0
...En total 141 empresas están desarrollando nuevos fármacos NSCLC										
TOTAL DEL PIPELINE	**336**	**9**	**32**	**225**	**70**	**58**	**3**	**7**	**153**	**11**

WE HAVE A DIFFERENTIATED THERAPEUTIC APPROACH: NEW SOLUTION



MEMBRANE LIPID THERAPY

RISK AND MITIGATING FACTORS

- Risk of failure in preclinical and clinical development.
- Failure in intellectual property protection.
- Drug Development in cancer indications and other life threatening conditions.
- Accelerated approval at Phase II reduces financial risk.
- Orphan drug status for some indications.
- Costs of marketing are controllable (limited market, little DTC).
- Market pressure on drug costs may reduce incentive for investments in this space.

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   d) **Current status of development**
   e) **IPR protection**
   f) **Pitfalls & Risks to be considered**
3. **Availability for cooperation**

Availability for cooperation

- AB-Therapeutics intends to develop its drug candidates until clinical proof of concept, to out-license them to pharmaceutical companies at this point (late 2013/early 2014).
- The company is also willing to reach research agreements with pharma companies including a first option rights to license the compounds after clinical POC

Programa Cooperación Farma-Biotech

Jornada IIb: **Oncología**

Novel derivatives of polyunsaturated fatty acids for the treatment of lung and pancreatic cancer

AB Therapeutics
real medicine for real life

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