VII Encuentro de Cooperación Farma-Biotech

Área Terapéutica de Oncología

ENAX003: Preclinical development of an oral wide spectrum antitumoral drug for pancreatic cancer

ARGON PHARMA

Bilbao, 21 de septiembre de 2012

biospain 2012

GOBIERNO DE ESPAÑA | MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD

MEDICAMENTOS INNOVADORES
Plataforma Tecnológica Española

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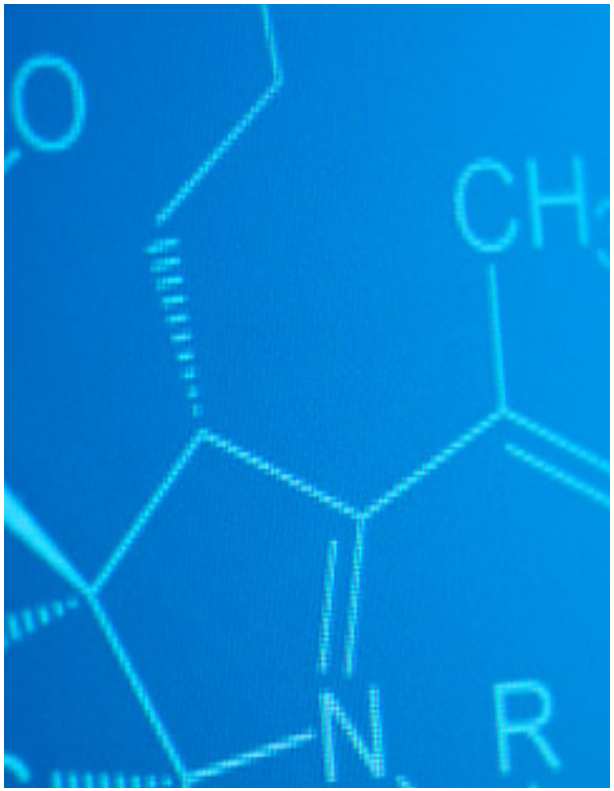
1. The Company - Origin

ARGON-PHARMA is a biotech company established at the Barcelona Science Park with the mission to develop new therapeutics and diagnostic tools based on drug discovery and drug delivery systems to combat cancer. Our vision is to become a global biotech reference by offering innovative solutions and profitable drugs to big pharmaceutical companies. Argon-Pharma supports the creativity of its committed human team to offer unique products to solve uncovered medical needs in the oncology field and with the same driving force to improve the quality of life of people.



1. The Company - HHRR

Advisrory board

Simo Schwartz — Director of CIBBIM Nanomedicine
Hospital Vall d' Hebron (Barcelona)
Deputy Director and transfer technology chief
CIBER BBN (Zaragoza)

Fernando Albericio — Group leader of combinatorial chemistry for the discovery of new compounds. **IBEC (Barcelona)**

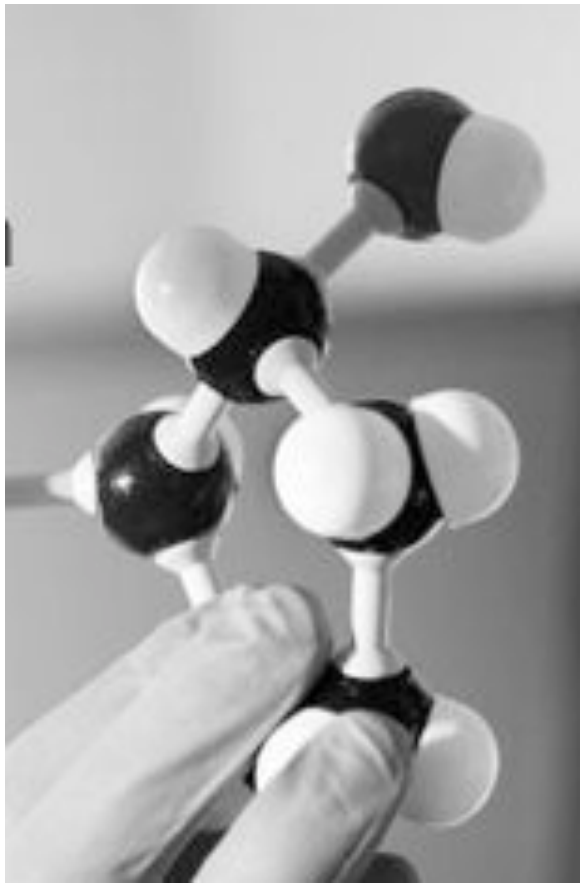
Ramon Mangues — Group leader of of Oncogenesis and Antitmoral lab.
Research Center Hospital Sant Pau (Barcelona)

Mª Jesús Vicent — Group leader of Polymer Therapeutics lab.
Centro de Investigación Principe Felipe (Valencia)

STAFF Experience

Ramon Roca	CEO (oncology (5 y) drug discovery (7 y) Project Management (4 y))
Oscar Peña	CSO (polymer therapeutics (5 y) Drug Discovery (1 y))
Nuria Bayó	R&D Scientist (Synthetic chemistry (5 y))

1. The Company - Strategy



ARGON PHARMA selects its research projects based on the potential to generate innovative solutions to bring real benefits to patients.

Two main strategic lines are covered by ARGON-PHARMA:

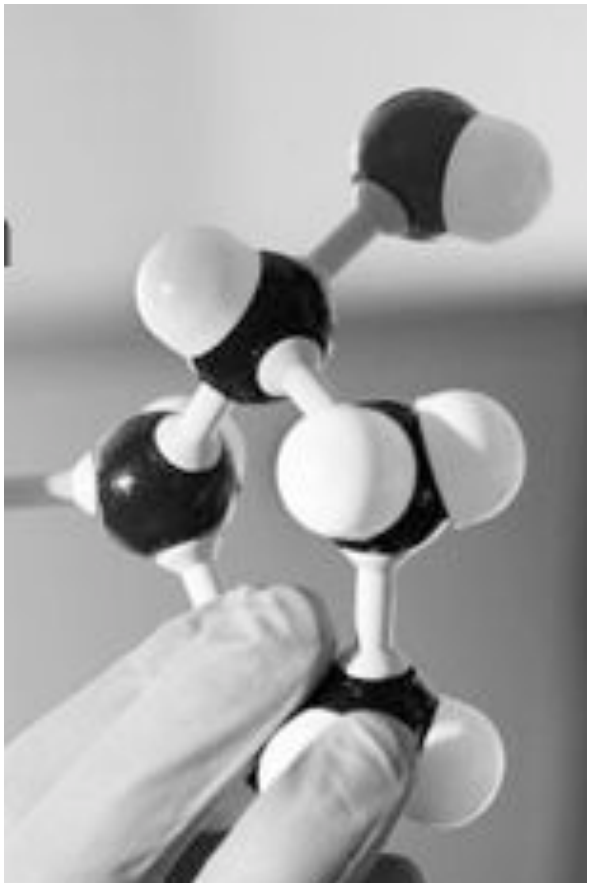
1.- Drug Discovery of antitumoral compounds.

2.- Biodegradable Polymers for several applications.

DEVELOPMENT OF ANTITUMORAL COMPOUNDS

.- Oral administration
.- Non Genotoxic profile
.- Antitumoral inhibition of wide spectrum.
.- Unique mechanism of action.
.- Addressed to indications of unmet medical needs

1. The Company - Technology



Development of antitumoral drugs.

ARGON PHARMA is currently developing new antitumor oral drugs, capable of inhibiting a mechanism of action of focal adhesions that is associated with carcinogenic processes for a variety of oncology indications. The inhibition of this promising mechanism induces apoptosis and causes irreversible cell death of tumor cells.

1. The Company – Business Development

BUSINESS DEVELOPMENT FOR ENAX003 CO-DEVELOPMENT
(Confidential – In process of assessment of NDA signature)

1 Spanish Pharma company has shown interest for the near future
1 Spanish Pharma company is assessing our project
1 International Pharma company is in the process of NDA signature
2 International Pharma companies will be contacted shortly

PARTNERS FOR ANTITUMORAL DRUG DISCOVERY PROJECTS

2. The Product - Target Indications

PANCREATIC CANCER as a main indication

1.- Today remains undetectable in the early stages, due to widespread non-specific symptoms.

2.- Has a poor prognosis, late diagnosis and poor survival of the affected.

3.- The prognosis is terminal, very few patients survive and complete remission is very rare.

4.- This disease remains a main unmet need because of the existing solutions are not a cure.

5.- Gold standard is “Gemcitabine-Gemzar” that is not a cure give serious side effects and toxicities.

6.- The disappointing results in recent years by competitors show that this disease is still a niche not occupied and in the absence of appropriate therapy becomes an unmet need.

2. The Product - Target Indications

The market for pancreatic Cancer

1.- Pancreatic cancer in one of the seven major markets and will continue in this position until 2016.

2.- Currently is a priority for the American and Japanese market in which it has almost become an epidemic.

3.- Being an unmet need, makes this market still a growing business opportunity.

				Forecast epidemiology				
Country	Prev. (000s)	Prev (%)	Share (%)	2012	2013	2014	2015	2016
EU5	9.80	0.01	29.77	19.82	19.85	19.91	19.97	20.02
US	23.12	0.01	34.51	23.32	23.53	23.59	23.66	23.73
Japan	23.73	0.02	35.72	23.74	23.75	23.82	23.89	23.96
Total	66.64	0.01	100.00	66.88	67.13	67.33	67.52	67.72

The Market for Gold Standard Gemzar Eli Lilly,
Second line treatment (Gemzar Eli Lilly and Tarceba (Erlotinib Roche)) as a main competitor

1.- Gemzar is approbed for many other indications in the clinic.

2.- Our candidate displays sinergy with Gemzar, opening the door to be used in combination for other indications.

Product(Company)	Growth 2009–10 (%)	Market share 2010 (%)	CAGR 2006–10 (%)
Gemzar-gemcitabine (Eli Lilly)	-15.7	2.5	-5.0
Tarceva-erlotinib (Roche)	1.6	2.8	13.0

Product (Company)	Sales 2010	Sales 2011	Sales 2012	Sales 2013	Sales 2014	Sales 2015	Sales 2016	CAGR 2010-2016
Gemzar-gemcitabine (Eli Lilly)	4,265	4,043	3,881	3,758	3,624	2,977	2,415	-9.0
Tarceva-erlotinib (Roche)	1,271	1,356	1,451	1,575	1,669	1,780	1,904	7.0

2. The Product - Alternative Indications

Our candidate also displays antitumoral activity in many others cancer cell lines.
This fact makes our candidate a possible wide spectrum drug suitable to be used for other prevalent indications such as Colon Cancer or Prostate Cancer

	Prostate Cancer			Colon Cancer		
Country	Prev. (000s)	Prev (%)	Share (%)	Prev. (000s)	Prev (%)	Share (%)
EU5	492.88	0.16	28.13	583.04	0.19	36.78
US	1194.05	0.38	68.15	629.10	0.21	23.53
Japan	65.25	0.05	3.72	372.99	0.29	23.53
Total	1752.18	0.24	100.00	1585.11	0.21	100.00

For Colon Cancer, the current best sellers are:

ProductName	Companies	2010	2011
Avastin	F. Hoffmann-La Roche Ltd	4.680,23	7.946,07
Avastin	Amgen Inc, Astellas Pharma Inc, A	4.689,53	3.841,05
Xeloda	Amgen Inc, Astellas Pharma Inc, A	1.328,19	2.300,32
Xeloda	F. Hoffmann-La Roche Ltd	1.032,97	2.010,29
Alimta	Eli Lilly & Co	1.666,95	1.869,52
Tarceva	F. Hoffmann-La Roche Ltd	959,81	1.850,40
Eloxatin	Sanofi (formerly Sanofi-aventis)	427,47	978,91
Velcade	Johnson & Johnson	815,13	925,33
Sutent	Amgen Inc, Astellas Pharma Inc, A	804,57	902,68
Sutent	Pfizer Inc	804,57	902,68
Iressa	Amgen Inc, Astellas Pharma Inc, A	296,62	803,06
Iressa	AstraZeneca Plc	296,62	803,06

2. The Product – Origin Scientific -Technologic

Technology transfer agreement (05-2009)

Antitumor 1,2-diphenylpyrrole compounds and their preparation process

Between Argon Pharma and:

- FISP Institut de Investigación del Hospital de Sant Pau de Barcelona
- PCB Parc Científic de Barcelona.

This product is based in the research performed by Dr. Mangues at Hospital of Sant Pau regarding the Focal Adhesion Mechanism (FAM), and the SAR performed between the Parc Cientific of Barcelona and Hospital de Sant Pau in order to optimize an antitumoral hit.

2. The Product – Current Status Development

Early preclinical development – Efficacy in vitro

It displays antitumoral activity in 18 different cancer cell lines from 6 different oncologic indicagtions

Pancreatic cancer cell lines show also antitumoral activity even in cell lines displaying resistance to Gemzar (gold standard for the indication)

PK

Single dose PK show a

Cmax = 40 uM

Repetitive dose PK show a

Cmax = 176 uM

Efficacy in vivo

Efficacy study in vivo in PANC-1 model shows:

Efficacy of our candidate
Sinergy with the gold standard

Efficacy study in vivo in NP-9 model shows:

Efficacy of our candidate at low concentrations
Sinergy with the gold standard at low concentrations

2. The Product – Next Steps

Regulatory preclinical development and First in man

Tareas y actividades	2012						2013												2014												2015					
	Jul.	Ago.	Sep.	Oct.	Nov.	Dic.	Ene.	Feb.	Mar.	Abr.	May.	Jun.	Jul.	Ago.	Sep.	Oct.	Nov.	Dic.	Ene.	Feb.	Mar.	Abr.	May.	Jun.	Jul.	Ago.	Sep.	Oct.	Nov.	Dic.	Ene.	Feb.	Mar.	Abr.	May.	Jun.
1. Escalado																																				
1.1. Síntesis																																				
1.2. Analisis																																				
1.3. Impurezas																																				
1. Validación de métodos																																				
2.1. Metodo																																				
2.2. Análisis de formulaciones																																				
2.3. Validación m.bioanalíticos																																				
3. Preclínica																																				
3.1. DRF																																				
3.2. MTD																																				
3.3. 4 week rat																																				
3.4. 4 week dog																																				
4. First in man																																				
4.1. Plan																																				
4.2. Document.																																				
4.3. Hospitales y reclutamiento																																				
4.4. Gestión producto																																				
4.5. Monitoriza.																																				
4.6 Gestión info.																																				
4.7 Estadistica Informe final																																				

2. The Product – Differentiation vs marketed drugs

GEMZAR (Eli Lilly) – first line treatment

.- IV hospitalary administration
.- Half life 94' (Dosing, IV 1000 mg/m2 once a week)
.- rapidly metabolized
.- Toxic profile, mutagenic, strong secondary effects
(Fatigue, Nausea, Vomiting, skin rash, Diarrhea, hair loss, difficult sleeping, shortness of breath…)
.- Non specific mechanism.
.- Pyrimidin antagonist.
Interfering with DNA synthesis.
.- Other marketed interfere DNA synthesis. (5-Fu)
.- Unspecific drug prescribed for several indications
pancreatic, bladder, brease and non-small cell lung cancer

Survival times were:
5.4 months on average, with Gemzar
4.4 months with 5-fluoracil

ENAX003

.- Oral administration
.- Half life 1 week (Backup half life of 93')
.- Slow metabolism (Backup has fast metabolism)
.- So far no toxicity has been detected. Is unexpected.

.- Specific inhibition mechanism of tumors.
.- No Target has been identified yet.
Inhibitor of Focal Adhesion Mechanism.
.- No current marketed drugs inhibit this mechanism
.- Specific of FAM, displays in vivo efficacy for pancreatic cancer and other 8 cancer indications.

2. The Product – Differentiation vs marketed drugs

ERLOTINIB (Roche) - second line treatment
In combination with Gemzar

.- IV administration for Gemzar and oral for Erlotinib
.- Half life 36,2 h (Daily dose of 150 mg)
.- rapidly metabolized
.- Toxic profile, mutagenic, strong secondary effects
Rash, diarrhea, weight loss, nausea, fatigue, mouth sores, dry skin, itchin, cough.
.- Non specific mechanism.
.- EGFR inhibitor,
Inhibits tumor growth and matastatic progression
.- Other marketed interfere DNA synthesis.
.- Drug combination used for several indications
pancreatic, advanced prostate and non-small cell lung cancer

ENAX003

.- Oral administration
.- Half life 1 week (Backup half life of 93')
.- Slow metabolism (Backup has fast metabolism)
.- So far no toxicity has been detected. Is unexpected.

.- Specific inhibition of focal adhesion mechanism.
.- No Target has been identified yet.
Induces apoptosis in tumoral cells.
.- No current marketed drugs inhibit this mechanism
.- Specific of FAM, displays in vivo efficacy for pancreatic cancer and other 8 cancer indications.

Patients lived for an average of:

12.1 weeks without their disease getting worse taking tarceva.
11.3 weeks in those taking placebo.

Survival times were:
11.9 months on average, with Tarceva
9.6 months with placebo

2. The Product – Differentiation vs drugs in development

No current drugs are under development for focal adhesion mechanism.

The closest targets could be FAK inhibitors.

1 compound for GSK is in Phase 1

8 compounds in preclinical for several indications

Current clinical assays in progress for pancreatic cancer

	Small	Large	other	Total
Approved	3	1		4
Fase III	12	13	6	31
Fase II	25	26	27	78
Fase I	1	6	4	11
Preclínical	8	9	16	33

The disappointing results in recent years by the results of all competitors show that this disease is still a niche not occupied and in the absence of appropriate therapy becomes an unmet need.

2. The Product – IPR Protection

IPR WO2011/012660
Antitumor 1,2-diphenylpyrrole compounds and their preparation process.

03-2009 Application
02-2011 PCT
04-2012 National phases: EuroPCT, USA, Canada, India y Japón.

2. The Product – Pitfalls & Risks to be considered

1.- HALF LiFE 1 week

Currently we are in early preclinical development of a backup with a shortest half life to determine which Compound has a better profile.

No main toxicities have been detected after repetitive hight doses g during 3 weeks.

2.- Scale up.

Yield remains still low and route optimization are under way.

3. Partnering Opportunities

ARGON PHARMA is actively seeking pharma companies interested to reach agreements to develop our drugs.

1.- Reaching agreements to co-develop our compounds for pancreatic cancer, sharing costs during the preclinical and clinical development.
Also interested in colon cancer, prostate cancer and breast cancer.

2.- Reaching licence agreements to develop our compounds for other indications of interest.

3.- Reaching agreements for the future exploitation of the products in different world markets.