





# For ferrer Advanced Biotherapeutics

### The Collaborative Research Division of

**F**ferrer



Barcelona, July 1st 2015

Spanish private pharmaceutical company Vertical integration from R&D to distribution International profile

### **Business areas**

Pharmaceuticals OTCs & personal health Molecular diagnostics Immunology & in vitro diagnostics Fine chemicals Food & feed additives

### **Worldwide operations**

Presence in 93 countries

### **25 international affiliates**

Central & Southern Europe Central & South America



### **Ferrer: The Innovation Factory G Ferrer** Corporate Product Clinical **G** ferrer Development Fight Advanced Biotherapeutics G ferrer HealthTech **ferrer** Venter Gendiag ORYZON S spherium Genmedico Therapeutics

# Explaining... FAB





### 99,99997 % of the world's population doesn't work at Ferrer



## An Exercise in Humility

### ... a smart exercise





#### **Ferrer Advanced Biotherapeutics**

Paul Isherwood

GlaxoSmithKline

# **R&D Evolving Paradigm**



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## Cooperation





### **Defining Our Strategic Vectors**







# **Connecting celestial bodies and drugs...**



### **Discovery & Platforms**





### **Discovery & Platforms**





### Technological **platforms**: their pivotal importance







## Platform **proliferation...**





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### **Defining Our Strategic Vectors**





# The **innovation** factory: a classical view





# The innovation factory: time to change





### **R&D** sustainability: Challenges



Modified from S.M. Paul et al. (2010)



### **Defining Our Strategic Vectors**





# For ferrer Advanced Biotherapeutics

#### The Aim & The Team





### **Ferrer Advanced Biotherapeutics**



#### Projects yielding high added value products



- Identifying, incorporating and (co-)managing projects originated outside the company.
- Concentrating most high-risk projects of the company.
- Focused on expanding Collaborative Research.



# FAB, a well-supported lean organization





## **BD&L and FAB**

A dedicated professional team with

- Broad experience in biomedical research.
- A previous successful acummulated track record: 10 new medicines registered and launched in EU, US and Japan.
- Business oriented attitude.
- An Extensive network of European and American stakeholders: Key Opinion Leaders, CROs, Regulatory Experts, Patient Associations...



# **Our role in a fragmented value-chain**





### **Therapeutic Focus... yes but...**







...and opportunities



# What do we pursue

# rsue

### **Pipeline: an idealized 3D representation**







## Our Projects





# PROGRAMA FARMA-BIOTECH 2011-2014





# **FAB projects**

Project	Code	Originators	1 <sup>st</sup> Indication	2 <sup>nd</sup> Indication	Advanced therapy	Small molec	EpiDx
NeuroSave	FAB-117		Spinal Cord Injury	ТВІ			
cellS4See	FAB-111	Centre for Genomic Regulation	Retinitis Pigmentosa	AMD			
EPICUP	FAB-115	INSTITUT DINVESTIGACIÓ BUGELO	Cancer of Unknown Primary	Poorly- differentiated primary			
Limbus	FAB-112	Institute for bioonging of Catalonia	Limbal deficiency (LSCD)	Corneal damage			
Stratum	FAB-116		Psoriasis	Other dermal AAID			
Lympho	FAB-114	vivia BIOTECH	NHL	Other lymphomas			
EPIbreast	FAB-118	INSTITUT DINVESTIGACIÓ BIOMÉDICA DE BELLVITGE	Breast Cancer				



### **Oncology @ Ferrer** New Frontiers in Tolerability

Drug Repositioning: lower risk & faster dev.



# Lympho Project (FAB-114)

- 3 months for internal valorization and info-discussion
- 4 months for deal structure (consortium) and signatures
- 2 months for detailed development plan
- 2 months for contracting (out-sourcing)
  - 5 companies
  - 3 continents





- The problem
- Our approach



### FAB-114

	<ul> <li>Non-Hodgkin lymphoma (NHL)</li> </ul>					
Hematologic	127 000 new cases /vear across the 7MM the largest HM market					
malignances (HM)	<ul> <li>- Iz7.000 new cases/year across the 7000, the largest HM market.</li> <li>- Prevalence increases faster than other cancer types.</li> </ul>					
therapies are <b>poorly</b>	<ul> <li>Indolent lymphoma remains incurable with standard therapy and eventually becomes refractory to rituximab, often within 3 years.</li> </ul>					
tolerated and yield a	- Combo chemotherapy is poorly tolerated but also the 'on top'					
high % of refractory	rituximab can produce tumor lysis syndrome, severe skin and mouth reactions, progressive multifocal leukoencephalopathy and reactivation of hepatitis B virus infection.					
patients						
	Chronic Lymphocytic Leukemia (CLL)					
	- Most frequent leukemia: <b>31.000 new cases/year</b> in the 7MM.					
	<ul> <li>- 30 % refractory patients due to p53 deletion          poor response , even to ofatumumab.     </li> </ul>					
	<ul> <li>- 50 % refractory patients due to be fragile elder -&gt; lack of tolerability to fludarabine.</li> </ul>					



# Our approach

An <b>old drug</b> orally	• An extensive <b>reprofiling</b> project
used in millions of	- Evaluation in fresh HM patient samples.
high <b>efficacy in B-</b>	- Parallel evaluation in healthy cells.
cell HM by	
parenteral route	<ul> <li>A generic-threat safe position</li> </ul>
	<ul> <li>The drug is only effective by a non-previously developed route.</li> <li>IP protection.</li> <li>No option for generic interference.</li> </ul>





### **Our results**





# Previous results (highlights)

• Excellent *in vitro* efficacy, higher than fludarabine in tumoral human B-cells

• Exciting preliminary in vivo results

• Results based on a non-industrially-developable formulation

• Lack of direct comparison with the new gold standard



## **Results**: Extensive formulation screening

**Discriminating PK and Distribution Properties in Mice (>40** formulations belonging to 6 types)

Due to confidentiality requirements detailed results are not published



### **Results**: Extensive formulation screening

Lymph Node vs Bone Marrow distribution ratio + local tolerability

Due to confidentiality requirements detailed results are not published



### **Eµ-Myc**: a genetic lymphoma model in mice





Eµ-Myc: a genetic lymphoma model in mice

#### **Experimental design**

Group #	Mice	FAB-114 (iv)	Ibrutinib (po)
1	Healthy	Vehicle	Vehicle
2	Еµ-Мус	Vehicle	Vehicle
3	Еµ-Мус	FAB-114	Vehicle
4	Еµ-Мус	Vehicle	Ibrutinib
5	Еµ-Мус	FAB-114	Ibrutinib



### **Eµ-Myc**: a genetic lymphoma model in mice

**Outcome: Overall Survival** 

Due to confidentiality requirements detailed results are not published



### **Eµ-Myc**: a genetic lymphoma model in mice

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### Conclusions

#### An exciting unprecedented profile

- Cancer treatments has been associated to severe adverse events limiting the dose and the duration of treatment.
- FAB-114 is extremely well-tolerated and effective.
- FAB-114 could be the ideal "on-top" medication to add synergic efficacy (different mechanism of action), especially relevant in p-53 and fragile patients, without adding adverse events.

#### Important market expectative

- External experts have evaluated the potential NHL market for FAB-114 in more than 500.000 MUSD.

#### **More opportunities**

- The same succesful reprofiling approach is yielding attractive additional opportunities in other indications.





# Making people better