“Benefits of Pharma-Biotech program for Spanish pharmaceutical industry”

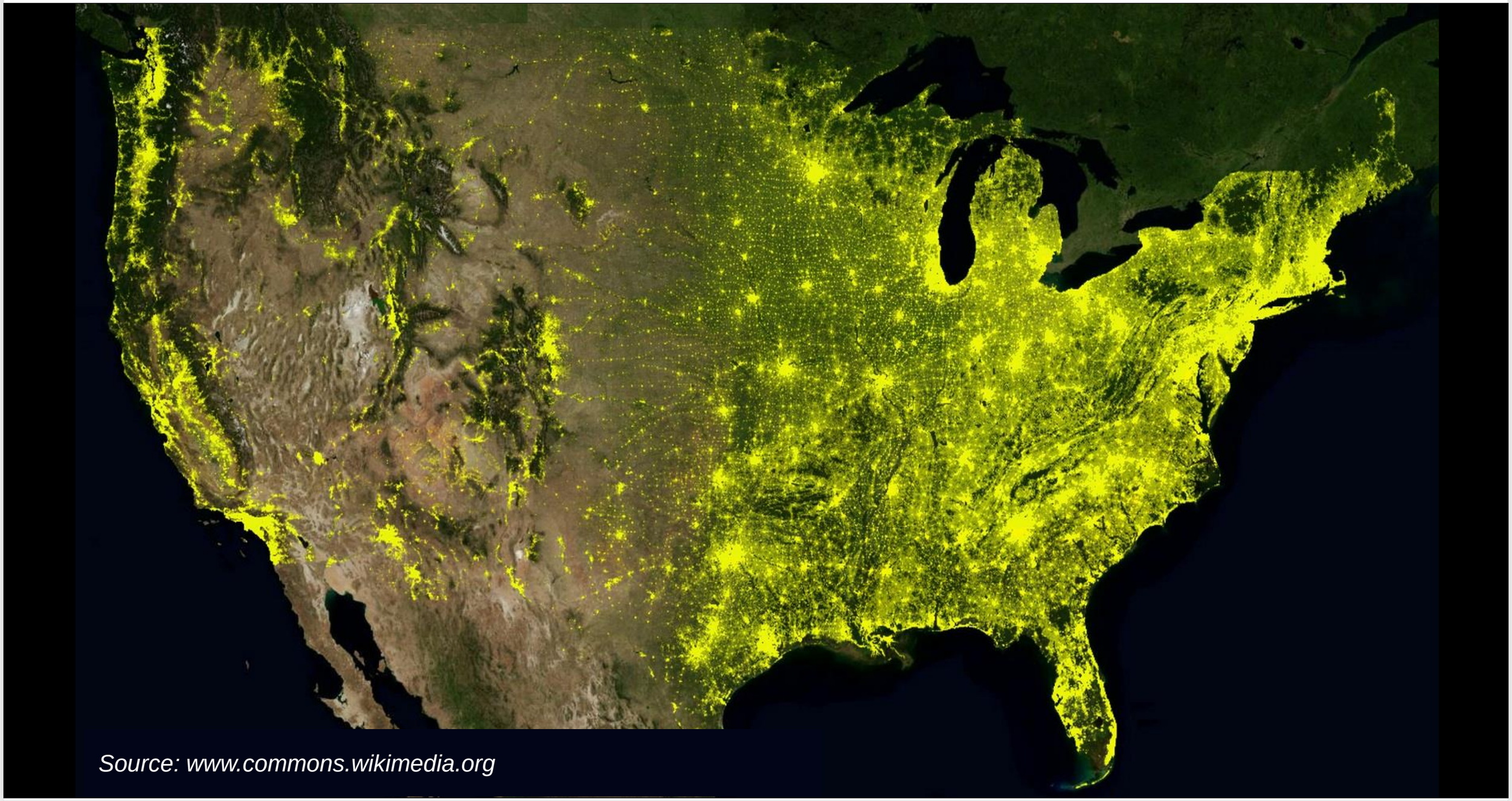
Bilbao, 30 September 2016

Dr. Andrés G. Fernández

Director

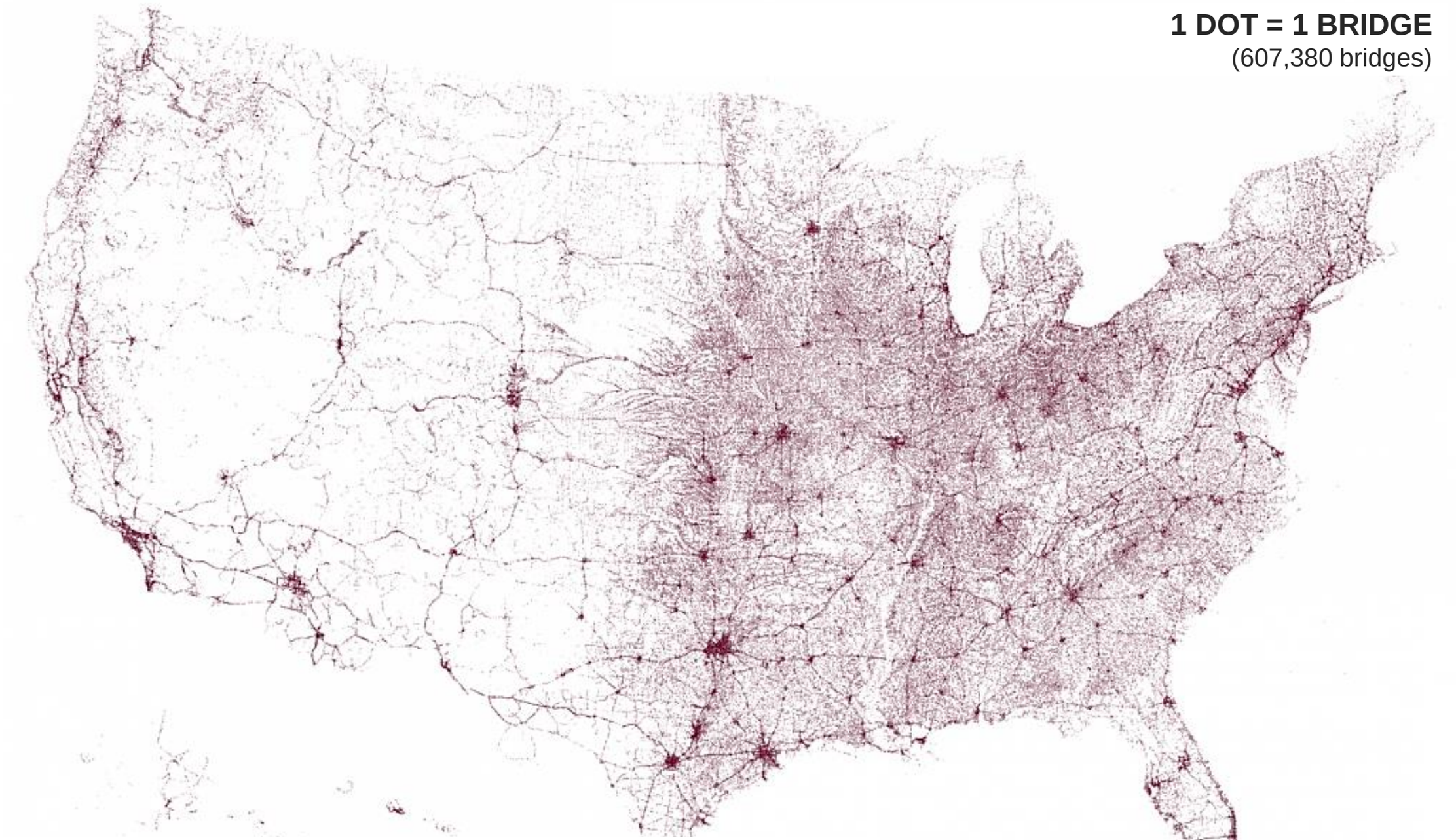
Ferrer Advanced Biotherapeutics

US population distribution



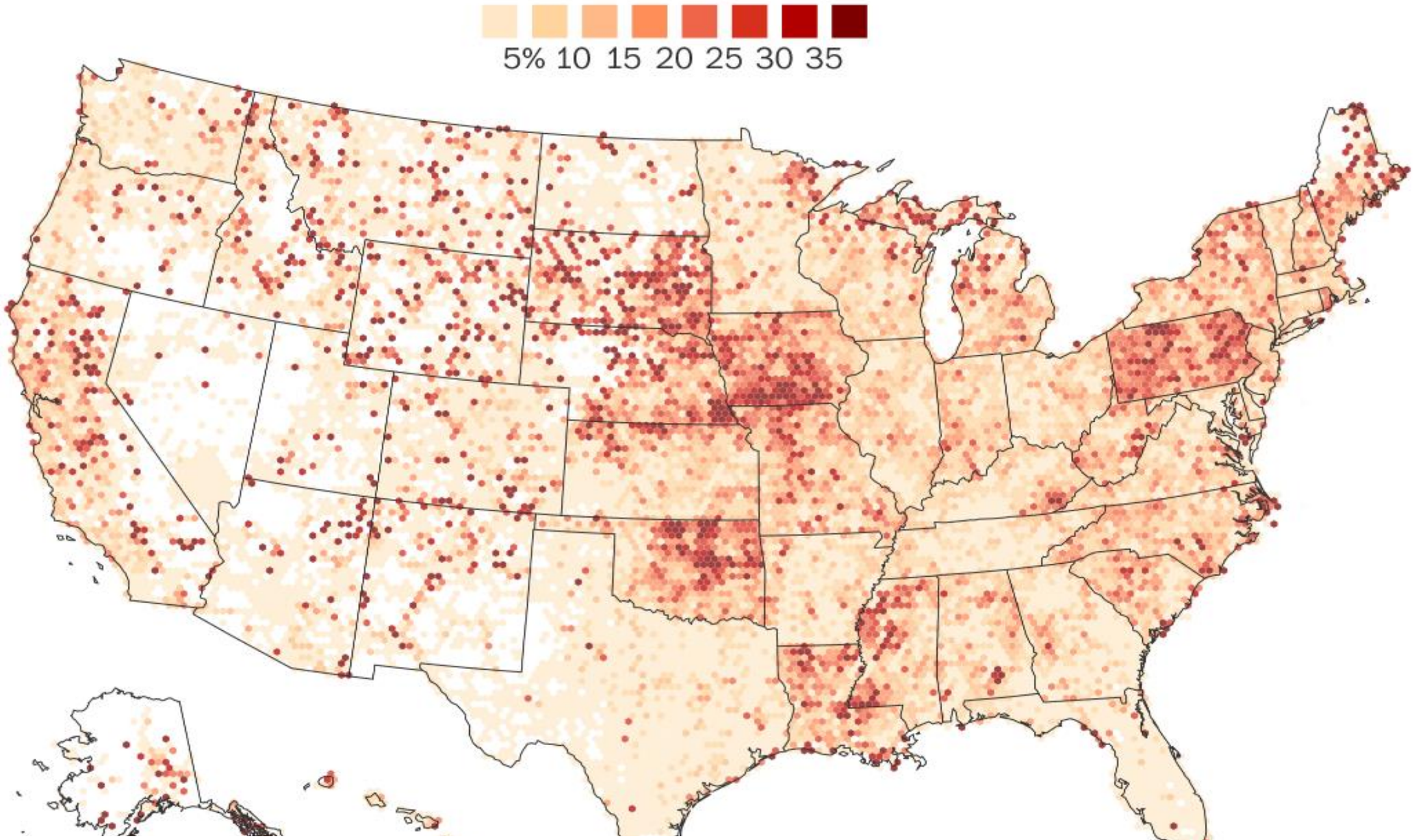
Source: www.commons.wikimedia.org

US bridge distribution



Source: Federal Highway Administration & WashingtonPost.com/wonkblog

US percent of bridges rated “structurally deficient“



Source: www.washingtonpost.com/news/wonk/wp/2015/02/04/mapping-americas-most-dangerous-bridges/

What if 50% of bridges instantly dissapeared?

The impact on GDP would be huge

Bridges = Richness

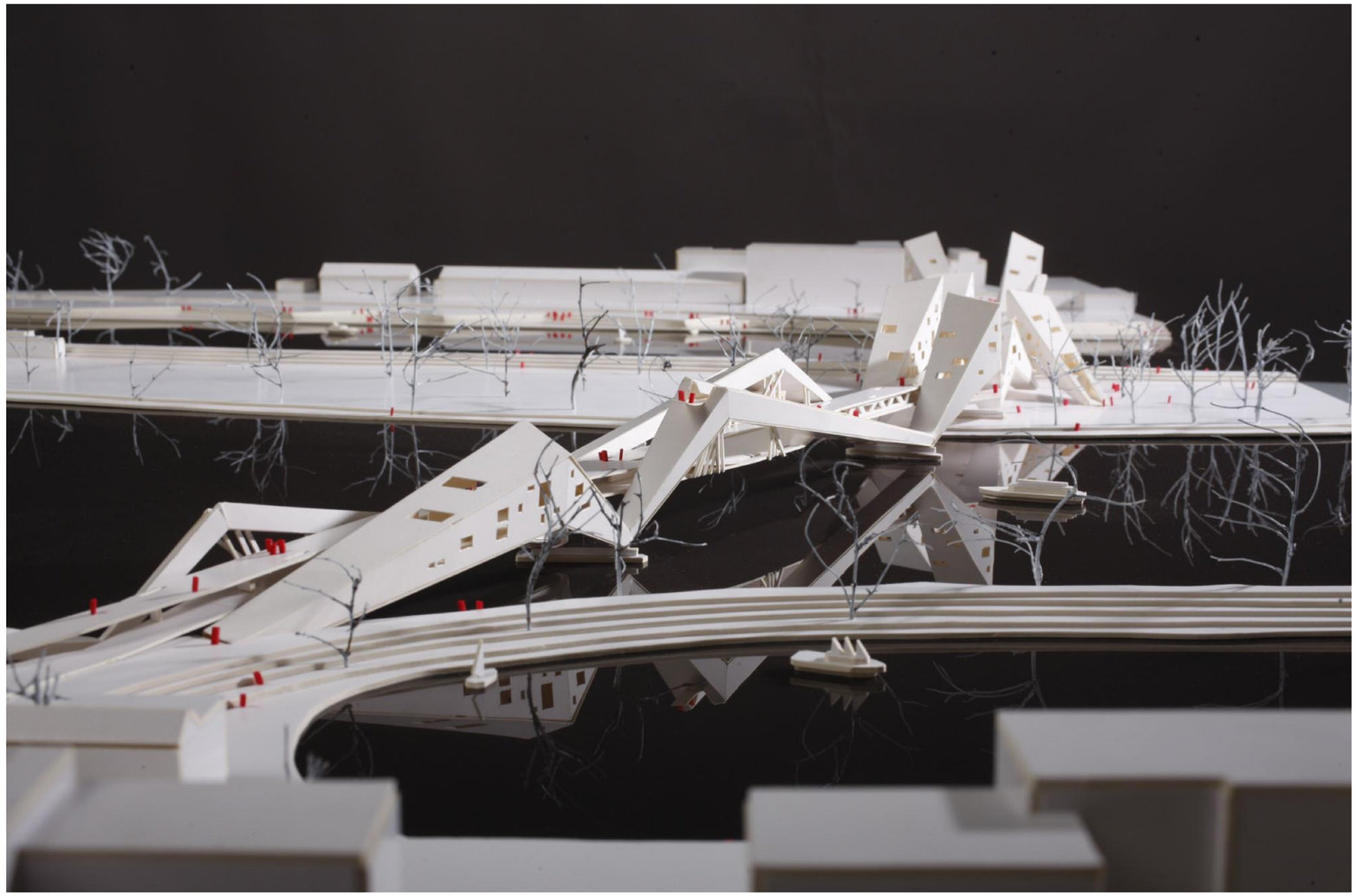
... but not always... results are ok...

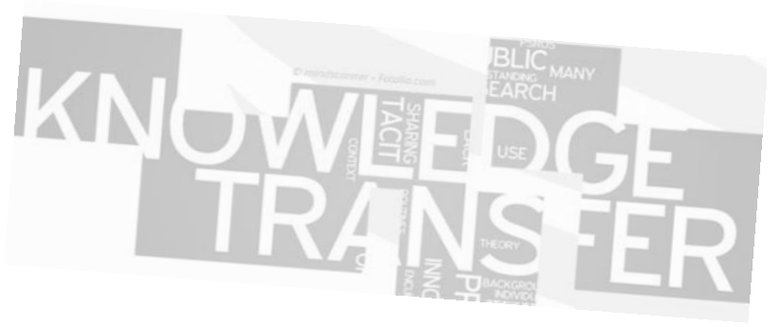
... lavish ceremonies without real content

... lack of simplicity

... not well oriented

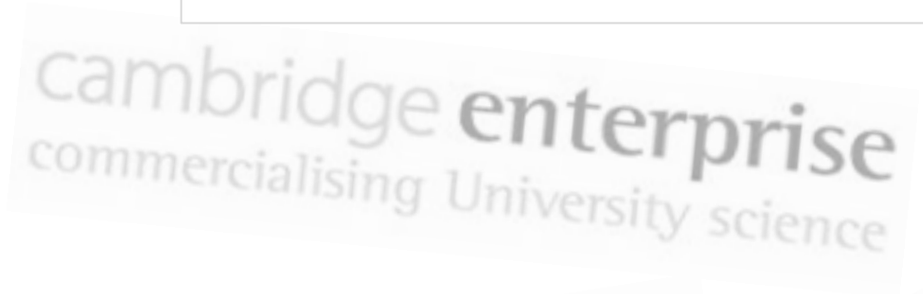
... or just a model... an idea



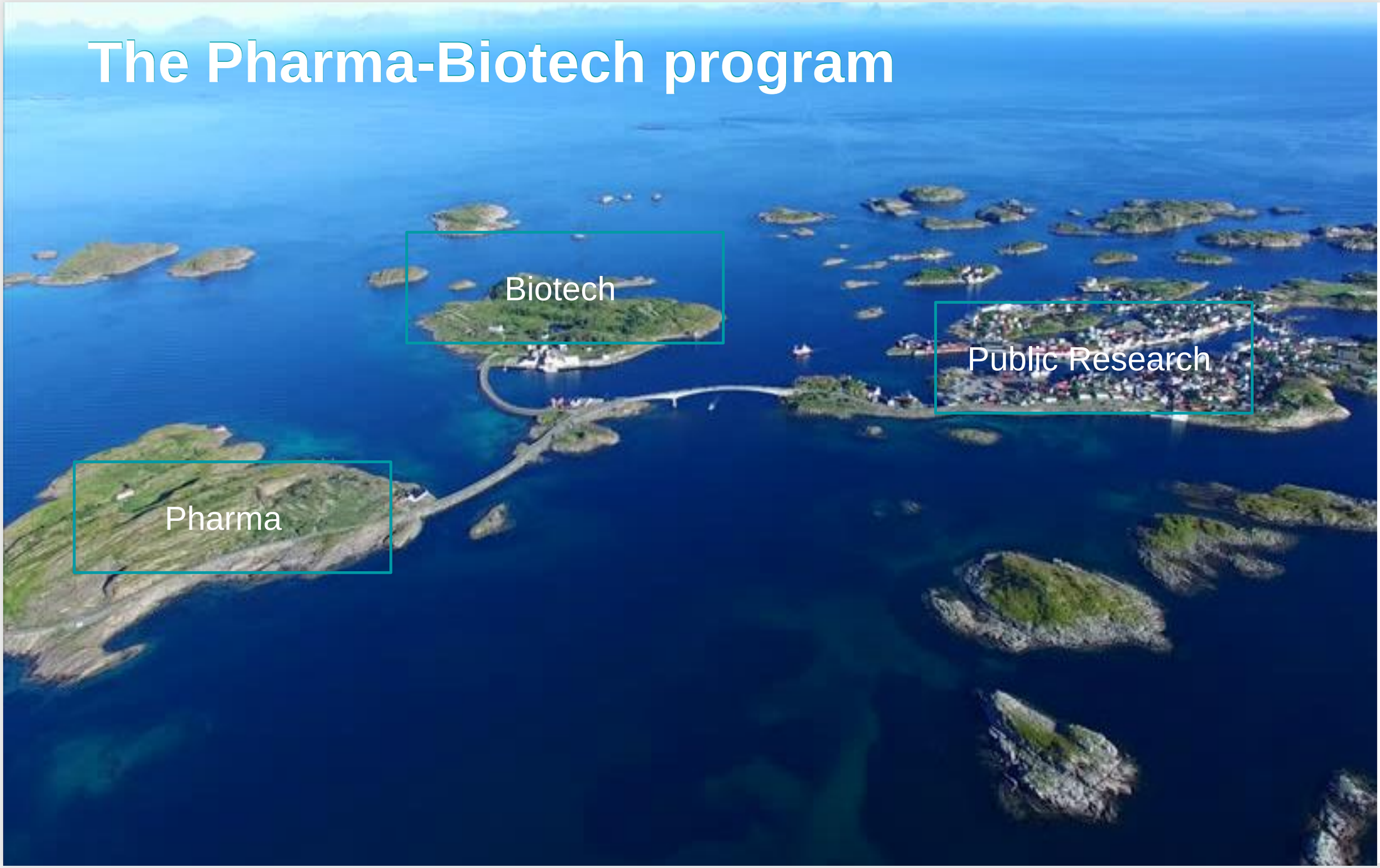


PROGRAMA FARMA-BIOTECH

2011-2016



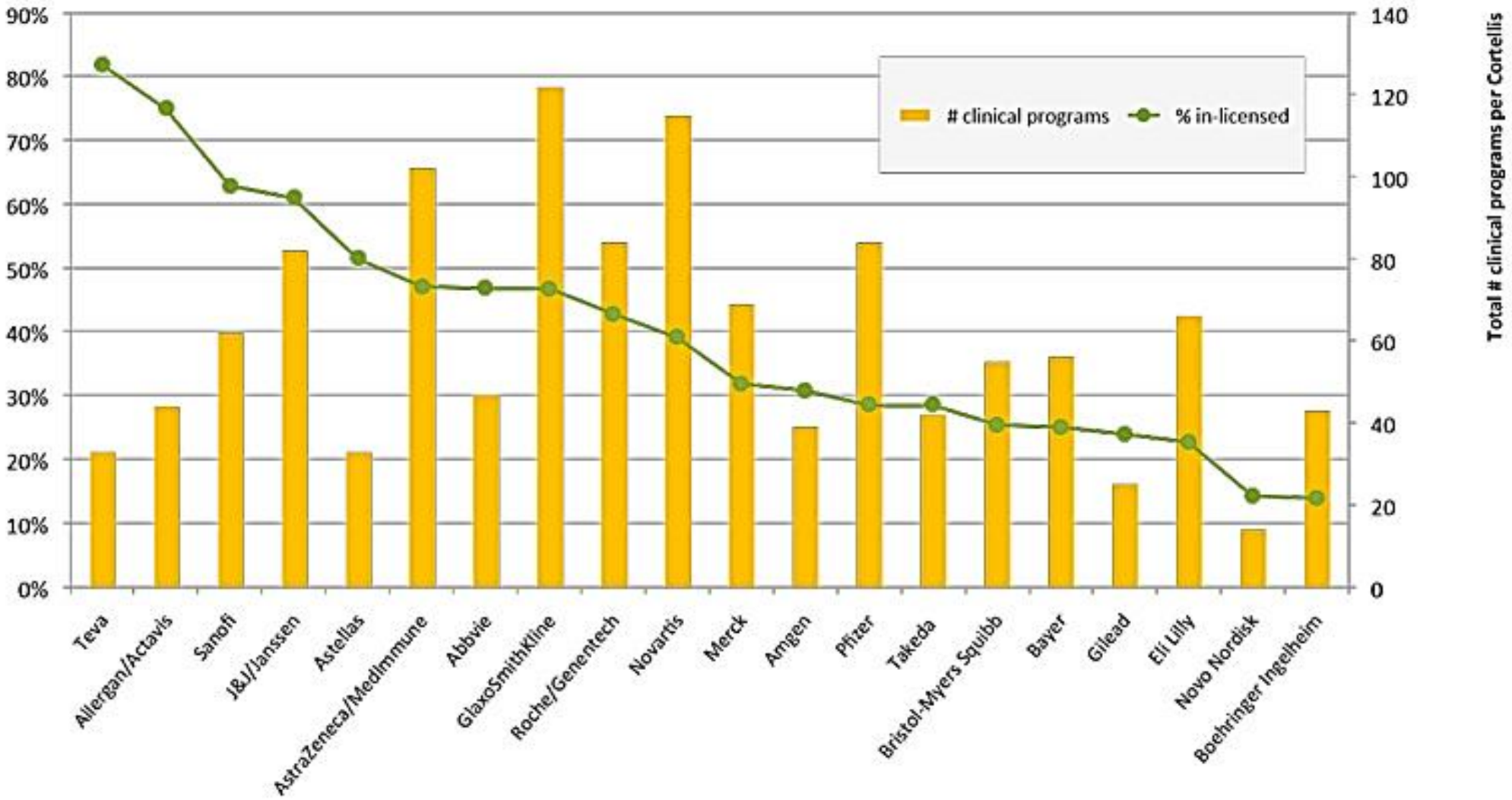
The Pharma-Biotech program



Extremely encouraging results

The response to a global need...

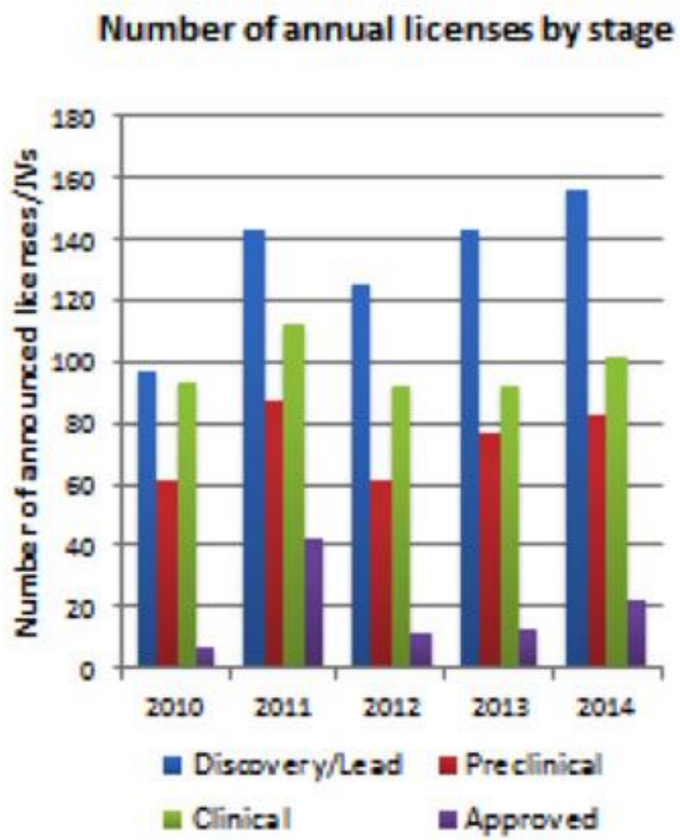
Clinical pipeline Sourcing for Top 20 Pharma

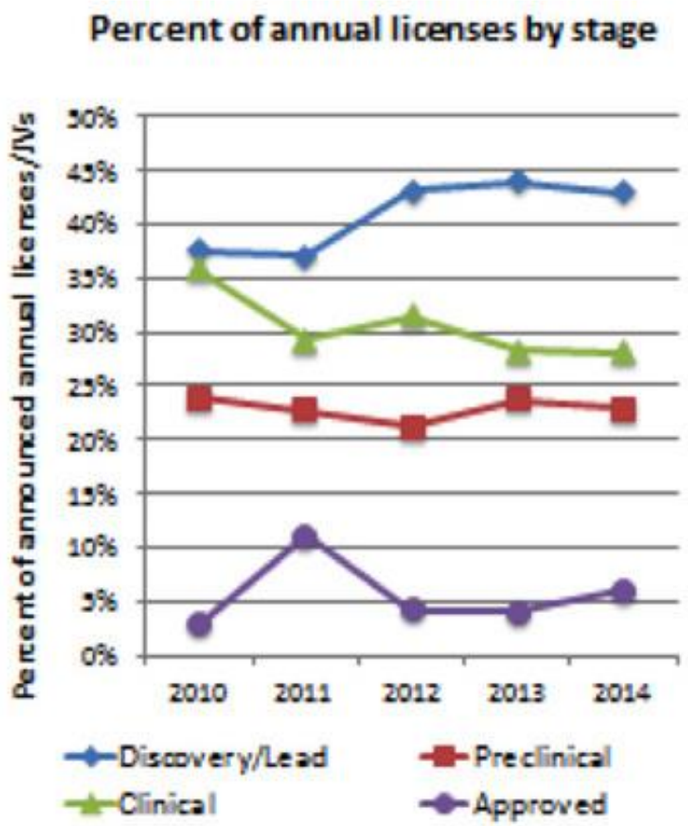


http://stateofinnovation.thomsonreuters.com/sites/default/files/content/articles_finding_cures_fig1.jpg

The response to a global need...

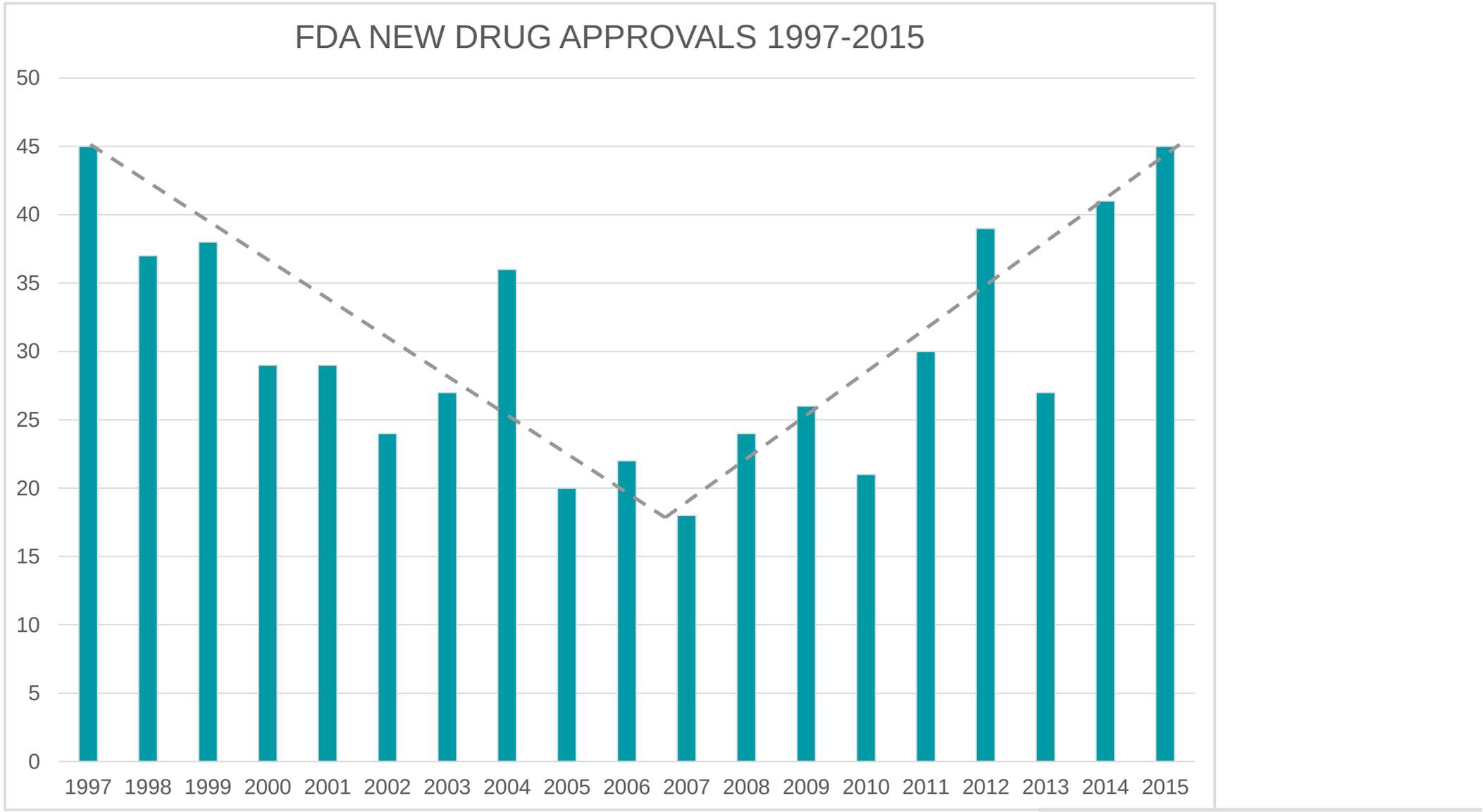
5-year Trend in Numbers of Therapeutics Licensing Deals by Stage of Lead Asset





http://stateofinnovation.thomsonreuters.com/sites/default/files/content/articles_finding_cures_fig2.jpg

Productivity is improving...



www.fda.gov/drugs/developmentapprovalprocess/druginnovation/ucm474696.htm

J. Owens, Nature Rev Drug Discovery 6, 99-101 (Feb 2007)

The Pharma-Biotech program

It is being particularly useful for Spanish pharmaceutical industry due to:

- *proximity of the centers of decision*
- *frequent attendance of key persons involved in the decision process*
- *ideal stage of maturity*
- *easy follow-up*
- *financial terms affordable*

The Pharma-Biotech program

It is particularly useful because

- *It has elaborated through years a complete and updated map of Spanish biomedicine innovation*
- *It has targeted both academic and biotech sectors*
- *It has instructed the offering side about the key points required to value their projects*
- *It has structured the offer according with a variety of fields and demand priorities.*
- *It has carefully followed-up/monitored the results of the program*

The Pharma-Biotech Program (PBP)

PBP and the failure rate in deal closing (after an initial mutual interest)

Reason	Without PBP	With PBP
Weak IP	+++	+
Not so mature as promised	++	+
Lack of robustness and/or relevance of preclinical results	++	+
J effect (the candidate is not feasible but "…we have an earlier one")	++	+
Lack of realistic competitor analysis	+++	++
Deep market analysis	+++	+++

Who we are

Who we are

Private pharmaceutical company headquartered in Barcelona

Vertical integration from R&D to distribution

International profile

Total turnover 2015	€879 million (+9%)
International turnover	€519 million (59% of total)
Total staff 2015	2,169
Abroad	420

Our Strategy

A quick guide

"Diversity: the art of thinking independently together"

Malcolm Forbes

ferrer 3D

- **B**usiness **D**iversification
- **I**nnovation **D**iversification
- **G**eographical **D**iversification

Business Channel Diversification

to cover whole healthcare spectrum

Dx	Rx	OTCs	Self-care
Basic diagnostics	Primary care	Cough & cold	Dermocosmetics
Genetic diagnostics	Specialties	Pain	Infant nutrition
Prognostic tools	Hospital based therapies	Inflammation	Antiparasitics
	Personalized immunotherapy		Repellents
			Nutraceuticals

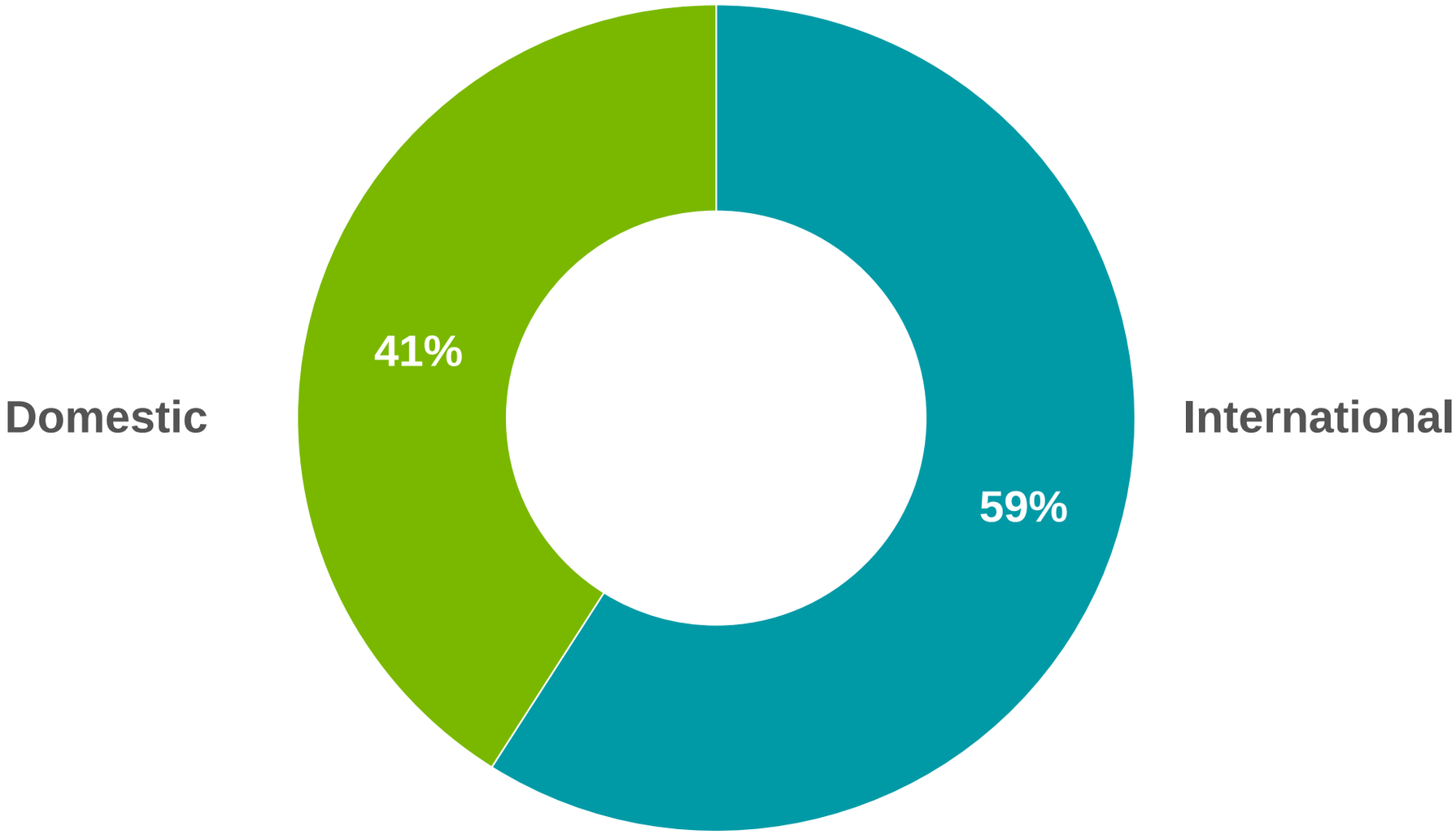
Geographical Diversification

Presence in 95 countries

Europe	26
Asia	21
Africa	21
Middle East	8
North America	2
Central America	7
South America	10

18 products
23 direct subsidiaries (including JVs)
72 partners and distributors

International vs domestic sales

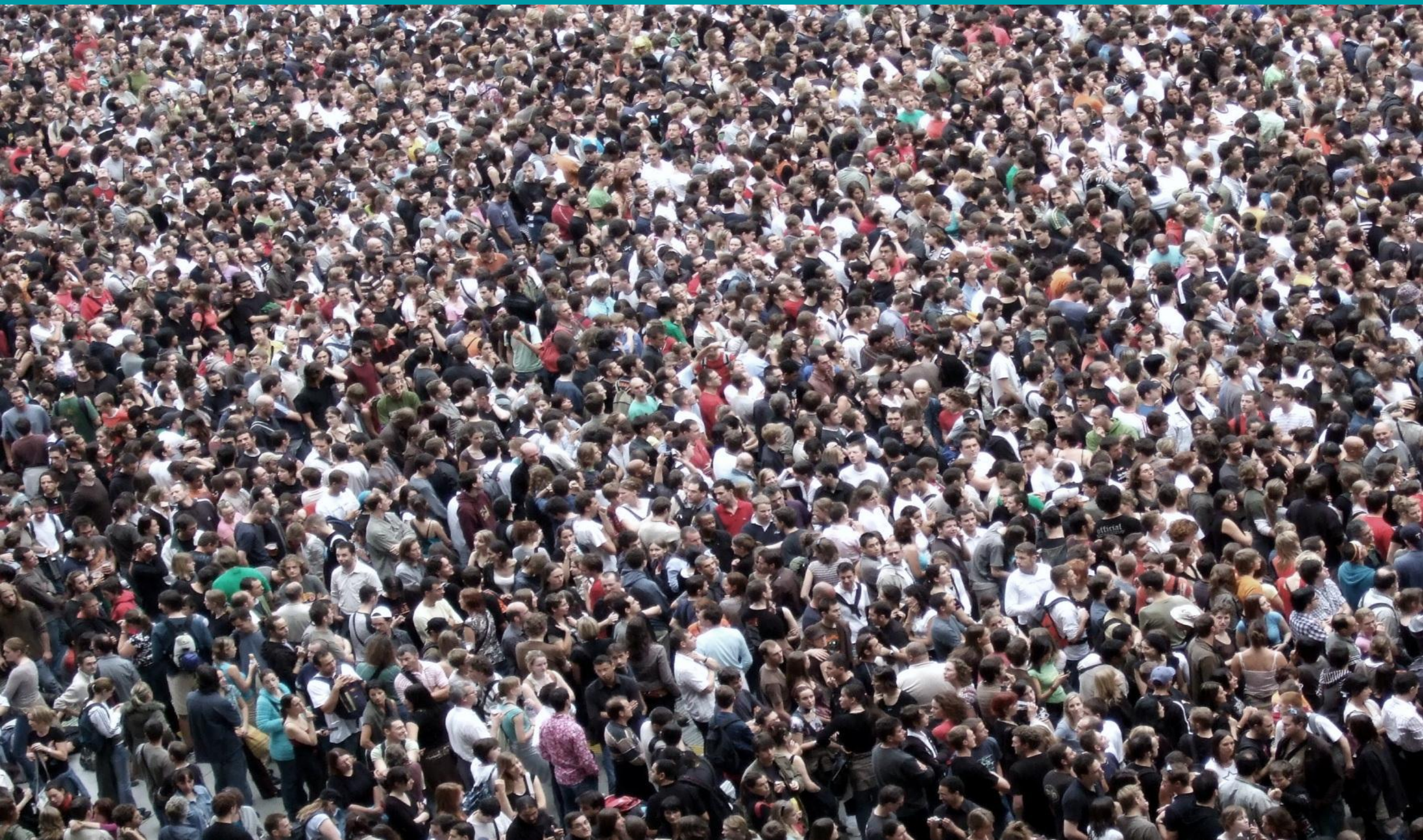


innovation

focus on value

Looking outside…

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



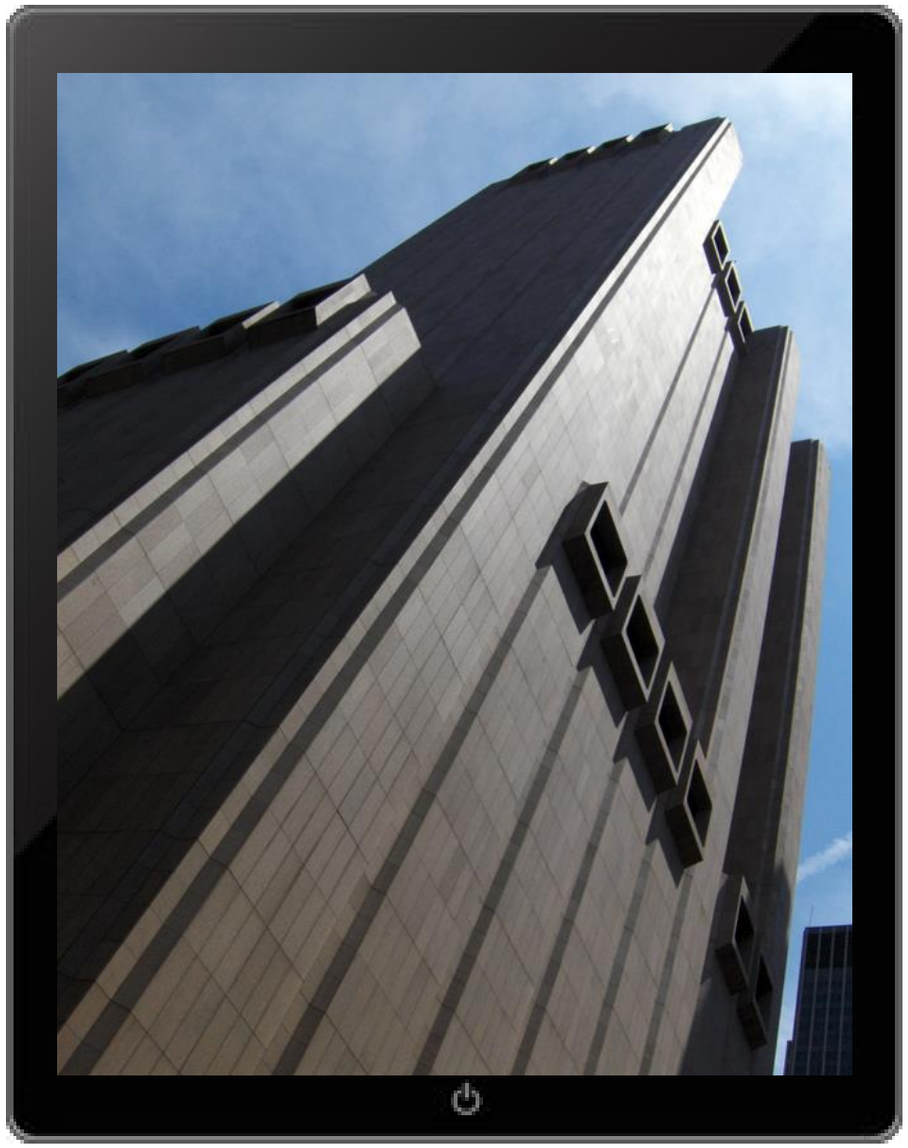
An Exercise in **Humility**

... a smart exercise

Paul Isherwood
GlaxoSmithKline
Director of Innovation

Our **Model**

Ferrer R&D: An evolving structure



AT&T Long Lines Building
New York, 1974

World Village of Woman Sports
Malmo, 2010

Ferrer R&D: An evolving structure

2016

2010

Focus on patient value

Biotech acquisitions & incubator

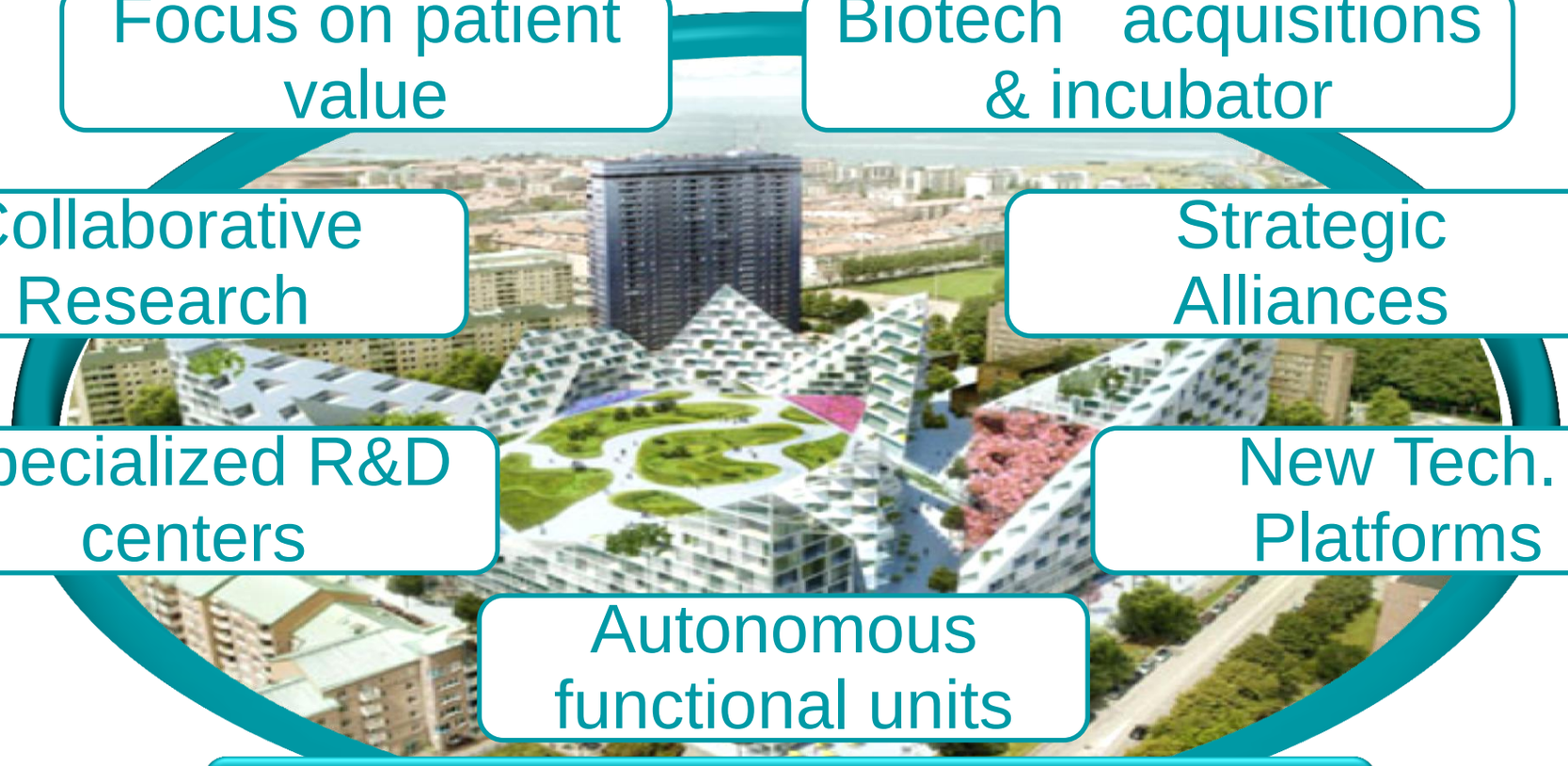
Collaborative Research

Strategic Alliances

Specialized R&D centers

New Tech. Platforms

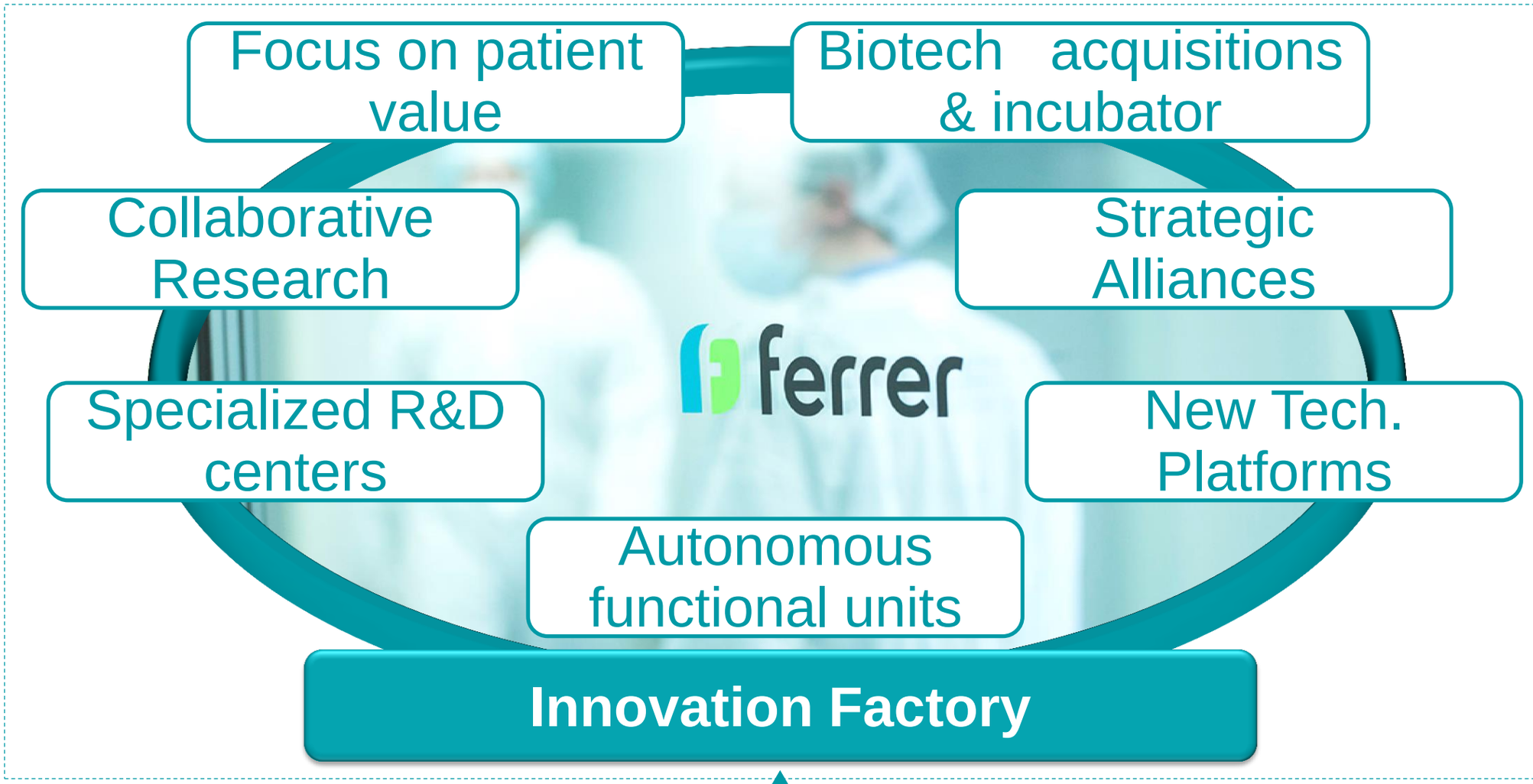
Autonomous functional units



Innovation Factory

Centralized R&D Corporate Lab

Ferrer R&D: An evolving structure



The Innovation Factory: 8 Functional Units

The Innovation Factory: 7 Specialized R&D Centers

Chemistry	Ferrer HealthTech		Sant Cugat Barcelona, Spain
Preclinical (chemolibrary, screening, NGS, biomarkers)	Ferrer Biotech Incubator (Synergy Building)		Esplugues de Llobregat Barcelona, Spain
Pharmaceutical Development & Bioequivalence	Corporate Product Development		Sant Cugat, Barcelona, Spain
Depot injectables (Proteins, peptides, small molecules)	Microcaps		Cerdanyola del Vallés Barcelona, Spain
Preclinical (allergy, immunotherapy, diagnostics)	Diater		Leganés Madrid, Spain
Chemistry / Natural products	Ferrer HealthTech		Beniel Murcia, Spain
Pharmac. Development	Ferrer HealthTech		Alsdorf, Germany

R&D Functional Units	R&D Centers (Spain)	Sant Cugat I (Barcelona)	Beniel (Murcia)	Sant Cugat II (Barcelona)	Cerdanyola (Barcelona)	Esplugues (Barcelona)	Leganés (Madrid)	L'Illa (Barcelona) (virtual)
								
ferrer HealthTech		■	■					
ferrer | Corporate Product Development				■	■			
ferrer | Advanced Biotherapeutics								■
ferrer | Clinical Research								■
ferrer inCode Personalised medicine						■		
ABAC Therapeutics						■		
spherium biomed®						■		
DIATER LABORATORIOS							■	

Bioincubator & preclinical facilities

ferrer inCode
Personalised medicine

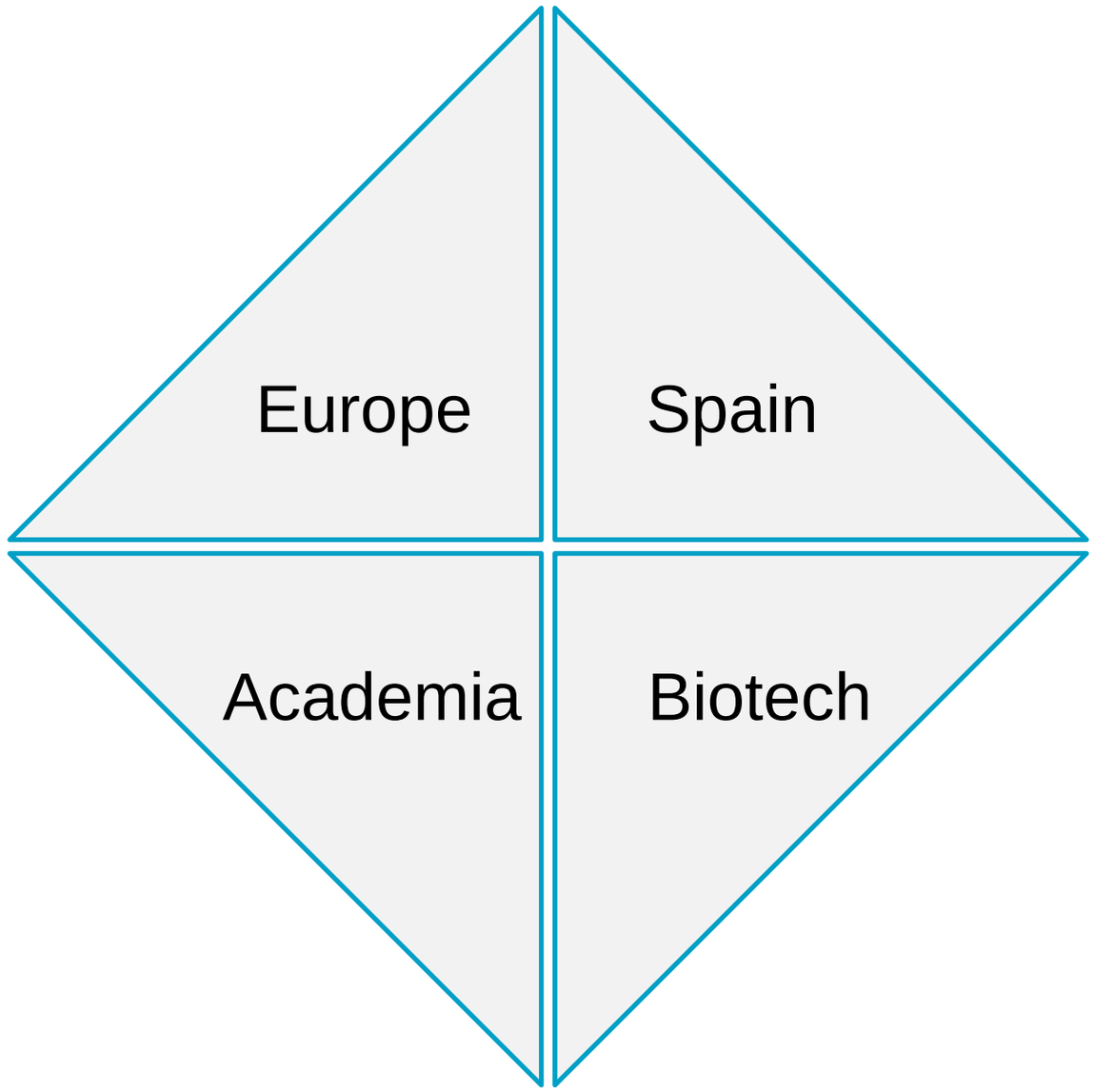
spherium biomed®

ABAC Therapeutics

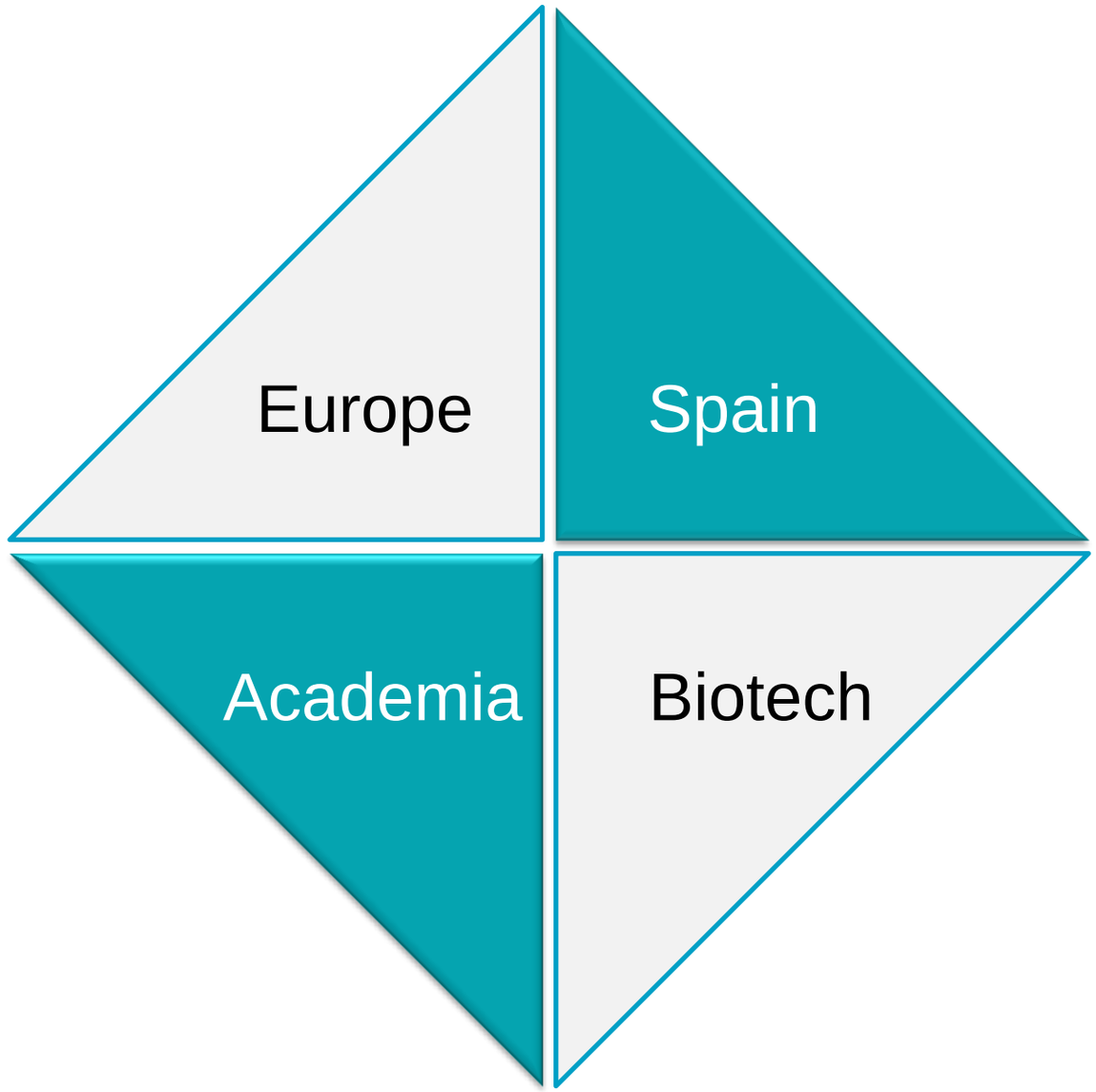
Genmedica Therapeutics

qgenomics
Genomics for Human Health

Collaborative projects by origin



Collaborative projects by origin



Collaborative Research (Public Institutions.es)

#	Project	Market	Originator	Localization
1	Trinomia		Centro Nacional de Investigaciones Cardiovasculares (CNIC)	Madrid
2	FAB-115 / EPICUP		Instituto de Investigación de Bellvitge (IDIBELL)	Barcelona
3	FAB-112		Universidad de Valladolid / Instituto de Oftalmobiología Aplicada (IOBA)	Valladolid
			Universidad del País Vasco	Vitoria
			Instituto de Bioingeniería de Cataluña (IBEC)	Barcelona
			CiberBBN	Madrid
4	FAB-121		Instituto de Bioingeniería de Cataluña (IBEC)	Barcelona
5	FAB-118		Instituto de Investigación de Bellvitge (IDIBELL)	Barcelona
6	FAB-119		Instituto de Investigación de Bellvitge (IDIBELL)	Barcelona
7	FAB-120		Hospital Vall d'Hebron - VHIR	Barcelona
8	SP13004		Universidad de Granada	Granada
9	SP09013		Universidad de Zaragoza	Zaragoza
			Universidad Autónoma de Barcelona	Barcelona
10	SP12008		Instituto de Investigación de Bellvitge (IDIBELL)	Barcelona
11	SP14037		Universidad de Lleida	Lleida
12	SP15016		Hospital Gregorio Marañón	Madrid

epicup

THE LANCET Oncology 2016

Articles

Epigenetic profiling to classify cancer of unknown primary: a multicentre, retrospective analysis

Sebastian Moran, MSc, Anna Martínez-Cardús, PhD, Sergi Sayols, MSc, Eva Musulén, MD, Carme Balañá, MD, Anna Estival-Gonzalez, MD, Cátia Moutinho, PhD, Holger Heyn, PhD, Angel Diaz-Lagares, PhD, Manuel Castro de Moura, MSc, Giulia M Stella, MD, Prof Paolo M Comoglio, MD, Maria Ruiz-Miró, PhD, Xavier Matias-Guiu, MD, Roberto Pazo-Cid, MD, Antonio Antón, MD, Rafael Lopez-Lopez, MD, Gemma Soler, MD, Federico Longo, MD, Isabel Guerra, MD, Sara Fernandez, MD, Yassen Assenov, PhD, Prof Christoph Plass, PhD, Rafael Morales, MD, Joan Carles, MD, Prof David Bowtell, PhD, Linda Mileshkin, MD, Daniela Sia, PhD, Richard Tothill, PhD, Josep Tabernero, MD, Prof Josep M Llovet, MD, Prof Manel Esteller, MD

Trinomia

ácido acetilsalicílico • simvastatina • ramipril

nature CLINICAL PRACTICE
CARDIOVASCULAR
MEDICINE

REVIEW

CME
Nature Clinical Practice Cardiovascular Medicine (2009) **6**, 101-110
doi:10.1038/ncpcardio1419
Received 15 May 2008 | Accepted 23 October 2008 | Published online: 23 December 2008

Fixed-dose combination therapy and secondary cardiovascular prevention: rationale, selection of drugs and target population

Ginés Sanz* and Valentin Fuster About the authors

Correspondence *Centro Nacional de Investigaciones Cardiovasculares, Melchor Fernández Almagro 3, 28029 Madrid, Spain

Email gsanz@cnic.es

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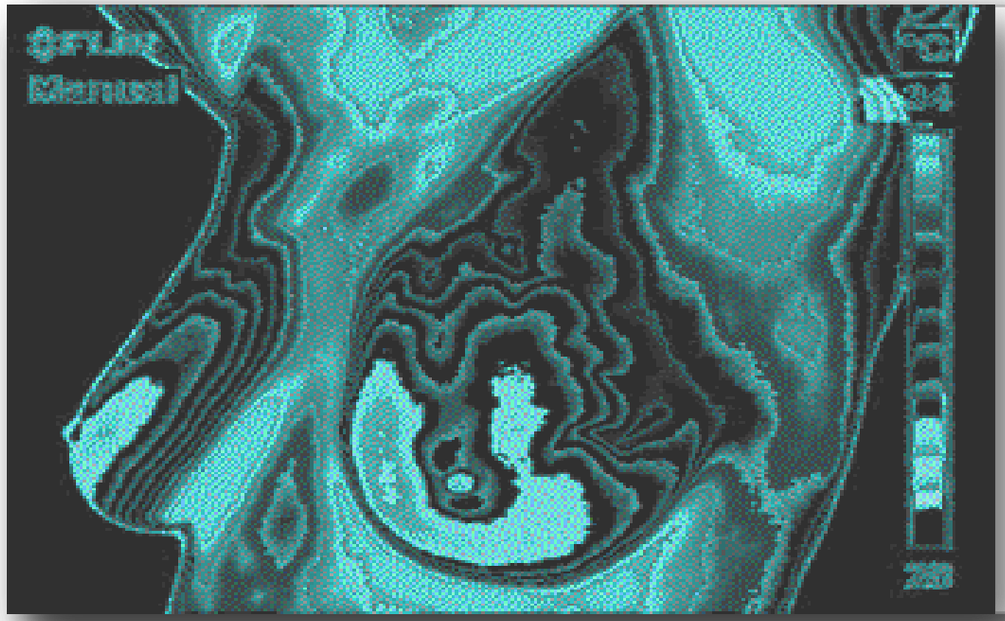
Ferrer Advanced Biotherapeutics

Oncology @ Ferrer

New Frontiers in Tolerability

A Farma-Biotech program success



LYMPHO

(Vivia009)

Project FAB-114

vivia BIOTECH

ferrer | Advanced Biotherapeutics

Lympho Project (FAB-114)

A Farma-Biotech program success

- 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**

Hematologic malignances (HM) therapies are **poorly tolerated** and yield a **high % of refractory** patients

- Non-Hodgkin lymphoma (NHL)

- **127.000 new cases/year** across the 7MM, the largest HM market.
- Prevalence increases faster than other cancer types.
- Indolent lymphoma remains incurable with standard therapy and eventually becomes refractory to rituximab, often within 3 years.
- **Combo chemotherapy is poorly tolerated** but also the 'on top' **rituximab can produce tumor lysis syndrome**, severe skin and mouth reactions, progressive multifocal leukoencephalopathy and reactivation of hepatitis B virus infection.

- Chronic Lymphocytic Leukemia (CLL)

- Most frequent leukemia: **31.000 new cases/year** in the 7MM.
- **30 % refractory patients due to p53 deletion→** poor response , even to ofatumumab.
- **50 % refractory patients due to be fragile elder →** lack of tolerability to fludarabine.

Our **approach**

An **old drug** orally used in millions of patients exhibits high **efficacy in B-cell HM** by **parenteral** route

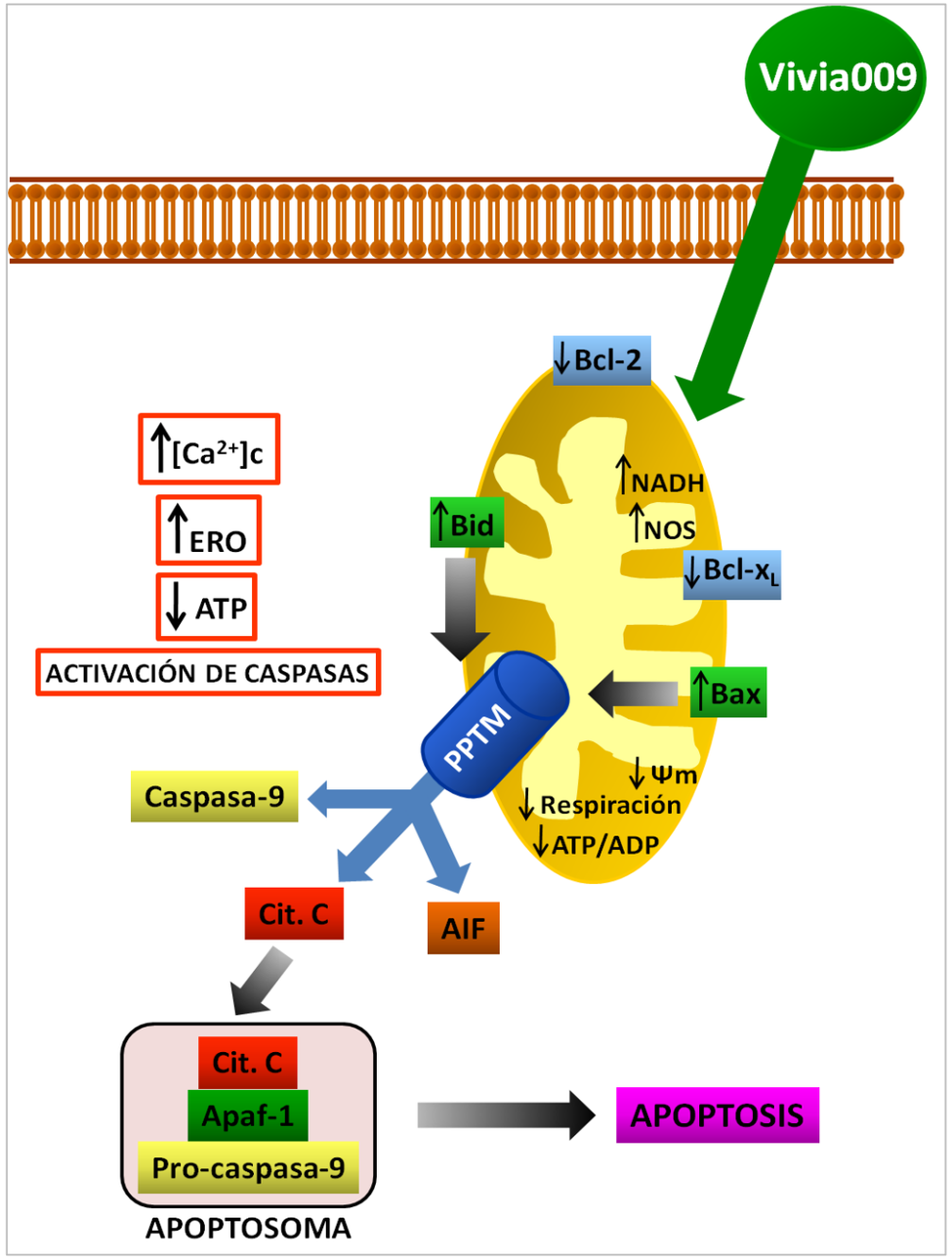
- An extensive **reprofiling** project
  - Evaluation in fresh HM patient samples.
  - Parallel evaluation in healthy cells.

- **A generic-threat safe position**
  - The drug is only effective by a non-previously developed route.
  - **IP protection.**
  - No option for generic interference.

Mechanism of Action (I)

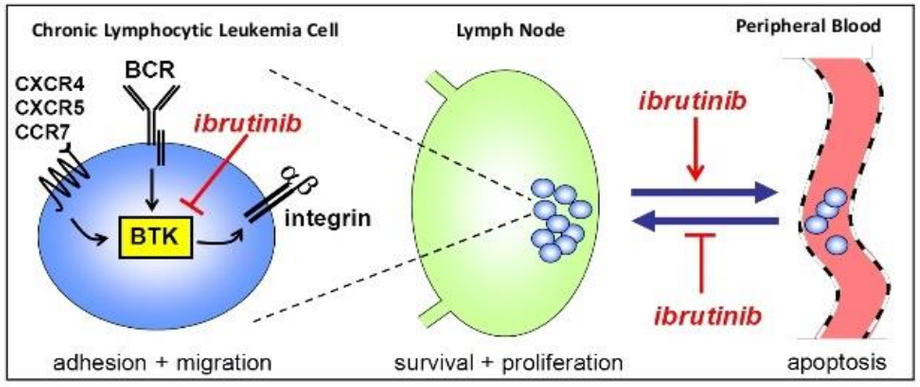
FAB-114 (Vivia009) accumulates in mitochondria

- Induces apoptosis from mitochondria skipping p53
- Could induce opening of Transient Mitochondrial Permeability Pore (TMPP), initiating release of pro-apoptotic molecules
- Anti-tumor mechanism to be further characterized.

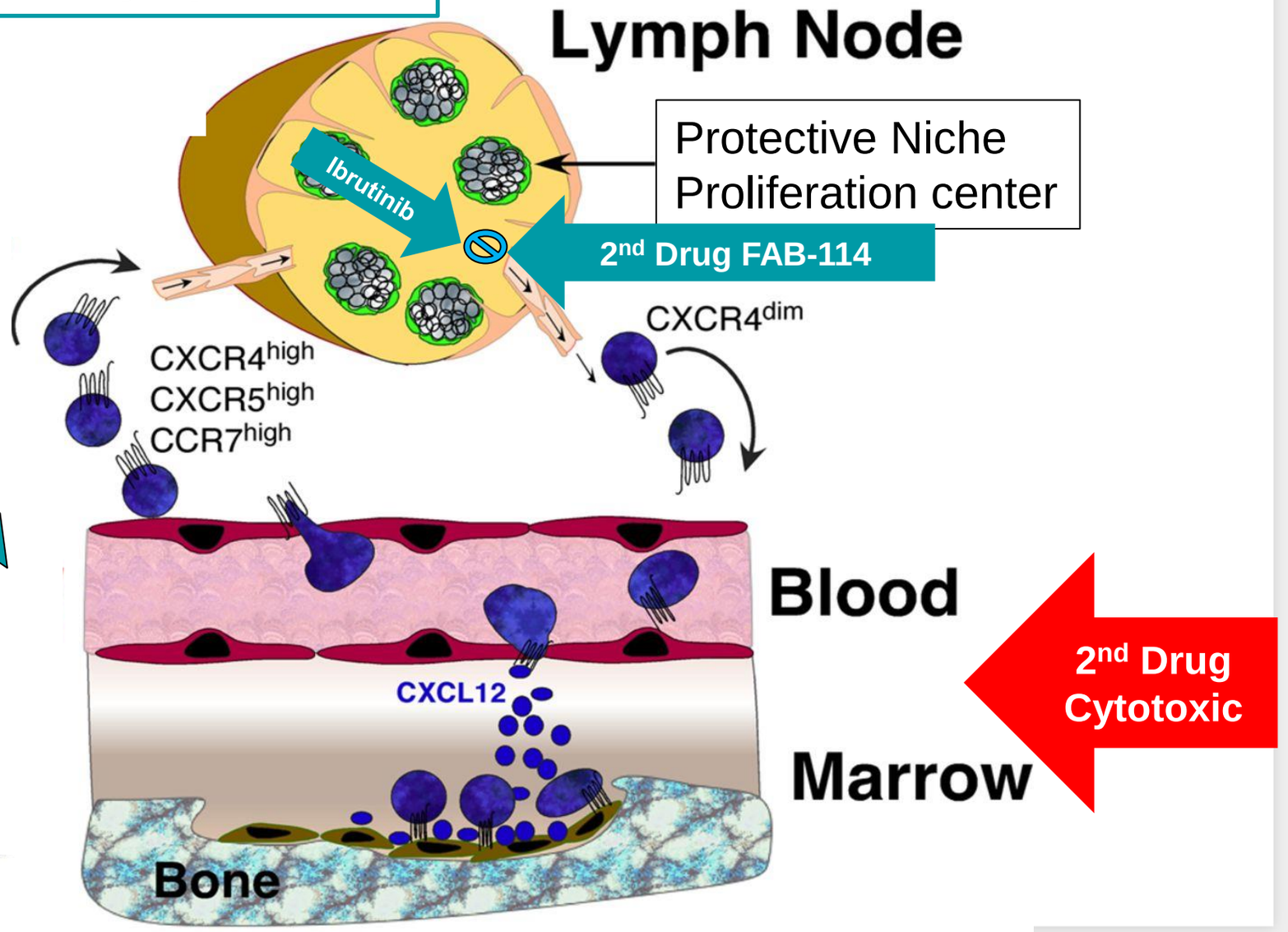


Mechanism of Action (&II)

Potentially Synergistic with Ibrutinib.
IBRUTINIB frees leukemic cells in lymph nodes
FAB-114 eliminates leukemic cells in lymph Nodes



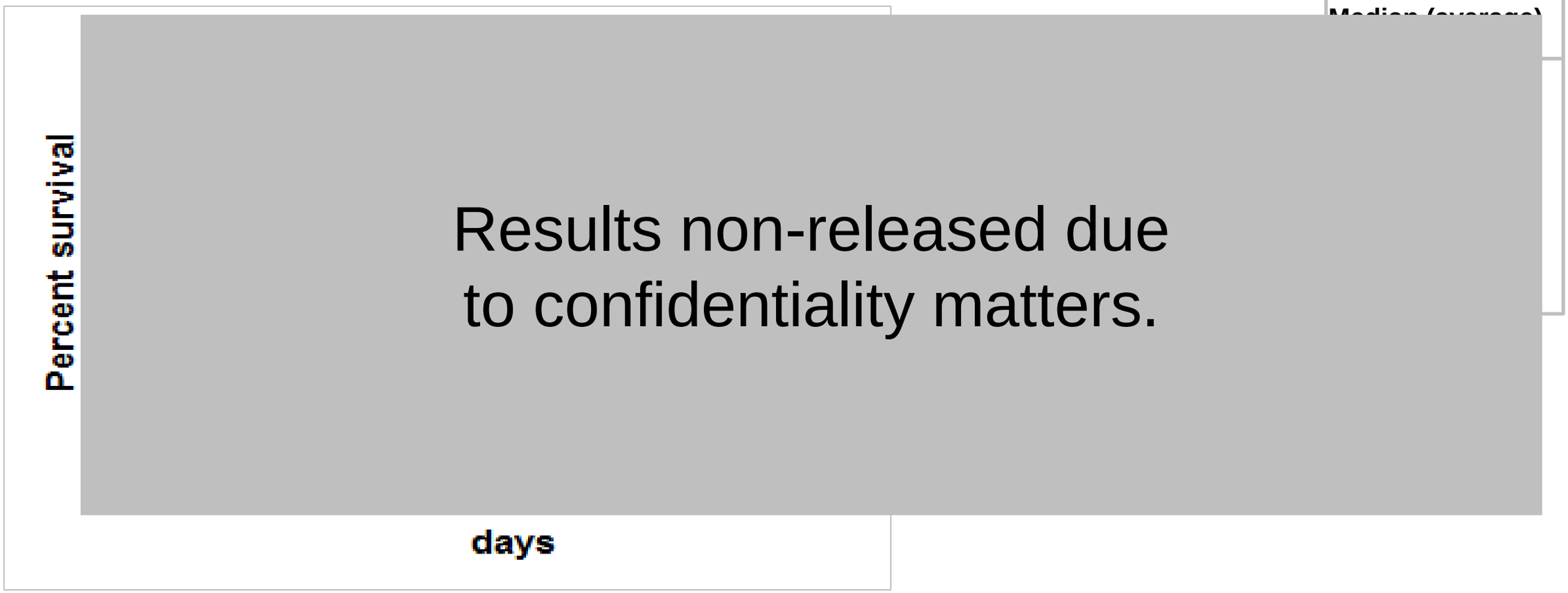
From: de R... *et al*, Blood 119: 2590-2594



Results: **In vivo efficacy**

Eμ-Myc: a genetic lymphoma model in mice

Outcome: Overall Survival



Making
people
better

ferrer