Innovative Medicines Initiative

The Innovative Medicines Initiative: Building New Models of Collaborative Research across Europe

Maria-Teresa De Magistris

Principal Scientific Manager, IMI

Innovative Medicines Initiative:
the Largest PPP in Life Sciences R&D

Launched in 2008

EFPIA = **E**uropean **F**ederation of **P**harmaceutical **I**ndustries and **A**ssociations

Importance of a *neutral platform* for the success of PPPs

IMI Executive Office acts as a neutral third party:

- Builds and maintains trust between the different project parties for the benefit of all partners
- Before and during the project life provides guidance and impartial advice to projects for intellectual property, data sharing, governance, etc.
- Facilitates the involvement of Regulatory Bodies in Projects

Public-private partnerships need honest brokering

Michel Goldman

Given the current challenges in research and development, it's increasingly apparent that collaboration between large pharmaceutical companies, academic teams and biotechnology enterprises is essential for converting basic biomedical discoveries into lifesaving medicines. But these partnerships work best when a neutral third party helps foster them.

Michel Goldman IMI

A trickling pipeline of new products at many pharmaceutical companies has led to a paradigm shift in the industry's research and development (R&D) strategy. Indeed, the integrated R&D model in which every step of drug development is conducted in-house has proved largely inefficient in delivering the novel therapies needed to address major health challenges. Therefore, this model is being progressively replaced by open innovation networks that allow the leveraging of external pools of knowledge, especially in universities and biotechnology companies[1].

The pharmaceutical industry realizes that the best approach is to apply an open innovation concept to precompetitive research that encourages companies to share expertise. These principles were the cornerstones of the Critical Path Initiative launched by the US Food and Drug Administration in 2004, which led to the creation of the Critical Path Institute, an Arizona-based nonprofit dedicated to fostering collaborations between industry, academia and regulators[2].

Across the pond, the Innovative Medicines Initiative (IMI), a public-private partnership between the EU and the European Federation of Pharmaceutical Industries and Associations, is a prototypic example of an organization created to support open innovation and pre-competitive research in the pharmaceutical sector. It has raised awareness about the principles of open collaboration and has launched several education and training programs for scientists from industry or academia interested in drug development and

> "A neutral organizer is key to ensure the sustainability of public-private partnerships and to restore trust in and among the stakeholders committed to the development of innovative therapies."

transparent competition, rather than through preexisting connections. For this reason, IMI organizes a competitive process to identify the best partners to match with the pharmaceutical companies that, for their part, invest considerable resources in the projects, propose the research topics and most often coordinate the projects.

This leading role of industry, which distinguishes IMI from most other public-private partnerships, guarantees the optimal exploitation of the knowledge created and its dissemination by the research consortia. As an example, within one of the IMI consortia for diabetes, the optimal exploitation of the first human beta cell line useable for the development of antidiabetic drugs[4] was made possible by the partnership between the academic team that made the basic discovery, a small enterprise that commercializes the cell product and the large pharmaceutical enterprises that will develop drug screening assays relying on this innovative tool.

Ensuring that consortia operate in a balanced manner in terms of intellectual property and allocation of resources requires a neutral party that can act as a referee whenever needed. To address this need, IMI facilitates consortium agreements by playing the role of impartial broker. A key mission of a neutral body such as IMI is, of course, to ensure the sound management and allocation of public funds in the interest of both industry and society. Here, IMI develops performance indicators suited to measure the added value of public-private partnerships[5]. As an example, IMI is closely

Nature Medicine
18: 341, 2012

What has IMI done so far?

IMI 2008 – July 2013

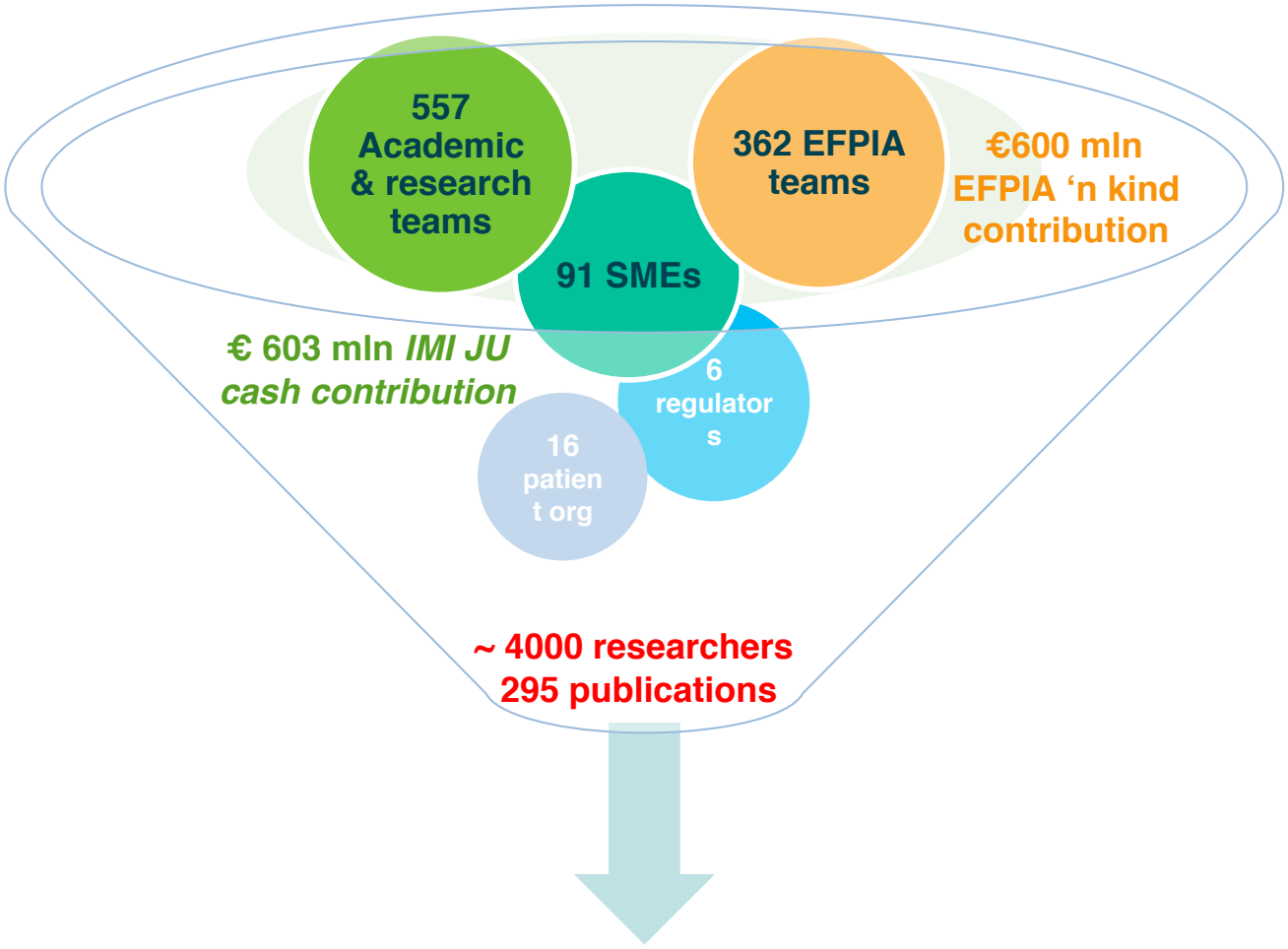
IMI has launched 8 Calls

-Projects of Calls 1 - 6 are ongoing (40 projects)

-Call 7 Projects are about to sign the Grant Agreement

-Call 8 Proposals are under evaluation

Key Figures of 40 on-going Projects



R&D Productivity Improvements

IMI projects

- Alzheimer
- Schizophrenia
- Depression
- Autism
- Chronic Pain
- Diabetes
- Cancer
- Infectious diseases
- Asthma
- COPD
- Tuberculosis
- RA

- Kidney, liver and vascular system toxicity
- Non genotoxic carcinogens
- In silico tox prediction
- Adverse drug reaction detection and monitoring
- Biopharmaceutical safety
- Vaccine safety

- Integrated drug development & safety
- Pharmacovigilance & pharmacoepidemiology
- Pan-European course catalog
- Patient education

- Model based drug development
- EHR in medical research
- Open access innovation platform
- Patient Health Information Framework
- Translational research informatics and analytics platform

Total budget (Calls 1-8) distributed across therapeutic areas

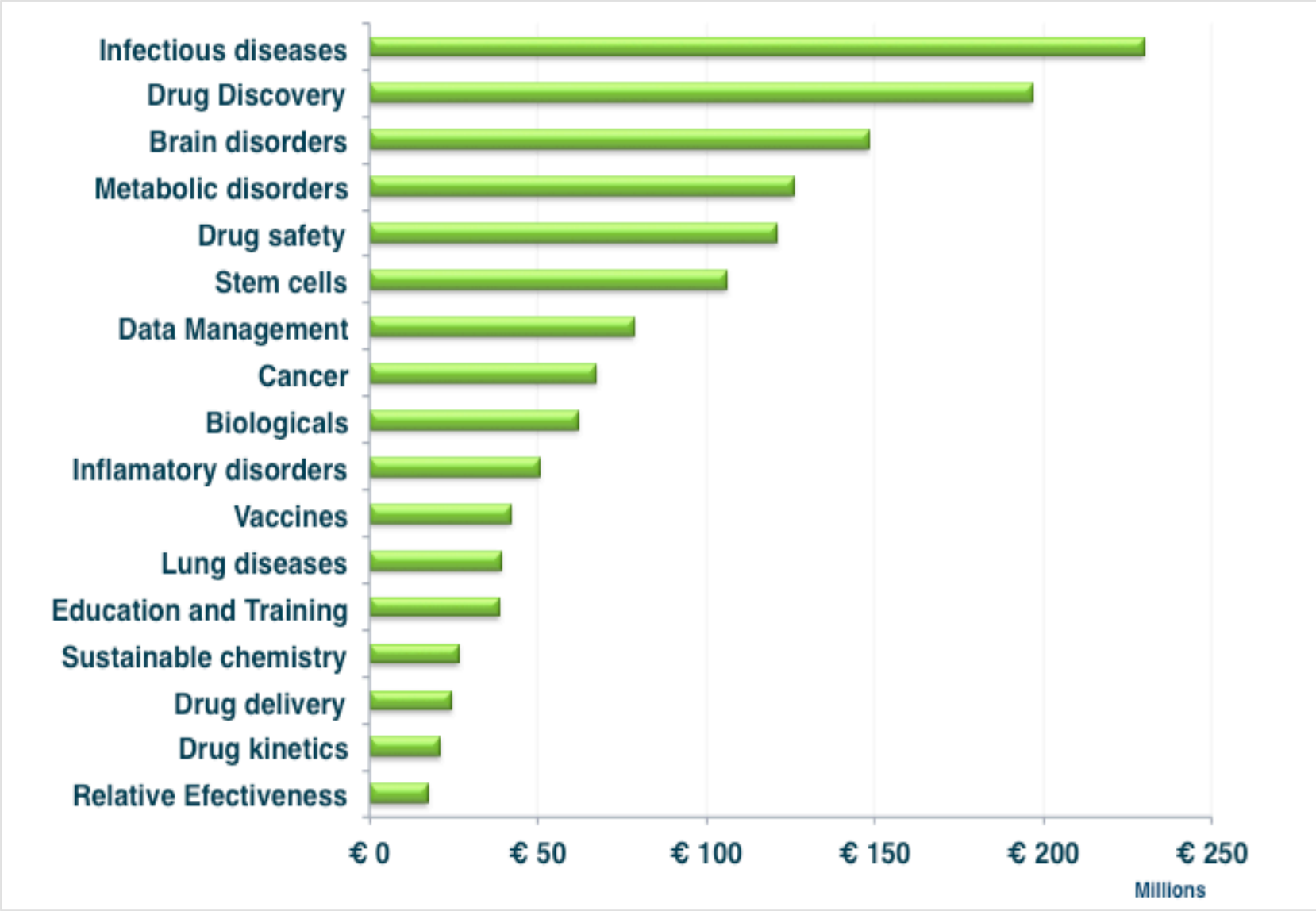


Table based on SOFIA extract Q1 2013

ND4BB*: the IMI Anti-Microbial Resistance Programme (will include several calls)

Innovative Medicines Initiative

European Commission and European Parliament → **Incentives for Pharma Industry**

("Action plan against the raising threats from Antimicrobial Resistance" launched by the European Commission in November 2011)

➢As a PPP aiming at removing bottlenecks in drug development, **IMI is the ideal instrument** to solve the scientific challenges, to provide the necessary incentives for industry and to revisit the regulatory environment in order **to reinvigorate R&D on antibiotics.**

Call 6, two Topics:

*ND4BB= New Drugs for Bad Bugs

>Clinical trials with a candidate antibiotic
>Antibiotic influx and efflux from bacterial cells

Budget: 229 M

efpia

Ongoing Projects

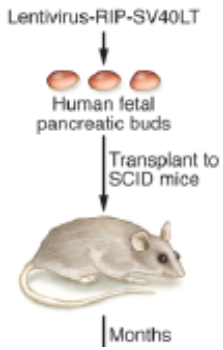
Key Achievements

Improving R&D productivity (1)

Establishment of robust validated models for drug development

Alzheimer's Disease	translatable sleep deprivation model developed
	characterized multiple Tg mice models
Chronic Pain	sleep deprivation model validation on-going
	menthol model validation on-going
	UVB irradiation model validation on-going
Schizophrenia Depression	new animal models developed, multiple models evaluated
	translatable imaging methodology develop
Autism	developed animal model that mimics nonsyndromathic autism
Diabetes	developed new animal models that mimic T1 and T2 diabetes, multiple models evaluated
	Tg mice developed
	developed human B cell line
Asthma	2 new animal models developed FCA/HDM and CT & MRI imaging of chronic HDM model
	evaluated and harmonized multiple animal models

IMIDIA: Development of a Key Tool for new Diabetes Therapies



Related Commentary, page 3395 Technical advance

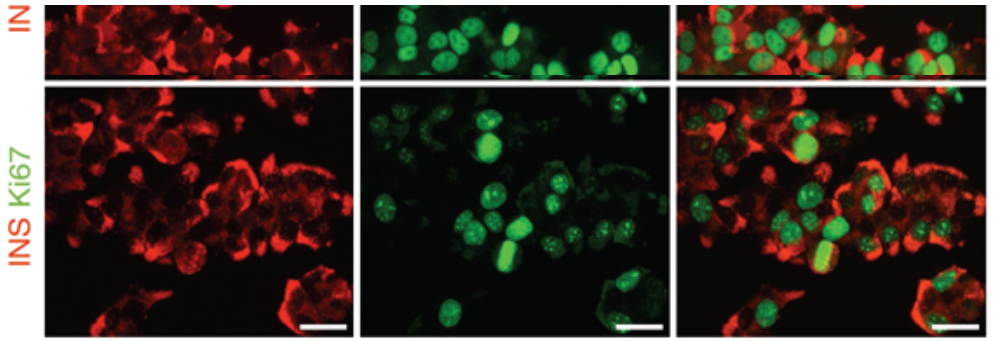
A genetically engineered human pancreatic β cell line exhibiting glucose-inducible insulin secretion

Philippe Ravassard,[1,2,3] Yasmine Hazhouz,[2,4] Séverine Pechberty,[4,5] Emilie Bricout-Neveu,[2,4] Mathieu Armanet,[6,7] Paul Czernichow,[4] and Raphael Scharfmann[5]

Finally! A human pancreatic β cell line

Gordon C. Weir and Susan Bonner-Weir

Section on Islet Cell Biology and Regenerative Medicine, Research Division, Joslin Diabetes Center, and Department of Medicine, Harvard Medical School, Boston, Massachusetts, USA.



The Journal of Clinical Investigation http://www.jci.org Volume 121 Number 9 September 2011

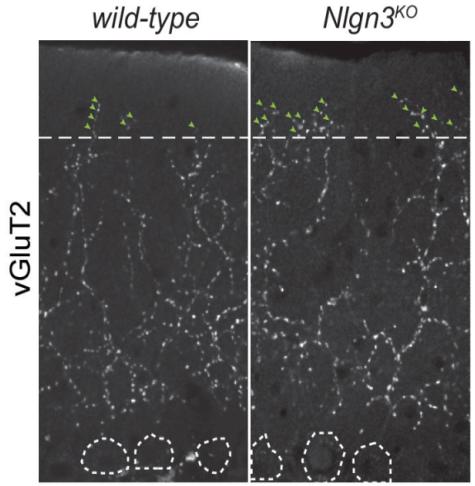
EU-AIMS
Autism Research in Europe

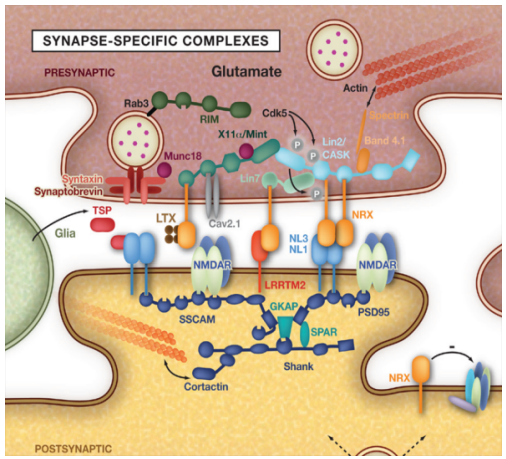
Science

October 5th 2012

Shared Synaptic Pathophysiology in Syndromic and Nonsyndromic Rodent Models of Autism

Stéphane J. Baudouin,[1] Julien Gaudias,[1] Stefan Gerharz,[1*] Laetitia Hatstatt,[1] Kuikui Zhou,[2] Pradeep Punnakkal,[1] Kenji F. Tanaka,[3,4] Will Spooren,[5] Rene Hen,[3] Chris I. De Zeeuw,[2,6] Kaspar Vogt,[1] Peter Scheiffele[1]†





The consortium has developed an animal model replicating a nonsyndromic autism and demonstrated that the condition can be reversed with specific therapy

This new development is be of great importance for clinical development of new treatments for autism

Improving R&D productivity (2)

Development of novel biomarkers for drug development

Alzheimer's Disease	novel biomarkers that follow disease progression in Tg mice
Chronic Pain	translatable imaging biomarkers of brain activation related to chronic pain
Schizophrenia Depression	clinical imaging biomarkers
	clinical and molecular biomarker candidates for antidepressant response
	surrogate proteomic biomarkers for efficacy prediction
Diabetes	candidate lipodomic and metabolomic biomarkers
	novel genetic markers identified
Asthma	genetic, proteomic, metabolomic, breathomic biomarker candidates – validation on-going
Safety	novel early non genotoxic carcinogen biomarkers identified
	potential biomarkers of drug induced injury of liver, kidney and vascular system

SAFE-T

Addresses the current lack of sensitive and specific clinical tests to diagnose and monitor drug-induced injury to the kidney, liver and vascular tissues in man, which is a major hurdle in drug development

A generic operational strategy to qualify translational safety biomarkers

Katja Matheis[1], David Laurie[2], Christiane Andriamandroso[3], Nadir Arber[4], Lina Badimon[5], Xavier Benain[6], Kaïdre Bendjama[7], Isabelle Clavier[6], Peter Colman[8], Hüseyin Firat[7], Jens Goepfert[9], Steve Hall[8], Thomas Joos[10], Sarah Kraus[4], Axel Kretschmer[11], Michael Merz[2], Teresa Padro[5], Hannes Planatscher[9], Annamaria Rossi[8], Nicole Schneiderhan-Marra[9], Ina Schuppe-Koistinen[12], Peter Thomann[7], Jean-Marc Vidal[13] and Béatrice Molac[7]

[1] Boehringer-Ingelheim Pharma GmbH & Co. KG, Biberach, Germany
[2] Novartis Pharma AG, Basel, Switzerland
[3] Interface Europe, Brussels, Belgium
[4] Tel-Aviv (Souraski) Medical Center, Tel-Aviv, Israel
[5] Barcelona Cardiovascular Research Center (ICCC-CISC), Barcelona, Spain
[6] Sanofi-Aventis, Paris, France
[7] Firalis SAS, 35 rue du Fort, 68330 Huningue, France
[8] Pfizer Ltd, Sandwich, UK
[9] Natural and Medical Sciences Institute, Reutlingen, Germany
[10] Experimental & Diagnostic Immunology GmbH, Reutlingen, Germany
[11] Bayer Schering Pharma AG, Leverkusen, Germany
[12] AstraZeneca R&D, Södertälje, Sweden
[13] EMA, London, UK

Drug Discov Today, in press

20 Partners

- 11 EFPIA Pharma Companies
- 5 Academic Institutions
- 4 SMEs

First achievements

✓ 153 potential biomarker candidates for drug-induced injury of the kidney, liver and vascular system have been evaluated and are currently undergoing clinical evaluation.

✓ The strategy adopted has been agreed with the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA).

Improving R&D productivity (3)

Joining forces to make a difference – data pooling

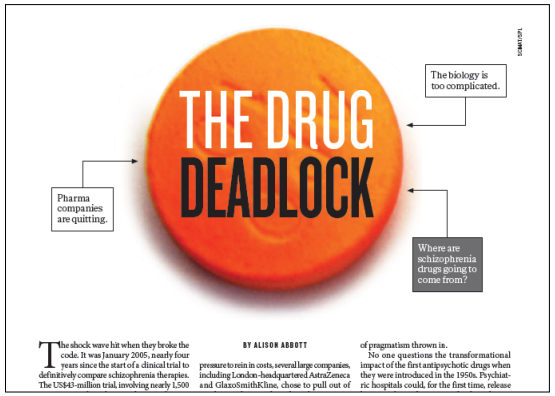
Schizophrenia Depression	combined data analysis of 23,401 schizophrenia patients
	Data from 45 randomized controlled studies of antidepressants on 11,000 patients – de novo analysis pending
	combined genetic data analysis on 2146 DNA samples
Autism	sequenced 78 Icelandic parent–offspring trios, a total of 219 distinct individuals (44 autistic, 21 schizophrenic offspring) and identified 4933 *de novo* mutations
Chronic Pain	pooled data from 43 past trials to understand the pain medicines mechanism of action and factors important in placebo response
Safety	building a toxicology information database utilising toxicology legacy reports to develop better in silico tools for toxicology prediction of new chemical entities (1274 reports extracted so far, 2092 were cleared, 3564 are planned in total)
	exploited EFPIA in vivo mouse and rat toxicology studies, tissue archives and molecular profiling data for >30 reference compounds to study NGC, genotoxic carcinogens and non-hepatocarcinogen controls

NEWMEDS

Develops biomarkers and tools and models to allow better targeted treatments for schizophrenia and depression

19 Partners

- 9 EFPIA companies
- 7 Public organisations
- 3 SMEs



Nature, 11 November 2010

- ✓ Has assembled the largest known repository of antipsychotic clinical trail data.
- ✓ The database contains information on 23 401 patients from 67 industry sponsored studies.
- ✓ Bringing together data from public projects and 3 companies on the genetics and clinical response in 1800 well characterized patients with depression.

Improving R&D productivity (4)

Agreeing development and regulatory submission of key standards for drug development

Asthma	diagnostic criteria on severe asthma
Schizophrenia Depression	clinical biomarker meaningfulness calculator for predicting biomarker candidate utility in predicting antidepressant response
	identified phenotypes associated with schizophrenia CNVs
Diabetes	developed non-invasive carotid histology for diabetic macroangiopathy
	generated phenotype definitions for diabetic complications
COPD	derived a conceptual model for physical activity
	developed patient reported outcome tools – validation on-going
Safety	established generic qualification strategy for translational biomarkers
	building ontology for preclinical pathology, 3917 terms and 2535 synonyms have been mapped

U-BIOPRED

By comparing data from several hundreds of people, the team will characterise different kinds of severe asthma, paving the way towards a new classification of asthma *and personalised treatments for patients*

38 Partners

- 9 EFPIA companies
- 23 Academic institutions
- 3 Patients' organisations
- 3 SMEs
- 1 non-SME company

First achievements

✓ Consensus statement on the definition of severe refractory asthma

Diagnosis and definition of severe refractory asthma: an international consensus statement from the Innovative Medicine Initiative (IMI)

Elisabeth H Bel,[1] Ana Sousa,[2] Louise Fleming,[3] Andrew Bush,[4] K Fan Chung,[5] Jennifer Versnel,[6] Ariane H Wagener,[1] Scott S Wagers,[7] Peter J Sterk,[1] Chris H Compton,[8] on behalf of the members of the Unbiased Biomarkers for the Prediction of Respiratory Disease Outcome (U-BIOPRED) Consortium, Consensus Generation[9]

ABSTRACT

Patients with severe refractory asthma pose a major healthcare problem. Over the last decade it has become increasingly clear that, for the development of new targeted therapies, there is an urgent need for further characterisation and classification of these patients. The

DIAGNOSIS AND DEFINITION OF SEVERE ASTHMA OVER THE LAST 15 YEARS

Various documents proposing different clinical definitions of 'severe asthma' in adults and children have been published over the last 15 years by international task forces, workshops, networks and

Thorax, in press

IMI Education & Training Projects

✓ European Medicines Research Training Network (EMTRAIN)
First course in Nov 2010 on drug discovery development

✓ European Program in Pharmacovigilance and Pharmacoepidemiology (EU2P)

✓ Pharmaceutical Medicines Training Program (PharmaTrain)

✓ European Modular education and Training Program in Safety Sciences and Medicines (SafeSciMET)
Database on over 700 master courses, 110 professional development courses, 380 learning tools

IMI Metrics Report – scientific outputs

	Nr.
New biomarker candidates (identified, or currently considered, or under validation)	**324**
New animal models (developed or standardized)	**53**
New in vitro models	**102**
New In silico models	**102**
New drug targets (identified, or currently considered, or under validation)	**21**
New tools to facilitate drug development (diagnostics, imaging)	**17**
Samples collected	**32676**
Clinical trials (completed or on-going)	**61**
Patients enrolled	**18083**
Data points pooled, curated, linked	**450 024 567**
People trained (industrial internships, personnel exchanges, E&T courses attendees)	**641**
Patents awarded/in preparation	**1/5**

New IMI Calls

CALL 9

Innovative Medicines Initiative

- Launched on July 9th (yesterday)
- Proposal submission: beginning of October!

WEBAE – Leveraging Emerging Technologies for Pharmacovigilance
Developing Innovative Therapeutic Interventions Against Physical Frailty and Sarcopenia (ITI-PF&S) as a Prototype Geriatric Indication
ND4BB TOPIC 4: Driving re-investment in R&D and Responsible Use of Antibiotics
ND4BB TOPIC 5: Clinical development of antibacterial agents for Gram-negative antibiotic resistant pathogens

WEBAE – Leveraging Emerging Technologies for Pharmacovigilance (1)

Background:

• European Pharmacovigilance legislation has strengthened safety monitoring of human medicines in the EU

• EMA has a responsibility to develop, in cooperation with the Member States, web-based forms for adverse reaction reporting by patients and healthcare professionals

• Emerging communication technology is changing the way people interact with their healthcare providers and products. Large body of health care data is being generated in social media

• The value of such data is not fully established

•Mining and analysis of social media is an emerging science

WEBAE – Leveraging Emerging Technologies for Pharmacovigilance (2)

Main Deliverables:

- An open platform for gathering content from different web sources in real time and organizing such content in a format suitable to analysis

- A series of algorithms that are coupled to the data gathering platform and enable the extraction and identification of Adverse Drug Reactions

- A series of algorithms and tools that are coupled to the data gathering platform and enable the provenance of data to be established across multiple social media source.

EFPIA participants: Novartis, Janssen, AstraZeneca, Sanofi, UCB
Duration: 3 years

Developing Innovative Therapeutic Interventions against Physical Frailty and Sarcopenia (ITI-PF&S) as a Prototype Geriatric Indication

Background

Physical frailty is a geriatric condition resulting from cumulative declines in multiple physiologic systems.

Sarcopenia is the loss of muscular mass and strength observed in older persons and is believed to be central to the development of frailty.

Currently there is no consensus on the definition of physical frailty and sarcopenia in older persons and there is also insufficient definition of the target population.

Innovative Medicines Initiative

Overall objectives

Generate real life data in older persons in order to determine/qualify:

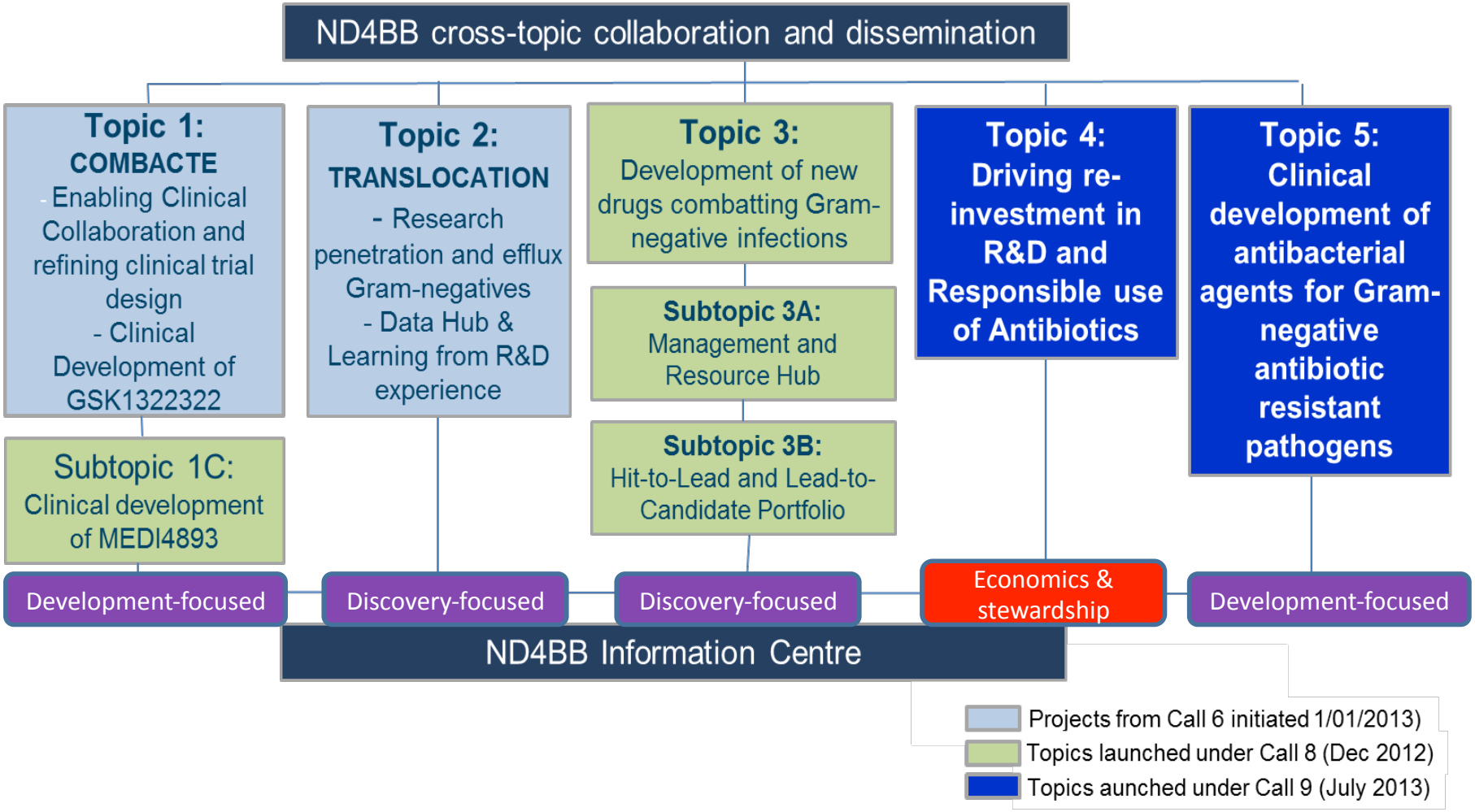
- Specific **at-risk populations**, specific therapeutic/preventative **targets** and related regulatory appraisal
- **Economic savings** in terms of public health costs
- Adapted study methodologies, including **biomarkers** and **functional endpoints**
- Adapted sustainable **clinical development** methodologies
- **Pharmaco-economic modelling** of the indication
- Delineate and agree with regulators the **regulatory framework** for a sustainable development of innovative geriatric indications

EFPIA participants: Sanofi, GSK, Novartis, Eli Lilly
Duration: 5 years

efpia

ND4BB* Overall Structure

July 2013



*ND4BB: New Drugs for Bad Bugs

ND4BB TOPIC 4 - Driving re-investment in R&D and Responsible Use of Antibiotics (1)

The ND4BB Topic 4 aims to develop options for a new **sustainable commercial model** that will ensure future R&D investment in antibacterials leading to new products to combat emerging resistance **while supporting the appropriate use of all antibiotics, both old and new**.

- There is a disconnect between the contribution that therapies to treat infection make to public health and the value attributed to antibiotics by public and payers.

- There is a misalignment of economic incentives: a pharmaceutical company aims to generate returns through sales volumes contrasted with the public health goals of minimising resistance by limiting use through antimicrobial stewardship initiatives.

ND4BB TOPIC 4 - Driving re-investment in R&D and Responsible Use of Antibiotics (2)

Objectives

- **Create a multi-disciplinary, multi-stakeholder community** with an in-depth comprehension of the complexities of antibacterial R&D and the challenges of the current model.
  - This group will meet serially over a 3-year period to review progress, commission new research, and update stakeholders
  - Involved: Public health, payors, HTAs, academic, Industry, patients

- **The multistakeholder community will conduct research** into the societal impact and cost of antibiotic resistance, and the predicted future cost to society now and into the future.

- The group will **define a research plan to define and explore alternative options**. The plan should address the need of multiple stakeholders, incentivise investment from the private sector, and provide a clear basis for action by policymakers.

- The group will **validate options through modelling** the effect on selected antibiotic case studies with recommendations for implementation. The plan will include metrics to use during implementation.

Duration : 3 years

ND4BB TOPIC 5 - Clinical development of antibacterial agents for Gram-negative antibiotic resistant pathogens (1)

Objectives

- **Create a multi-disciplinary, multi-stakeholder community** with an in-depth comprehension of the complexities of antibacterial R&D and the challenges of the current model.
  - This group will meet serially over a 3-year period to review progress, commission new research, and update stakeholders
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- **The multistakeholder community will conduct research** into the societal impact and cost of antibiotic resistance, and the predicted future cost to society now and into the future.

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- The group will **validate options through modelling** the effect on selected antibiotic case studies with recommendations for implementation. The plan will include metrics to use during implementation.

ND4BB Topic 5 - Clinical Development of antibacterial agents for Gram-negative antibiotic resistant pathogens (2)

Innovative Medicines Initiative

OVERALL OBJECTIVES

- Increase the efficiency of antibiotic R&D through analysing observational clinical and microbiological data sets and making recommendations for the development of novel antibiotic agents for MDR Gram-negative pathogens

- Understand the clinical management and outcomes of patients with serious hospitalised infections to validate our understanding of the clinical outcomes for patients in areas of emerging and endemic antibiotic resistance.

- Conduct prospective clinical trials with novel trial designs to deliver safety, pharmacology, and proof of efficacy data for a novel agents/combinations, in particular aztreonam-avibactam (ATM-AVI) directed towards treatment of infections due to priority pathogens.

efpia

ND4BB Topic 5 - Clinical Development of antibacterial agents for Gram-negative antibiotic resistant pathogens (2)

PART A – Conduct of observational clinical research to inform the design, conduct and interpretation of development programmes for antibacterial agents targeted MDR gram-negative bacteria.

PART B - Conduct of Clinical therapeutic studies to support the development of Aztreonam-Avibactam (ATM-AVI)

Intended applicant consortia are expected to apply for both PART A and PART B

HOW TO WRITE A SUCCESSFUL PROPOSAL

- Read carefully the rules for participation as well as the Topic text
- All the Topic objectives have to be addressed
- The size of the consortium should be adapted to the scientific goals
- When preparing your scientific plan check complementarities or potential overlaps with other projects ongoing in IMI or any other program
- if you have doubts contact IMI (infodesk or scientific officers)

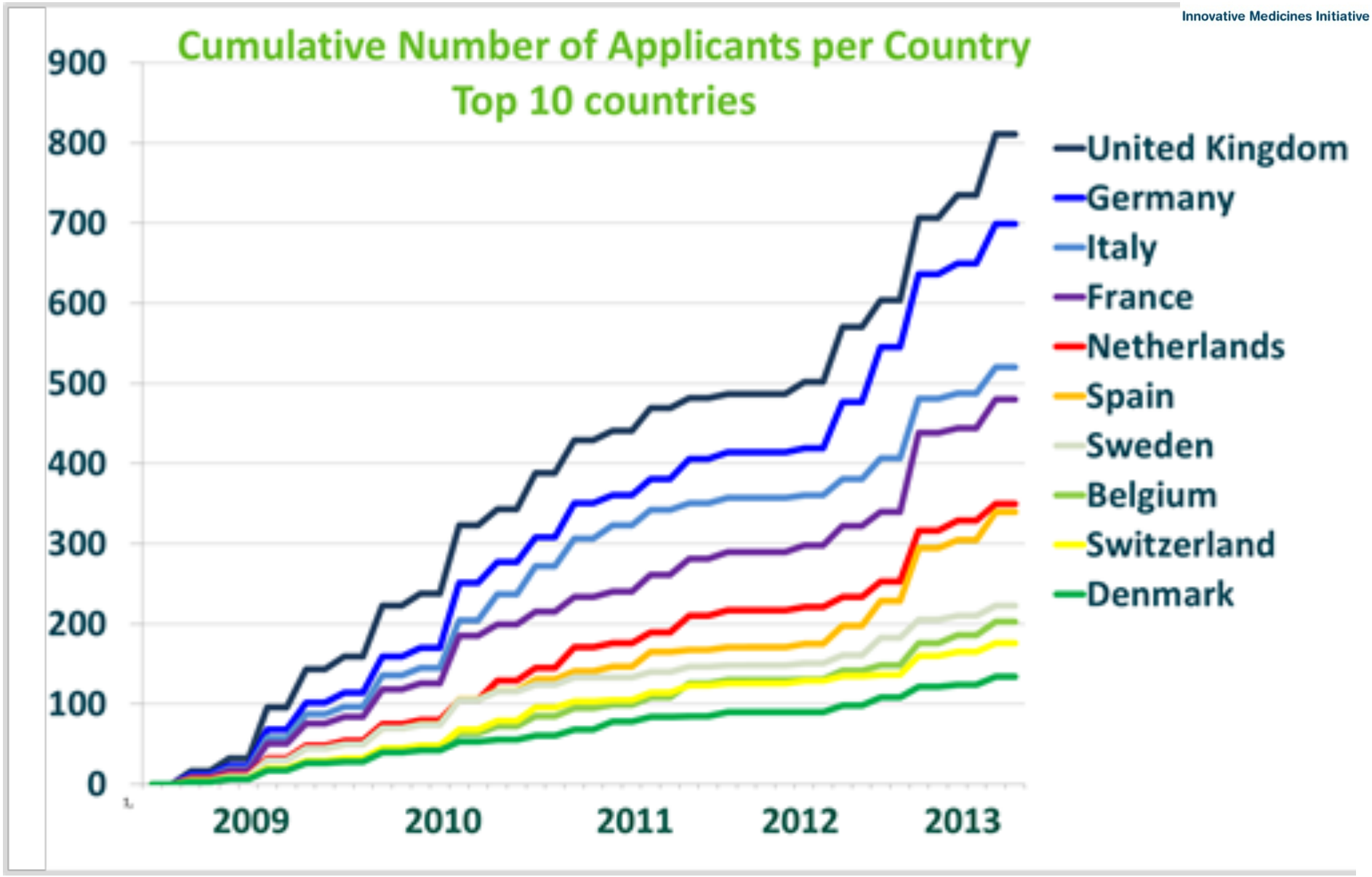
Potential future Calls

(under discussion within EFPIA)

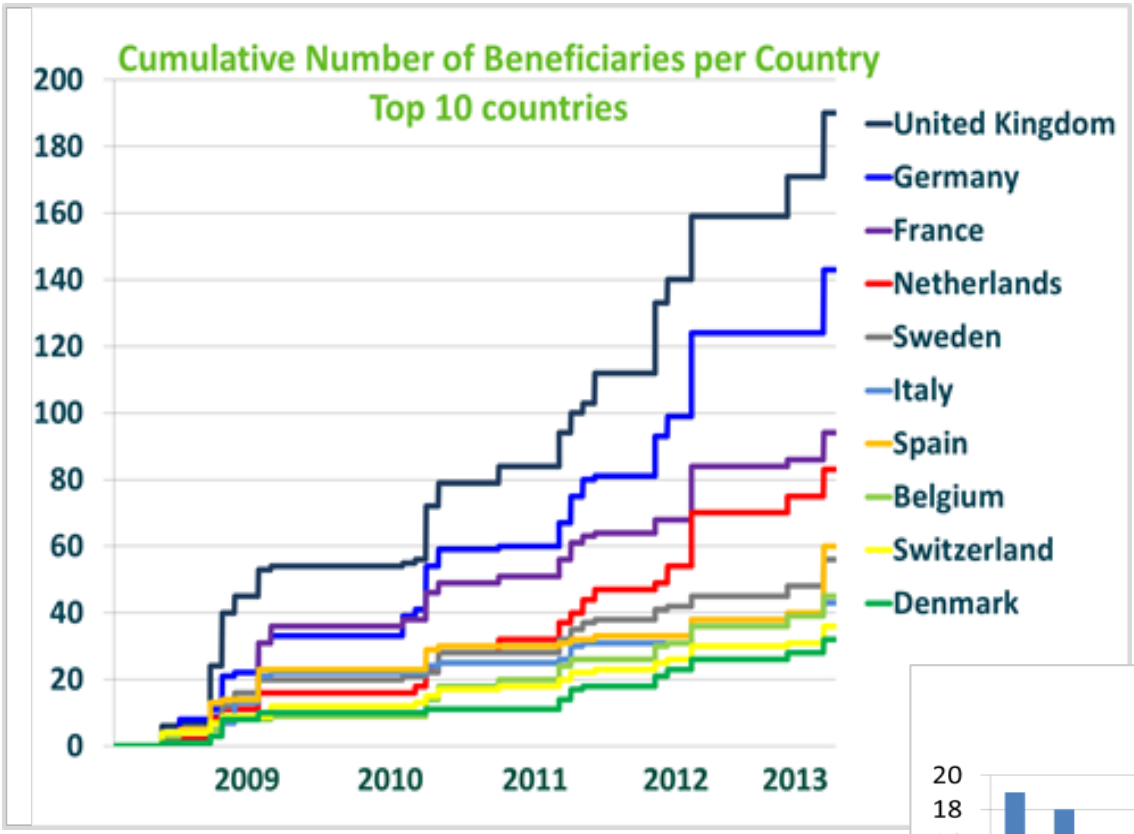
- A European genotype-phenotype repository

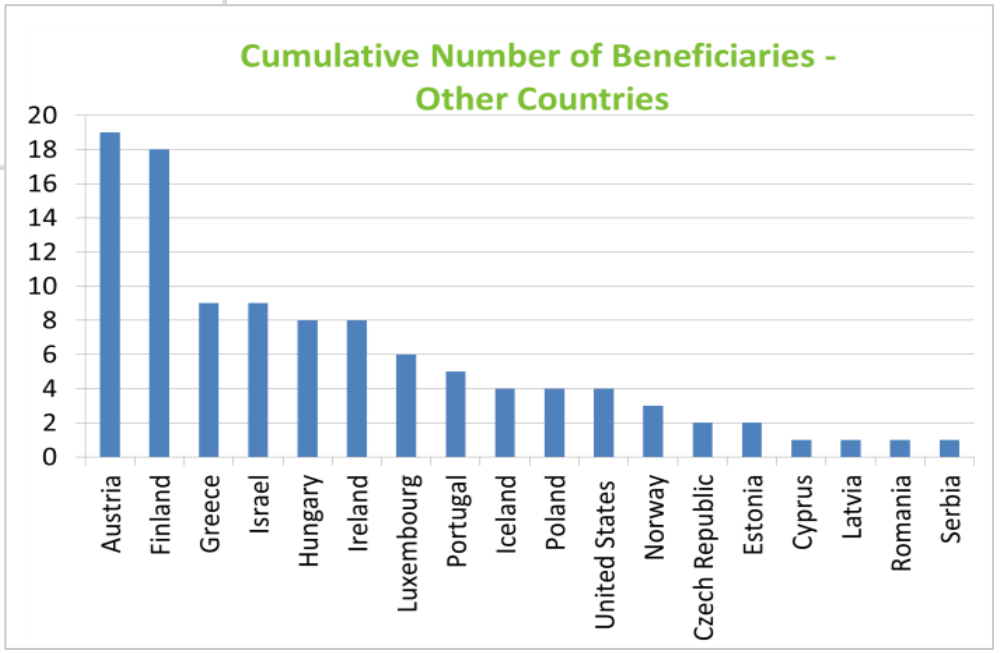
- Osteoathritis biomarker analysis to enable patient stratification and disease modifying experimental medicine clinical trials

IMI Metrics Report - applicants



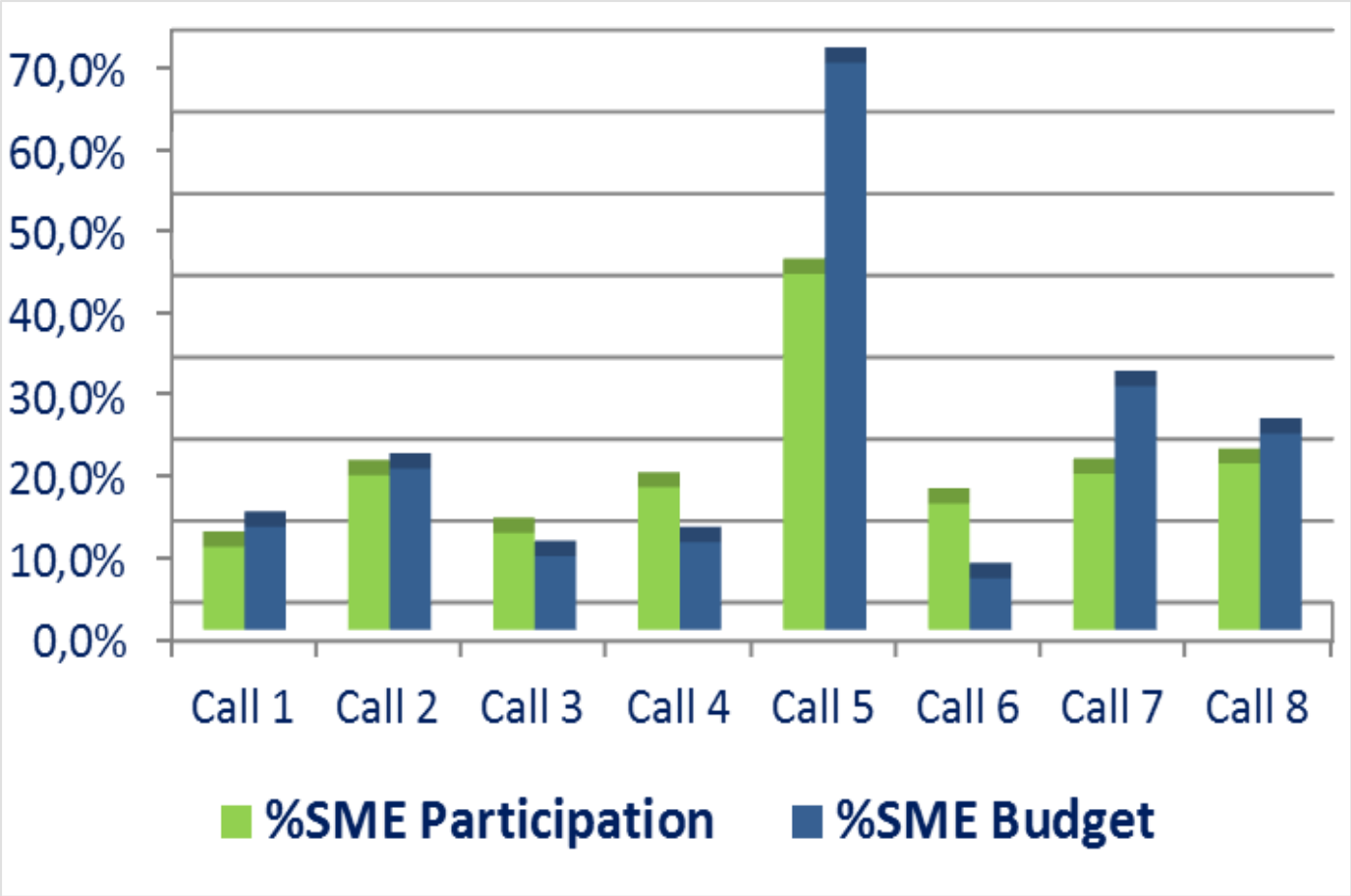
IMI Metrics Report - beneficiaries





IMI Metrics Report – SME's

15.9% of beneficiaries (=141) are SME's receiving
22.6% of IMI JU funding



Find project partners

- IMI InfoDay (check for date on IMI website)
- Use the **IMI Partner Search Tool** http://www.imi.europa.eu/content/partner-search
- Get in touch with your **local IMI contact point**: www.imi.europa.eu/content/states-representatives-groups
- Talk to your **FP7 Health National Contact Point** (NCP)

Keep up to date

- Sign up to the IMI **Newsletter**
- Follow us on Twitter: @IMI_JU
- Join the IMI group on LinkedIn
- For questions: infodesk@imi.europa.eu

www.imi.europa.eu

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Innovative Medicines Initiative

Thank you for your attention!