Innovative Medicines Initiative

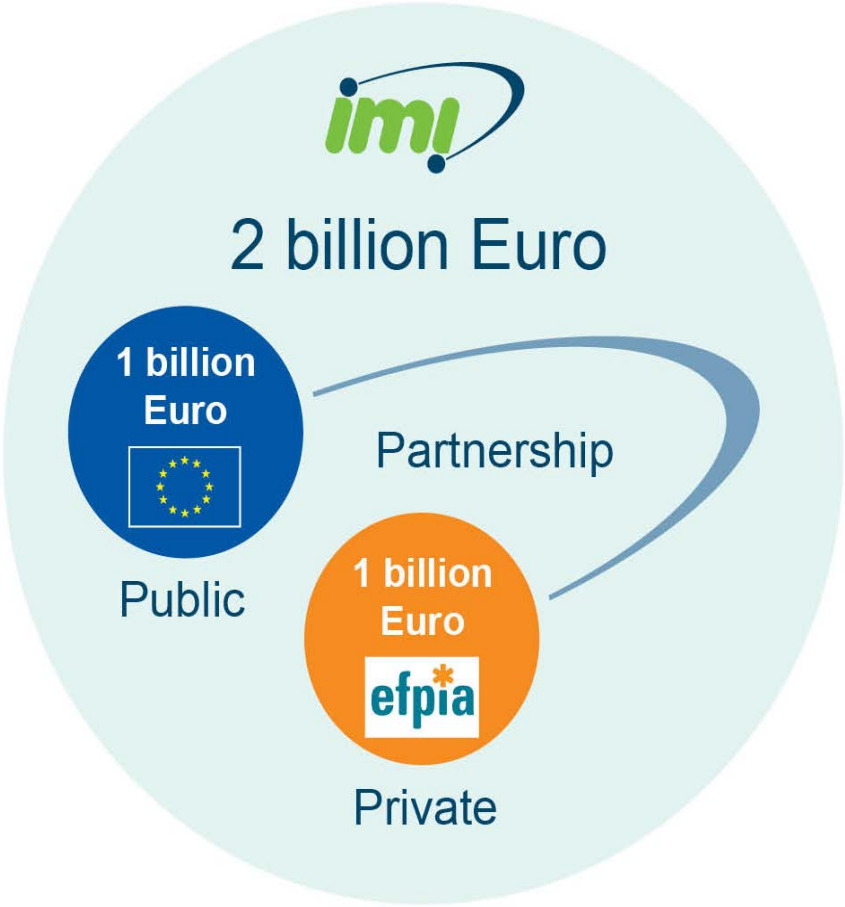
From IMI to IMI2

Hugh Laverty

Senior Scientific Project Manager

FitForHealth June 2014

Innovative Medicines Initiative:
Joining forces in the healthcare sector



The biggest public/private partnership in Life Science aiming to:

- Make drug R&D processes in Europe more **innovative** and **efficient**
- Enhance Europe's **competitiveness**
- Address key **societal challenges**

Features:

- 1:1 funding, joint decision making
- All EU funds go to SMEs, academia, patient organisations and regulatory agencies
- Large pharmaceutical industry, represented by EFPIA, contributes in-kind

How it works

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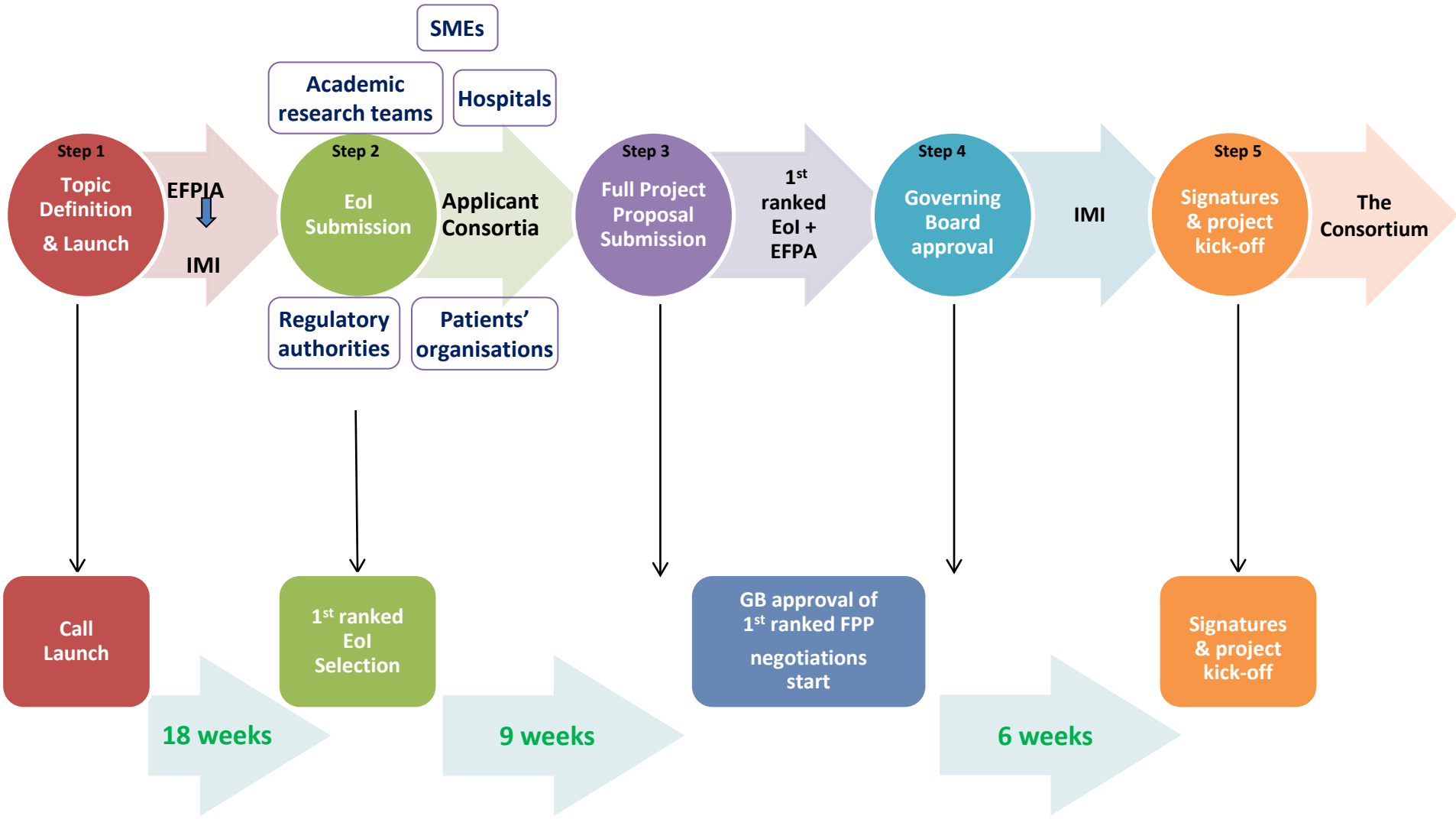

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The IMI community

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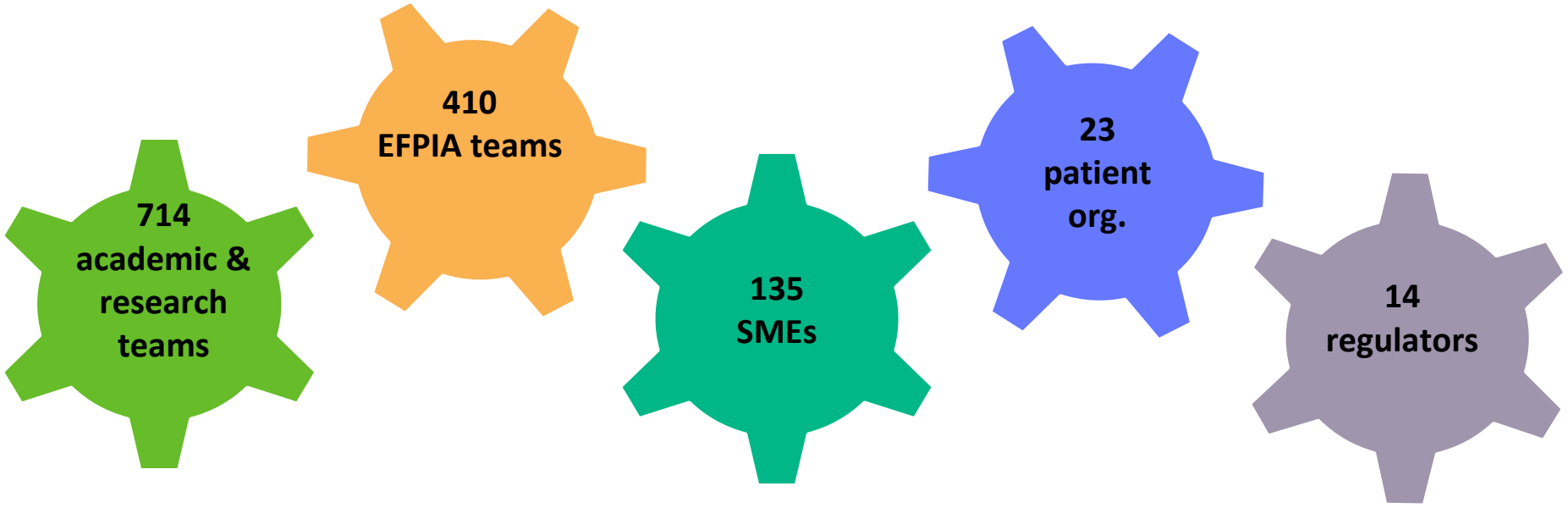
Calls 1-8 → **46 projects** → **> 6000 researchers**



61% of projects reported some form of **PATIENT INVOLVEMENT**

REGULATORS ON BOARD OF **12** PROJECTS

50% of projects have **REGULATORY AUTHORITIES** representatives in Scientific Advisory Boards

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The IMI portfolio

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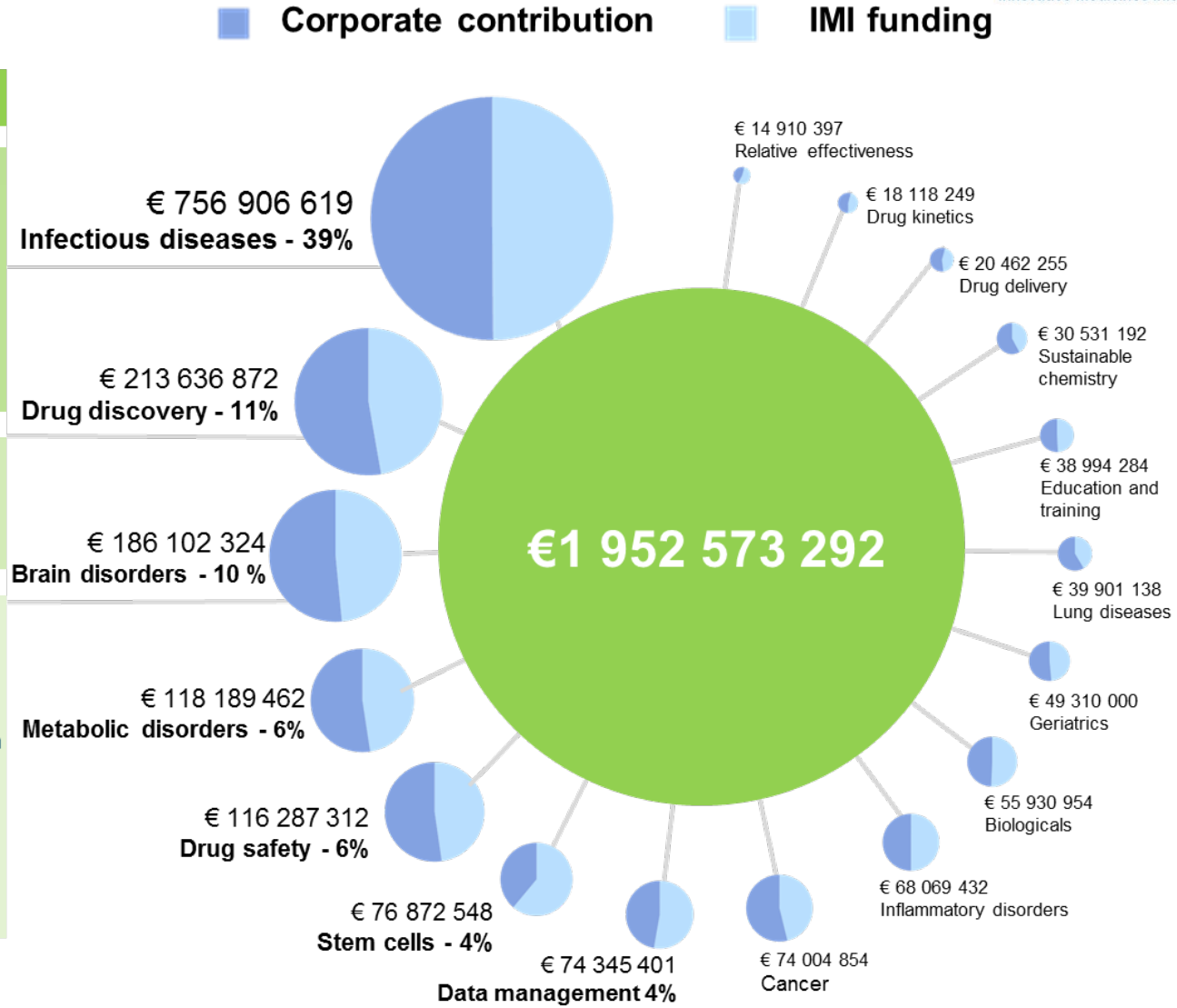
Partners

AiCuris	**Johnson&Johnson**
Animal Health	Medimmune
Division of Sanofi	**Merck**
Astellas	Merck Sharp
AstraZeneca	& Dohme Corp
Basilea	**Merial**
Boehringer Ingelheim	Novartis
Cubist	**Pfizer**
GSK	Rempex
Janssen	**Sanofi**

AstraZeneca	**Novartis**
Bayer	Pfizer
Janssen	**Sanofi**
Lundbeck	UCB
Merck	

Abbott	Janssen
AbbVie	**Lundbeck**
AC IMMUNE	Merck
Amgen	**Novartis**
Astellas	NOVO NORDISK
AstraZeneca	**Orion Corporation**
BIOGEN IDEC	Pfizer
Boehringer Ingelheim	**Roche**
Eisai	Sanofi
Eli Lilly	**SERVIER**
ESTEVE	UCB
Grunenthal	**Vifor**
GSK	



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IMI scientific output

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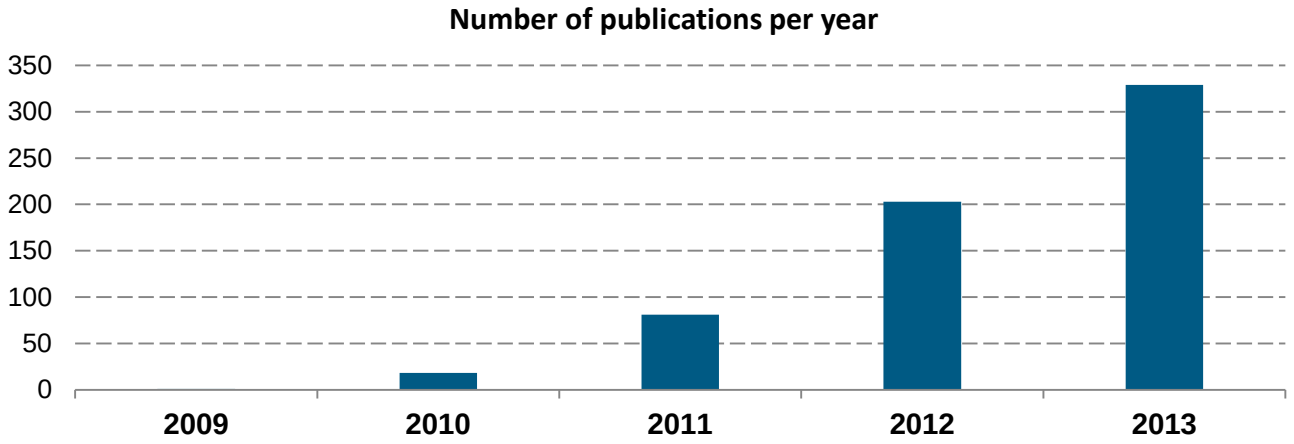
708	3709	2.04	19%
PUBLICATIONS	CITATIONS	CITATION IMPACT	HIGHLY CITED



Science AAAS

PLoS one www.plosone.org

nature

PNAS

JAMA® The Journal of the American Medical Association

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Making a difference

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Implementation of project results inside industry

Project	Area	Results description
IMIDIA	**diabetes**	The human beta cell line EndoC BetaH1 has been validated by Endocells and 3 pharma partners confirming their initial insulin secretion capacity. These cells have been **successfully transferred as a research tool for drug discovery to industrial partners.**
DDMORE	**knowledge management**	Several drug/disease models identified by DDMORE are **adopted or further developed inside the industry.**
eTRIKS	**knowledge management**	Adoption of the eTRIKS results, **TransMART system deployments in 5 pharmaceutical companies.**
EUROPAIN	**Chronic pain**	Preclinical model of spontaneous pain in rodents has been developed, standardized, validated, and is already **used for internal decision making in the drug development process**. The ultraviolet B (UVB) pain model has also started to be **used for in house R&D**.

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Impact on regulatory framework

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Project	Area	Results description
PROactive	COPD	**Qualification Advice completed** at the EMA
EU-AIMS	autism	Started EMA formal scientific advice procedure for **qualification of 5 biomarkers in ASD**
eTOX	drug safety	Provided an update on the eTOX database and the prediction system to the CHMP Safety Working Party (SWP) at EMA. **Scientific Advice Procedure was initiated**.
MARCAR	cancer	Has developed new biomarkers, technologies, and alternative test systems that help explain or predict animal and/or human carcinogenic pathways and mechanisms for non-genotoxic carcinogenesis. This will provide enhanced scientific rationale for Carcinogenicity Assessment Document (CAD) submissions, with **potential impact for ICH S1 carcinogenicity testing guideline revisions**.
Safe-T	drug safety	Developed and now **progressed towards an aligned EMA/FDA qualification** a set of novel safety biomarkers for drug-induced kidney, liver, and vascular injury.
DDMORE	knowledge management	In May 2012 an advisory meeting with EMA and FDA representatives was held. Through a Modelling Review Group , DDMoRe is in regular contact with both the EMA and FDA regarding the qualification of the content of the project's Model Library.

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IMI supports small and medium-sized enterprises engaged in drug innovation

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- Communication
- Meetings
- Website
- Advice

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SME participation in IMI projects (up to 8th Call)

Total IMI commitment	€ 723 million
Total received by SMEs	€ 133 million
% SME	18.4%
Total IMI participations	886
Total SME participations	135
% SME	15%

SME success stories

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SME involved in **SAFE-T** project
"Thanks to IMI our company went from **6 to 50 employees.**
Now we are ready to go to further expand."

SME involved in **IMIDIA** project –
"1st product released to the market in 2013 – **IMI was instrumental in validation of the first cell line product**, 2nd product release planned this year, 3rd diagnostic product in development.

In preparation: **a new patent filing** to protect technologies for the creation of third generation human beta cell lines.

SME involved in **PharmaCog** project
"We are developing a blood panel for AD for diagnosis, stratification and companion diagnostics in AD. **The Panel was tested on 300 patients in IMI project**"

SME involved in **eTOX** project
"We have developed in silico models for predicting toxicity, which were validated by pharmas in eTOX. Now **we have signed a contract with one of the companies to use our models in house**."

Promoting patient involvement

- ✓ IMI makes efforts to enhance **patient centric approach**
  - **Patient dedicated workshops**
  - Involving **patients at all levels**
  - Providing **forum for discussion**
- ✓ IMI best practice examples:

EUPATI

U-BIOPRED

PROactive

For patient-centric R&D more trained patients are needed

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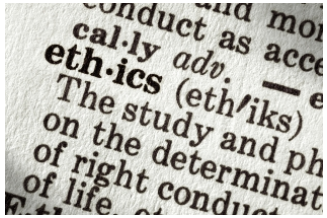
Public

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH
BfArM
MHRA
swissmedic

Competent authorities

Policy makers

Trial protocol design, informed consent, ethical review, marketing authorization, value assessment, health policy



Research Ethics Committees

HTA agencies & committees

Clinical Research

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EUPATI
European Patients' Academy on Therapeutic Innovation

Paradigm shift in empowering patients on medicines R&D

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Key European initiative to provide **objective, credible, correct and up-to-date public knowledge about medical research**

Will **build competencies & expert capacity** among patients & public

Will **facilitate patient involvement in R&D** to collaborate in academic research, industry research, authorities and ethics committees

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Collaboration

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Key collaborative activity areas:

Diabetes, CNS disorders, Tuberculosis, Patient Reported Outcomes, Cancer, Preclinical Safety and Education & Training.

IMI projects have signed

14

MEMORANDA of UNDERSTANDING

with other international consortia

IMI signed horizontal agreements with:

Critical Path, **Juvenile Diabetes Research Foundation** as well as with **Clinical Data Interchange Standards Consortium**.

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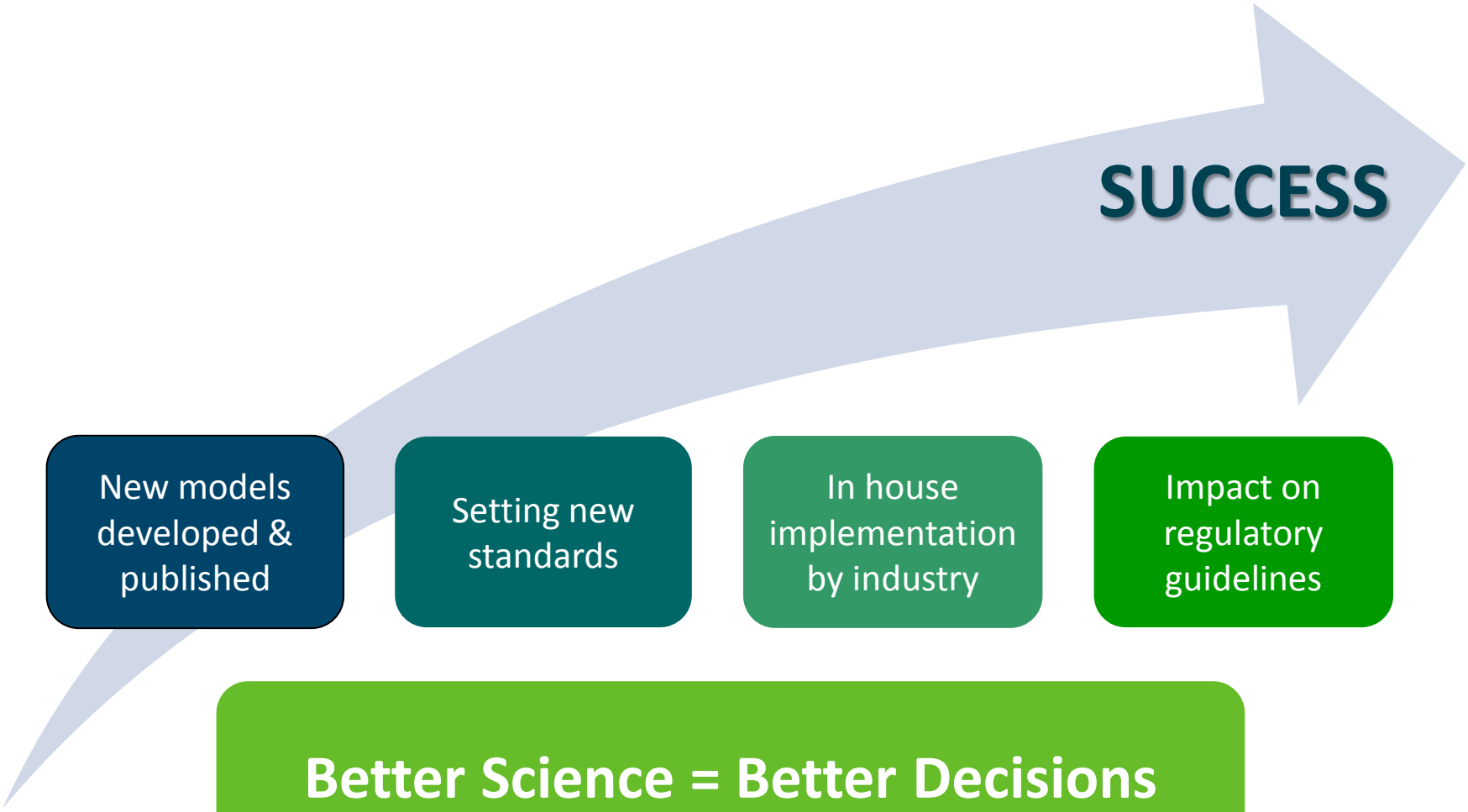
The measures of success



Towards IMI2

The Evolution of IMI: From bottlenecks in industry – to bottlenecks in Industry and Society

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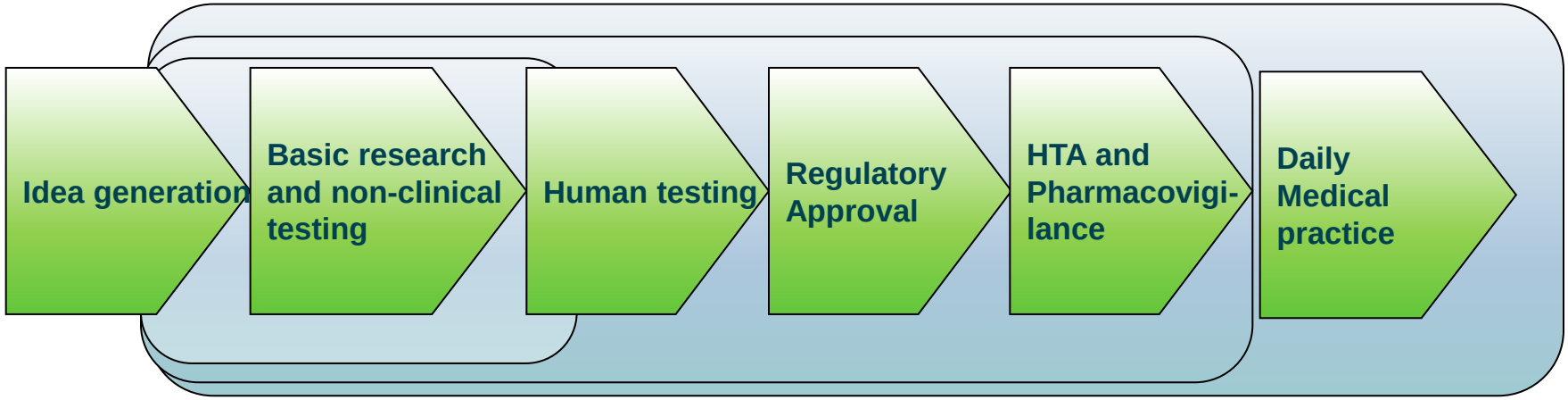
Make Drug R&D processes in Europe more efficient and effective and enhance Europe's competitiveness in the Pharma sector



Primary focus of early IMI calls 2007 SRA

Shift to also addressing challenges in in society and healthcare 2011 SRA

IMI 2 includes real life medical practice 2013 SRA

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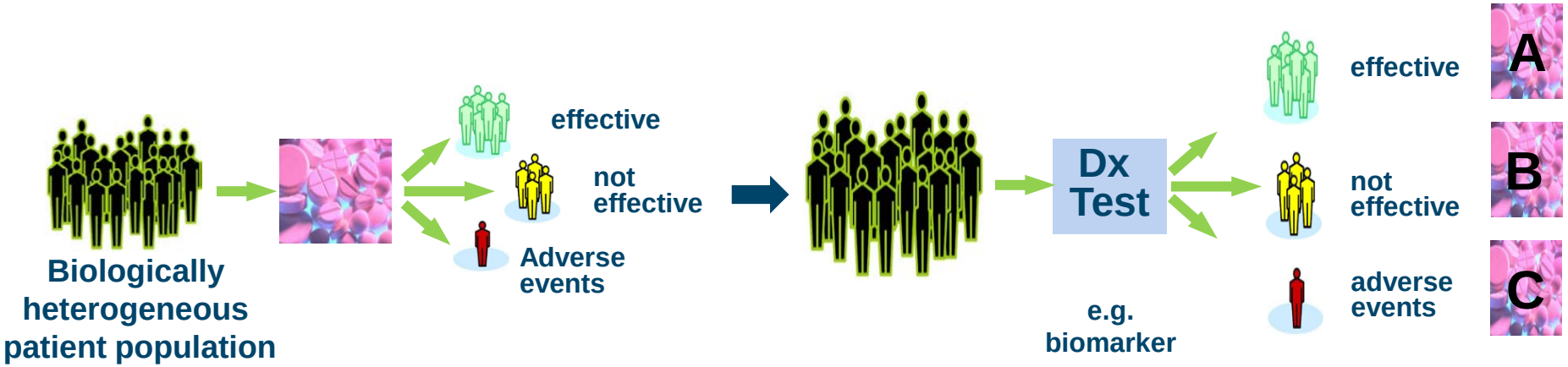
The Vision for IMI2 – The right prevention and treatment for the right patient at the right time



Trial and Error vs **Information based treatment decisions**

*Graphic adapted from C. Carini, C. Fratazzi, Eur. Pharm. Rev. **2008**, 2, 39-45*

Objectives of IMI2 – what the Regulation says

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- increase the success rate in clinical trials
- where possible, reduce the time to reach clinical proof of concept in medicine development
- develop new therapies for diseases for which there is a high unmet need and limited market incentives
- develop diagnostic and treatment biomarkers for diseases clearly linked to clinical relevance and approved by regulators;
- reduce the failure rate of vaccine candidates in phase III clinical trials through new biomarkers for initial efficacy and safety checks;
- provide support for the development of tools, standards and approaches to assess efficacy, safety and quality of regulated health products.

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The premises

- Alignment with **Horizon 2020** objectives of the Health challenge
- Addressing healthcare priorities identified by the WHO 2013 report on priority medicines for Europe and the world
- Strategic Research Agenda aimed at progressing the vision of personalised medicines, for both prevention and treatment
- Collaboration across sectors to harness all knowledge and technologies which can contribute to IMI2 vision - diagnostics, imaging, IT, medical devices, …

Strategic Research Agenda

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Comprehensive framework for a 10-year programme

Prepared with input from 80+ organisations (internet and targeted)

Project ideas from industry and third parties will be screened against it

http://goo.gl/jqMP9g

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IMI2 - Broad participation to be able to set ambitious goals

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IMI is evolving, with a stronger focus on the needs of patients and society and with simpler rules and procedures

Evolution in scientific focus

- Stronger focus on needs of patients and society, including unmet needs
- Increased emphasis on improving patient access to innovative medicines (in addition to medicines development)
- Focus on personalised medicine (**the right treatment for the right patient at the right time**)

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IMI2 - Broad Participation to achieve ambitious goals:

Bigger budget: 3,45 Billion Euro, equally shared by EU and industry

- **Not limited to EFPIA members**: open for other industries / companies, which can contribute to the PPP goals (Healthcare IT, medical devices,…) giving them the opportunity to establish their own projects
- The principle of large companies providing an inkind contribution matched by IMI funding for public beneficiaries will be retained.

IMI2 - Broad Participation to achieve ambitious goals:

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Specified Budget: 225 million Euros reserved for non-EFPIA led projects (to be matched by inkind contributions)

- Objectives, deliverables and timelines determined by the company(ies) proposing the project
- Inkind contribution determined by the company(ies)
- Once approved by IMI's Governing Board the Programme Office will launch a call for proposals to identify public partners for the project
- The call process and review of submitted proposals will be independent of the company(ies)

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IMI2: the first call

- Two topics are under consideration:
  - **Translational approaches to disease modifying therapy of type 1 diabetes mellitus (T1DM)**
  - **Discovery and validation of novel endpoints in dry age-related macular degeneration and diabetic retinopathy**
- Webinars will be organised immediately after the Call is officially launched: **9th July 2014**
- IMI is also planning an Open Info Day in September, with topic workshops presented by EFPIA

IMI2 indicative call topic: Discovery and validation of novel endpoints in retinal diseases

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Project Background:

- Retinal diseases are among the leading causes of blindness worldwide
- While substantial progress has been made in the treatment of neovascular age-related macular degeneration (neovascular AMD) and diabetic macular edema (DME), for other common retinal conditions such as the dry form of AMD (dry AMD) or diabetic retinopathy (DR) beyond DME, treatment options remain limited
- One major development hurdle is the lack of suitable endpoints for investigating these conditions in early exploratory and pivotal trials

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IMI2 indicative call topic: Discovery and validation of novel endpoints in retinal diseases

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Objective:

To evaluate novel endpoint candidates for retinal diseases (dry AMD and DR). The evaluation should cover the technical, medical and the health economic appropriateness of a method and bridge pre-clinical and clinical studies. The following methods are in scope:

- Visual function testing beyond BCVA
- Electrophysiology
- Imaging methods to assess retinal structure
- Patient reported outcome tools and QoL-related endpoints
- A combination of the aforementioned methods.

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IMI2 indicative call topic: Discovery and validation of novel endpoints in retinal diseases

Key deliverables of the full project

- Generation of robust data from retrospective and/or prospective studies serving as basis for discussion of regulatory acceptability of endpoints for future clinical programs.

- It is expected that the proposed research program delivers data on:
  - Technical evaluation of methods (validity, repeatability, reliability, interpretability, translatability and acceptability by patients).
  - Development of novel methods and tools.
  - Clinical validation of methods/tools in patient studies for dry AMD and DR.
  - Collection of biomarkers for selection of high risk populations.
  - Synergies between dry AMD and DR vs condition-specific aspects.

IMI2 indicative call topic: Translational approaches to disease modifying therapy of type 1 diabetes mellitus (T1DM)

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Facts

- Type 1 diabetes mellitus (T1DM) is a chronic disease affecting worldwide around 17 Million people.
- The incidence rate is highest in Europe affecting ~ 22 / 100.000 per year, with major regional differences.
- The incidence of childhood T1DM is reported to be rising rapidly worldwide, especially in the under 5 year old age group.

Diagnosis

- T1DM is typically characterized by hyperglycemia due to destruction and loss of beta cells & function over time. The earliest detectable change in biomarkers is the occurrence of one or several autoantibodies directed towards antigens of the endocrine pancreatic islets (GADA, ICA, IA-2, ZnT8). The disease T1DM is generally seen today as an autoimmune disease.
- The precise cause of type 1 diabetes is unknown and believed to be caused by one or more of the following: genetic susceptibility, diabetogenic trigger(s) and/or exposure to a driving antigen.

Therapy

- The disease is currently not preventable and no cure is available.
- The only available pharmacotherapy for T1DM patients is the lifelong injection of insulin.
- An alternative approach to subcutaneous insulin replacement therapy is pancreas or pancreatic islet cell transplantation. Both methods acquire immunosuppression and are time limited in their effectiveness.

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IMI2 indicative call topic: Translational approaches to disease modifying therapy of type 1 diabetes mellitus (T1DM)

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Objectives:

- Systematic retro- & prospective collection and characterization (broad "–Omics" approach) of human biological samples from children/ adolescents at risk of developing diabetes as well as early diagnosed T1DM patient cohorts undergoing standard glucose controlling therapy.
- Phenotypical characterization (in silico based on medical records as well as active through experimental medical studies).
- Establishment of systematic large-data repository enabling extensive cross functional data mining and integrated data analysis
- Development and characterization of the most appropriate preclinical T1DM animal model(s) for discovery of novel clinical therapies.
- Establish the opportunity to apply the newly acquired molecular knowledge to be verified for their human disease translatability

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Key deliverables of the full project

- Improved understanding of the heterogeneous disease T1DM in their immunological and beta cell biology aspects in children/adolescents at risk of developing diabetes as well as on early diagnosed T1DM patient cohorts undergoing standard glucose controlling therapy.
- Complex clinical & standardised molecular “real world data” obtained from T1DM patients and the application of novel bio-statistical methodologies will result in compositions of relevant endpoints & readouts for T1DM clinical trials.
- The pre-clinical T1DM models in their translational value will be improved.
- Improved understanding of the complex human T1DM disease offers the opportunity to test novel mono- and combination approaches in an optimised clinical trial setting.

IMI2: Call timings

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- Indicative call topic text is available on IMI's website: http://www.imi.europa.eu/content/future-topics
- Launch of first call: **9th July 2014**
- EoI submission: 12 November 2014
- 2nd Call: Nov - Dec 2014

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Questions?

Hugh.Laverty@imi.europa.eu

www.imi.europa.eu