Innovative Medicines Initiative

EMA - EBE Regulatory Conference on ATMPs
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Global Head Discovery & Investigative Safety/Global Head Preclinical Safety Therapeutic Areas
IMI accelerates innovation

Multiple companies join force where they would fail alone:
Identify missing or weak links in medicines pathways that hold progress
Combine (often) proprietary knowledge, data and assets
Open them up for challenge by and collaboration with public partners
Validate proposed solutions during project lifetime in R&D practice

- Solutions for diseases with high burden and cost for patients and society
- Solutions that challenge current business models and focus on value for patients and sustainable healthcare
- Tracking and addressing science gaps and inefficiencies from discovery to disease management
Essential features for research and policy agendas

- Public private partnership
  - Companies and public partners work together
  - Industry cost is not reimbursed: it is our in kind contribution
  - Public partners (including companies up to € 500 mio turnover) cost is reimbursed by EU: grants for collaborating with industry

- Industry defines the research agenda and projects (but does not chose with whom to work)
  - Beyond the publication: impact on research, regulatory and medical practice

- Managed by a neutral broker that allows participation of authorities and patients
The Innovative Medicines Initiative: the largest public-private partnership for health research worldwide

€5,276 billion

IMI1 €2 billion from 2008 – 2014
IMI2 €3,276 billion from 2014 - 2024

Part of the EU FP7 and Horizon 2020 R&D funding
1. What are the results?

2. From H2020

3. Public Partners + Private Partners = in IMI2 consortia

EFPIA direct and indirect members

1,638 Billion €

1,425
EFPIA direct and indirect members

213
Other sectors

CASH for grants for PUBLIC PARTNERS

1,638 Billion €

3,276 Billion €

2014 - 2024

Improve R&D

Speed up patient access

Improve outcomes & safety
Distribution of IMI funding per area

- Infectious diseases
- Drug discovery
- Brain disorders
- Metabolic disorders
- Stem cells
- Drug safety
- Cancer
- Data management
- Inflammatory disorders
- Biologicals
- Geriatrics
- Lung diseases
- Education & training
- Sustainable chemistry
- Drug delivery
- Drug kinetics
- Relative effectiveness
Major Axis of Research

Biomarker identification/validation (precision medicine)

Reclassification of disease by molecular means

Target Identification and validation (human biology)

Determinants of drug/vaccine safety and efficacy

Innovative drug delivery methodologies

Manufacturing for personalised medicines

Discovery and Development of novel preventative and therapeutic agents

Innovative clinical trial paradigms

European Health Priorities

Innovative medicines

Patient tailored adherence programmes

Innovative methodologies to evaluate treatment effect

Adoption of innovative clinical trial designs

Benefit/Risk Assessment

Healthcare delivery: focus on the treatment programmes not just the medicine

DRIVE CHANGE IN DELIVERY OF MEDICAL PRACTICE
End-to-End: Alzheimer’s Example

Aetiology Interventions and Modelling

EMIF-AD Characterisation and Modelling

EMIF
Legal and Ethical framework, Parent cohorts, fingerprinting, data browser

ROADMAP Outcomes definition and tracking
Patient access, healthcare systems

EPAD Trial and Modelling
Trial, Hypothesis validation

Pharma-Cog Biomarkers
Combination of tools to accurately measure disease progression

Knowlege base, novel hypotheses and biomarkers
End-to-End: R&D accelerator

- Target validation: ELF
  - Clinical trials Networks: EU-AIMS COMBACTE
  - Hit to Lead: Enable
  - Big Data: EMIF EHR4CR
  - Biomarker acceleration: SAFE-T
European Lead Factory

Rationale

Need

1. Access to **high-quality chemical library** for academics/SMEs to translate academic biological discoveries/targets into suitable chemical matter
2. Access to otherwise **unattainable chemical space** for pharma partners through compound sharing and synthesis of novel chemical libraries
3. Access **new biology from academia/biotech**

Aim

• **Provide starting points for lead discovery or high-quality pharmacological tools** both for academics/SMEs proposing targets and EFPIA companies.
• **Create partnering opportunities** for public partners and EFPIA companies to progress hits along the pharma value chain

Partnership Project Profile

- **Methods and Tools**
- **Direct Pipeline Impact**
- **Collaboration Indispensable**
- **Standardization and Regulatory Body Interaction**
- **Share Burden and Risk**

Funds

- **IMI funding**: € 80 Mio
- **Academia / Biotech cont.**: € 25 Mio
- **Pharma resources**: € 91 Mio

**TOTAL PROJECT COST**: € 196 Mio

**Duration**: 01.01.2013 – 31.12.2017
Boosting Drug Discovery

European Lead Factory

- Seven Pharma companies provided a high-quality cross-section of their in-house libraries.
- Chemistry consortium designs and synthesized Public Compound Collection (PCC).
- EFPIA contribution (>300,000 cpds)
- Public contribution (200,000 cpds by 2017)

Public targets through crowd-sourcing process

- 50% EFPIA targets
- 50% public targets

Total budget: € 196 million
European Lead Factory
Short and long-term benefits

Individual
Target owner
Chemical library designer

Small- to medium sized enterprise
Target owner
Chemical library designer
ELF partner

Academia
Target owner
Chemical library designer
ELF partner

Established pharmaceutical company
ELF partner
Target owner
Chemical compound provider
Cost contributions

Drug candidates/ Research tools
Start-ups
Publications & dissemination

Patents
Knowledge transfer

European Life Science Community

Public Health

European Lead Factory

Drug targets

Small molecules

Hit compounds

Collaborations

Business opportunities
European Lead Factory
What’s in it for the stakeholders?

### Output
- **Public target proposals**: 129
- **Accepted targets**: 73
- **Public screens completed**: 49
- **Qualified hit lists (QHLs)**: 43
- **Improved hit lists (IHLs)**: 12

### Capabilities
Access to a unique, unprecedented screening library, assay development, and state-of-the-art screening including hit validation capabilities.

### Progress
Public programme advanced to be developed within **NDiBB ENABLE** programme; a further project lead progressed as asset in **ScandiCure** start-up.

### Knowledge
Training and education activities increased public knowledge on early drug discovery; establishment of a network of scientists working in drug discovery across Europe; more than 40 publication in peer-reviewed journals.
The Big Data for Better Outcomes programme

Goal: Support the evolution towards outcomes-focused and sustainable healthcare systems, exploiting the opportunities offered by big and deep data sources

1. Design sets of standard outcomes and demonstrate value
2. Increase access to high quality outcomes data
3. Use data to improve value of HC delivery
4. Increase patient engagement through digital solutions

COORDINATION AND SUPPORT ACTION (CSA)

DISTRIBUTED DATA NETWORK

ROADS: ALZHEIMER’S DISEASE

HEMATOLOGIC MALIGNANCIES
CARDIOVASCULAR
PROSTATE CANCER
MULTI-DISEASE / MULTI-MORBID PATIENTS

Coordination and operational topics
Themes / Enablers
Disease-specific topics
HARMONY project

To improve outcomes in Hematologic Malignancies, we are teaming with leading institutions across Europe.

Largest funded project within IMI2

51 partners, including 44 public partners from 10 different EU countries

"IMI projects are best practice in the industry" – FDA representative
ATMPs

Key challenges and future IMI2 topics

Based on feedback from the IMI Stakeholder Forum on Advanced Therapies, **five potential IMI2 topics** are currently being considered:

- Precision Genome Editing (PGE)
- Clinical development and patient access
- Clinical development of cell therapies in cancer
- Manufacturing
- Immunogenicity

*Prioritised for development in 2017*
Scope
- Address gaps in our understanding of precision genome editing (PGE) biology, function and applicability.
- Increase confidence in the accuracy, safety and efficacy of the technologies for both research and therapeutic applications.

Examples of deliverables
- Novel characterization assays and tools for the quantification of on-target/ off-target effects, ie. New DNA analytic technologies or advanced ‘next generation sequencing’ (NGS) platforms.
- Optimization of existing PGE platforms - ie. Bioinformatic tools and design guidelines to increase target selectivity.
- Development of new pre-clinical cell/animal testing paradigms, ie: Develop and provide access to qualified reagents, platforms and data.
- Define the boundaries between the competitive and precompetitive space, through continued dialogue between researchers, manufacturers and platform development, throughout the programme.
Clinical development

**Scope**
- Framework for the data-enabled optimization of clinical trials for different types of ATMPs.
- Infrastructure and methodologies for the efficient utilization of existing and new registries and other data repositories.
- Enhance interoperability between databases and integration of data
- Update policies, processes and qualification pathways to assess clinical utility of existing data and new evidence requirements.

**Examples of deliverables**
- Technical capabilities around data source standards and interoperability.
- Quality standards, accuracy and regularity of data entry, reporting and analytics.
- Develop new data network architectures and links, as well as dataset query protocol designs, to avoid fragmentation.
- Increase built in flexibility to accommodate emerging knowledge and changing requirements.
- Address challenges in database sustainability
- Clarify status of patient level data protection, access controls and surveillance.
- Clinical trial registries could also expand to provide evidence in further support of HTA evaluations, focused on patient outcomes.
Patient access

**Scope**
- Capture the challenges across the pathway from the bench to the bedside, and across the different types of ATMPs.
- Clarify evidence requirements for a comprehensive assessment and commercialization framework.
- Allow sufficient flexibility to accommodate the pace of scientific progress.
- Secure the appropriate use of hospital exemption and leverage existing schemes, i.e. Orphan/rare disease funds.

**Examples of deliverables**
- Analysis of pipeline projects and commercial products, investment decisions etc.
- Identify success/failure drivers and key go/no-go decision factors across the product journey from R&D to the health systems (case studies).
- Devise analytical frameworks and performance indicators to compare EU countries, with US and other global competitors.
- Model/propose novel reimbursement and payment schemes.
- Tabulate the key HTA considerations and contrast with evidence for regulatory approvals and surveillance.
- Analyze case examples on hospital exemption across Member States.
- Identify and evaluate existing and propose new modelling methods and data tools (i.e. Registries) through specific projects and work streams.
How an overarching project could look like: Clinical Development of Cell Therapies in Cancer

**Scope**
- Address gaps in early financing of proof-of-concept studies.
- Improve comparability of clinical benefit of cell therapies in cancer.
- Enable combination therapy with checkpoint inhibitors and targeted therapies

**Examples of deliverables**
- Public-private partnership in pre-PoC stage to improve number and quality of clinically tested approaches.
- Early focus on demonstrating clinical benefit – alone or in combination with checkpoint inhibitors and targeted therapies- of cellular therapies.
- Search for biomarkers of activity and mode of action of cell therapies.
- Define and standardize production quality standards & specifications.
- Analyse feasibility of production on an adequate scale.
- Focus investigators on „affordability and profitability“.
- Use of historical and real-world evidence to compare outcomes in ATMP clinical trials.

Define the boundaries between the competitive and precompetitive space.
ATMP Manufacturing

**Scope**
- Technological innovation in cell therapy and gene therapy production, with specific attention to closed systems, automation and monitoring technologies.
- Particular emphasis on therapeutic scale production and GMP standards at reasonable cost, achieving regulatory compliance.

**Deliverables**
- Two main types of automation processes should be developed in order to address both conditions of optimal cell growth, namely for adherent cells in flasks and for cells in suspension or semi-suspension in bioreactors.
- Robotised technologies and controlled methodologies for cGMP banking of cell therapy products. Large-scale banking of clinical-grade cell therapy end-products requires increasing appropriately all safety measures and designing fully controlled procedures both for freezing and thawing.
- Addressing the question of a huge diversity of cell and gene therapy products.
- Quality controls and standards using the procedures of Quality by Design and Quality Risk Management (ICH paradigm used for chemical compounds production).
- Rules for continued engagement between scientists/manufacturers and regulators based on risk assessment along the programme.
Immunogenicity

Scope

- Immunogenicity of different types of allogeneic cell sources.
- Impact of the disease on the immune responses.
- Impact of the route and schedule of cell administration.
- Clinical investigation of immune responses and their impact on safety and efficacy of the ATMP.

Deliverables

- Understanding the innate and adaptive immune responses against different allogeneic cell types.
- Insight in the intensity, specificity, kinetics, and persistence of such immune responses.
- Dynamics of memory responses upon repeated administration.
- Understanding the influence of given pathologies on the anti-cell immune responses.
- Clinical assessment of the associated safety aspects.
- Clinical assessment of the impact of immune responses on ATMP efficacy.
- Knowledge of the impact of HLA matching and mismatching on safety/efficacy.
Conclusion

- IMI is delivering
- This is a true partnership, where companies, public partners and SMEs work together
- There is an opportunity to transform the ATMP landscape