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Institut de Recerca

Iniciativas internacionales para el fomento de la cooperación en investigación clínica

European Advanced Translational Research Infrastructure - EATRIS

Fátima Núñez
Institut de Recerca Hospital Universitari Vall d'Hebron
05/03/2014

The European landscape

- 2002: The European Strategy Forum Research Infrastructure (ESFRI) is formed at the mandate of the European Council to develop the scientific integration of Europe and to strengthen its international outreach

- 2006: First roadmap for pan-European research infrastructures. Updated in 2008 and 2010

The European landscape

Status as reported by the implementation group to the ESFRI forum in 2012:

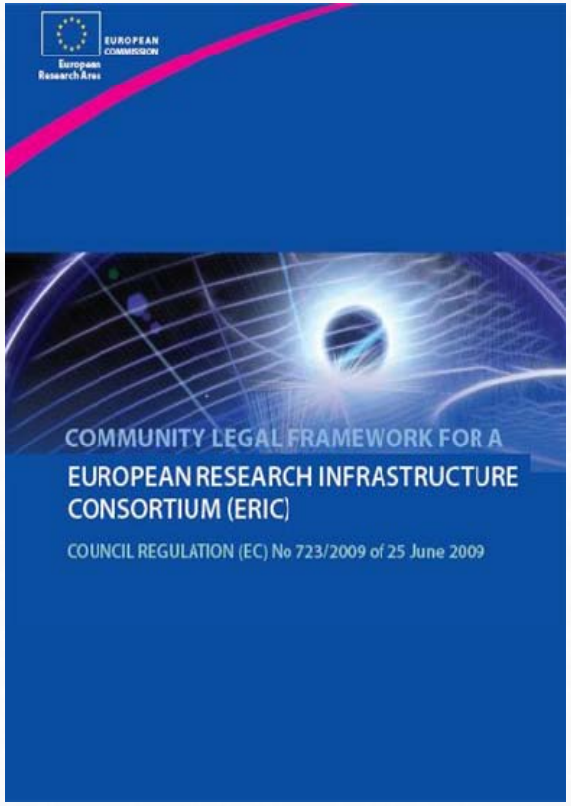
- 48 ESFRI projects in various areas:
  - Social Sciences and Humanities
  - Environmental Sciences
  - Energy
  - Health and Food Domain
  - Material and Analytical facilities
  - Physical Sciences and Engineering

http://ec.europa.eu/research/infrastructures/pdf/esfri_implementation_report_2012.pdf#view=fit&pagemode=none

EATRIS Short History

- 2008-2010: EATRIS is awarded and goes through the Preparatory Phase
- 2011-2013: apply for the ERIC legal status and prepare operations sustained by 8 member states
- July 2012: Application for the ERIC status

2013 EATRIS-ERIC
European Research Infrastructure Consortium



- Legal form - directly applicable across EU
- Independent & non-commercial
- Long term commitment of member governments

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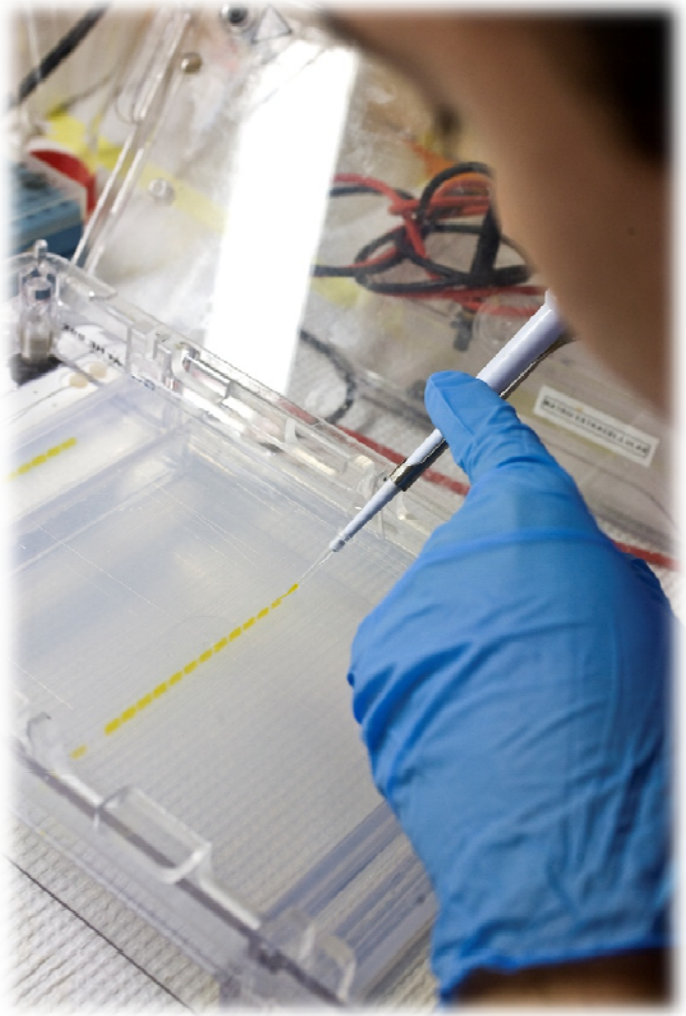
Current status



- ERIC status achieved
- Operations ready
- Infrastructure database ready, expert database in development
- Pilot projects in preparation

➢ Open to innovative industry partners for sustainable collaboration

EATRIS: Positioning

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European Advanced Translational Research InfraStructure in Medicine

Vision

Making translation of scientific discoveries into medical products more effective to improve human health and quality of life.

Mission

To support our clients in developing their biomedical discoveries for novel preventive, diagnostic or therapeutic products up to clinical proof of concept.

EATRIS
European Infrastructure for Translational Medicine

Supporting academia, funders, SME & biotech/pharma

EATRIS: Members

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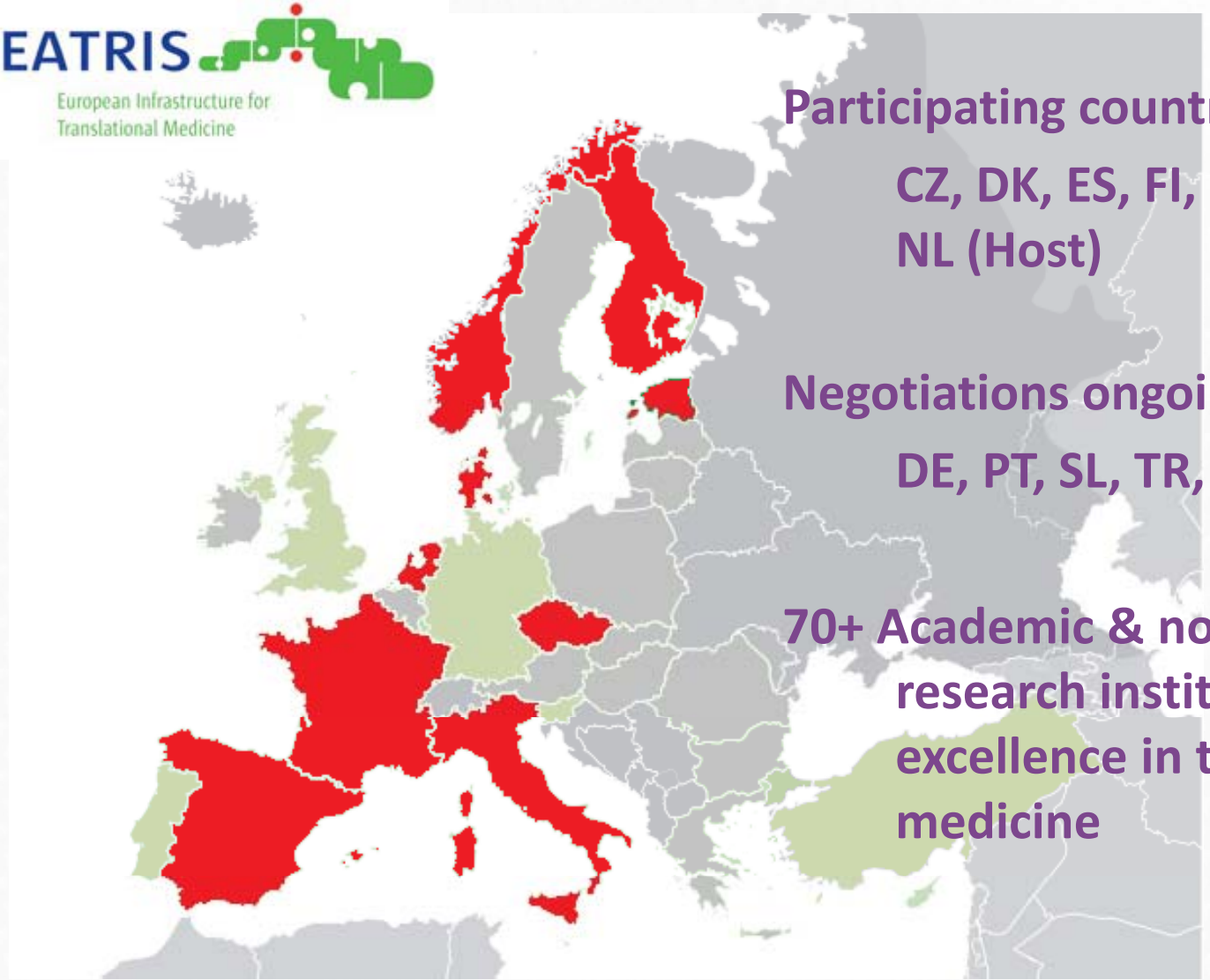

Participating countries :

CZ, DK, ES, FI, FR, IT, NO, EE, NL (Host)

Negotiations ongoing with:

DE, PT, SL, TR, UK

70+ Academic & non-profit research institutions of excellence in translational medicine

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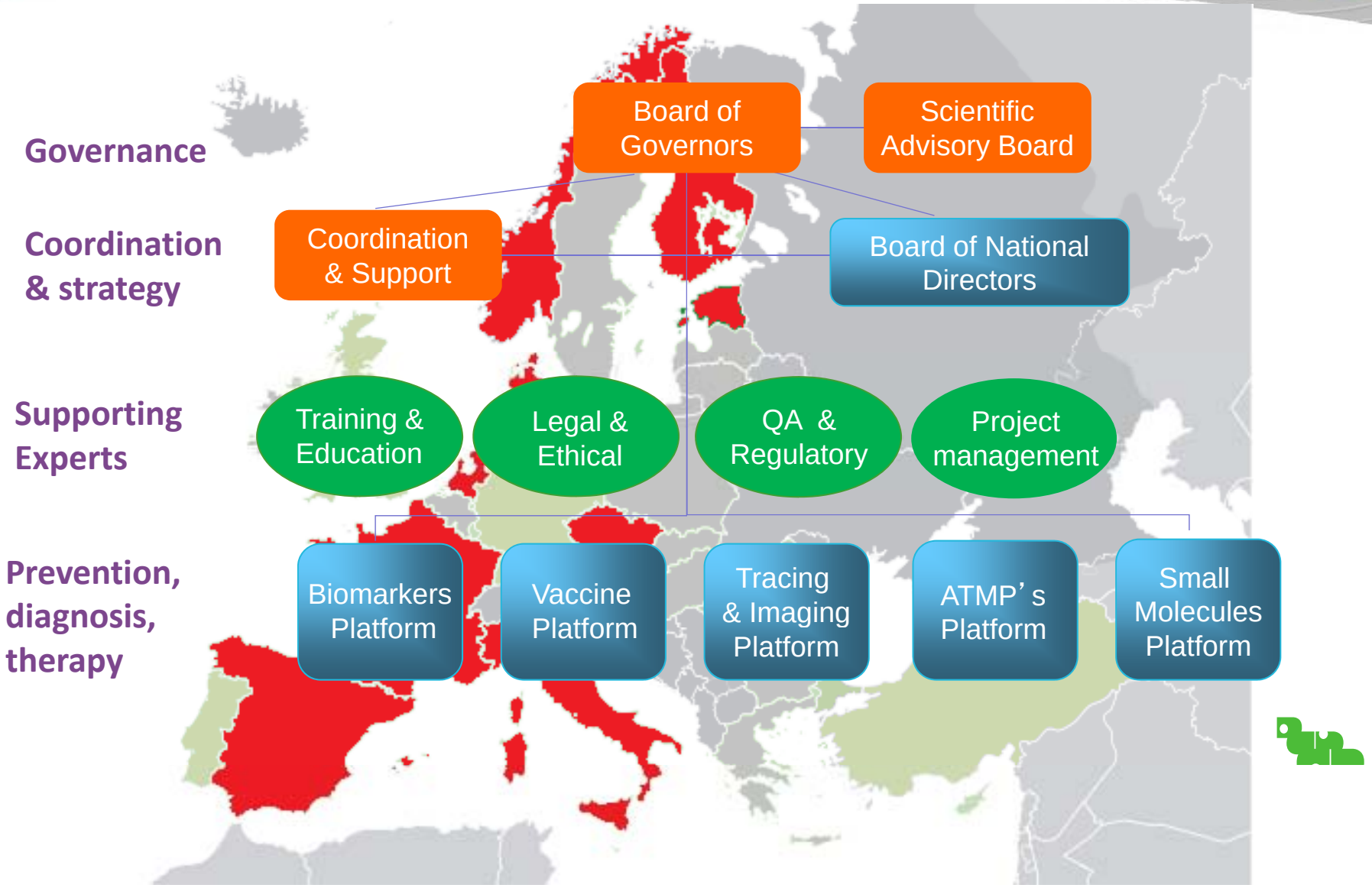
EATRIS: Governance and Structure



EATRIS-PLATFORMS-ATMPs
Advanced Therapy Medicinal Products

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Filippo Belardelli, ISS

- 20 State-of-the-art centres
- Cutting-edge technologies:
- Specialised GMP facilities
- Imaging facilities for *in vivo* animal studies
- Tailored animal models
- Clinical expertise and access to patients

➢ Supports from discovery to clinical proof of concept for novel ATMP

➢ Offers the entire spectrum of high-end research infrastructures and patient cohorts

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EATRIS-PLATFORMS-Biomarkers

Olli Kallioniemi, FIMM

- 27 European advanced biomarker development centres
- State-of-the-art technologies and expertise
  - Biobanks
  - Assay development and validation
  - Multi-centre clinical trials
  - Medical data & clinical experts

- Facilitates the validation and development of biomarkers for the prevention, diagnosis and prognostic assessment of disease

- Facilitates the validation and development of biomarkers for the prediction of therapy response and precision medicine

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EATRIS-PLATFORMS-Imaging and tracing

Guus van Dongen, VUmc

- 25 World class European centres
- Cover the entire scope of tracer development and molecular imaging
- Manufacturing of disease specific tracers and radiolabeled drugs
- High-end imaging techniques (PET/MRI, PET/CT…)
- Multi-centre clinical trials
- Images analysis

- Enhances prediction of efficacy of new drug compounds at an early stage and reduce development time

- Helps to understand critical disease processes and patient selection

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EATRIS-PLATFORMS-Small molecules

Mario Salmona, Mario Negri

- 20 Leading European centres
- Compound screening with innovative cell based assays
- Tailored animal models
- Experts in pharmacology medicinal and analytical chemistry and toxicology
- Multi-centre clinical trials
- Patients materials and cohorts

- Supports the development of (orphan) drug candidates around novel innovative targets and molecular scaffolds

- Cross synergy with Imaging and Tracing and Biomarkers EATRIS platforms

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EATRIS-PLATFORMS-Vaccines

Jan Langermans, BPRC

- 12 European high-end facilities
- Antigen characterisation
- Specialised GMP manufacturing facilities covering USP and DSP; Formulation & adjuvantation
- Animal facilities up to BSL3
- Animal models including non-human primates and GLP-toxicology
- Immunomonitoring and clinical capacity

➢ Supports the translation of scientific discoveries into more effective novel novel preventive and therapeutic vaccine products

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The product platforms: Mapping of the infrastructure

Example: Imaging and Tracing

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IMAGING & TRACING PLATFORM SURVEY 2012	INSTITUTION:	Translational Bottleneck	The Italian NIH (ISS), Rome	Nuclear Physics Institute of the ASCR/UJF, Rez	Fondazione Giovanni Pascale (IRCCS, CROM), Napoli	August Pi i Sunyer Biomedical Research Institute (IDIBAP	Fondazione Giovanni Pascale (IRCCS) INT, Milan	Neuratris-CEA, Fontenay	UMCN, Nijmegen	UMCU, Utrecht	PET Center, Turku	UoC, Copenhagen	IR-HSCSP, Barcelona	Neuratris-IRU, Paris	Centre for Molecular Biology and Neuroscience (IMB, C	Norwegian University of Science and Technology (NTNU) Trondheim	IMTM, Olomouc	IMINET, Italy* (inlcuding UNIBO)	Neuratris - Mondor, C.Cedex	UoC, Frederickberg	MedViz, Haukeland Univ. Hospital	UMCG, Groningen	Neuratris-Bicetre	Hevesy
Draft Translational Pipeline	Country:	*	IT	CZ	IT	ES	IT	FR	NL	NL	FI	DK	ES	FR	NO	NO	CZ	IT	FR	DK	NO	NL	FR	DK	NL
Pre-clinical Imaging	Bioluminescence																								
	Fluorescence																								
	OCT																								
	DOT																								
	Photo-acoustics																								
	uCT																								
	MRI																								
	PET																								
	SPECT																								
	PET/MRI																								
	PET/CT																								
	Ultrasound																								
	MR Guided HIFU																								
Pre-clinical Radionuclide Production	15O																								
	13N																								
	11C																								
	18F																								
	124I/89Zr																								
	81Rb/81mKr																								
	Other radionuclides																								
Pre-clinical Tracer Production	Equipment (research)																								
	11C																								
	18F																								
	15O																								
	PET																								
	SPECT																								
	Optical																								
Animal facilities and disease models, surgeries and techniques	Small animal facility																								
	BSL 1/2																								
	BSL 3/4																								
	Mouse																								
	Rat																								
	Rabbit																								
	Large animal facility																								
	BSL 1/2																								
	BSL 3/4																								
	Non-human primate facility																								
	BSL 1/2																								
	BSL 3/4																								
Clinical Imaging	Kinetic modelling	*																							
	Optical-general	*																							
	Bioluminescence																								
	Fluorescence																								
	OCT																								
	DOT																								
	Photo-acoustics																								
	CT																								
	MRI	*																							
	PET	*																							

Partnering - greasing the wheels

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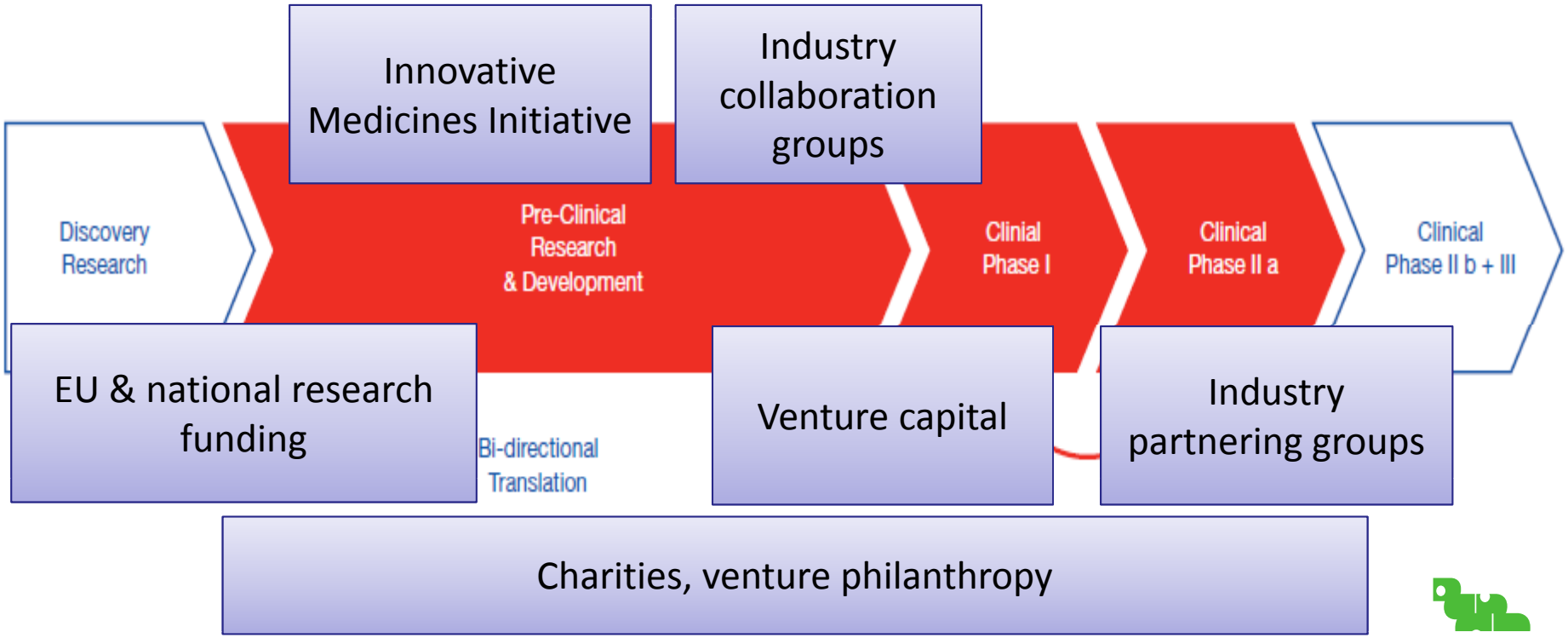
Structural collaboration with funders & industry for faster & more efficient development



EATRIS SPAIN: How?

On the 18th November 2013, Carmen Vela, Secretary of State for Research, Development and Innovation at the Ministerio de Economia y Competitividad in Spain, confirmed in a letter Spains' decision to ascend from Observer Membership to Full Membership of EATRIS-ERIC with a five year commitment.

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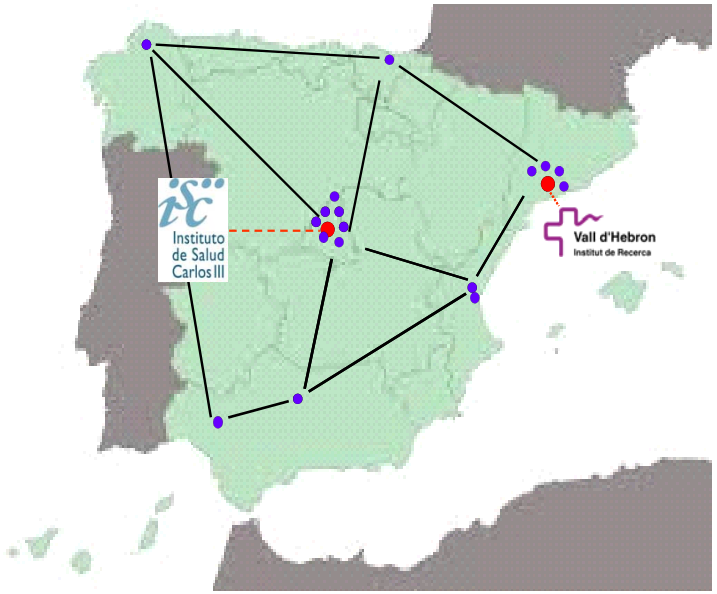
EATRIS SPAIN: Who?

EATRIS.ES is the Spanish mirror of EATRIS and represents the biggest EATRIS contribution…



Governmental Partner
Coordinating centre
Hospital of excelence-IIS

COORDINATOR: VHIR (Vall d'Hebron Institut de Recerca)

IDIBAPS (Institut d'Investigaciones Biomédicas August Pi y Sunyer

IBIS (Instituto de Biomedicina de Sevilla)

IDIBELL (Institut d'Investigació Biomédica de Bellvitge)

IGTP (Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol)

IIS LA FE (Fundación para la Investigación del Hospital Universitario la Fe)

IDIS (Instituto de Investigación Sanitaria de Santiago de Compostela)

IDIPAZ (Instituto de Investigación Sanitaria Hospital la Paz)

IIS-PRINCESA (Instituto de Investigación Sanitaria Hospital Universitario de la Princesa)

IISFJD (Instituto de Investigación Sanitaria Fundación Jiménez Díaz)

IIB SANT PAU (Instituto de Investigación Biomédico Sant Pau)

IRYCIS (Instituto Ramón y Cajal de Investigación Sanitaria)

i+12 (Instituto de Investigación Hospital 12 de Octubre)

INCLIVA (Instituto de Investigación Sanitaria Fundación para la investigación del Hospital Clínico de Valencia)

IMIBIC (Instituto Maimónides de Investigación Biomédica de Córdoba)

IIS BIODONOSTIA (Instituto de Investigación Sanitaria Biodonostia)

IiSGM (Instituto de Investigación Sanitaria Gregorio Marañón)

IdISSC (Instituto de Investigación Sanitaria del Hospital Clínico San Carlos)

IMIM (Institut Hospital del Mar d'Investigacions Mèdiques)

IBSAL (Instituto de Investigación Biomédica de Salamanca)

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EATRIS SPAIN: What's in it for the IISs?

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- Access to network of centres with proven track record in translational research
- Support in all aspects of translational research
- Way to offer our existing infrastructures to extensive network of clients (no need for upfront investment)
- Access to wider sources of funding
- Internationalisation: opportunity to increase our activity at an international level and to introduce our experts in international networks
- Visibility as an network of international prestige
- Opportunity for self-organisation and harmonisation

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EATRIS : What's in it for the clients?

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To make collaboration faster & less risky:

- 70 translational institutes under 1 framework agreement
  - Common IP policy
  - Harmonised quality framework
  - Standardised operational framework
  - Template agreements under development
- Faster time to contract, support in negotiating & IP
- One-on-one client/institute contract - no liability or IP issues
- Efficient links to complete innovation pathway

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Thank you for your attention.

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Translational Medicine

Backup

EATRIS: Governance and Structure

National support & embedding

Board of Governors - ultimate decision-making authority

- Composed of representatives from national governments/research councils, responsible for:
- Overall direction and supervision of EATRIS
- Appointing executive board (C&S)
- Establish bodies (e.g. Advisory board)

Board of National Directors - representing national EATRIS institutes

- Translational expert from country:
    - Appointed by governing body/research council
    - Not necessarily EATRIS Institution
    - Responsible for scientific strategy & overall coherence

EATRIS: Governance and Structure

EATRIS daily support

Coordination & Support (C&S) - day-to-day operations

Run by executive board – scientific director & finance director

- Implementation of strategies
- Assure short time lines to contracts
- Monitoring project milestones
- Keep database of EATRIS centers capabilities up-to-date
- Match project needs to infrastructure and expertise solutions
- Support the EATRIS community
- Facilitate collaboration between Institutions

EATRIS: the product platforms

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Composed of academic & non-profit research institutions

- **Active in biomedical translational research**
  - With track record in entering clinical development
  - With unique infrastructure, expertise and licenses
  - With access to broad array patient cohorts (also rare diseases)
  - Working to top quality level in harmonized manner

- **Working together to create a complete translational pipeline**
  - Via distributed infrastructure
  - Supported by C&S 'hub'

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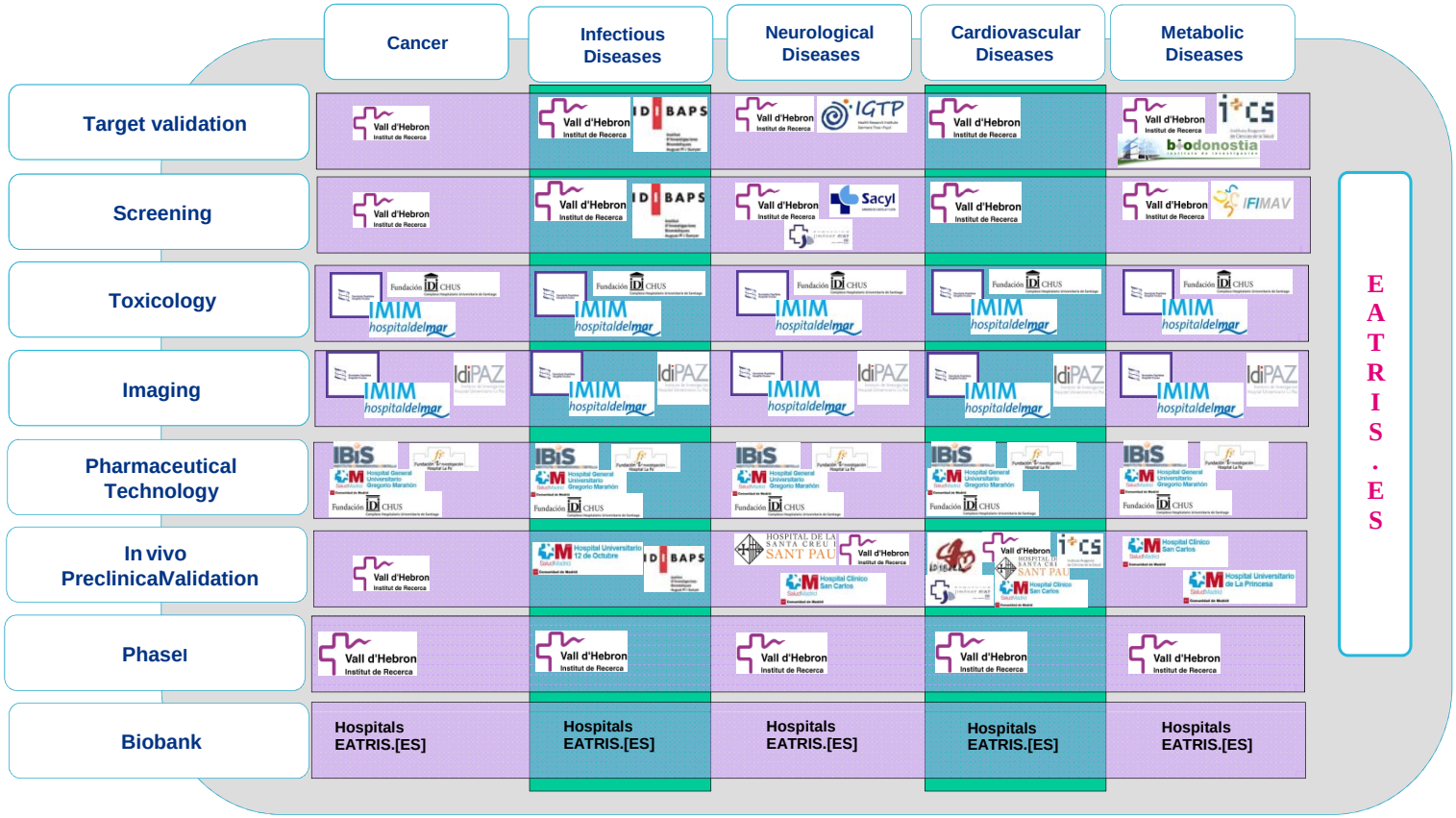
EATRIS SPAIN: Our capacities (work in progress)

…which in itself covers the key elements of the translational pipeline, providing coordinated access to infrastructures, biobanks, clinical trials and management skills.



Project initiation and implementation

1. Translational Assessment

- Core C&S activity
- Involve expert reviewers as needed
- Involve P.I. & his/her TTO

2. Matchmaking

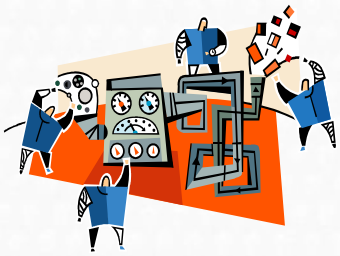
- Database identifies relevant infrastructure, disease knowledge and patient cohorts
- P.I. has lead in selecting partners

3. Exploration

- Institutes explore project with P.I.
- Project team assembled, including experts
- Product Development Plan created

4. Project implementation

- Define steps, milestones, budgets
- Draw up bilateral contracts - from template
- Start multi-step, multi-party international project



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Value Proposition: Facilitating efficient collaboration

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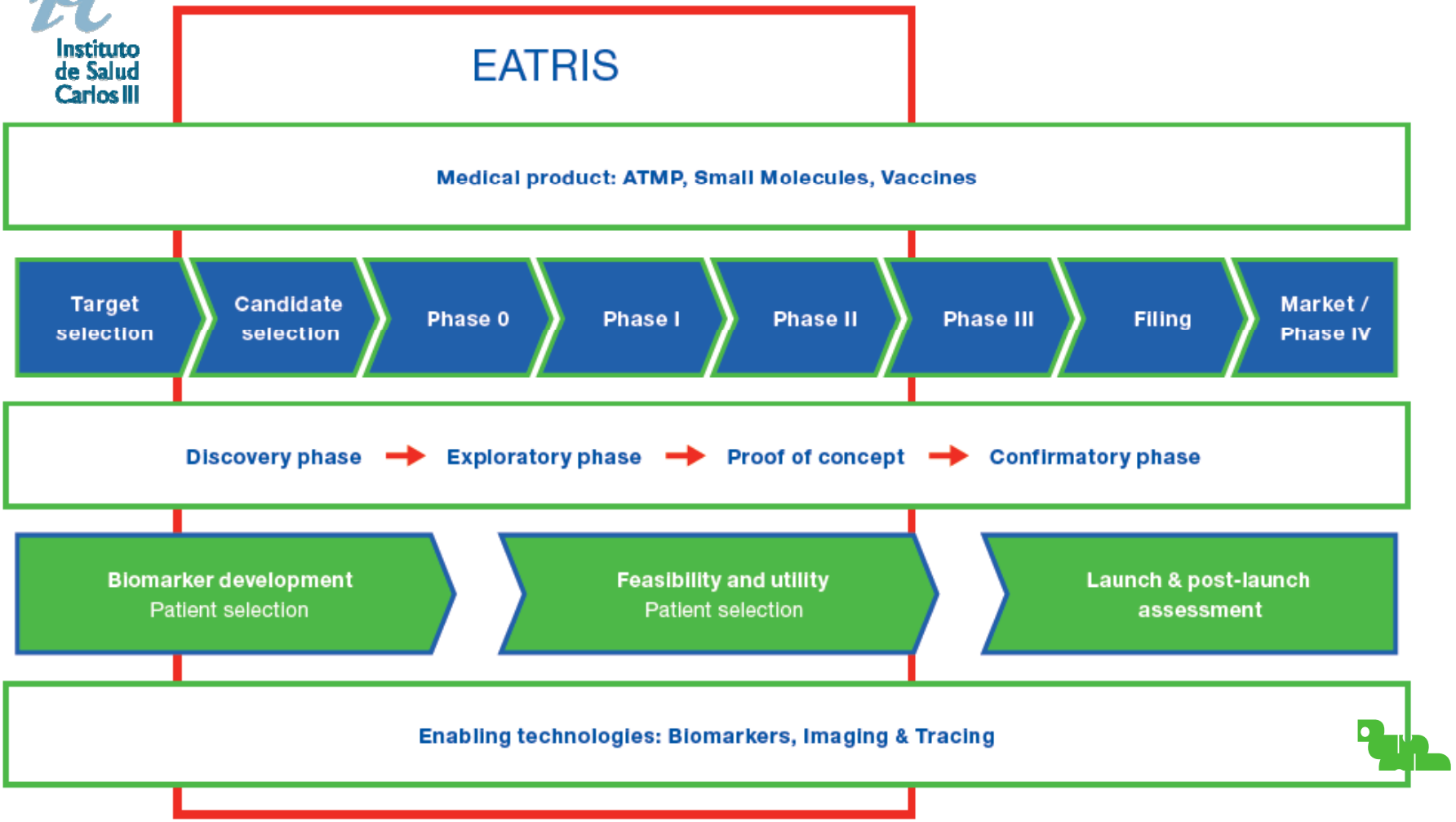
To make collaboration faster & less risky:

- 70 translational institutes under 1 framework agreement
    - Common IP policy
    - Harmonised quality framework
    - Standardised operational framework
    - Template agreements under development

- Faster time to contract, support in negotiating & IP
- One-on-one client/institute contract - no liability or IP issues
- Efficient links to complete innovation pathway, industry

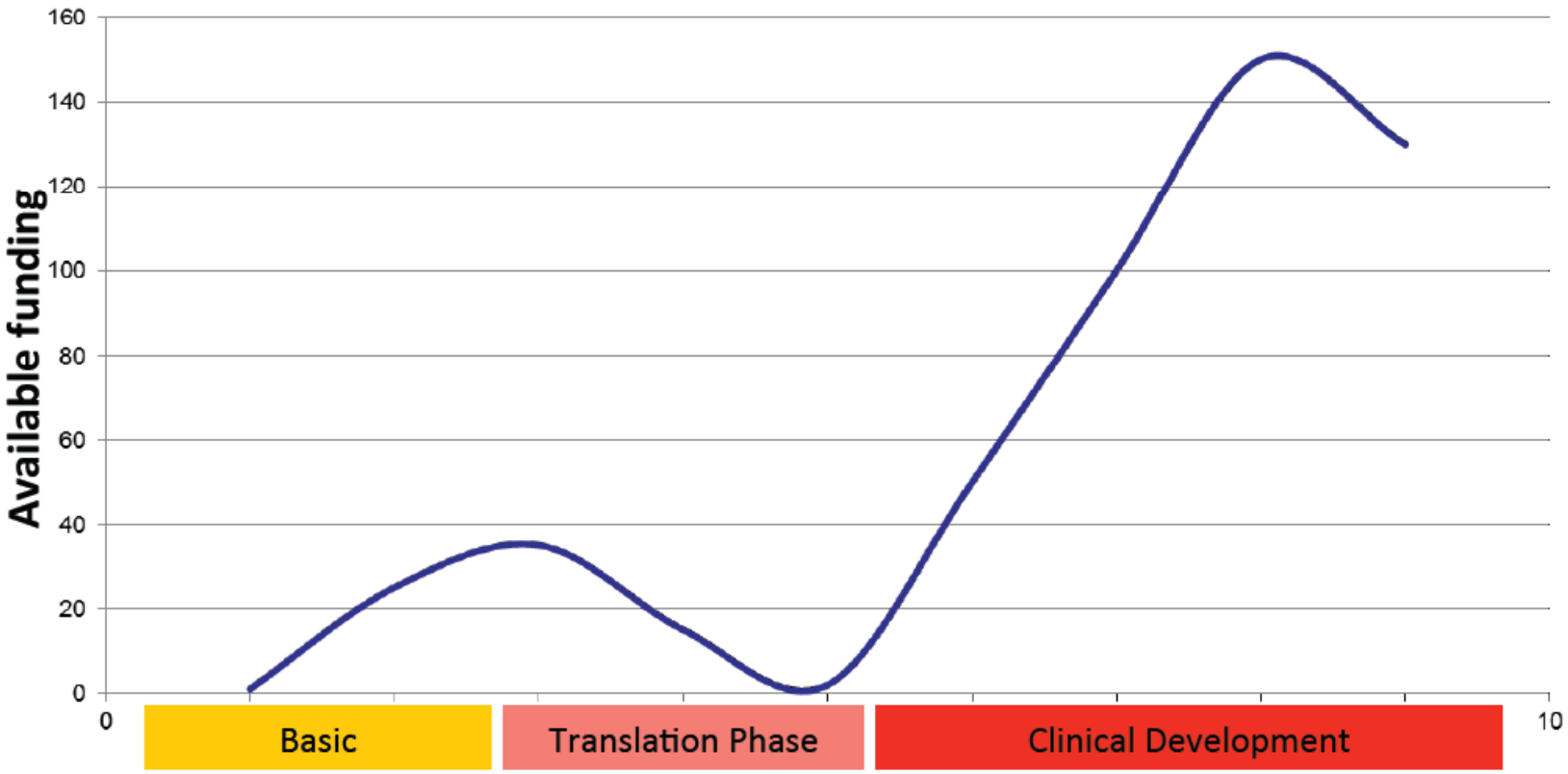
EATRIS SPAIN: Perfect fit



Value Proposition: Reduce risk – increase output

- Only high potential projects selected for development – **reduce failure rate**
- Executed by top quality infrastructure with track record – **reduce systemic risk**
- Optimal strategy with early imaging, biomarker, clinical, regulatory, input – **maximise resource efficiency**
- Seamless transition to external partners/collaborators – **Reduce transactional risk & lead times**

➢ **Higher output per research Euro**


160
140
120
100
80
60
40
20
0
Available funding
0
10
Basic
Translation Phase
Clinical Development
Stage of development

The product platform chairs at EATRIS

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Imaging & Tracing

Guus van Dongen, VUmc

Small Molecules

Mario Salmona, Mario Negri

Vaccines

Jan Langermans, BPRC

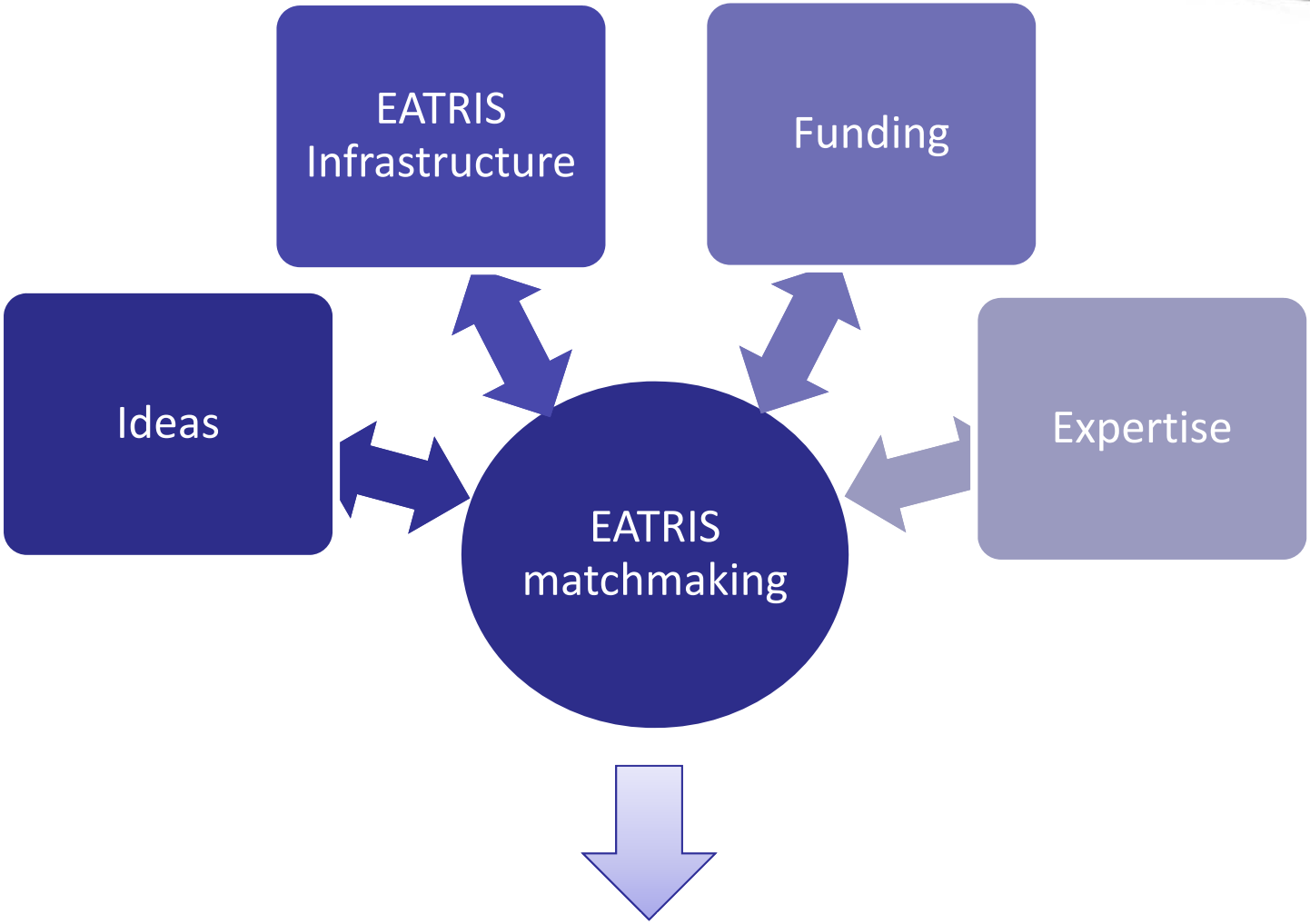
ATMPs

Filippo Belardelli, ISS

Biomarkers

Olli Kallioniemi, FIMM

Plug-&-play - matching needs



High potential projects - purpose built operational teams

Current status

- Operations ready
- Infrastructure database ready, expert database in development
- Pilot projects in preparation

You are invited to participate in pilot projects!
Open to innovative industry partners for sustainable collaboration

Building an effective organisation

The EATRIS way..

- Long term relationships: internally and externally
- Actively supporting each other and clients
- Operation Big Ears: ‘learning through listening’
- Shaping the EATRIS community, build the strength ‘from wi
- Build trust and comfort: inside – out
- Team workers by DNA
- Always focused on the benefit of the patient

Index

Drug development today

Tick box approach to Proof of Concept

Efficacy	Proof of Mechanism & Clinical End Points affected
	Target Population identified
Pharmacokinetics	PK/PD Relationship
	Dose and Regimen
Safety	On- and off-Target Effects
	Relevant Clinical Measures
Pharmaceutics	Dose Form and Formulation
	Manufacturing Process and Cost of Goods
Commercial	Unmet Medical Need
	Reimbursement and Intellectual Property secured
Regulatory	Approvable Indication
	Target Population and End Points acceptable

Drug development today: A multidisciplinary exercise approach

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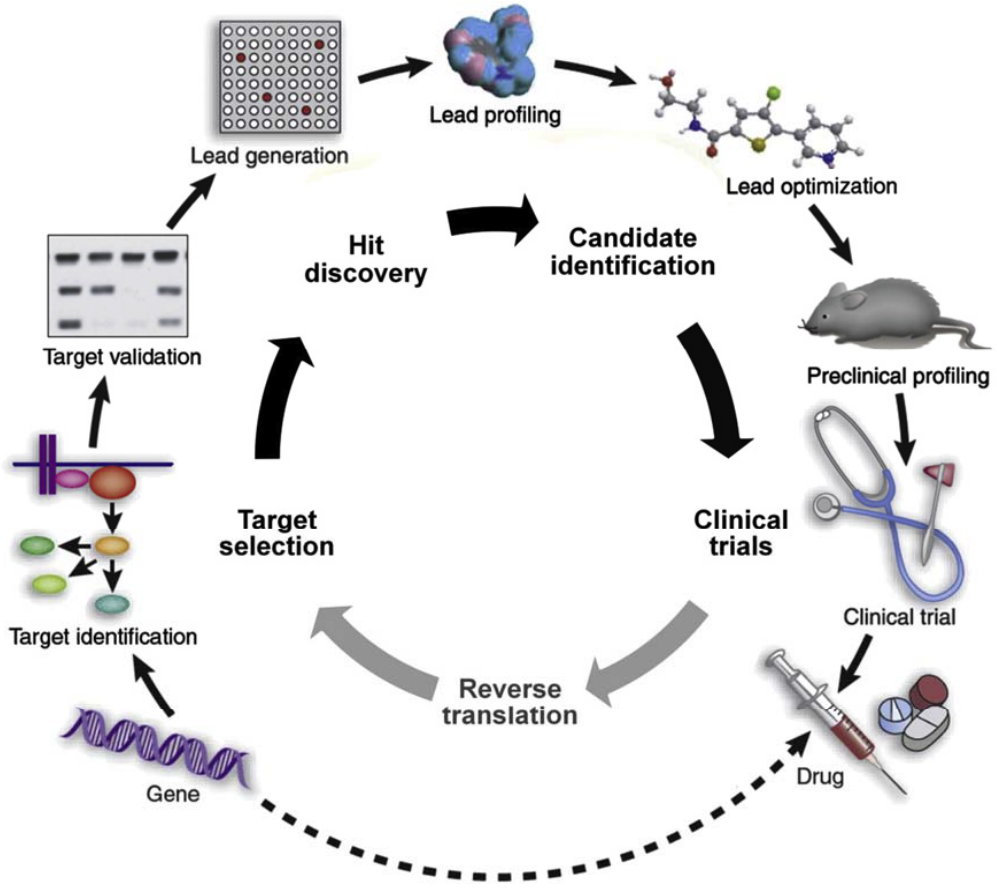
"From bench to bedside, from bedside to bench"



Hoelder et al, Molecular Oncology 2012

- Clinical
- Regulatory affairs
- Toxicology
- Manufacturing
- Quality
- Health technology
- Legal/IP
- Chemistry
- Pharmacology
- Omics…

Drug development today

- **Pipeline productivity stalling**

  Failure rate at phase II ~65%

- **Industry early R&D moving to acquisition**

  Development cost of new drug ~$1.8 billion, 12-15 years

- **High price of marketed drugs**

  FDA approved 4 new drugs in 2012, cost >$200k per patient

- **Pressure on public funds for research, healthcare**

  Dementia care cost 1% ($600 billion) of global GDP – 2010

- **High fundamental output – little innovation**

  8% success rate from pre-clinical candidate to launch

- **Substantial expertise – severely fragmented**

  Contract negotiating time ~300 days

- **Demand for high end infrastructure & licenses**

  Median time to clinical trial 12-18 months

Drug development today

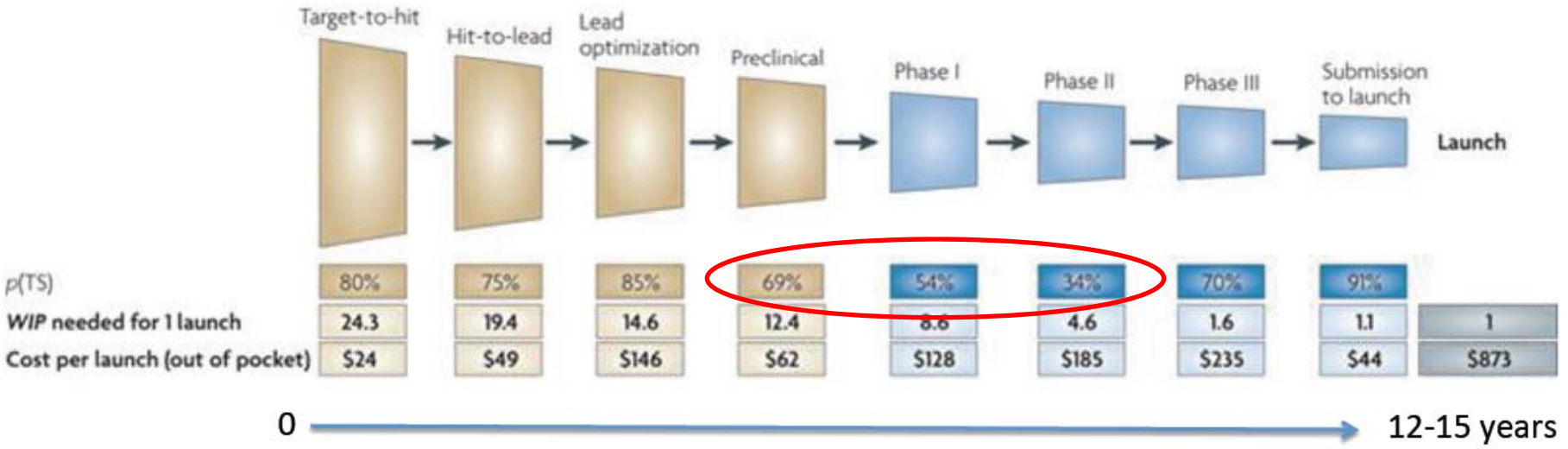
Which factors are relevant for failure?

- Poor predictive pre-clinical models
- Mode of action not fully validated
- Sub-optimal clinical trial design
- Clinical need not confirmed
- IP not secured

Risk of failure needs to be reduced

Drug development today

Translational research: the riskiest part



Paul et al, Nat Rev Drug Discov 2010

EATRIS: Positioning

Components of the translational path

- Academia
- Research /charities
- SME/biotech
- Pharma

Client projects

- GMP manufacturing
- Imaging facilities
- Biobanks
- Clinical trial units
- Patient groups

Infrastructure

- Nat'l governments
- Regional dev. Funds
- H2020
- Venture capital
- Pharma partnering

Funding

- Clinicians
- Technologies
- Biomarkers
- Regulatory
- IP, partnering

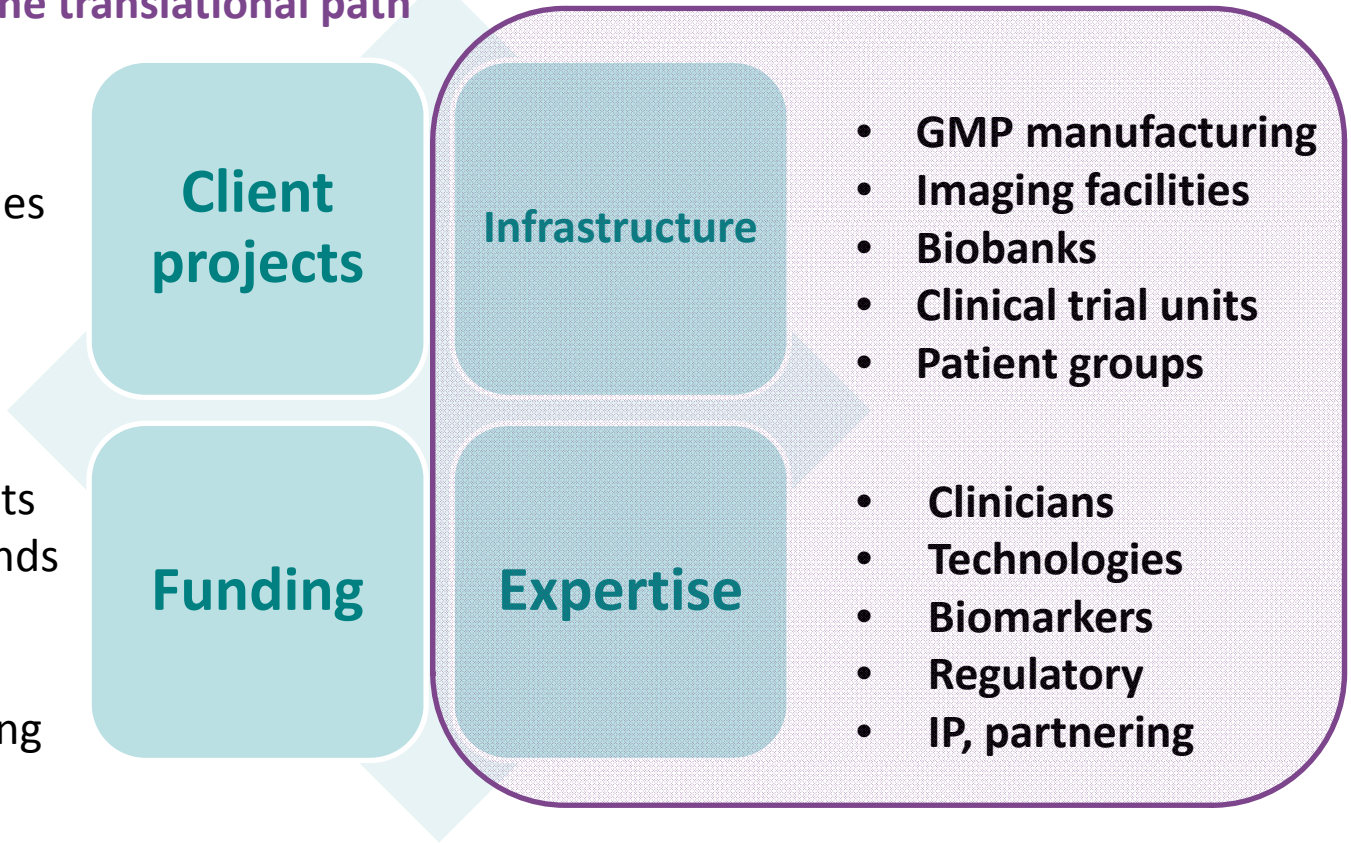
Expertise

EATRIS: Positioning

Components of the translational path

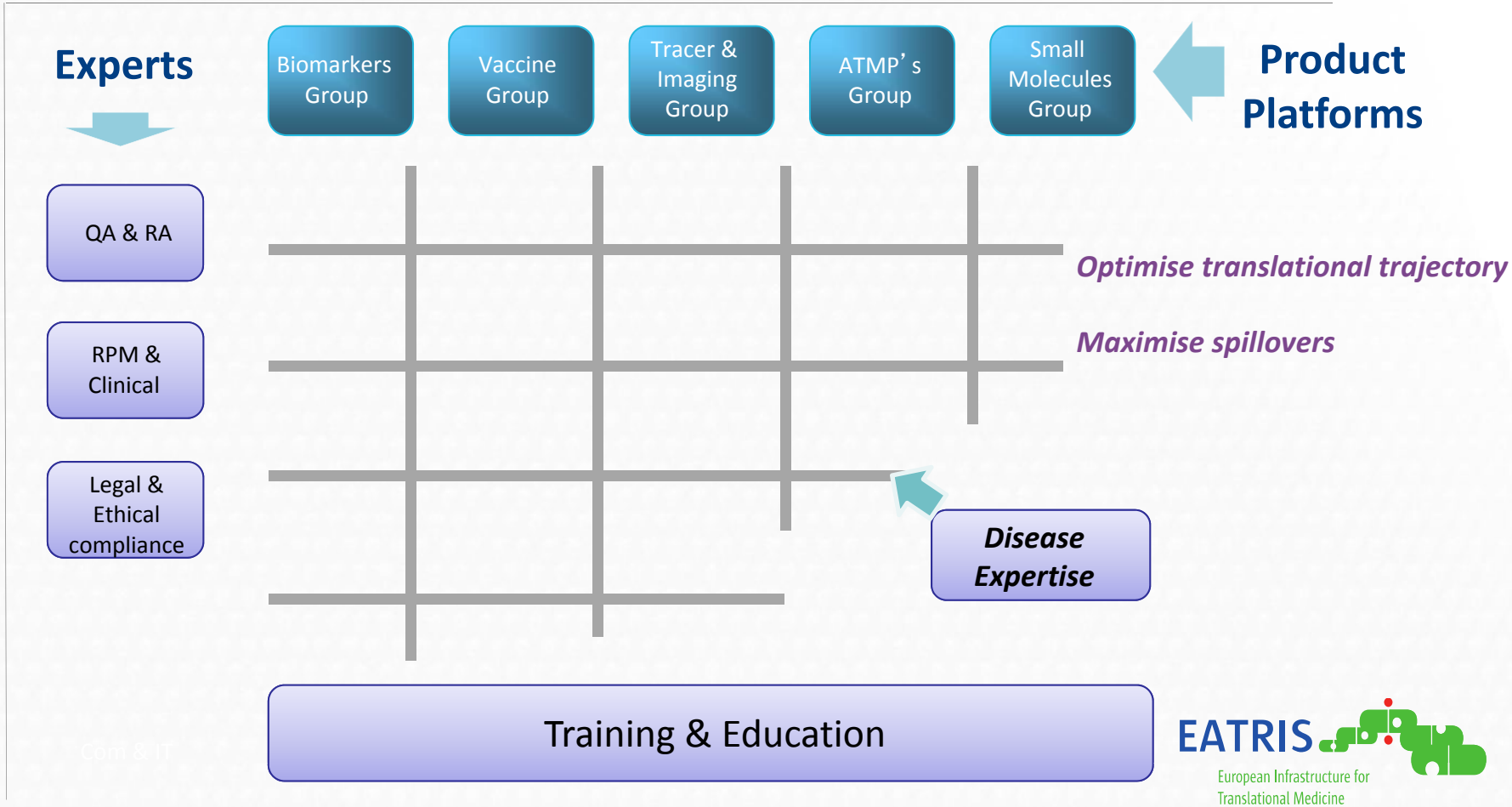
- Academia
- Research /charities
- SME/biotech
- Pharma

- Nat'l governments
- Regional dev. Funds
- H2020
- Venture capital
- Pharma partnering



EATRIS: operational strategy

Consortia of centres of excellence in a 3D matrix model



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