Creating Value through Biomedical Innovation Ecosystems

Isabelle Thizon-de Gaulle
VP, Scouting & Partnering – R&D
SANOFI Global R&D

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Frustrating and disappointing past decade

In spite of remarkable scientific progress, **our capacity to translate those advances into health benefits** has decreased

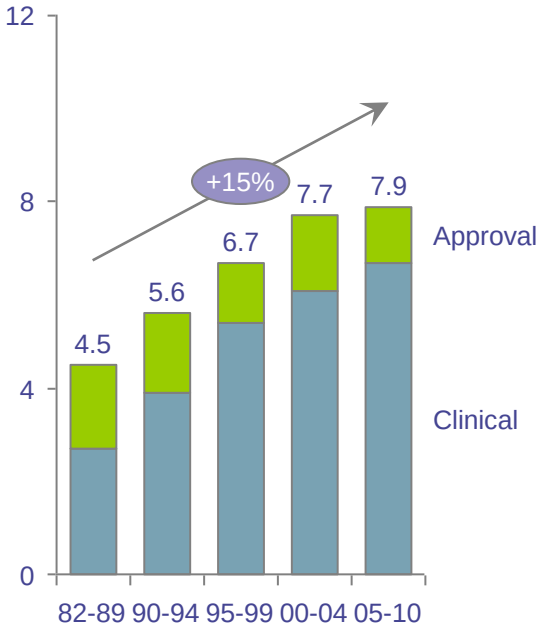
The number of biological targets has dramatically increased thanks to **progress made in the field of genomics**

In the biopharmaceutical sector **success rate has dropped** from 1/8 to 1/14 and **the length of development has doubled**

Spectacular drop in R&D productivity

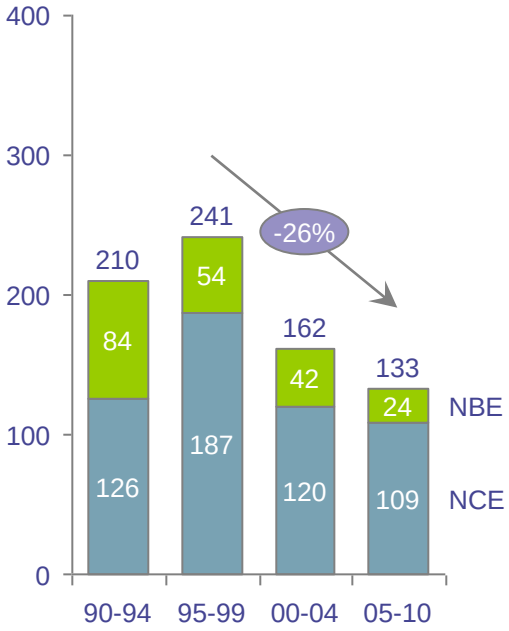
Clinical timelines increasing

Mean clinical development time (years)



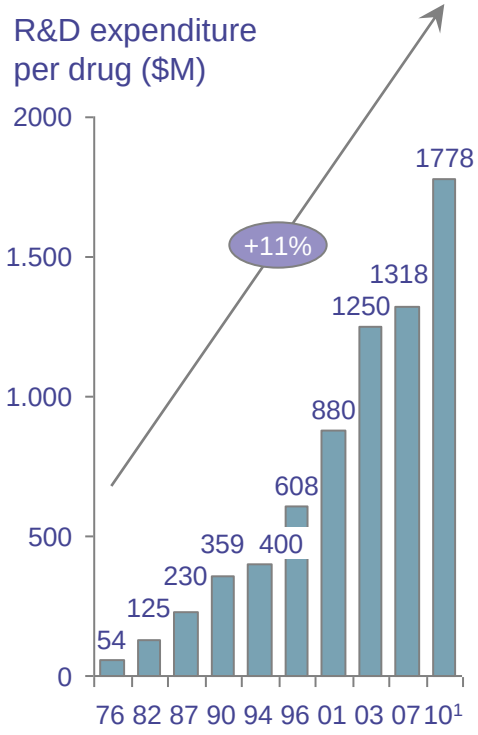
NME approvals by FDA decreasing

Number of NCEs and NBEs approved



Rising R&D costs

R&D expenditure per drug ($M)



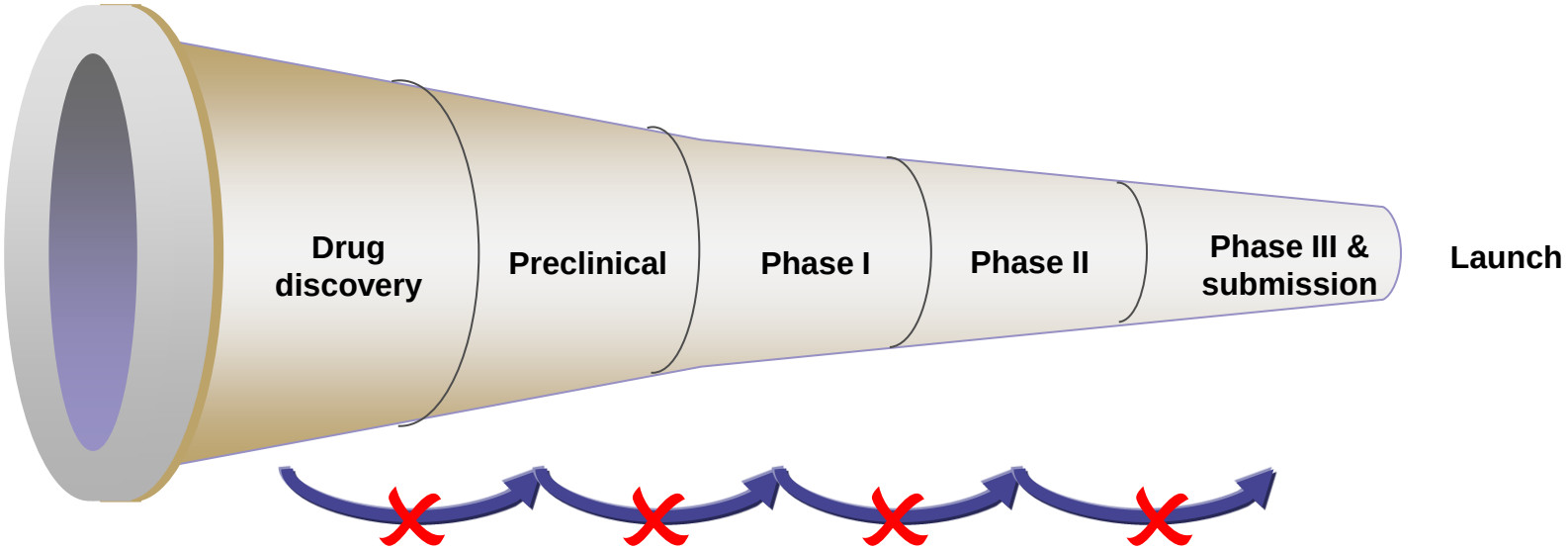
NME: New molecular entity NCE: New chemical entity NBE: New biological entity
1 2010 data is from Paul et al Nature Feb-10, rest of data from Tufts
Source: FDA; EvaluatePharma; Tufts CSDD 2007; Parexel; CMR; Paul et al, 2010,

What Changed?

The entire healthcare ecosystem is under pressure

- **Patient needs**
  - Acute to chronic
  - Personalized
  - Generics
- **Regulation**
  - Regulatory burden
  - Safety thresholds
  - Postmarketing requirement
  - Longer R&D cycles
- **Payer driven market**
  - Differential medical value
  - Rise of formularies
  - Payment restrictions
  - Price controls
- **Science**
  - Low predictability in Humans
  - Too concentrated on a few targets
  - Low success rates
  - Low overall efficiency

What went wrong?



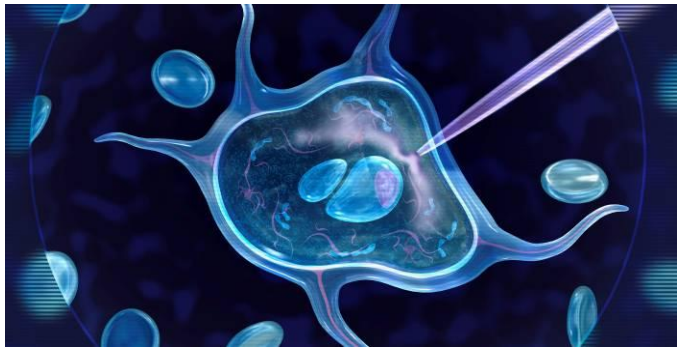
Advances in basic science leading to more unvalidated targets	*More focus on molecular biology vs translational medicine*	*Incentives to continue advancing projects leading to late and costly failure*

What went wrong?

- **The innovation model**
  - Belief that advances in basic sciences could be easily translated to human disease
  - Too many novel but not validated targets in humans
  - Linear process from discovery to development to market
  - Number of research projects focused on « ME-TOO » drugs
  - Quantity over Quality
  - Strategy of « MANY SHOTS ON GOAL »

- **The organizational model**
  - Large complex organizations inherited from successive mergers
  - Internally driven research with little interaction with larger world of external innovation
  - Resource allocations driven by functions rather than specific projects and programs
  - Disconnect between R&D strategies and rapid changes in Science, Medicine and Markets

What will it take to be?



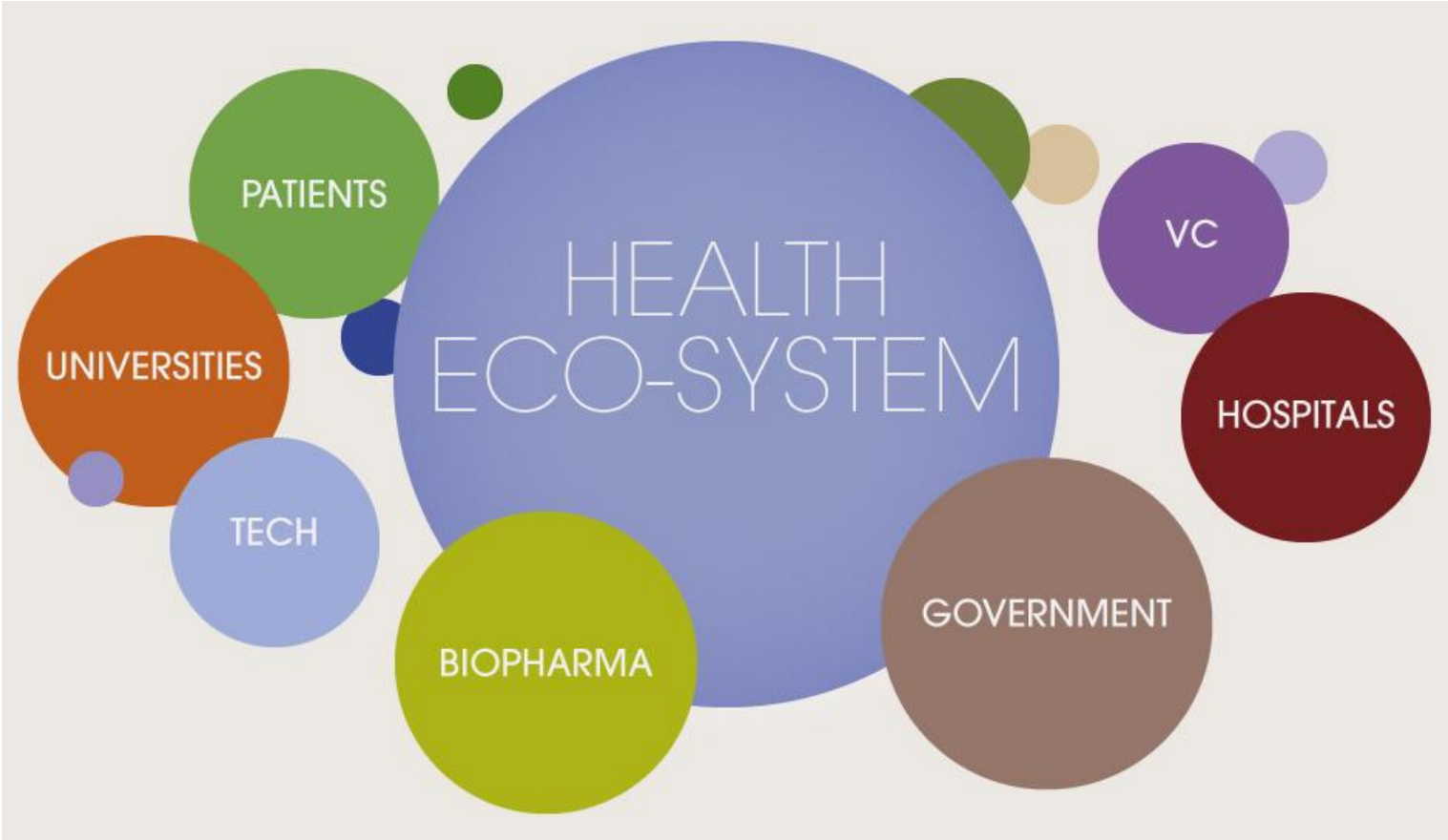
Translational medicine

Because strengthening cooperation between laboratory researchers, clinical trial directors and clinical researchers whose work focuses on patients and populations, is of paramount importance to make our science available to those who need it

Open innovation

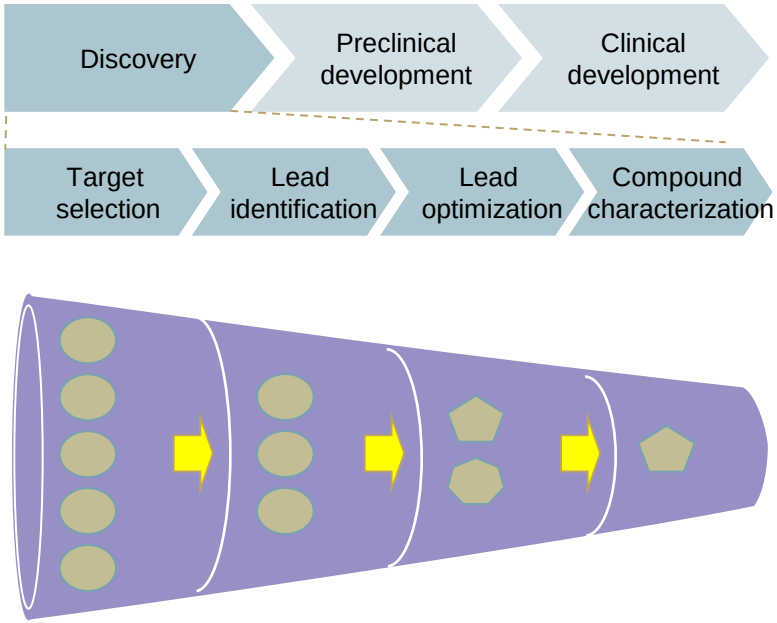
Because we recognize that inside and outside our walls, there is astounding scientific discovery going on and that it is through collaboration that we will deliver the best, the most innovative and the most awaited solutions patients are hoping for

We need to rethink innovation

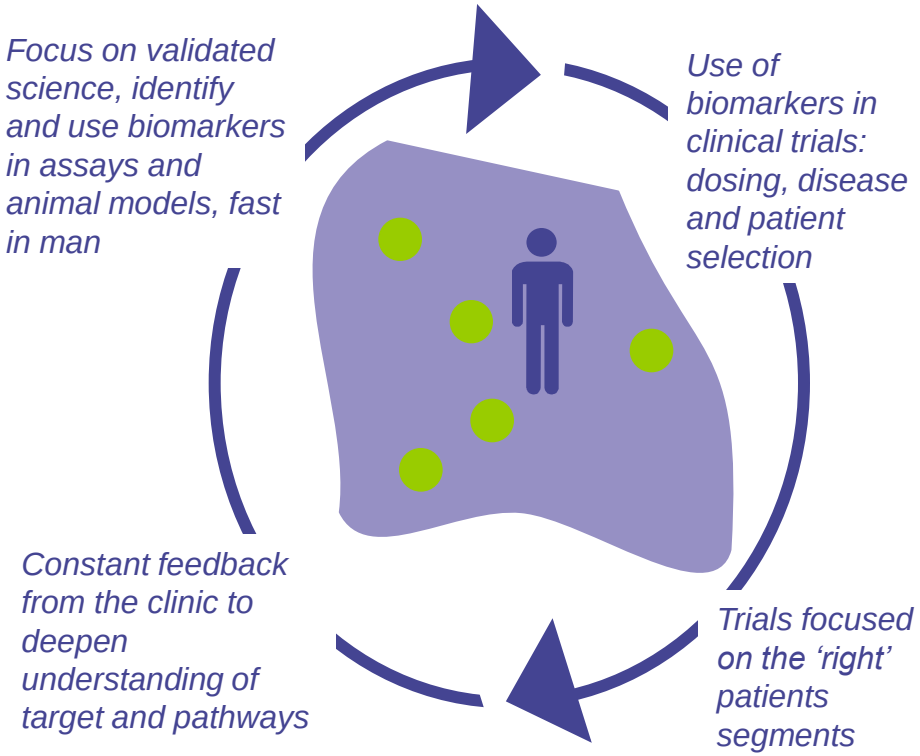


How can we get there?

Traditional approach:
Feed forward and linear; most parameters not predictable or controllable



New Translational Medicine approach:
Putting the human disease at the center of the drug discovery & develp't process



Our Way of Working
Leveraging Local Innovative Ecosystems

Our ambition is to create integrated R&D Hubs

To make the best of the **opportunities, science, talents** and **resources** available in local innovative ecosystems

Our Way of Working

Innovating with our partners for the benefit of mankind

Academic Partnerships

aviesan
alliance nationale pour les sciences de la vie et de la santé
CHARITÉ
SIBS
DANA-FARBER CANCER INSTITUTE
CALTECH
CRG Centre de Regulació Genòmica
imi Innovative Medicines Initiative
HARVARD UNIVERSITY
SALK INSTITUTE FOR BIOLOGICAL STUDIES
Massachusetts Institute of Technology
JOHNS HOPKINS UNIVERSITY
UCSF University of California San Francisco
THE ROCKEFELLER UNIVERSITY
Science for the benefit of humanity

Pharmaceuticals Partnerships

Dyax
EXELIXIS
micromet
ALOPEXX
KYOWA KIRIN 協和発酵キリン株式会社
bioMedica OXFORD
IMMUNOGEN, INC.
REGULUS THERAPEUTICS
ascendispharma
ASCENTA THERAPEUTICS
REGENERON
AgaMatrix
MERRIMACK PHARMACEUTICALS
glenmark A new way for a new world

Vaccines Partnerships

NAVAL MEDICAL RESEARCH CENTER U.S. NAVY
Syntiron
CSL
KALOBIOS
to therapeutics Vivalis

R&D Acquisitions

TargeGen
fovea PHARMACEUTICALS
SHANTHA BIOTECHNICS
BiPar sciences

Foundation Partnerships

JDRF Juvenile Diabetes Research Foundation International
dedicated to finding a cure
THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH
BILL & MELINDA GATES *foundation*

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Accelerate the maturation of promising projects

aviesan
alliance nationale
pour les sciences de la vie et de la santé

ATIP-AVENIR*

- Sponsorship to 15 young scientists to create and lead a team within a CNRS or INSERM structure, during 3 years
- Selection based on the excellence and the internationalization of their career, and their research subject
- Co-financing of the grant
- Allocation of a Sanofi tutor to each young researcher

COPIO**

- Identify, develop and co-finance innovative projects leading to medical and industrial applications
- Maturation phase of the project in collaboration with different institutions and industrial partners

Collaborative Programs

- Selection, co-financing of collaborative programs of highest added value with research teams of excellence at the leading edge of their scientific and technological fields
- First identified focus areas:
  - **Immuno-inflammation**
  - **Aging**
  - **Infectious diseases**
  - **Regenerative medicine**
  - **Oncology**

ATIP: Action Thématique et Incitative sur Programme

****COPIO: COmité de Pilotage Inter-Organismes***

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Enable the easy and effective deployment of global resources

Centre d'Immunologie de Marseille-Luminy

- **Built collectively**
  - by CIML, Sanofi Immuno-Inflammation and Sanofi Pasteur
- **Principle of:**
  - Open innovation, exchange of expertise
  - Dynamic reallocation of resources to evolve with new science and adapt to new opportunities
- **Innovative contract to ensure mutual benefits for both partners**
  - Joint funding
  - Delivering long term mutual benefits
  - Ownership and Exploitation of results reflecting and protecting the core business of each partner
- **Goal:**
  - Identify therapeutic opportunities in innate immunity
  - Focus on mucosal interfaces of skin and gut
  - Develop mechanistic mouse models
  - Translate key findings to human cells and tissues
  - Integrate teams so that they work for the success of ONE collaboration
  - Foster transversal activities that build a lasting partnership spirit

Focus disciplines on the right level of understanding to make things work

Pasteur Institute: Understanding of Science (Paris)

- Opportunity for new type of collaboration with the aim of confirming disease hypotheses and new targets
- Platform for Integrative Biology (IBEID)

➔Scientific Research Agreements

"Institut de Recherche Technologique" (Lyon/Paris):

Sharing access to scientific skills and infrastructures

- Better understanding of Science
- Development of tools and technologies

➔Sanofi Pasteur/Sanofi/Merial part of the Governance ("Fondateur")

"Institut Hospitalo-Universitaire" (Marseille):

Translational approach in infectiology

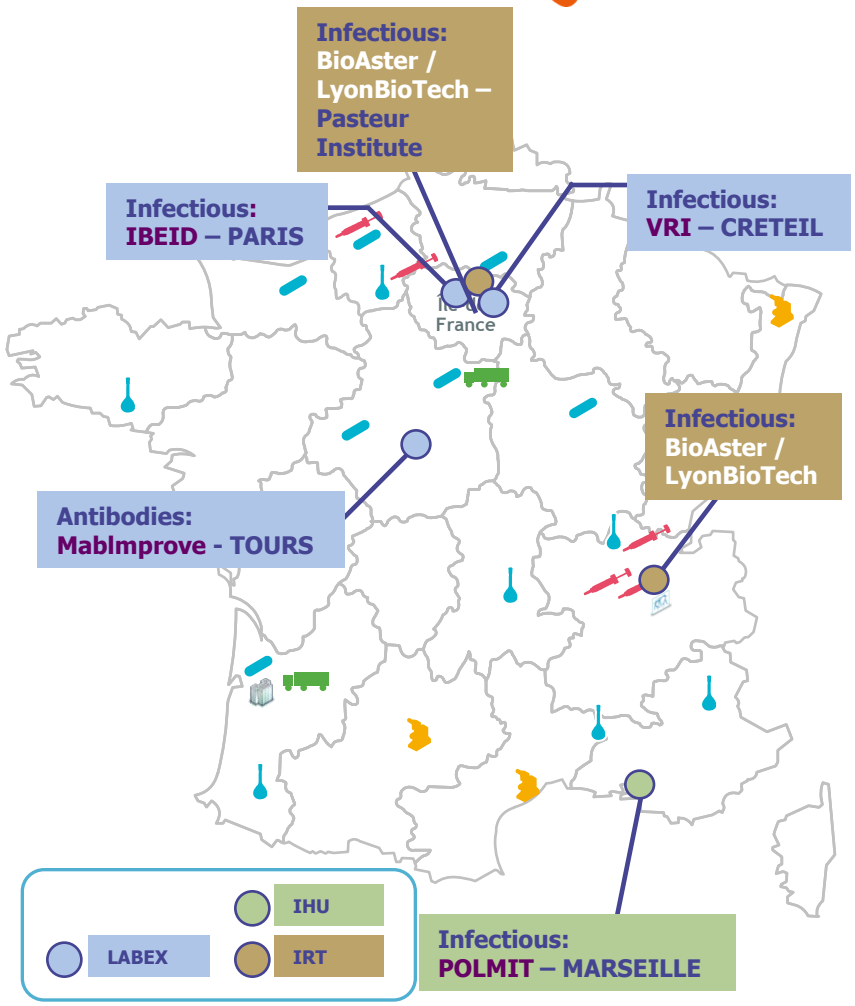
- Patients centric approach – Potential for rapid evaluation in Human

➔Sanofi is partner

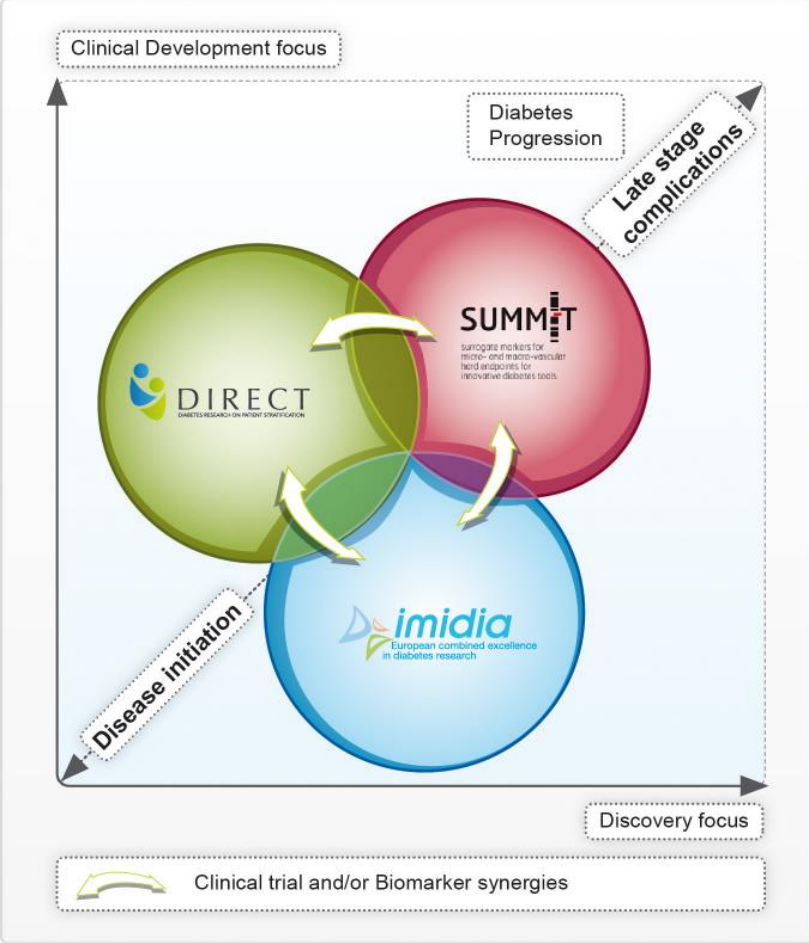
MabImprove (Tours/Montpellier):

Optimization of monoclonal antibodies therapies

- CRB-CIC center for dose adjustment during the treatment with antibodies: on-going discussions.



Leverage the best expertise & efficient funding from industry, academia & public institutions



- **Pathways & Systems Biology**
  - *Sanofi, BI, Lilly, Novartis, Novo, Univ. Dresden, Univ. Pisa, ICL, Swiss Institute of Bioinformatics; Univ. Turko, Univ. Lund, Univ. Lausanne, Univ. Pisa*
- **In vitro models**
  - *Sanofi, AZ, BI, Endocells, INSERM, CNRS, Univ. Brussels*
- **In vivo models**
  - *AZ, BI, Servier, Sanofi, Roche, CNRS, UP7, Karolinska Institute*
- **(Imaging) Biomarker**
  - *Sanofi, BI, Lilly, Novartis, Novo, Roche, AZ, CEA, Univ. Geneva, Univ. Dundee, Univ. Bath, , GSF – Helmholtz Centre Munich, Uni. Lund, CNRS, Univ. Lund, Karolinska Institute, National Institute of Health (Finland), Univ. Oxford, Univ. Turko, Univ. Exeter*
- **Clinical studies**
  - *Sanofi, Lilly, Novartis, Univ. Dundee, Univ. Bath, GSF – Helmholtz Centre Munich, ICL, CNRS*

Innovative Medicines Initiative

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Align incentives through adapted partnerships and investment models

THIRD ROCK VENTURES

greylockpartners.

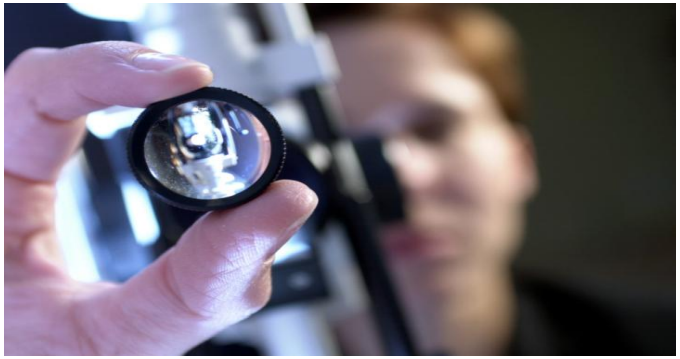
Warp Drive

Breakthrough approach leveraging recent discoveries to generate enhanced new drugs based on natural products

Launched jointly with venture capital firms Third Rock Ventures and Greylock Partners

Mutually beneficial partnership where Sanofi can internally provide value to an external pathway

Collaborating with the youngest Harvard Professor whose discoveries could revolutionize development of natural products therapies



Fovea

Acquisition of Fovea in 2009 and creation of a new Ophthalmology division in May 2012

Take advantage of Fovea's unique position & expertise with access to first class science in ophthalmology and to cohorts of patients and clinical experts, while Sanofi providing global marketing and development capabilities

Co-location of teams in local ecosystem (Institut de la vision/ Hopital des Quinze-Vingts)

Huge unmet and growing medical needs in both developed and in emerging countries, especially in Asia and Latin America

We need to rethink innovation