

La médecine personnalisée appliqué aux neurosciences :

Rôle des biomarqueurs & des dispositifs médicaux

Ecole de l'innovation
thérapeutique Ariis/Aviesan
Seine Port 13 juin 2014

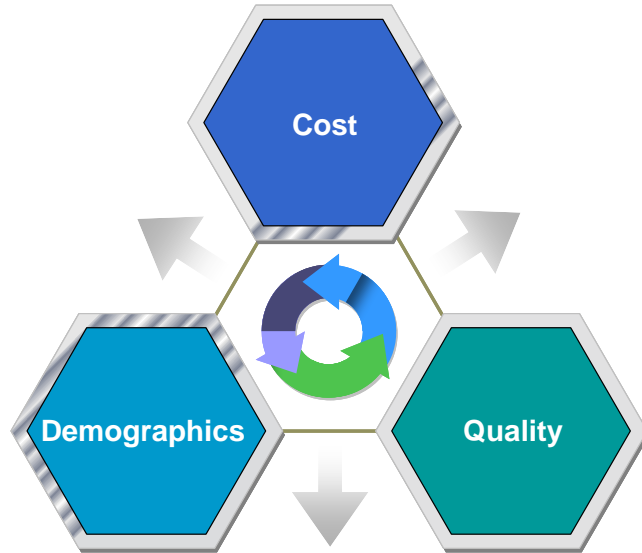
Bertrand LOUBATON
VP Santé

- Situation and Trends
 - ✓ *Economical*
 - ✓ *Pharmaceutical & Diagnostic Industry*
 - ✓ *Personalized medicine & Biomarkers*
- Medical Devices
 - ✓ *In-Vivo Diagnostic*
 - ✓ *In-Vitro Diagnostic*

Healthcare Is Challenged By Three Interlocking Crises That Make Present Healthcare Systems Unsustainable

- ❑ Healthcare is challenged by three interlocking crises that make present healthcare systems unsustainable:

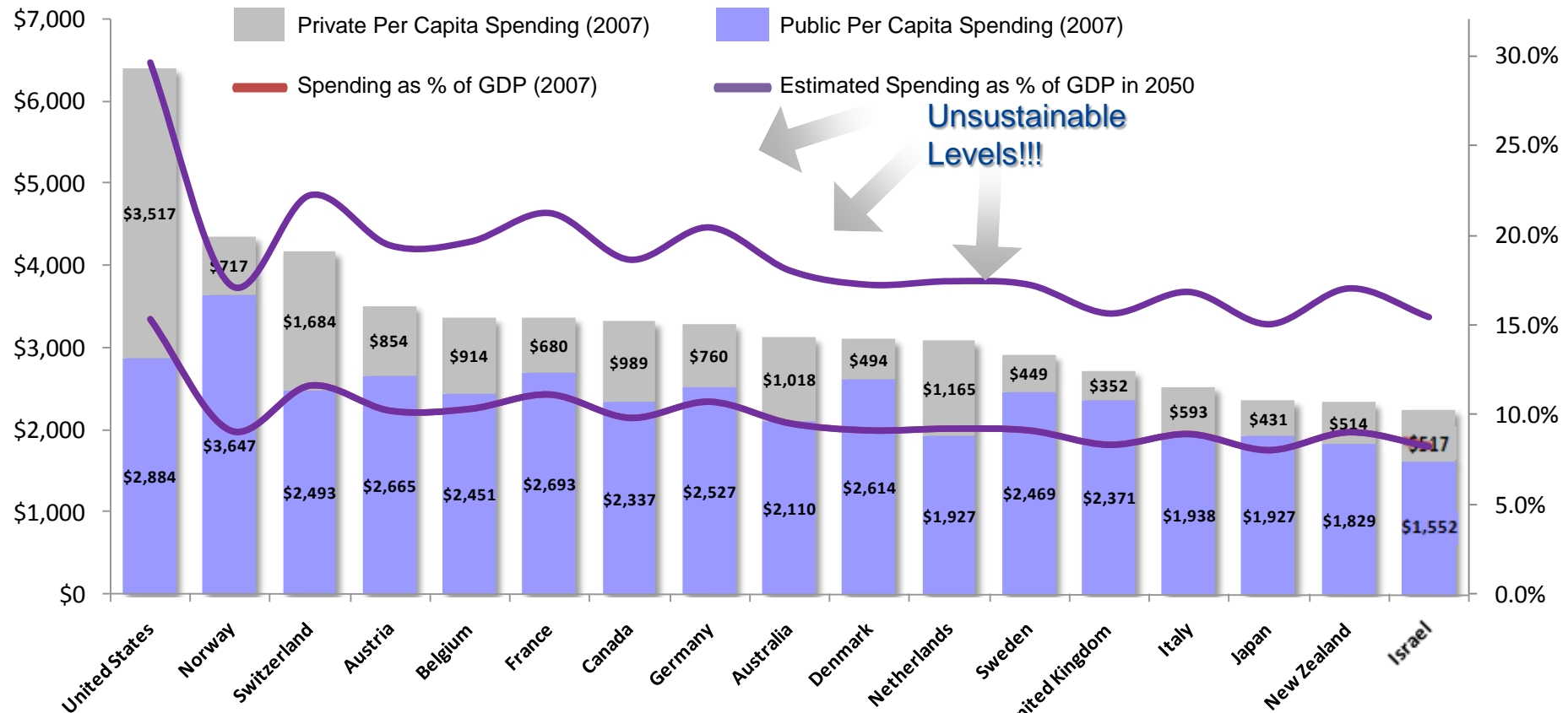
- ☑ Rising costs
- ☑ Changing demographics
- ☑ Quality



The Size of the Problem – Quality

- ❑ 15% of patients admitted to hospital suffer an adverse event.
- ❑ 8% of adverse events result in death.
- ❑ 6% of adverse events result in permanent disability.
- ❑ 10-20% of all adverse events are caused by medication errors.
- ❑ 10-15% of hospital admissions occur because providers do not have access to previous care records.
- ❑ 20% of laboratory tests are requested because the results of previous investigations are not accessible.

If Current Trends Hold, By 2050 Health Care Spending Will Almost Double Claiming 20% – 30% Of GDP For Some Economies

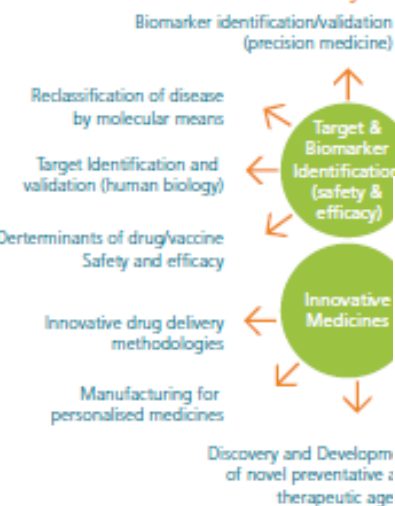


- ❑ In almost all countries worldwide, per capita healthcare spending is rising faster than per capita income.
- ❑ No country can spend an ever-rising share of its output on health care, indefinitely. Spending growth must eventually fall in line with growth in per capita income.
- ❑ The fundamental driver of high costs and quality issues is the inconsistency of healthcare delivery and outcomes from region to region, state to state, and even hospital to hospital. Such variance is bad for your health & the healthcare system as a whole

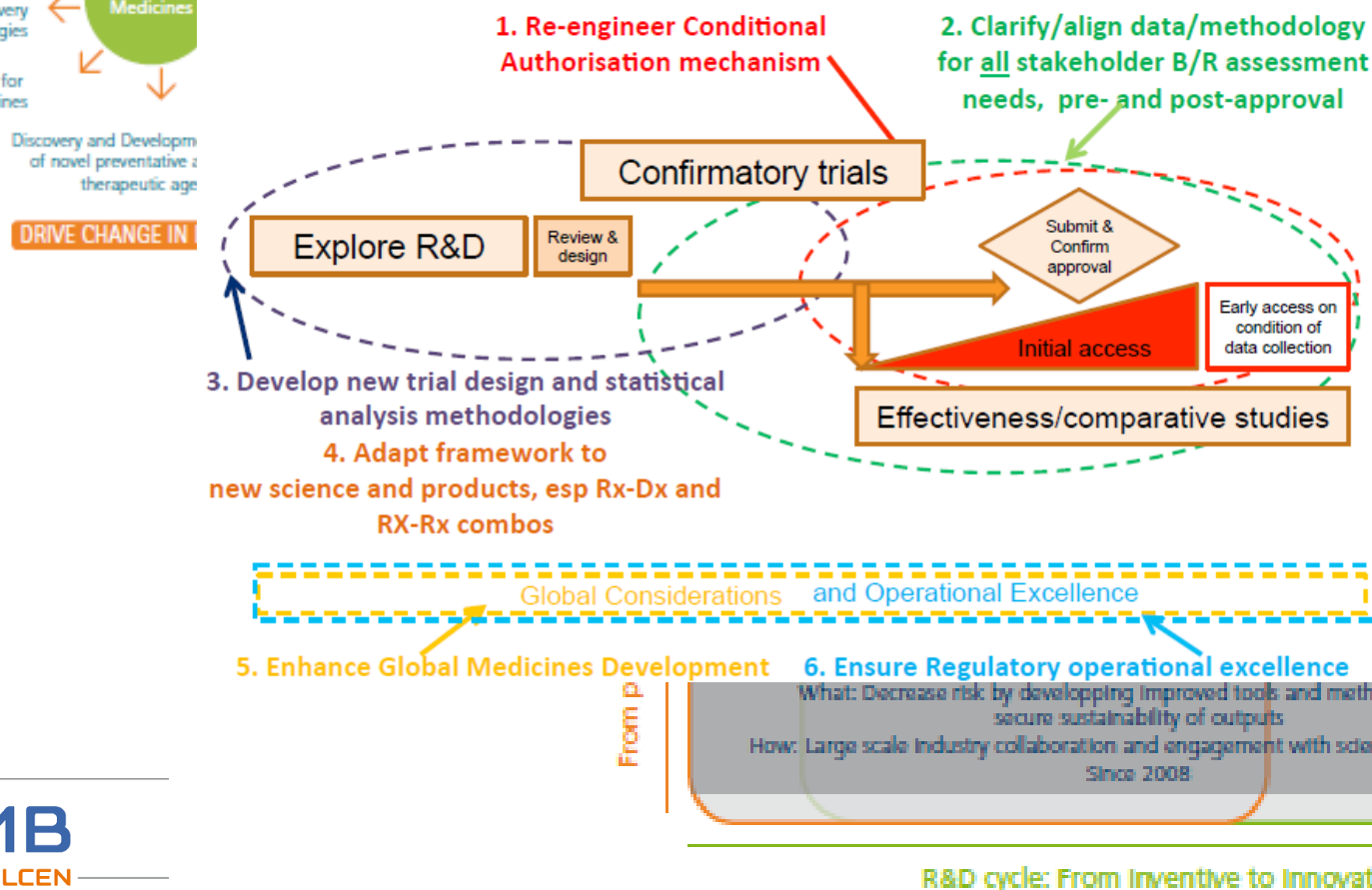
IMI Strategic Research Agenda



Major Axis of Research



Proposals for Regulatory/Development Initiatives



ORIZON 2020
PHARMA PPP

Regulatory Change
Move into regulatory
and life data
regulators and payers
2012

Medicines ("pull")
with care agendas
and payers

Need for a neutral platform

PMB

ALCEN

Personalized Medicine

Promise of new 'omic targets and validated Biomarkers

Disease mechanism understanding

Patient Stratification

Predisposition to disease

Early indicator of disease

Disease type

Drug selection

Dose selection

Toxicity avoidance



Patient Monitoring

Disease initiation

Progression

Severity

Drug efficacy/toxicity

In-Vitro Diagnostic “LOTUS”

a paradigm shift for Molecular Imaging

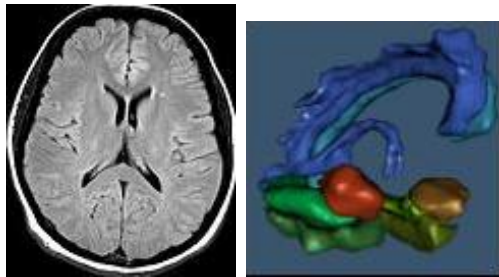
- *Locally Produced PET imaging Biomarkers*
- *Translational research & personalized medicine*



“GMP PETpresso Solution”

Trend Towards Molecular Imaging

**Anatomical
imaging**

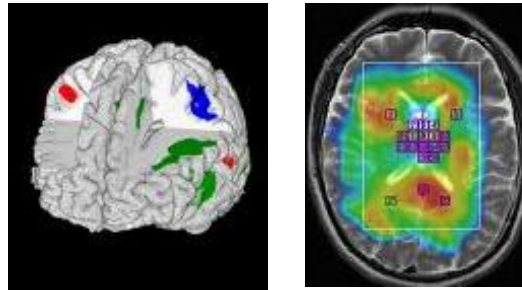


**Morphology
Morphometry**

Structure



**Physiological
imaging**

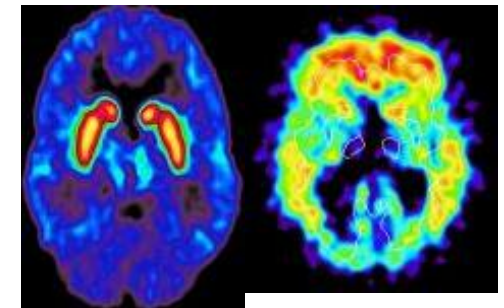


**Haemodynamics
Vascular permeability
Tissue oxygenation/hypoxia
CNS activity
Metabolites
pH**

Mechanism



**Molecular
imaging**



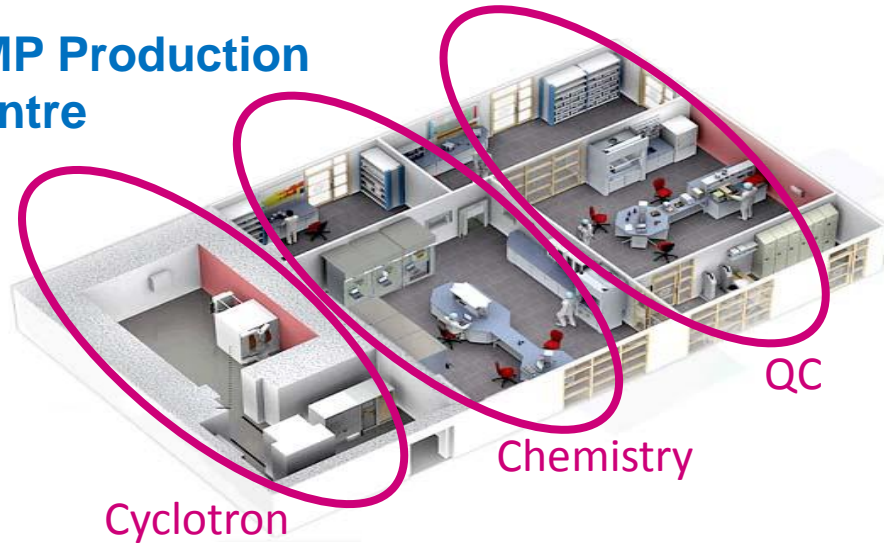
**Functional receptor
imaging
Target specific
contrast agents
Pharmacokinetics**

Target

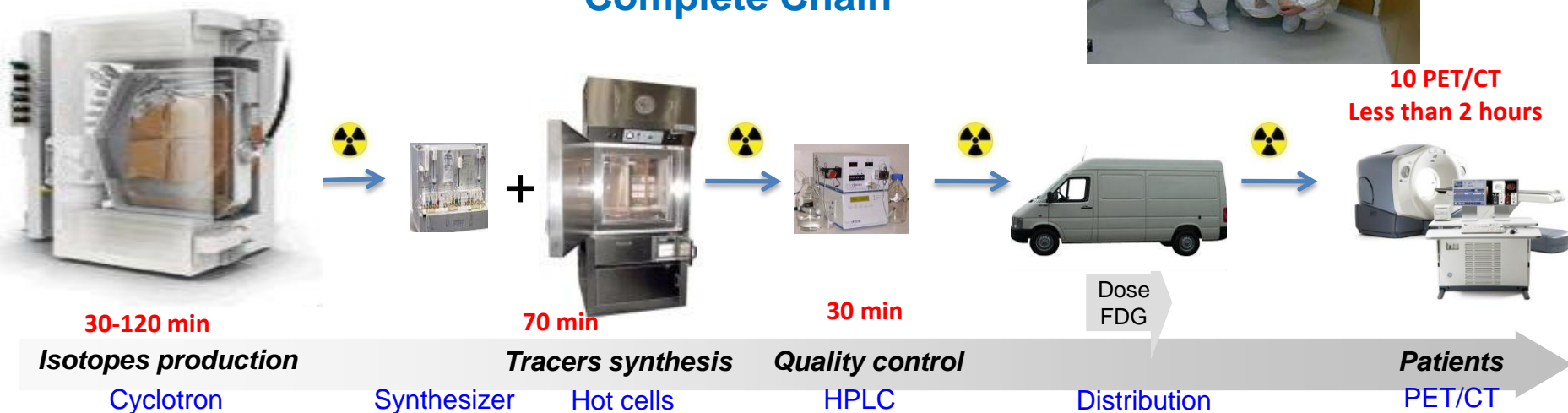


Situation

GMP Production Centre



Complete Chain



Paradigm shift for Molecular Imaging

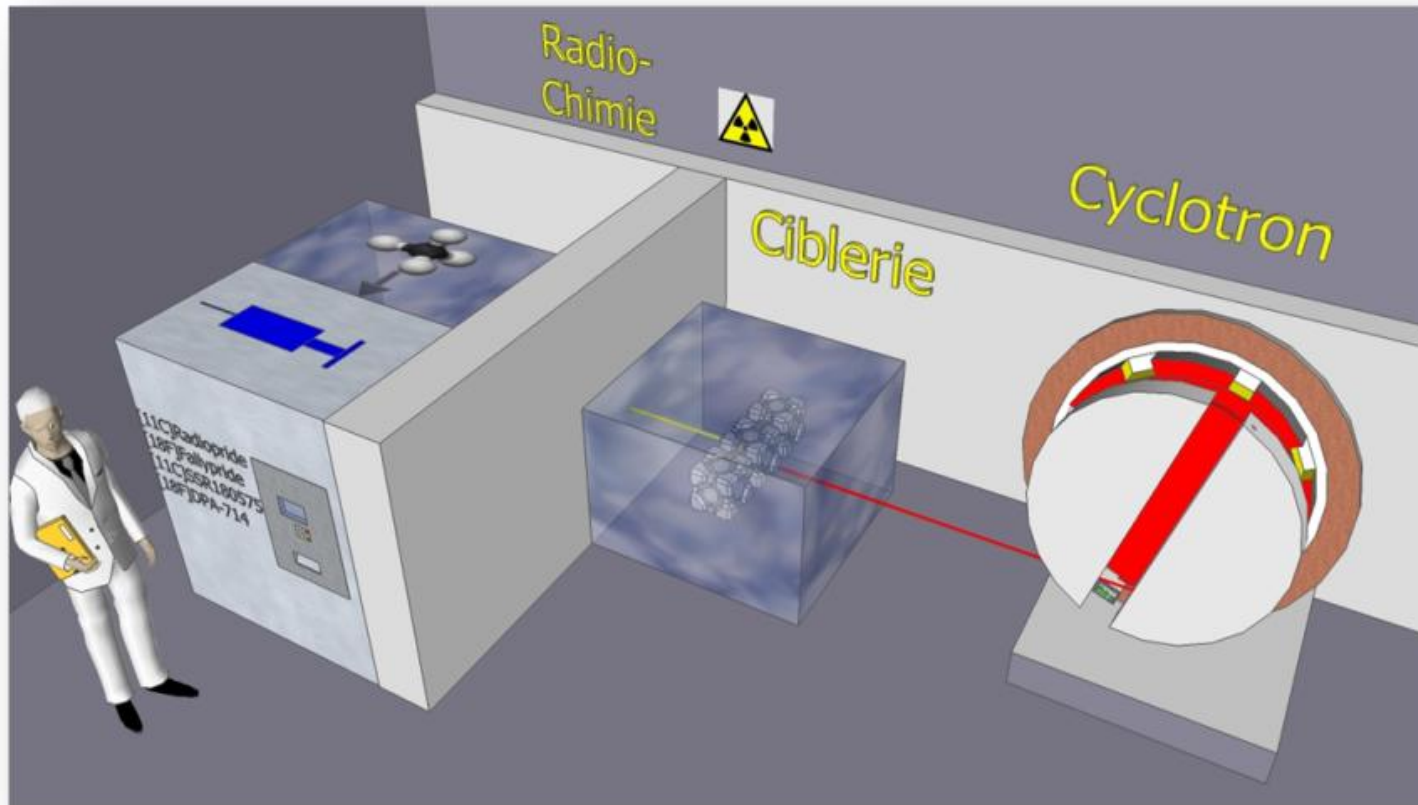
Short term/In Site/ **Open Innovation** (Public & Private)

- Distribute the technologies (*not the tracers*) to end users biologists and clinicians (*not expert in radiochemistry*) for the clinical validation
- Easy to use & to be installed “every where”
- On demand: μ -fluidic “1 dose 1 patient”, versatile & not limited by the Chemistry, or market size (*even the rare diseases - personalized medicine*)
- Access:
 - ✓ to all nuclides
 - *no labeling limit*
 - Very Short $\frac{1}{2}$ life (^{15}O , ^{11}C , ^{13}N) allowing “Multitracers protocols”
 - Long $\frac{1}{2}$ life & high energy nuclides for targeted radiotherapy
 - ✓ to all molecules even endogenous compounds, proprietary and in public domain
- High Specific Radio-Activity to allow quantification
- New Business model “Apple Store”:
 - ✓ Imaging Biomarkers & its μ -fluidic cassette co-developed with Academia & Pharma
 - ✓ the value is on the cassette & precursor not the “hot molecule”

Our vision:

Provide a platform to change the Molecular Imaging practice

LOTUS Project



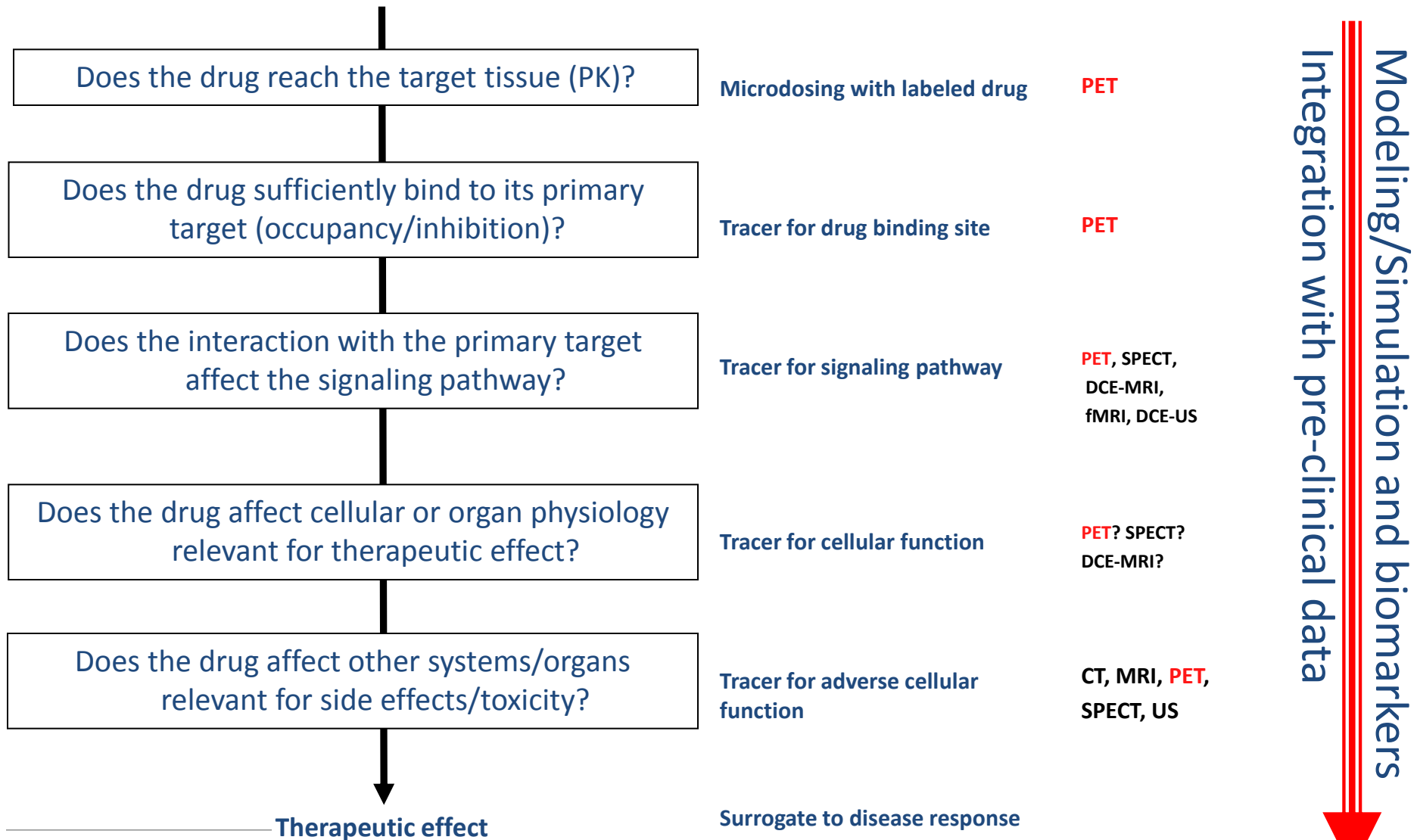
Complete GMP integrated functional solution instead of technology parts

12MeV*: minimum to garanty efficient radiochemistry (SRA) & high specific activity

LOTUS & Phrama industry

Translational Imaging in drug development

Questions & Answers



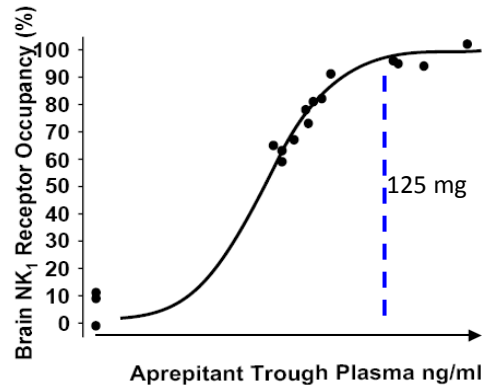
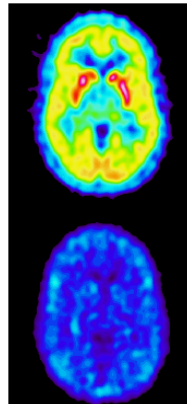
PET in Drug Development

Dose-occupancy profiles

^{18}F -SPARQ NK1 marker

Binding of PET tracer to NK₁ receptors

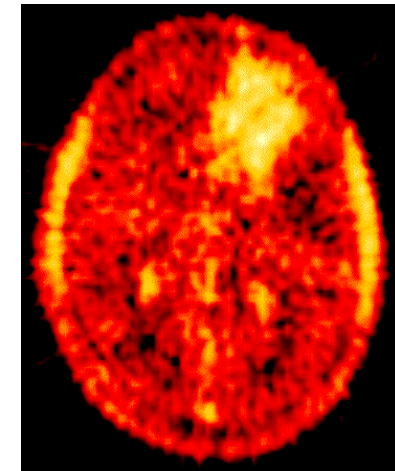
Blockade of PET tracer binding to NK₁ receptors by aprepitant



Tracer Binding
Low High

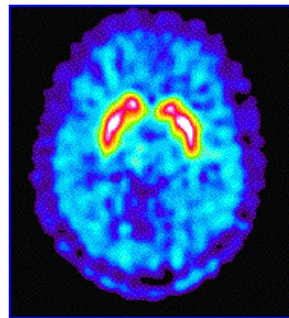
^{11}C -temozolamide

uptake by a glioma

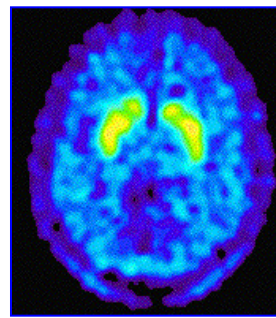


^{11}C -raclopride

(D2 site availability)



baseline

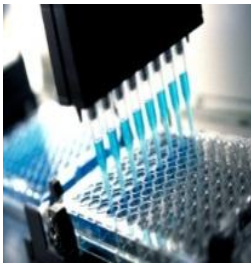


20mg ziprasidone

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from technology to innovation



In-Vitro Diagnostic

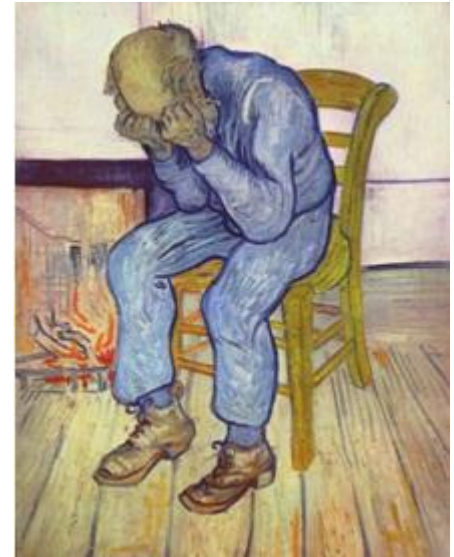
“Biomarkers in Psychiatry”

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Réunion annuelle 2013

Mental health: A major issue for public health



- **¼ of population concerned**
- **1st rank disability worldwide**
- **More deaths by suicide than car accidents (US, EU)**
- **Top ranked item of hospital expenses**
- **2nd cause for sick leave**
- **Huge direct and indirect costs: 240Md€ in EU (> cancer, diabetes)**

The Challenge

- Drug **toxicity** on the central nervous system can not be predicted nor measured today
- **In-vitro diagnostic test** of psychiatric illness does not exist
- Drug selection to the right patient could reduce side effects (suicide)



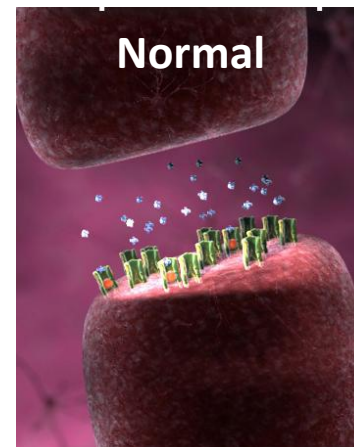
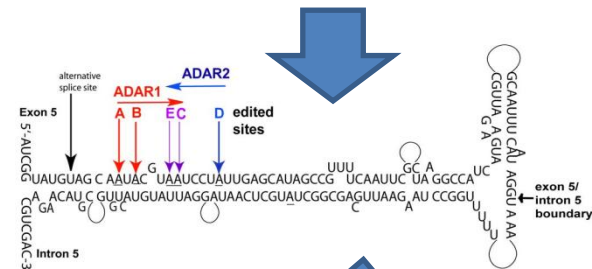
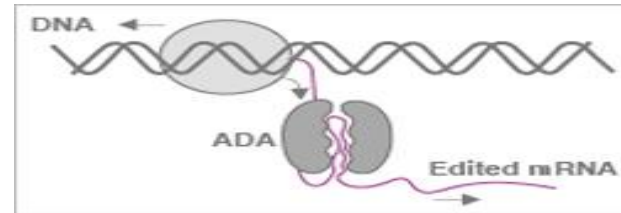
Need to move towards **personalized medicine**

Our project:

Development of an innovative biological test to enhance and to personalize the management of patients with psychiatric disorders

Regulation of serotonergic neurotransmission by RNA Editing

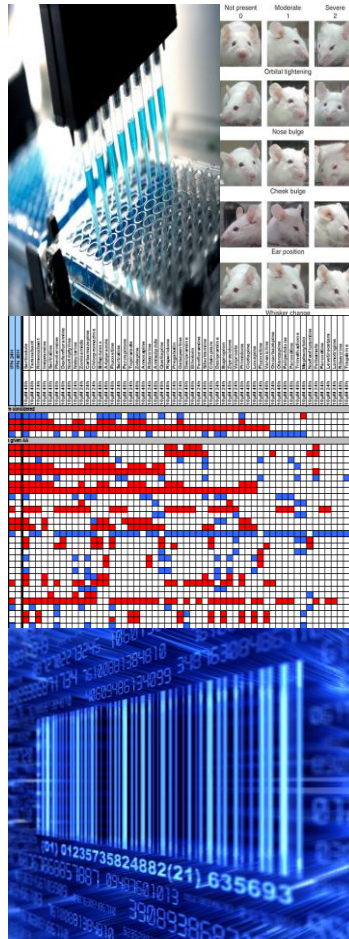
The 5HT2C RNA editing process



ALCEDIAG Tests consist in

Drug testing

Exposing human cells to candidate drugs



Characterizing induced alterations of RNA editing

Specifying drugs editing bioprints
Safety- Toxicity

Patient testing

Sampling patients' blood



Measuring expression and activity of RNA editing biomarkers



Interpreting changes to **personalize and monitor treatment**

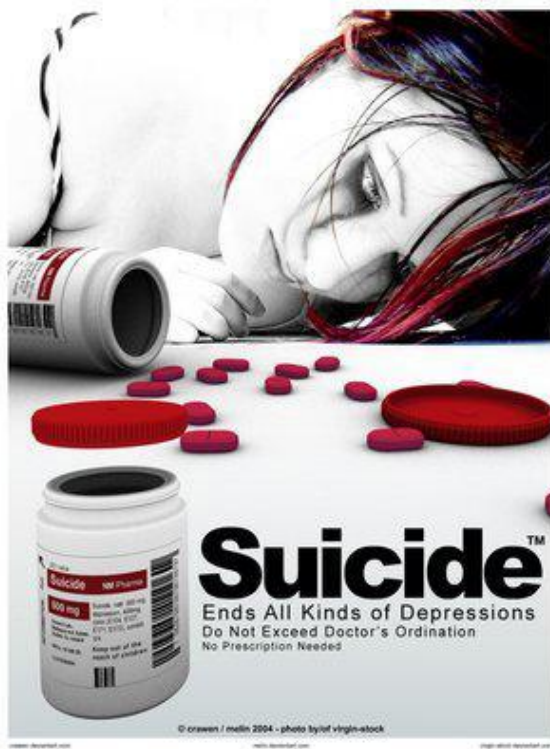


Overview of technology and products

- 1) Biological tests to **stratify** patients populations and to assess **drug responses**
- 2) Exploiting properties of a key regulation mechanism known as “RNA editing” as a source of **biomarkers**
- 3) Assays consist in:
 - **Drug** testing
 - **Patient** testing
- 4) Unique **dual approach** for **personalized medicine**

Predictive neurotoxicity drug screening

First application: drug-induced depression/suicide risk



Warning label

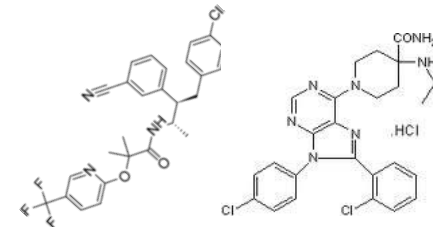


Guidance for Industry
Suicidality: Prospective
Assessment of Occurrence in
Clinical Trials

Clinical Trials
Assessment of Occurrence in
Suicidality: Prospective
Guidance for Industry



Market
withdrawal



Halted
development



Thank you