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from technology to innovation

diagnostic for personalized medicine

# EFPIA & Partners in Research: Mutual benefit

# "Diagnostic Industry Vision"

*EFPIA 2015 Annual Meeting*
*Luxembourg*

Bertrand LOUBATON
Vice President Healthcare

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# “LOTUS”

An open platform

*to validate and to use all types of*

*PET quantitative imaging biomarkers*

in research & clinical practice.

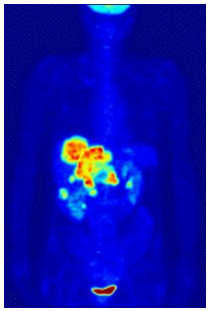
# LOTUS
## a paradigm shift for Molecular Imaging

## Situation

1. Few and rare isolated Key Leading PET research centers

   Able to develop, to produce and to use in-site a large number of potential useful PET quantitative imaging biomarkers labeled with various nuclides $^{15}O$ *(½ life =2minutes ),* $^{11}C$ *(20 minutes),* $^{68}Ga$ *(68 minutes),* $^{18}F$ *(110 minutes), ….. but not used in clinical practice nor multicenter clinical trials.*

2. A network of private PET production and distribution



   But with limited numbers of marketed PET Contrast Agents:

   - ✓ Limited to $^{18}F$ chemistry:
     - for logistic reason but less than 30% of the molecules can be labeled
     - "Contrast Agent" *(just Nice Image S/N)* not Imaging Biomarker *(quantification).*
   - ✓ Limited to large number of patients (ROI):
     - not adapted to Personalized Medicine *(ex: companion diagnostic)*
     - Expensive PET tracers doses
   - ✓ Limited to patentable molecules *(ex: endogenous)*

# LOTUS

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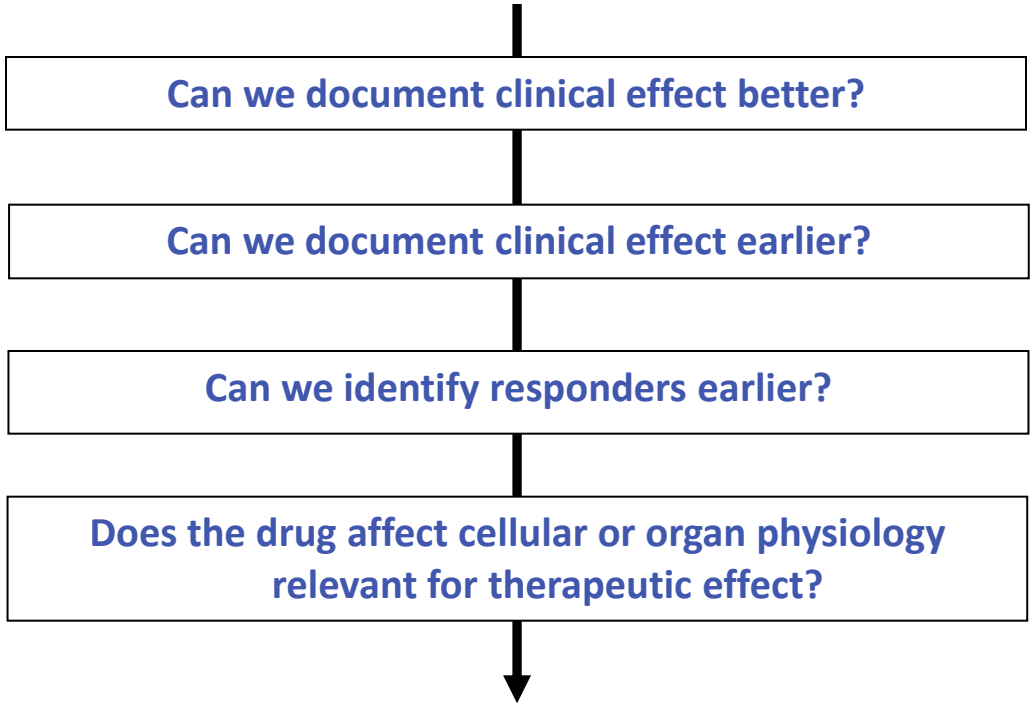
# Pharmaceutical industry

# Traditional imaging approach in drug development is insufficient for early decision making




CT – RECIST

Volumetric MRI

DCE-MRI

FDG

fMRI

***We are looking for Clinical therapeutic effect***

***<u>But all are late pharmacological effects:</u>***

**« Tumor concentration of drugs cannot be determined from plasma concentrations »**

**Bob Pinedo (July 1986)**

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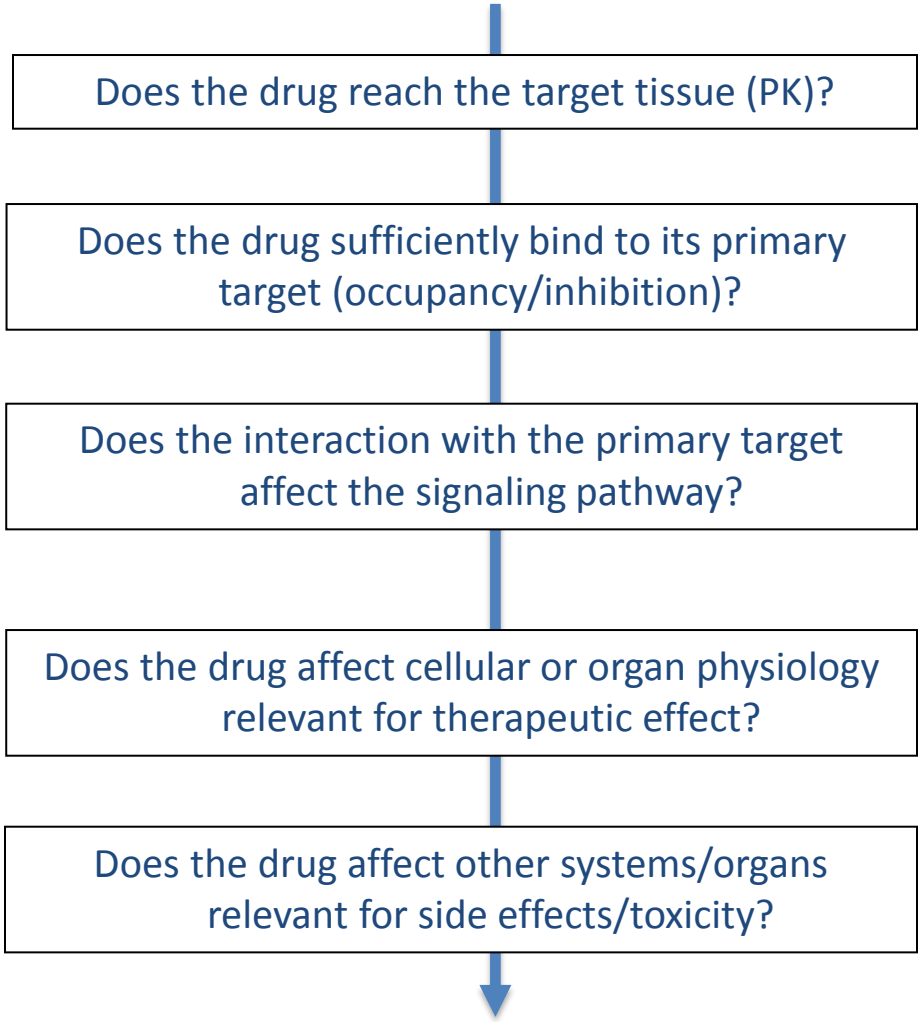
# Imaging Biomarkers in drug development

## *Questions & Answers*




| | |
|---|---|
| **Microdosing with labeled drug** | **PET** |
| **Tracer for drug binding site** | **PET** |
| **Tracer for signaling pathway** | **PET, SPECT, DCE-MRI, fMRI, DCE-US** |
| **Tracer for cellular function** | **PET? SPECT? DCE-MRI?** |
| **Tracer for adverse cellular function** | **CT, MRI, PET, SPECT, US** |
| **Surrogate to disease response** | |

Modeling/Simulation and biomarkers Integration with pre-clinical data

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# Personalized medicine in psychiatry

## EDITDIAG®: Blood test for diagnostic & treatment efficacy

*"One of the fundamental insights emerging from contemporary neuroscience is that mental illnesses are brain disorders."*

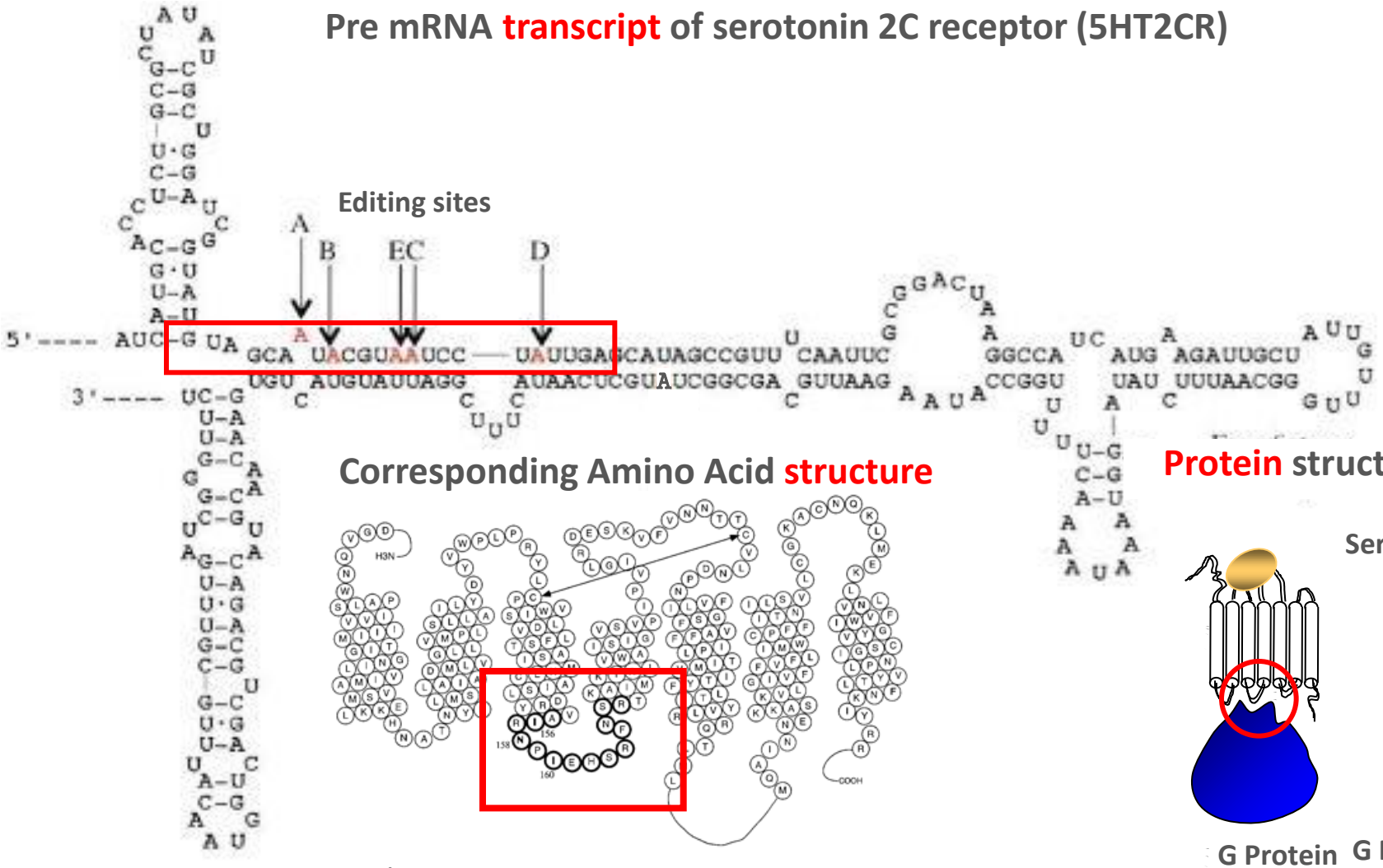
Thomas R. Insel, Director, National Institute of Mental Health

# Mental health: A major societal challenge


- ¼ of population concerned
- 1rst 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)

# 5HT2C Receptor RNA Editing mechanism

Pre mRNA **transcript** of serotonin 2C receptor (5HT2CR)




Corresponding Amino Acid **structure**



**Protein** structure



Serotonin

G Protein G Protein

2nd intracellular loop: G protein binding site

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# Pharmaceutical industry

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# Induced Depression & suicide

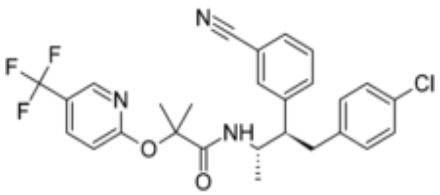
## A risk to be evaluate early

### Warning label

### Litigation


### Market withdrawal


### Halted development




Taranabant

August 2012

**Guidance for Industry**

**Suicidality: Prospective Assessment of Occurrence in Clinical Trials**

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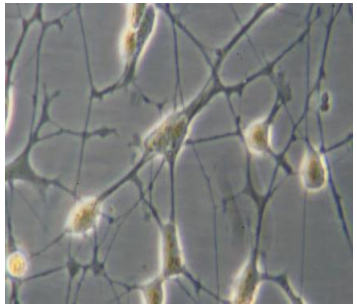
# EDITOX® & EDITDIAG®
## New Drug Development

### Predictive psychiatric toxicology & safety

Human culture cells exposition to drug candidates



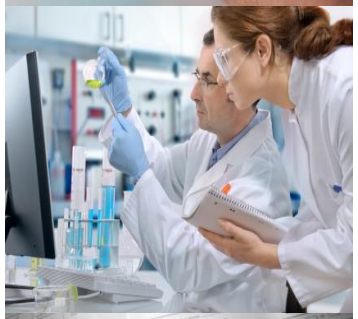
Characterisation of induced alterations of RNA edition

Drug 5HT2CR editing profile *for* ***Toxicity & Safety risk evaluation***

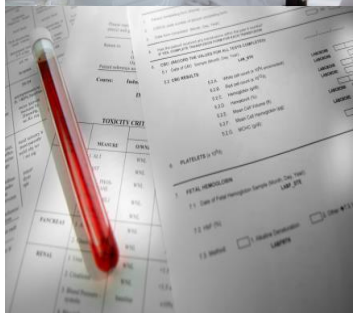

### Patient stratification & treatment follow up

Sampling patients' blood

Measuring expression and activity of RNA edited biomarkers



Patients ***Stratification, Treatment selection & monitoring***



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# Pharmaceutical & Diagnostic industries
## Rules for a successful convergence

The evolution toward stratified medicines & personalized care requires new or adapted marketed “diagnostic” solutions:

### I. For New Drug Development based on validated biomarkers

- ✓ The evolution toward “Imaging Biomarkers” needs a paradigm shift for imaging .
  - PET tracers: Contrast Agents VS Quantitative Imaging Biomarkers *(Time is an issue to use PET as a “Quantitative imaging biomarker”).*
  - MRI sequence: Manual VS Automatic & Standardized *( ex: Hippocampus measurement for AD)*
  - For all modalities: Standardization *(imaging agent & consistent performance of imaging equipments)*, Harmonization *(consistencies of data between different sites),* Evolution *(additional features & functionalities) .*

- ✓ Extend in-vitro tests beyond diagnosis:
  - Suicide risk identification: From diagnosis to Predictive toxicology, patients stratification & treatments follow up.

# Pharmaceutical & Diagnostic industries
## Rules for a successful convergence

## II. New Environment

- ✓ Medical Practices:
  - Healthcare practitioners need to be trained *(ei: "Nice image" Vs dynamic – "noise" can be valuable data).*
- ✓ Regulatory requirements:
  - New standards (*between manufacturers*), "market authorization" for useful not profitable solutions.

## III. New Economical Model

- ✓ Cost efficient:
  - Ei. PET tracers production: Distribution VS In-House *(adapted to personalized medicine).*
- ✓ Reimbursement and Perceptions of Value:
  - "Personalized Diagnosis" needs to demonstrate economic impact on healthcare delivery.
  - For "useful diagnostic solutions" that can't be developed by industry for operational & economical reasons (*ex: endogenous molecules, too small market*).

# Pharmaceutical & Diagnostic industries

## Rules for a successful convergence

### My vision

- **The Pharmaceutical Industry & Regulatory bodies**
  - ✓ Need to define their specific needs *("Biomarkers", Standardization & Harmonization)*.
  - ✓ Don't limit the development of the "Personalized medicine" to existing diagnostic solutions (*based on current medical practice*) but ask for mandatory improvements.

- **The Diagnostic industry:**
  - ✓ Have to play a more fundamental role in advancing personalized medicine, it needs to pursue Discovery and Validation adapted to future medical practices.
  - ✓ The collaboration with the pharmaceutical industry to develop the "Personalized medicine" is an opportunity to increase the value of "Diagnostic" (*ex: leveraging "Imaging" to "quantitative Imaging Biomarker"*).
  - ✓ But we need to find a way to propose to the clinicians the "useful diagnostic solutions" that can't be developed by the diagnostic industry (*profitability, public domain, …*)