Open Innovation in action: IMI flagship projects
PRISM and RADAR-AD

Emilio Merlo Pich, MD

Head, Quantitative Medicine, CNS TAU, Takeda Pharmaceutical International, Zurich, CH

IMI Stake-Holder Forum 2017 – Open Innovation
Crowne Plaza Le Palace • Rue Gineste 3, Brussels
Takeda is a global Pharma company & EPFIA member

Core therapeutic areas

- Oncology
- Gastroenterology
- CNS (vaccines)

Today we focus on CNS
Takeda R&D is committed to partnering and open innovation in concert with the external environment.

In 18 months, 43 partnerships signed and 28 consortia/PPP participations.

THE POWER OF PLUS
Takeda R&D CNS pipeline is driven by the patient’s needs

Patients with these selected disorders...

- Show significant suffering
- Pose a significant cost burden to society
- Have no treatments available

Psychiatry

- **Depression**
  - Treatment resistant depression

- **Schizophrenia**
  - Negative symptoms and cognitive impairment

Neurology

- **Neurodegenerative diseases**
  - Alzheimer’s Disease
  - Parkinson’s Disease
  - Rare Disease
Why should Pharma be involved in precompetitive consortia (private-public partnership - PPP)?

**Takeda's view**: if the consortia activities are aligned with R&D priorities, they provide deep insight into the external environment. This allows us to:

- Understand Emerging R&D trends
- Generate Portfolio Relevant Data
- Advance Science Policy and Regulatory Policy Issues
- Address Challenges in Clinical Development
- Accelerate Discovery & Development
- Fuel Partnering Capabilities

...and push scientific frontiers through collaboration across the healthcare ecosystem

**OUTCOME:**
PPP / precompetitive consortia activity facilitates and expedites our Portfolio Delivery and Broader Strategic Priorities
IMI is the prototypical PPP funding institution
Critical role of precompetitive consortia in addressing historical challenges to CNS drug development

- Poor disease biology understanding
  - human genetic / pathology repository
  - Patient-centric disease-related needs
  - Computational approach to novel target

- Heterogeneous patient populations
  - Enrichment strategy
    - Biomarker driven patient selection
    - Deep phenotype modeling

- Low precision of clinical endpoints
  - Digital surrogate vs. clinical score
  - Disease specific signal driven by the enrichment biomarker

- Operational challenges (failed trials)
  - Remote assessment, digital tools for patients identification, tracking, assessment and compliance

Today we focus on CNS

IMI
- PHAGO
- ADAPTED
- StemBANCC
- AETIONOMY
- AMYPAD
- PHARMACOG
- PRISM
- RADAR-CNS
- RADAR-AD
- DIAMOND
- THINK BIG”
  Digital – Remote and decentralized clinical trial
PRISM: Psychiatric Ratings using Intermediate Stratified Markers

Project coordinator: Martien Kas, University of Groningen, the Netherlands
Project leader: Hugh Marston, Eli Lilly and Company, United Kingdom

Takeda coordinator: Emilio Merlo Pich, Takeda Pharmaceutical International, Switzerland

The project leading to this application has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 115916. This Joint Undertaking receives support from the European Union’s Horizon 2020 research and innovation programme and EFPIA.
PRISM’s general concept:
“Providing quantitative biological measures to facilitate the discovery and development of new treatments for social and cognitive deficits in Alzheimer’s disease, schizophrenia and depression”
PRISM: 23 partners, including major EU Academic Centres, SME’s and Pharmaceutical Industry

**Academic consortium**
- University Medical Center Utrecht, Utrecht (UMCU)
- P1vital, LTD, Wallingford (P1vital)
- Radboud University Medical Center, Nijmegen (RUMC)
- Centro de Investigacion Biomedica en red, Madrid (CIBER)
- University of Bologna, Bologna (UNIBO)
- VU University Medical Center, Amsterdam (VUMC)
- Biotrial SAS, Rennes (BIOTRIAL)
- Drug Target ID BV, Nijmegen (DTID)
- University of Exeter, Exeter (UNEXE)
- SBGneuro Ltd, Oxford (SBG)
- concentris research management GmbH, Fürstenfeldbruck (concentris)
- Leiden University Medical Center, Leiden (LUMC)
- Erasmus Universitair Medisch Centrum Rotterdam, Rotterdam (EMC)
- European College of Neuropsychopharmacology, Utrecht (ECNP)
- European Federation of Associations of Families of People with Mental Illness, Leuven (EUFAMI)

**Industry consortium**
- Boehringer Ingelheim International GmbH, Ingelheim (BI)
- Novartis Pharma AG, Basel (Novartis)
- Pfizer Ltd, Sandwich (Pfizer)
- F. Hoffmann-La Roche Ltd, Basel (Roche)
- Takeda Development Centre Europe Ltd, London (Takeda)
- Eli Lilly and Company Ltd, Basingstoke (Lilly)
- Janssen Pharmaceutica NV, Beerse (Janssen)
Translational approach to social withdrawal: Human and rodent neurobiological homologies
1. Diagnosis and levels of social withdrawal (WHODAS)

2. Deep phenotyping of patients relevant for the neurobiology of social withdrawal

3. Existing database analysis

4. Integrated evaluation for stratification

PRISM: Proof of Concept in 160 patients (AD or SCZ)
PRISM: Testing a smartphone app for measuring sociability

Smartphone BeHapp (sensors)

Encrypted data

Secured data server - UMCU

WHODAS scale
fMRI
EEG
Genomics
Genetics

Clinical & biomarker correlation

Sociability scores

Behavioral profiles

Data analyses

Medical Ethical Approval UMCU (protocol: 14-395/D)
IMI initiative around Digital Technology solutions to profile patients symptoms relevant for novel drug development

**Remote assessment of disease and relapse – CNS**
- Develop a platform to collect and analyse digital data collected with mobile devise/sensors
- Started 2015
- Target patients with Epilepsy, Major Depressive Disorder and Multiple Sclerosis

**RADAR – AD**: Remote assessment of disease and relapse for patients with Alzheimer Disease - 2018

**DIAMOND**: Linking digital assessment of mobility to clinical endpoints to drive regulatory acceptance and clinical practice

**THINK BIG**:
- DataLakes (big data)
- Remote and decentralized clinical trials
- Digital endpoint validation for clinical trials
GOALS:

• To provide digital measures of the functional and cognitive status of AD patients at the early stages of the disease and correlate with standard clinical scale and neuropsychologic tests.

• To identify robust, scalable technology-enabled systems and specific endpoints that can be deployed and used in Real World settings (This search will include the experience of RADAR CNS)
Suggested architecture of the RADAD-AD project

- **Work package 1:** Management & Operations
- **Work package 2:** Assessment of patients-reported functional domains relevant to early Alzheimer’s Disease progression
- **Work package 3:** Communication with regulatory authorities, patient associations, payers and ethics
- **Work package 4:** Development of a technology-enabled system to measure identified functional domains via smartphone, wearable and fixed home-based sensors
- **Work package 5:** Validation of the technology in assessing functioning in a Real World setting and clinical assessment
RADAR–AD: key facts

- **Industry consortium**: Janssen (lead), Takeda, Eli Lilly, Novartis, Nokia, Software AG
- **Duration**: 36 months.
- **Budget**: expected EUR 5.0M + current in-kind contribution is EUR 3.6M.
- **Status** (October 2017): Industry Proposal under reviewer assessment
- **Academic Consortia**: unknown yet. It is expected that among the members of the consortium there are representatives of patient association(s), of regulatory agencies and of payers.
Precompetitive partnering and open innovation is perceived as a necessary risk-reducing step for industries aiming to deliver novel treatments to patients.

PPPs should provide a tremendous opportunity to partner in advancing science, speeding up R&D and faster access to new medicines.

These opportunities require the presence in the PPPs of not only academics, but also representatives of patient associations, regulatory agencies and payers (or at least the access to them).

IMI PPPs should deliver results/product that will effectively improve the development and the regulatory filing of novel treatments, e.g.:

- Validation of a novel methods to assess biomarkers or clinical efficacy to stratify patients;
- Regulators support of the validated biomarkers/endpoints that should be used in future clinical trials;
- Payer recognition of some validated biomarker/endpoint/outcome that can be used in Real World to assess the actual impact of novel treatments.
Acknowledgement

- All members of PRISM (in particular Martien Kaas)
- All colleagues that worked in the preparation of RADAR-AD (in particular Vaibhav Narayan)
- The component of the Takeda PPP Steering Group.
- The colleagues of the Takeda CNS TAU, DAT and Data Science.
- The colleagues of GMA, Takeda in Zurich