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

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IMI Stake-Holder Forum 2017 – Open Innovation

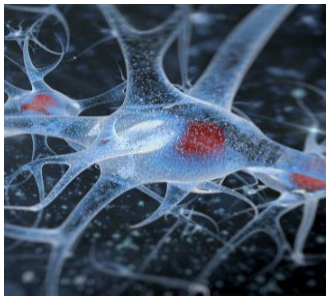
Crowne Plaza Le Palace • Rue Gineste 3, Brussels

Takeda is an global Pharma company & EPFIA member

Takeda Pharma

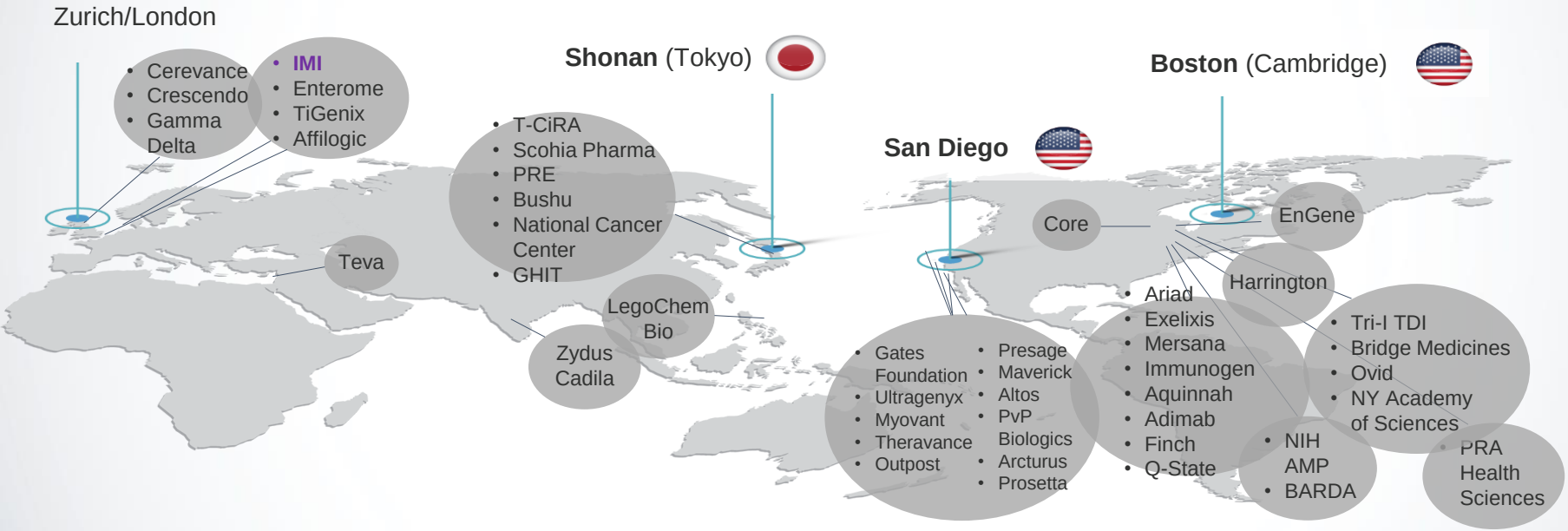
Core therapeutic areas

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



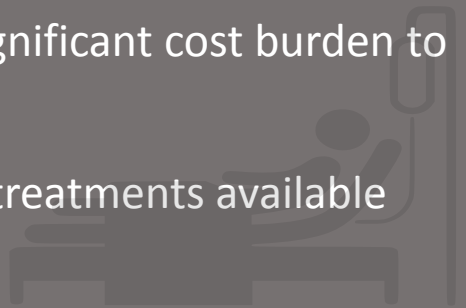
In 18 month 43 partnerships signed and 28 consortia / PPP participations

Takeda R&D CNS pipeline is driven by the patient's needs

Psychiatry	**Depression**	Treatment resistant depression
	Schizophrenia	Negative symptoms and cognitive impairment
Neurology	**Neurodegenerative diseases**	Alzheimer's Disease Parkinson's Disease Rare Disease

Patients with these selected disorders…

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



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

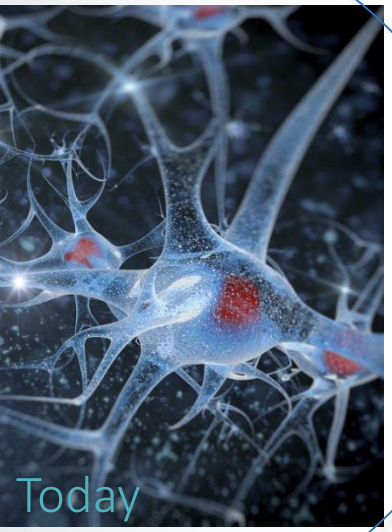
…and
push scientific frontiers through collaboration across the healthcare ecosystem

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



Today we focus on CNS

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**

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

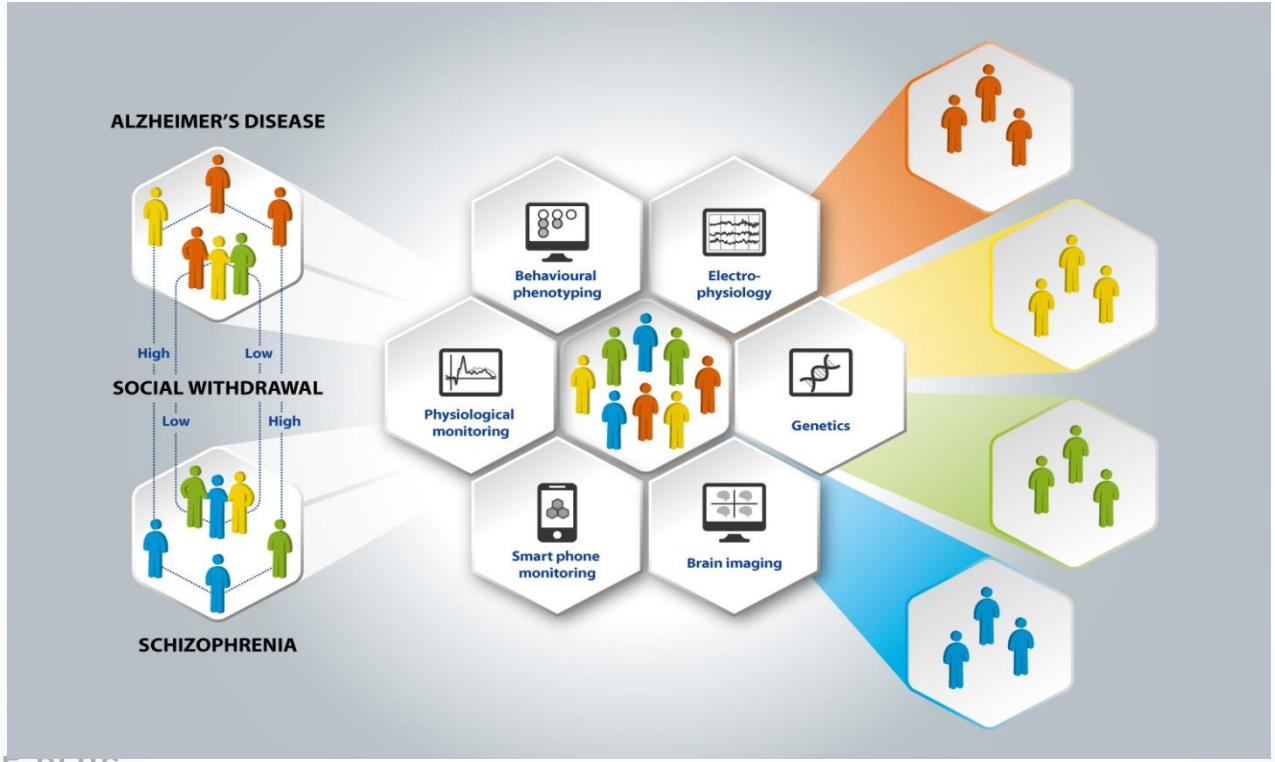
Project leader: Hugh Marston, Eli Lilly and Company, United Kingdom

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

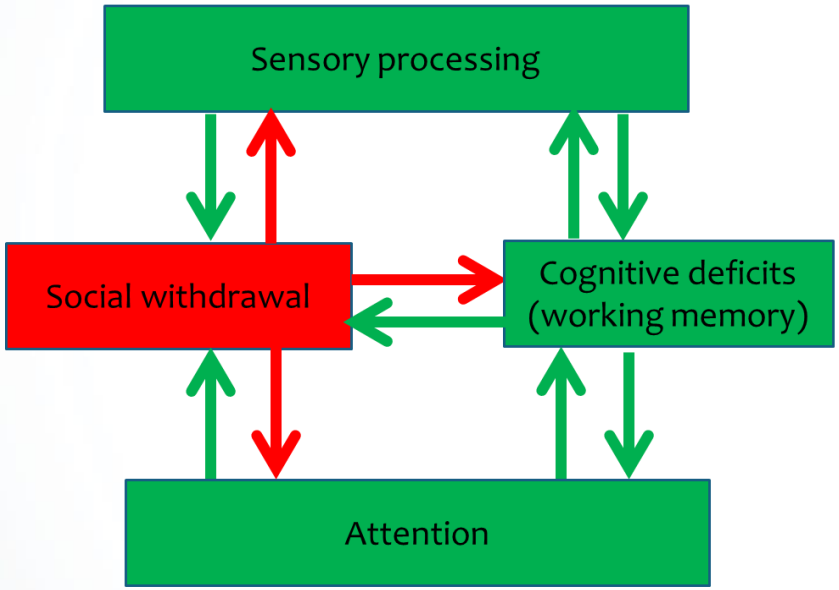
Academic consortium

- 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

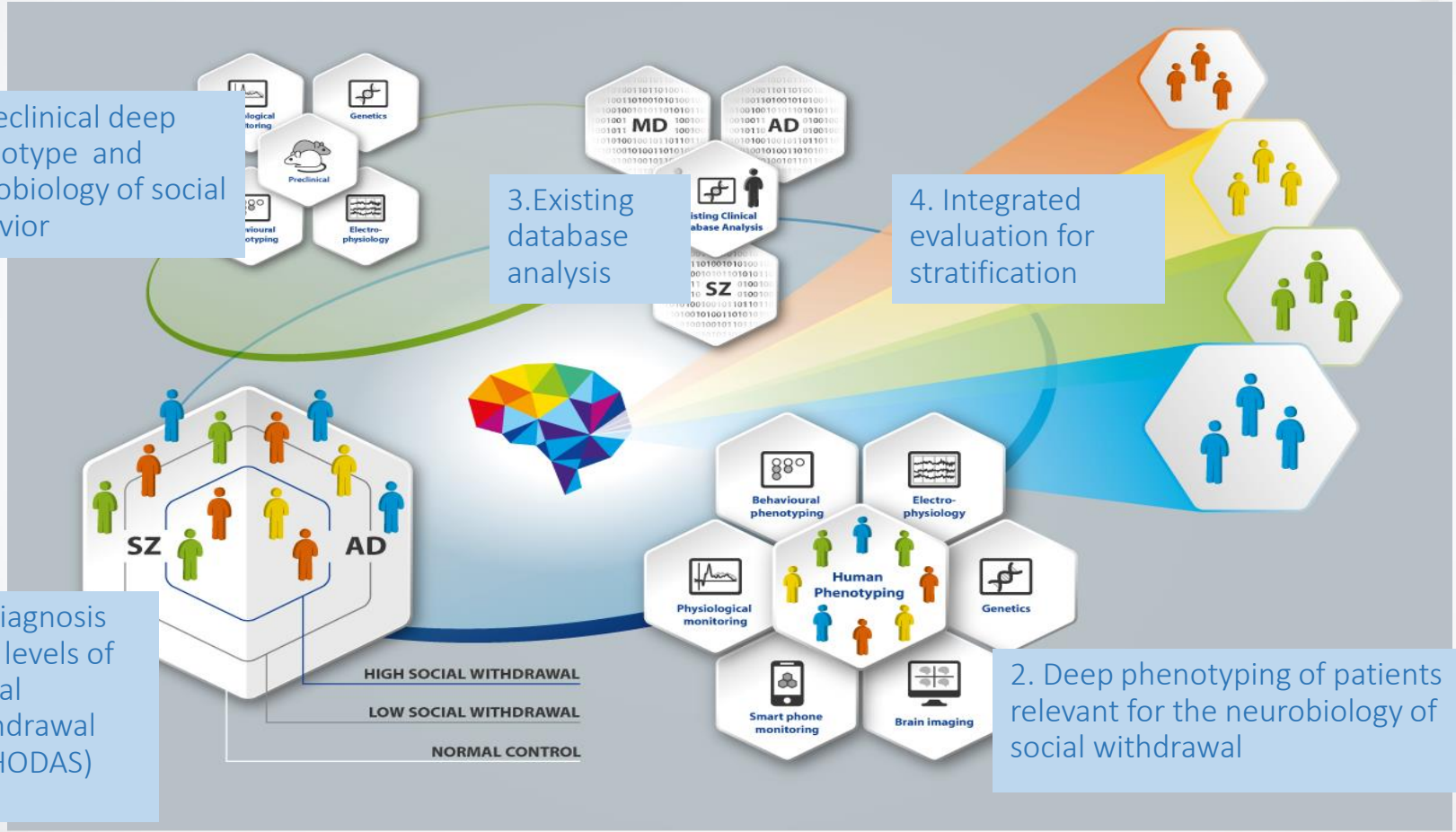


PRISM: Proof of Concept in 160 patients (AD or SCZ)

2. Preclinical deep phenotype and neurobiology of social behavior

3.Existing database analysis

4. Integrated evaluation for stratification



1. Diagnosis and levels of social withdrawal (WHODAS)

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

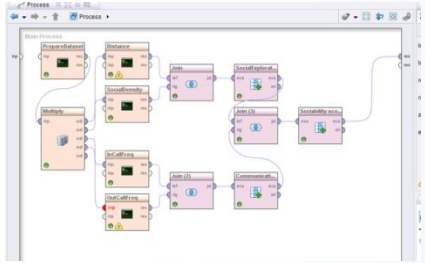
PRISM: Testing a smartphone app for measuring sociability

Smartphone BeHapp (sensors)

Encrypted data

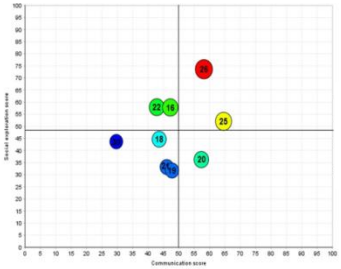
Secured data server - UMCU

read outs



Data analyses

Behavioral profiles



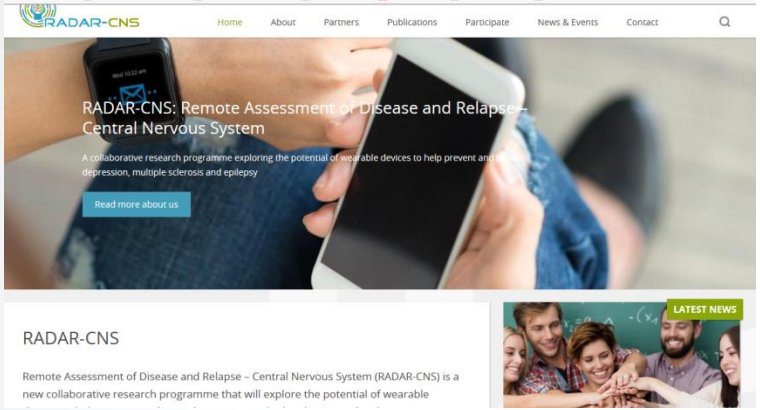
Sociability scores

Clinical & biomarker correlation

WHODAS scale
fMRI
EEG
Genomics
Genetics

Medical Ethical Approval UMCU (protocol: 14-395/D)

IMI initiative around Digital Technology solutions to profile patients symptoms relevant for novel drug development



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

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

THINK BIG :

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

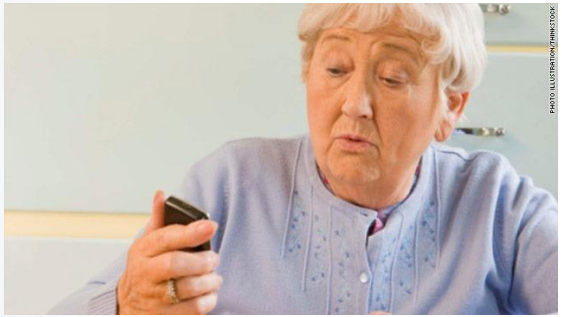
RADAR–AD: aims

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 system s** 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.

Critical Summary

- Precompetitive partnering and open innovation is perceived as a necessary risk-reducing step for industries aiming to delivery 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