



**PharmaCog: advancing science and treatment of AD"**

**Coordination**

**Dr Elaine A IRVING**  
**GlaxoSmithKline**  
**Gunnels Wood Road**  
**Stevenage SG1 2NY**  
**UK**  
**Tel : +44 (0) 7500765703**  
**E-mail : Elaine.A.Irving@gsk.com**

**Prof Olivier BLIN**  
**Université Méditerranée**  
**CIC-CPCT, Hôpital Timone,**  
**13385 Marseille Cedex 5**  
**France**  
**Tel : +33 491384646**  
**E-mail : olivier.blin@ap-hm.fr**

Recently the EU Council of Ministers for Health underlined the importance of generating novel therapeutic agents both for symptomatic and disease modifying treatment of Alzheimer's disease (AD). However, despite the increase in translational medicine activities attrition rates still remain high and progress in bringing these biomarkers and models to a state of readiness as effective decision making tools is slow as each academic and pharmaceutical company work in isolation.

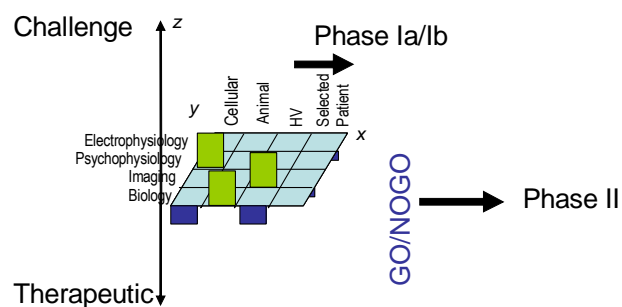
The €22M project PHARMA-COG was launched which funded under the Innovative Medicine Initiative (an initiative co-funded by the European Commission and the European Federation of Pharma Industries Association (EFPIA), the focus of which is to develop tools to streamline AD drug discovery and accelerate the delivery of effective agents to patients.

The PHARMA-COG consortium consists of 30 public (12 Universities, Research Centres, Hospitals) and private partners (5 SMEs and 11 EFPIA members), as well as a patients' Association Alzheimer Europe, coming from 10 different EU Members states. PHARMA-COG will also work closely with the EMEA, as an associated partner of this project, to share project progress and discuss the implications for drug development in Europe. The combined size and expertise of PHARMA-COG provides a truly unique opportunity to validate the tools required to fundamentally change the drug discovery process in AD and accelerate efficacious drug to patients across Europe.

Bringing together European experts in technologies fully translatable from animal to human, experts in translational medicine, drug discovery and mathematical modelling, PHARMA-COG proposes to accelerate this validation using a 'MATRIX' approach *i.e.* conducting parallel experiments in animals and human using a comprehensive and standardised battery of behavioural, neurophysiological, morphological/functional imaging, and biochemical endpoints to:

- develop models with greater predictive capacity for the clinics
- develop and validate translatable pharmacodynamic markers to support dose selection
- develop challenge models to support early hint of efficacy studies
- identify and validate of markers of disease progression and patient stratification.

### Matrix development strategy

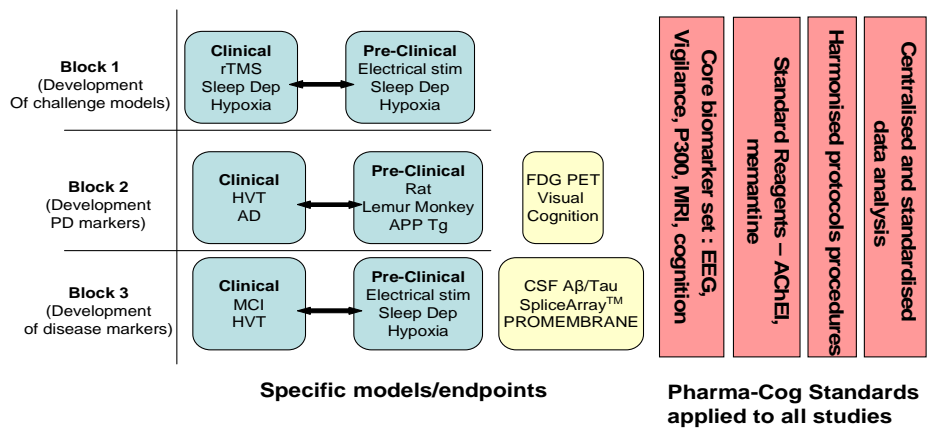


- A multidimensional "MATRIX" approach will be implemented throughout this project by conducting parallel pharmacodynamic studies in animals, healthy volunteers and selected patient cohorts (x axis), using the same fully translational pharmacodynamic endpoints (y axis), the same provocation challenges and therapeutic interventions (z axis) using single dose and medium-term treatment. This approach is based on i) multi-modal data collection from harmonized animal and human models, ii) extraction of selected features from this data collection (biomarkers/animals, healthy volunteer models, physiological and pharmacological challenges), and iii) advanced quantitative pharmacological assessment of the data generated across modalities and studies. The markers of the clinical section on disease modifying drugs will be collected following the ADNI protocols for clinical, neuropsychological, structural imaging, CSF, and blood data and sample

collection. Novel imaging and peripheral markers will also be added to this battery. Single and double transgenic mice overexpressing human mutated forms of amyloid precursor protein, PS1 and tau will also be characterised using the same marker MATRIX to increase our translational understanding of the Tg mice currently used to support disease modifying drug development. Novel models potentially more representative of AD patients will also be explored.

- The overall objective of this project is to develop and validate tools to facilitate the delivery of effective symptomatic and disease-modifying agents for Alzheimer’s disease to the patient. PHARMA-COG will achieve this through utilising the MATRIX approach combining both routinely used and innovative neurophysiological and biochemical approaches. The main objectives outlined in the call will be addressed by:

- 1) identifying and validating **healthy volunteer (HVT) challenge models** suitable for use in early clinical development of symptomatic treatment to support **‘hint of efficacy’ studies** which can be back-translated to pre-clinical studies
- 2) identifying and validating a **pharmacodynamic marker MATRIX** sensitive to central pharmacological activity of a symptomatic or disease modifying agent to determine **pharmacologically effective dose ranges and markers indicative of clinical efficacy**
- 3) identifying and validating a pharmacodynamic marker MATRIX sensitive to the **early onset of disease and subsequent progression thus identifying those markers most likely to be sensitive to pharmacological manipulation**
- 4) identifying a **pharmacodynamic marker MATRIX** (pre-clinically) sensitive to disease progression, central amyloid lowering and to other **disease-modifying approaches** which can be translated forward into early disease modifying trials to demonstrate **proof of mechanism**.
- 5) identifying **animal models** with biomarker signatures similar to that seen in mild cognitive impairment (MCI)/AD patients **offering improved predictive capacity** of disease progression for the clinic.



By the end of this 5-year project PHARMA-COG will have a) validated the tools necessary to streamline AD drug discovery and accelerate effective medicine to patients, b) set the standard for European drug discovery providing optimised and validated protocols c) provided the infrastructure to sustain world class drug discovery in Europe and driven the development of a new generation of leading scientists focussed on the translation from animal to human d) boost intersectoral collaborations and trainings as well as disseminate the obtained results from health professionals to patients.

## List of participants:

Participant No.	Participant organisation name	Participant organisation short name
1 (Coordinator)/EFPIA	GlaxoSmithKline R&D Ltd	GSK
2 (Managing entity of IMI JU funding)/HE-HOSP	Université de la Méditerranée, Aix Marseille II	UnivMed
3 RES-HOSP	Institut d'investigacions Biomediques August Pi I Sunyer	IDIBAPS
4 HE-HOSP	Université de Lille 2	UL2
5 HE-HOSP	Universitätsklinikum Leipzig	ULEI
6 HE	Universidad de Murcia	UMU
7 HE-HOSP	Universität Duisburg-Essen	UKEssen
8 RES	Centre National de la Recherche Scientifique	CNRS
9 RES	Institut National de la Santé et de la Recherche Médicale	INSERM
10 HE	University of Verona	UNIVR
11 RES	Provincia Lombardo-Veneta - Ordine Ospedaliero di San Giovanni di Dio – Fatebenefratelli	IRCCS-FBF
12 HE	Universita degli Studi di Foggia	UNIFG
13 HE-HOSP	Mario Negri Institute	MNI
14 SME	Innovative Concepts in Drug Development	ICDD
15 SME	Alzprotect	ALZP
16 SME	Qualissima	QUAL
17 SME	ExonHit Therapeutics	EHT
18 SME	Innovative Health Diagnostics	IHD
19 ASSO	Alzheimer Europe	AlzE
20 EFPIA	Astra Zeneca AB	AZ
21 EFPIA	Boehringer-Ingelheim International GMBH	BI
22 EFPIA	Novartis pharma AG	Novartis
23 EFPIA	Institut de Recherche Servier	Servier
24 EFPIA	UCB Pharma, SA	UCB
25 EFPIA	Merck Serono	Merck
26 EFPIA	Lilly	Lilly
27 EFPIA	Janssen Pharmaceutica N.V.	Janssen
28 EFPIA	F. Hoffmann-LaRoche	Roche
29 EFPIA	H. Lundbeck A/S	LDB
Associated Partner ORG	European Medicines Agency	EMA