Blood biomarkers for the early diagnosis of dementia with Lewy bodies

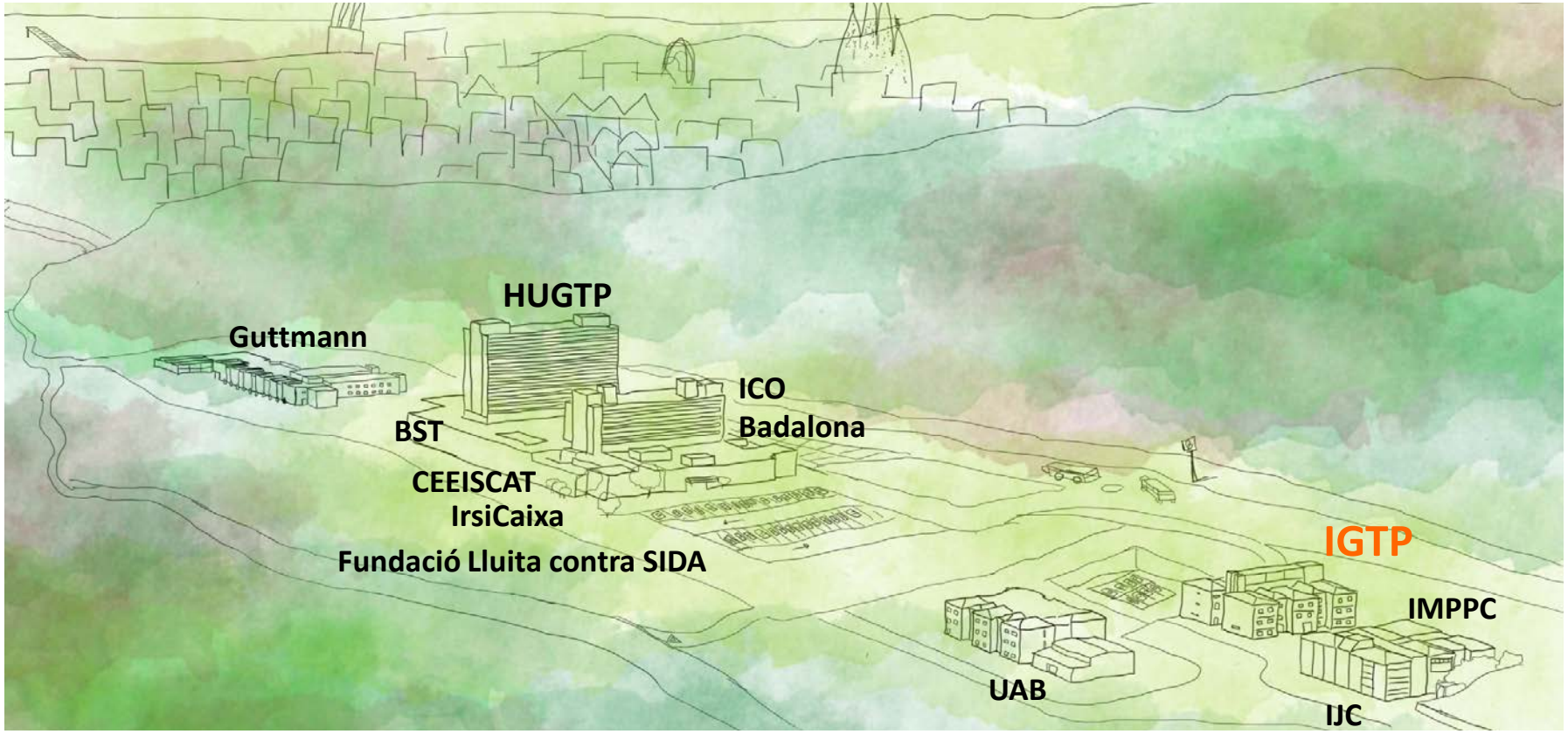
Fundació Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol

Barcelona, 20 de octubre de 2015

Content

1. The Institution
2. The Product
   a) Target Indications
   b) The biomarkers
   c) Differential features facing the market
   d) Current status of development
   e) IPR protection
   f) Pitfalls & Risks to be considered
3. Partnering Opportunities

1. The Institution



The Health Sciences Research Institute Germans Trias i Pujol (IGTP) is a CERCA biomedical research centre on the Can Ruti Campus, around the Germans Trias i Pujol Hospital in Badalona just outside Barcelona. As accredited centre of excellence for Medical Research accredited by the "Instituto Carlos III", the IGTP coordinates research and innovation activities on the campus as well as providing technical platforms and know-how to the scientific and medical community. The Can Ruti Campus is home to diverse research centres, including several which are outstanding in their fields, a teaching unit of the Autonomous University of Barcelona and various spin-offs.

The Research Group

Patología estructural y molecular; Director: Prof A Ariza

Área de cáncer

- Tumores cutáneos
- Linfomas
- Tumores gastro-intestinales

Área de neurociencias

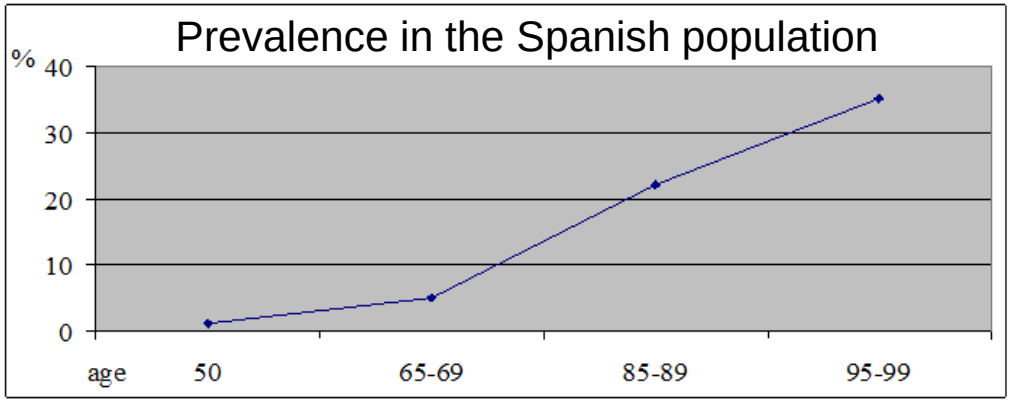
- Neuro-oncología
- **Neuro-degeneración**
- Neuro-infección

K Beyer, PhD
A Gámez, MSc
L Pérez, MSc
J Canet, MSc

- Transcriptómica y genómica de las sinucleinopatías
- Identificación de biomarcadores diagnósticos

2. The Product: a) Target Indications

DEMENTIAS



Alzheimer's disease (AD)	Dementia with Lewy bodies (DLB)	other dementias
45-50%	25-30%	

- polygenic / multi-factorial, heterogeneous disease

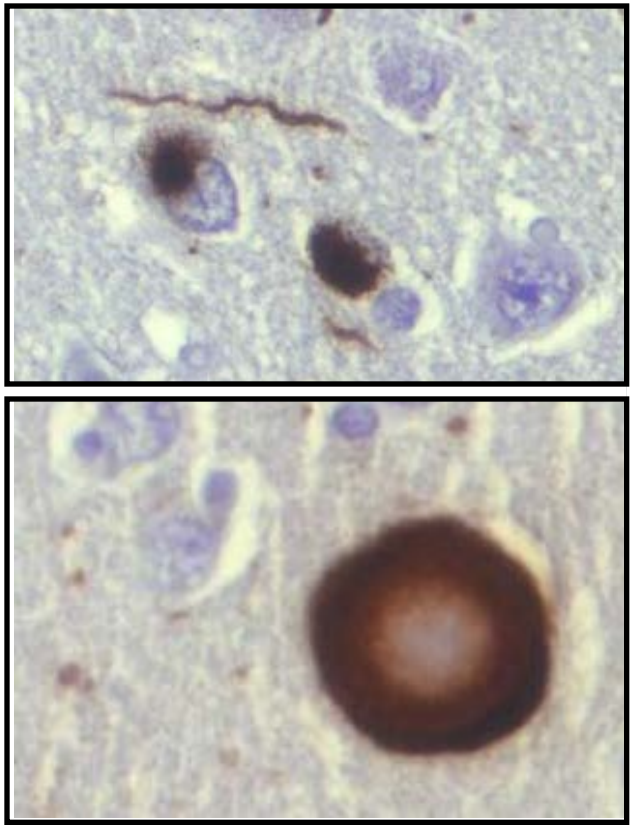
2. The Product: a) Target Indications

SYNUCLEINOPATHIES

= group of three diseases:
1. Parkinson´s disease (PD)
2. DLB
3. Multisystem atrophy (MSA)

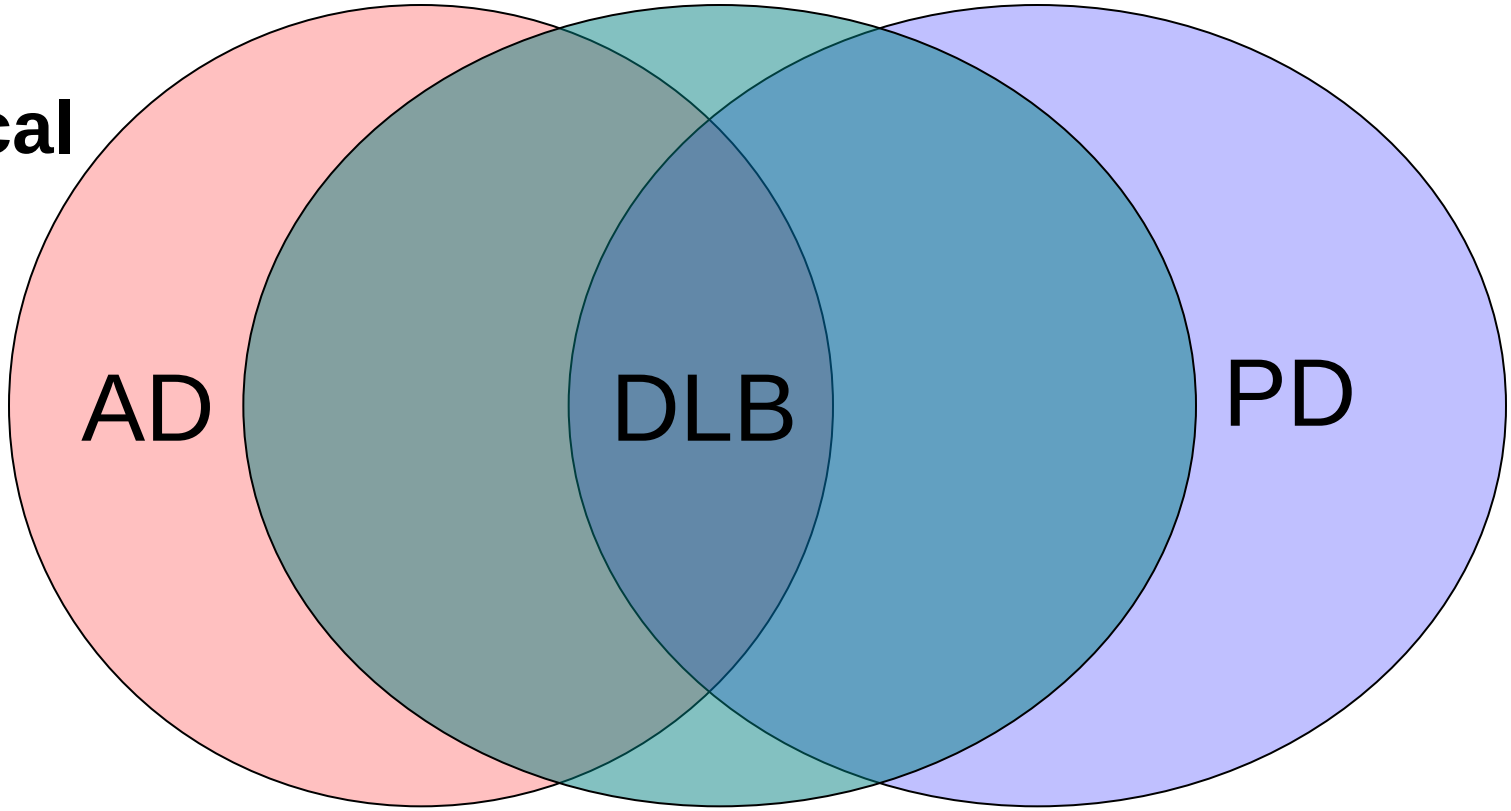
Primary pathological mechanism → oligomerization y aggregation of alpha-synuclein

Alpha-synuclein → formation of intra-neuronal inclusion bodies



2. The Product: a) Target Indications

AD / DLB / PD → neuro-pathological overlap:



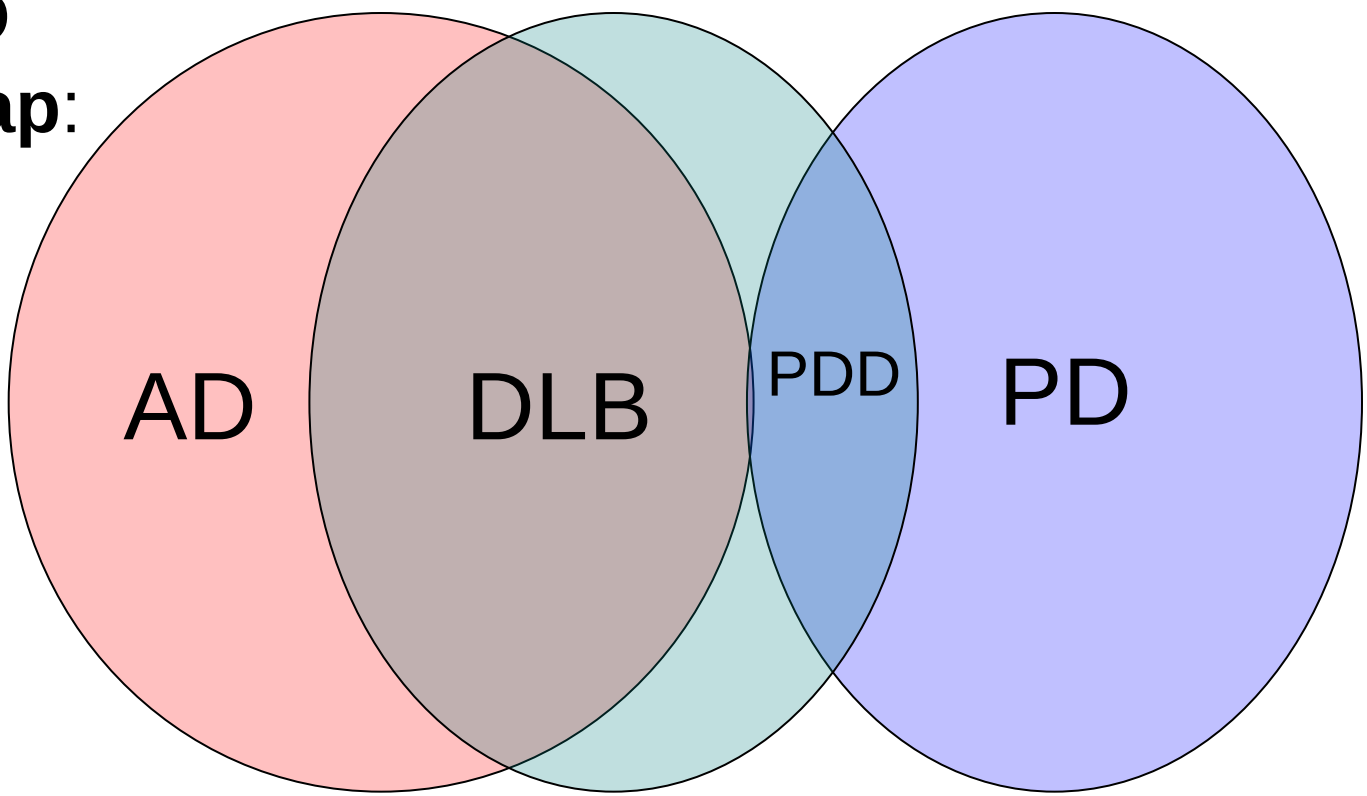
2. The Product: a) Target Indications

AD / DLB / PD clinical overlap:

→ DLB misdiagnosis

→ wrong treatment

→ adverse reaction

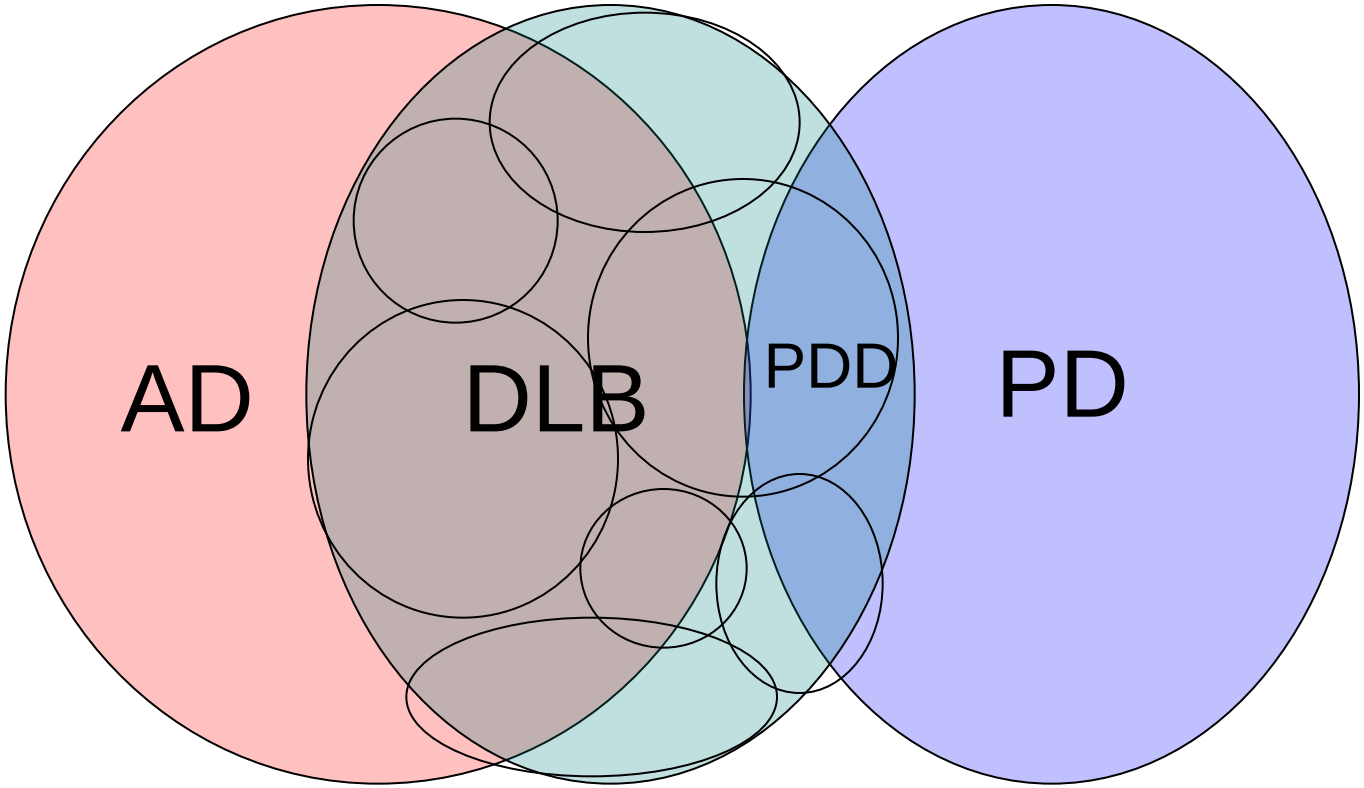


2. The Product: a) Target Indications

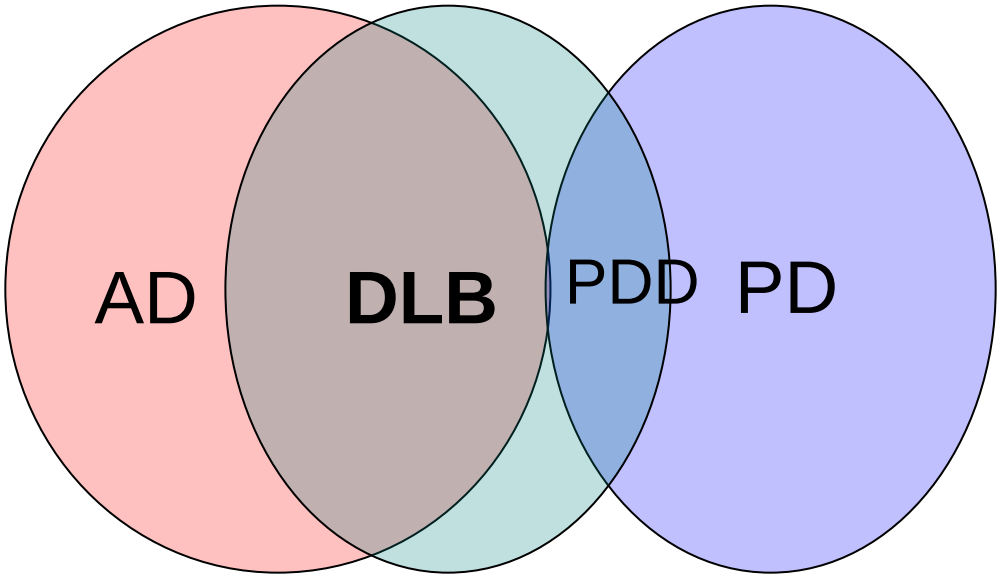
Genetic heterogenity:
- Subgroups
- different molecular mechanisms

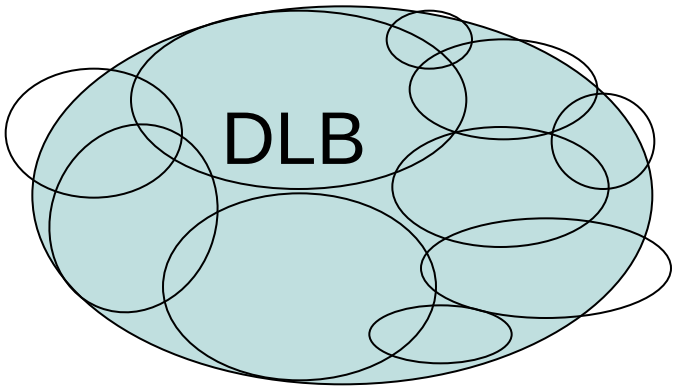
→

one pathology



2. The Product: a) Target Indications





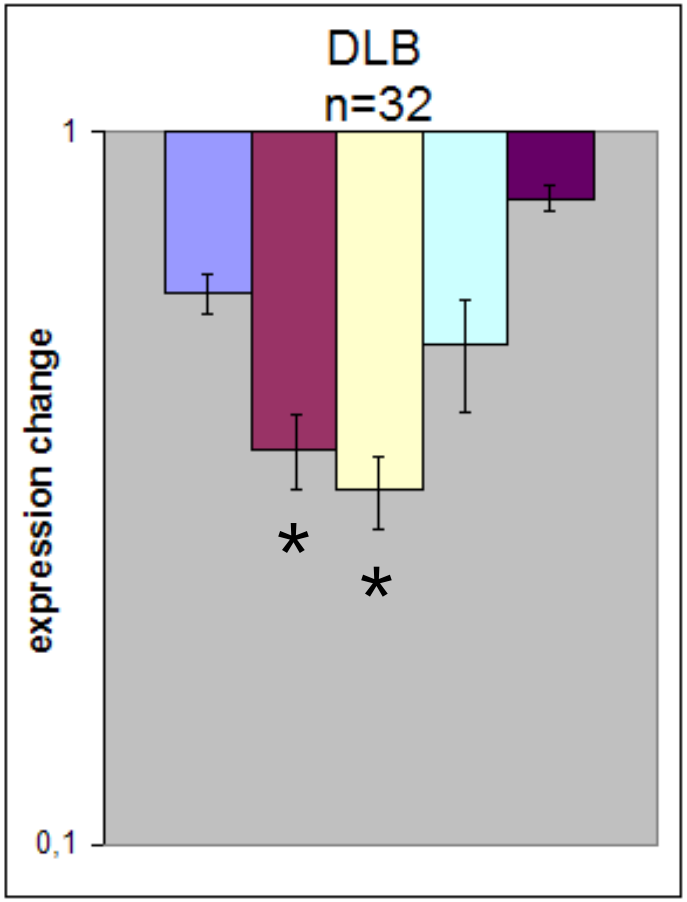
Main question:

HOW TO DIAGNOSE DLB CORRECTLY?

DLB = heterogeneous disease → How to diagnose the different subgroups?

2. The Product: b) The biomarkers

Genetic biomarkers for the early diagnosis of DLB



Biomarker 1

Analysis of relative expression of 5 Lewy body disease-related transcripts in blood of DLB patients in comparison with healthy controls.

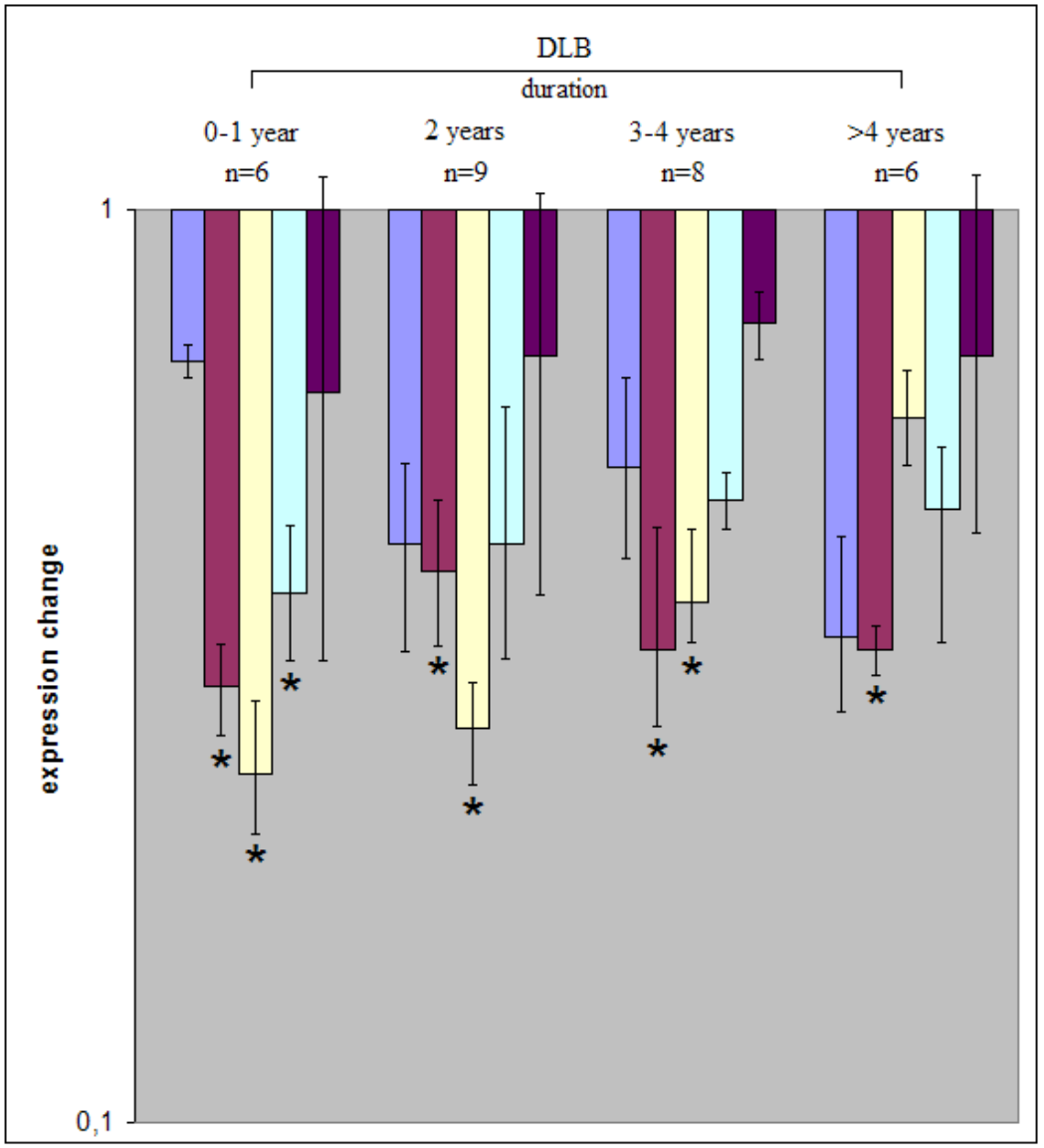
- PAX-blood RNA tubes
- RNA extraction with QIAcube
- real-time PCR with SybrGreen
- beta-actin (ACTB) and porphobilinogen deaminase (PBGD)
- ΔΔCt method

2. The Product:
b) The biomarkers

Genetic biomarkers for the early diagnosis of DLB

Biomarker 1

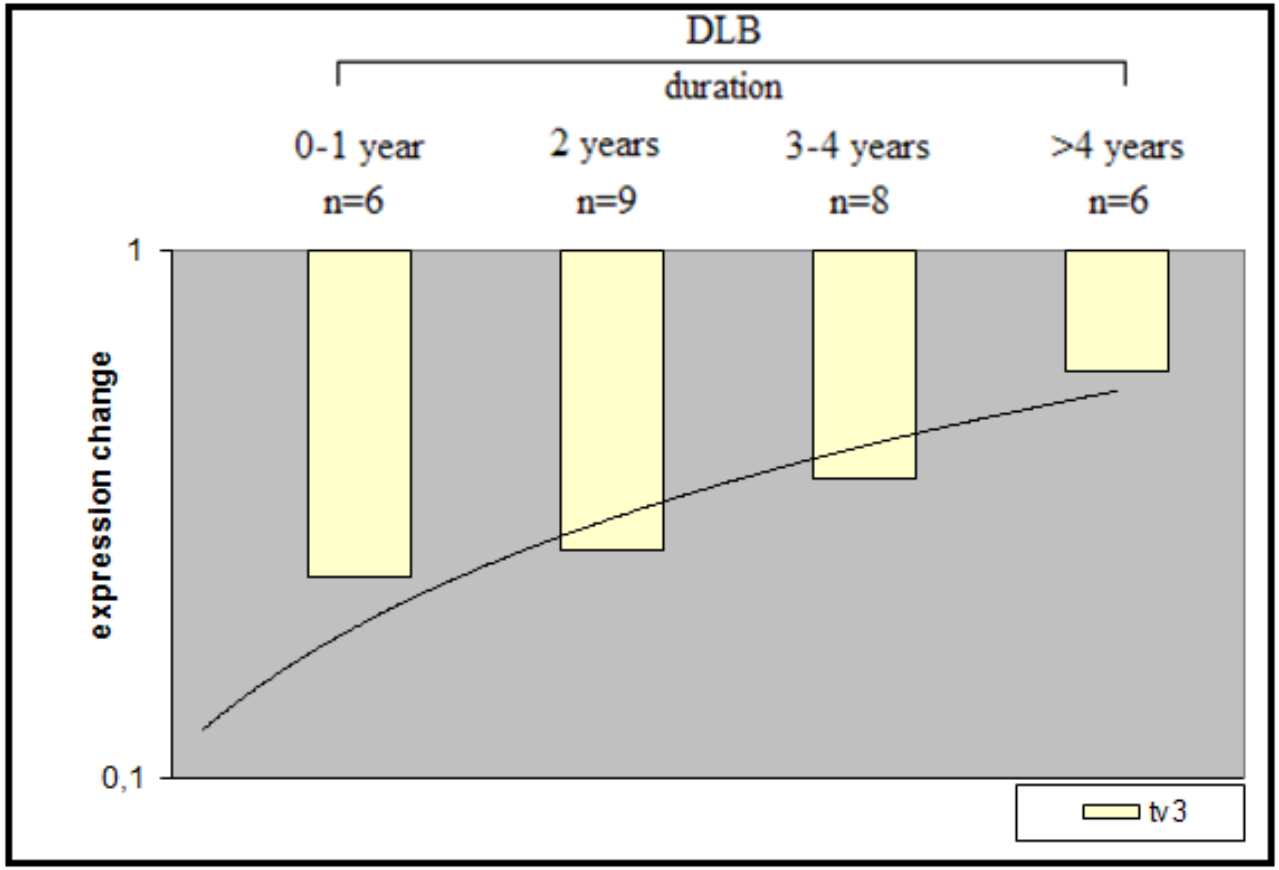
DLB patients divided by disease duration from onset



2. The Product: b) The biomarkers

Genetic biomarker to monitor the progression of Lewy body disease

Biomarker 1



2. The Product: b) The biomarkers

Genetic biomarkers for the early diagnosis of DLB

Biomarker 2

Analysis of 5 polymorphisms within the regulatory region of a Lewy body disease-related gene.

- DNA extraction from blood (QIAcube)
- Fragment analysis
- Sequencing
- Obtaining of the genotype combination

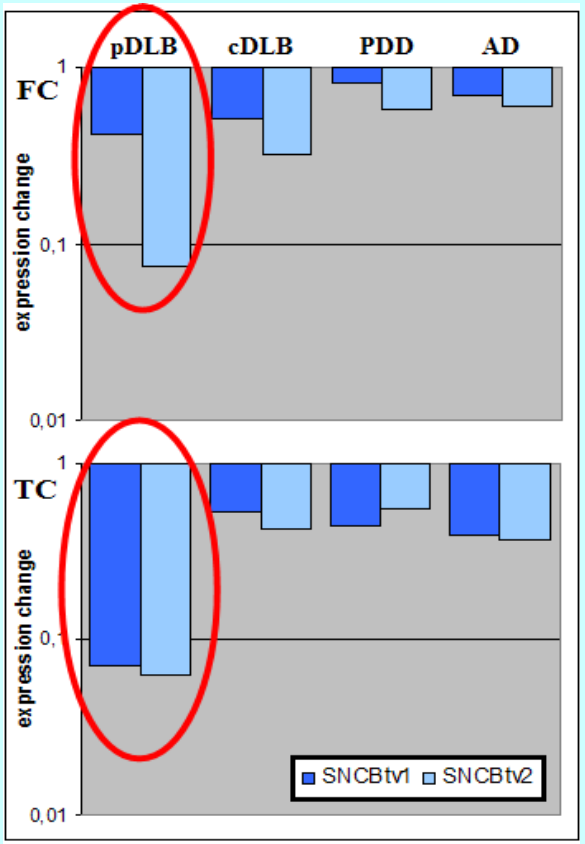
2. The Product: b) The biomarkers

2010: Drastic beta-synuclein diminution in the cerebral cortex defines a molecular subgroup of DLB

Characteristics:
- fast progression and short duration of DLB
- clinical presentation as DLB but not as PDD
- pure Lewy pathology in the brain

Identification: of the molecular mechanism as a possible therapeutic target
NO determination: the associated peripheral marker to this mechanism for the pre-mortem and early identification of affected patients

Expression of two beta-synuclein transcripts in the cortex of brains with:

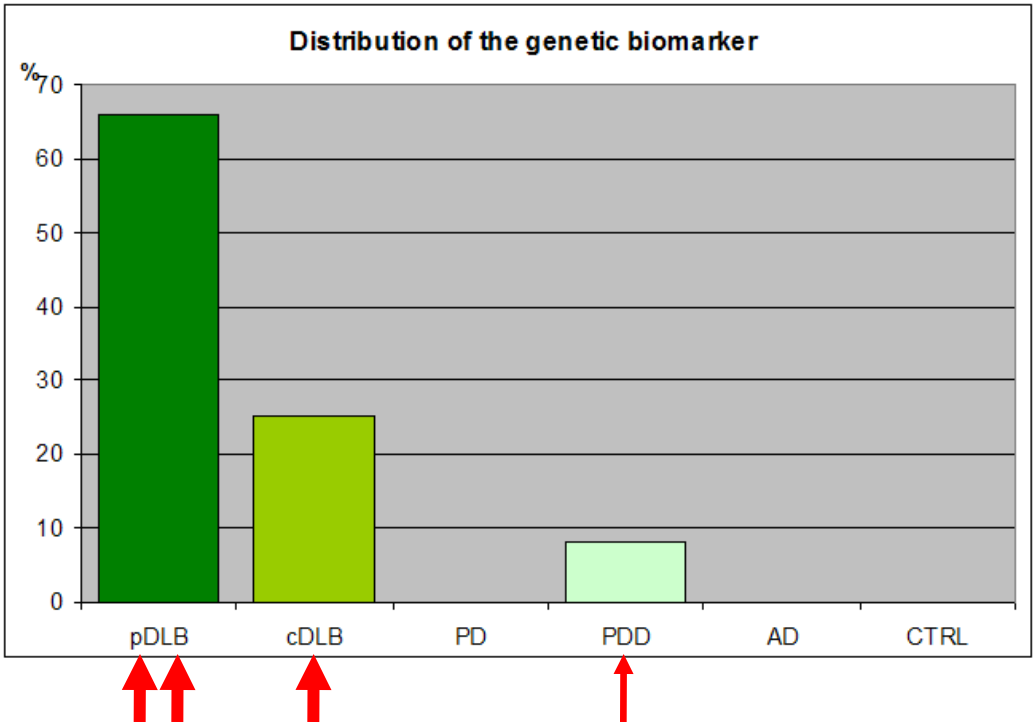


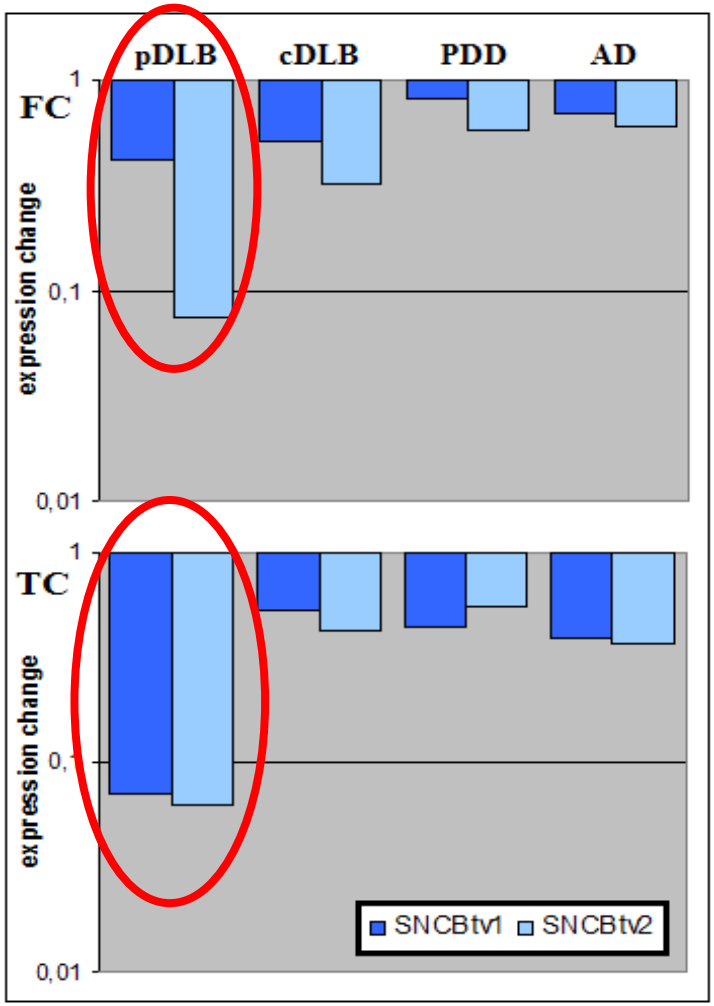
Beyer et al., Brain 2010

2. The Product: b) The biomarkers

Genetic biomarkers for the early diagnosis of DLB

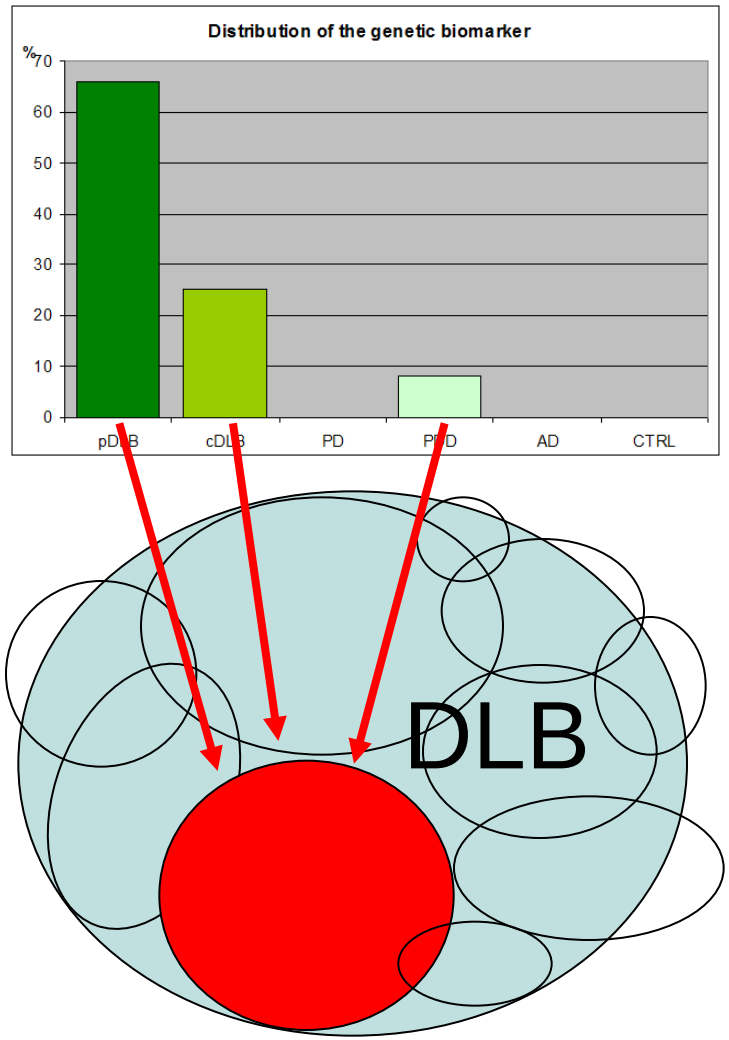
Biomarker 2





Beyer et al., Brain 2010

2. The Product: b) The biomarkers



ADVANTAGES

- The use of this **genetic biomarker** will permit to identify those patients with DLB that belong to a subgroup with known molecular changes in the brain.
- The potential to **personalize** the diagnosis and possibly also treatment is becoming a promising strategy for clinical use.
- The facility of **standardization** and relative **low-cost of analysis** are key characteristics for the use of the biomarker in clinics.

2. The Product:
c) Differential features facing the market

- **urgent need of diagnostic biomarkers for DLB**

- to achieve a correct diagnosis

- facing the ageing of the population

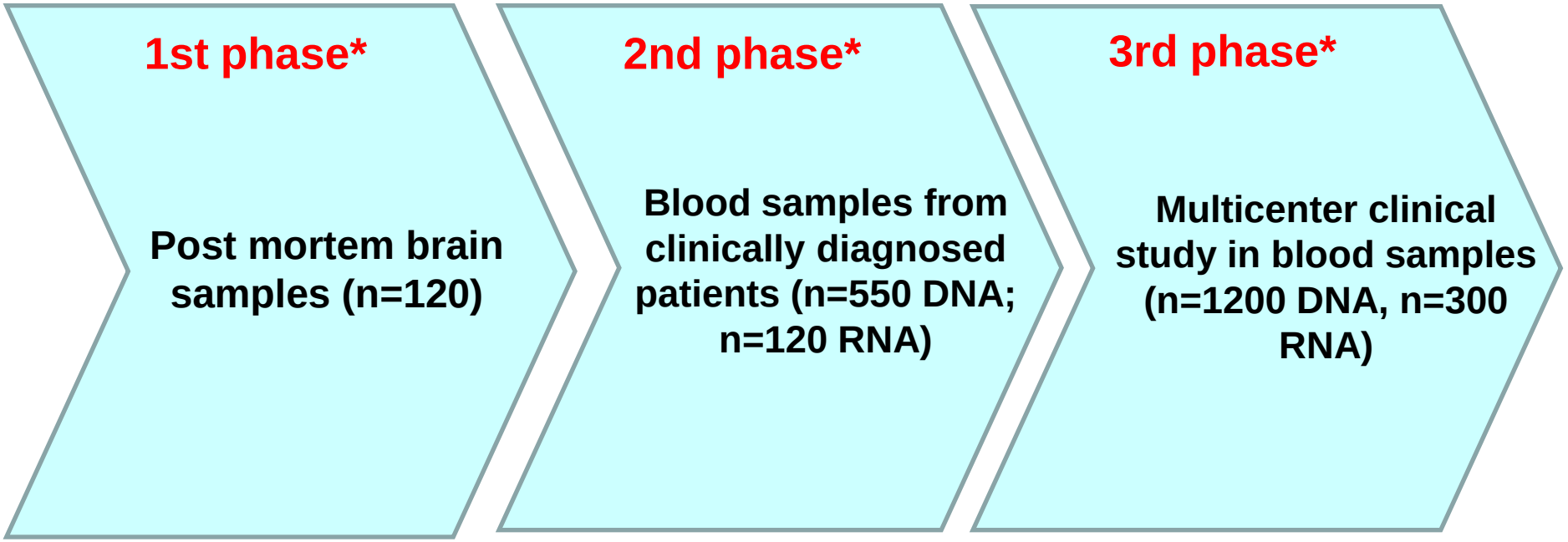
- **current diagnostic tools:**

- purely clinical

- radiodiagnostic tools (DATscan = expensive and invasive)

- **no genetic markers have been identified so far**

2. The Product:
d) Current status of development



Biomarker 2	Biomarker 1
Sensitivity: >> 85% Specificity: >> 93%	Sensitivity: >> 83% Specificity: >> 90%

** phase refers to stage of biomarker development*

2. The Product: e) IPR protection

Two Prioritary European patents applications filed

2. The Product: f) Pitfalls & Risks to be considered

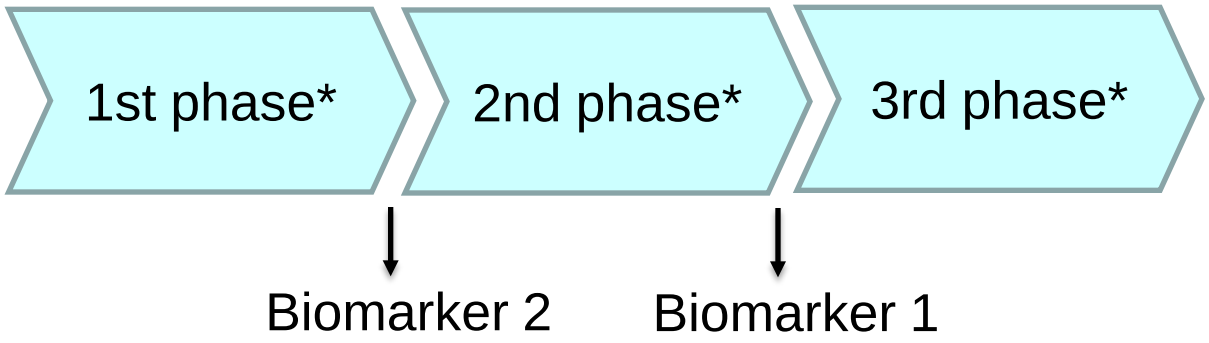
Biomarker 1

- to be validated vs AD
- to be validated in other populations

Biomarker 2

- to check the biomarker in a cohort with clinical diagnosis:
  - vs control subjects
  - vs AD patients
- to check the biomarker in a multicenter/international study

3. Partnering Opportunities



We are open to any kind of partnership with pharmaceutical and biotech industry that lead us to achieve final development including validation in step 3 for “Biomarker 1”, and validation in steps 2 and 3 for “Biomarker 2” and/or for licensing out the biomarkers.

**** phase refers to stage of biomarker development***