



# Personalised Medicine Approaches in Autism Spectrum Disorders

**Will Spooren**  
Webinar call 10 • Brussels

# Autism Spectrum Disorders

## Incidence

- 1 in 88 births

## Gender differences

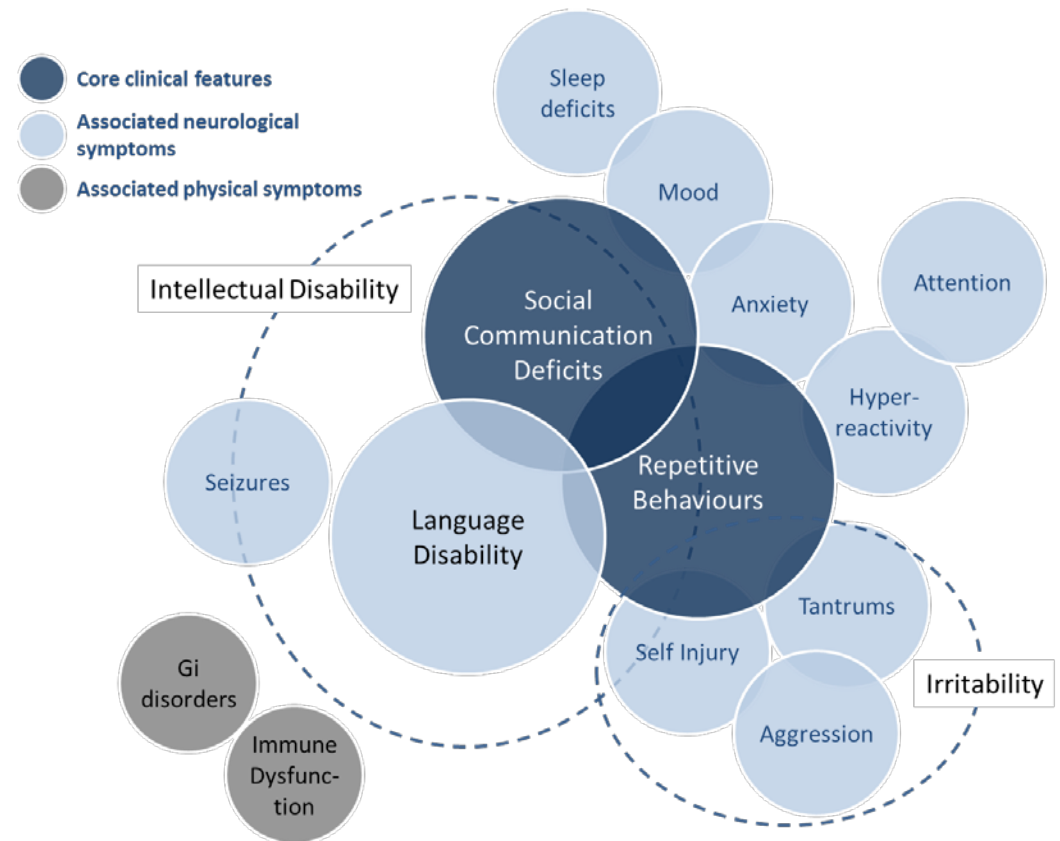
- 4x more frequent in males versus females

## Strong Genetic link

- 10-40% defined genetic alterations; high penetrance

## Treatment

- No treatment for core symptoms
  - Risperdal and Abilify for irritability



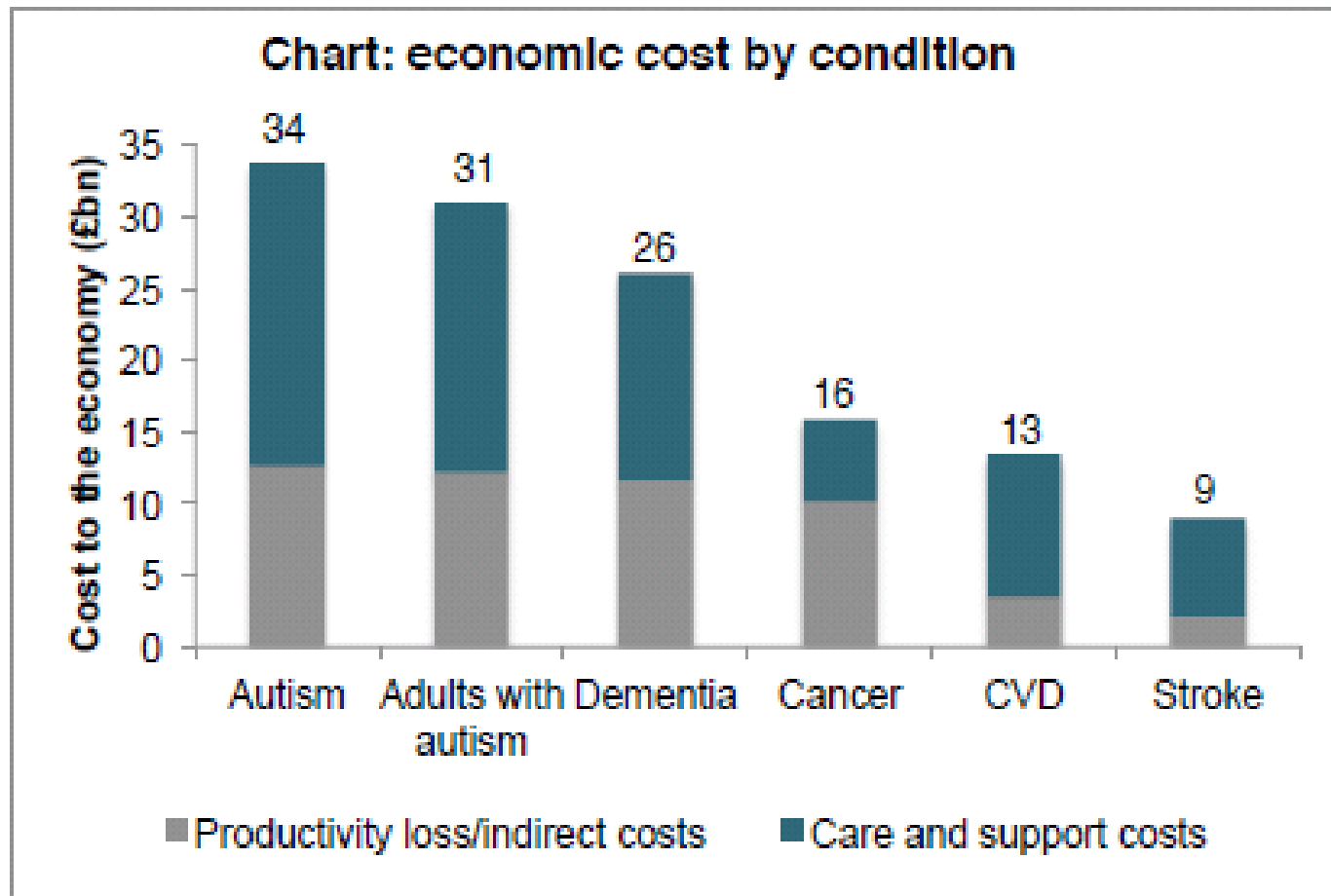
**High medical need with no therapy available**



# Autism research spend does not match economic cost\*



Autism has a higher cost to the economy than dementia, CVD, cancer or stroke



**Autism among the highest of socio-economic costs**

# Autism spectrum disorders

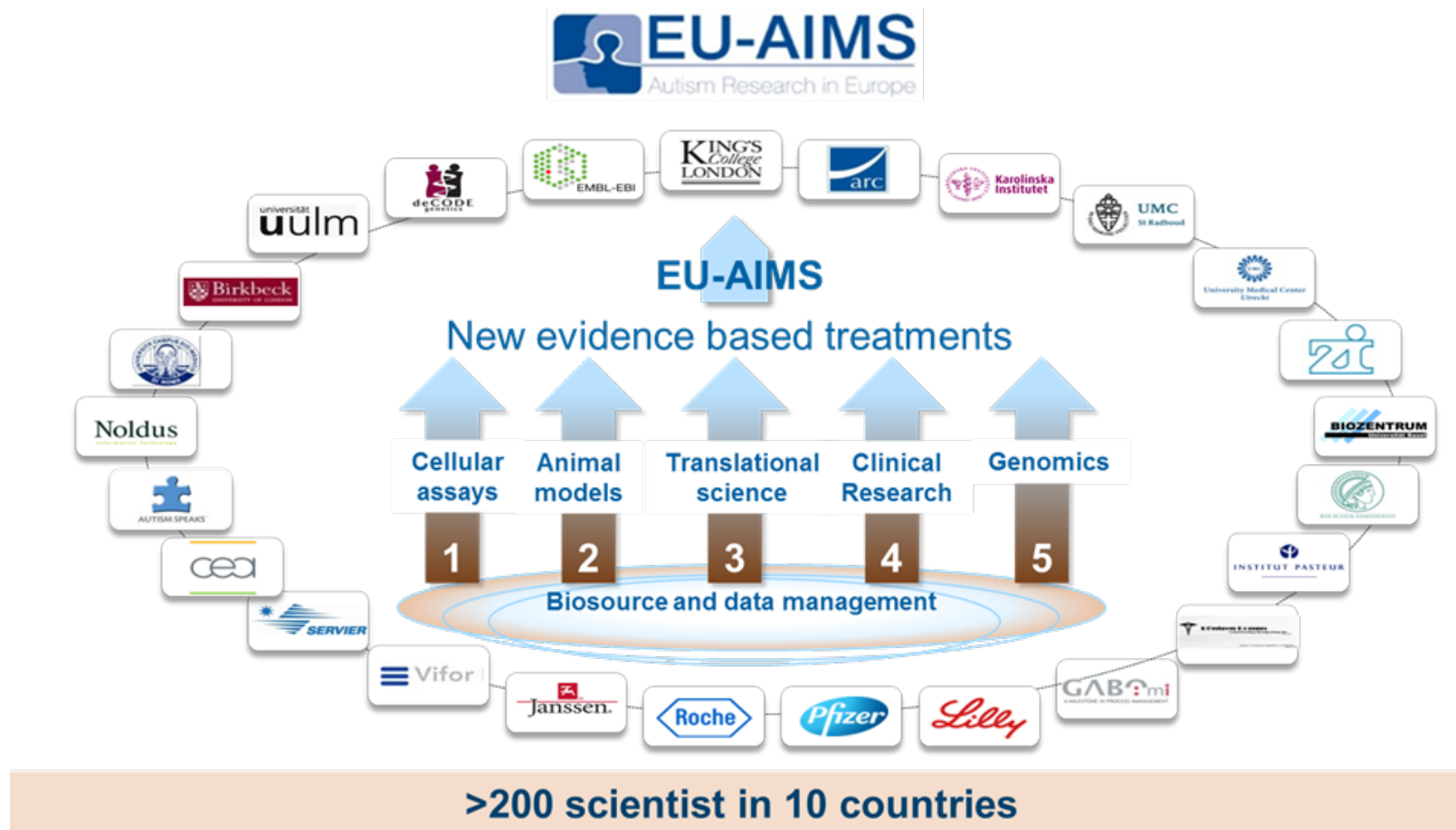
## *Europe and the rest of the world @ 2012*

- No major strategy defined within Europe
- No major or concerted efforts in drug discovery
- No pre-clinical network
- No clinical trial network
- No validated clinical endpoints
- No regulatory strategy
- Late diagnosis and poor awareness (adults)
- Poor knowledge of patients needs across life-course (teens into adulthood)



**A concerted effort of key stakeholders is needed Private Public Partnership**

# Autism Spectrum Disorders - Consortia



2012 - 2017

# Autism spectrum disorders

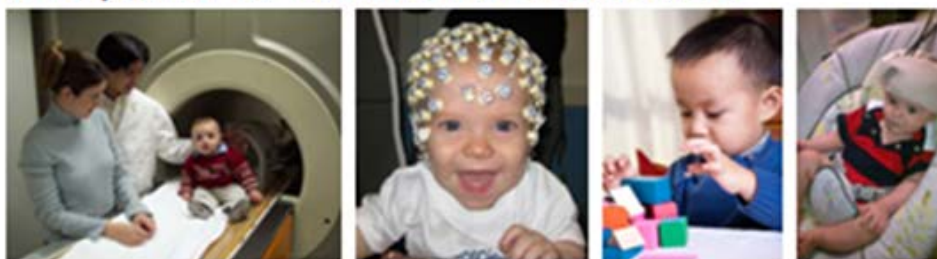
## *Predictive and diagnostic biomarkers*

### EU AIMS WP4 activities

#### *Task 1: High-risk sibling study*

#### Identification of early predictive/diagnostic biomarkers for ASD

- Prospective study of infants with older sibling with ASD
- Cognition, Behaviour, Neuroimaging and Neurophysiology
- Relation to symptoms/diagnosis of ASD at outcome
- Subjects: **405** N = 305 (High-Risk infants; 4 – 36 months)  
N = 100 (Low-Risk infants; 4 – 36 months)
- Time points: 5, 10, 14, 24 and 36 months



Clinical sites: London, Cambridge, Stockholm, Nijmegen, Ghent

Risk factors and early diagnosis

# Autism spectrum disorders

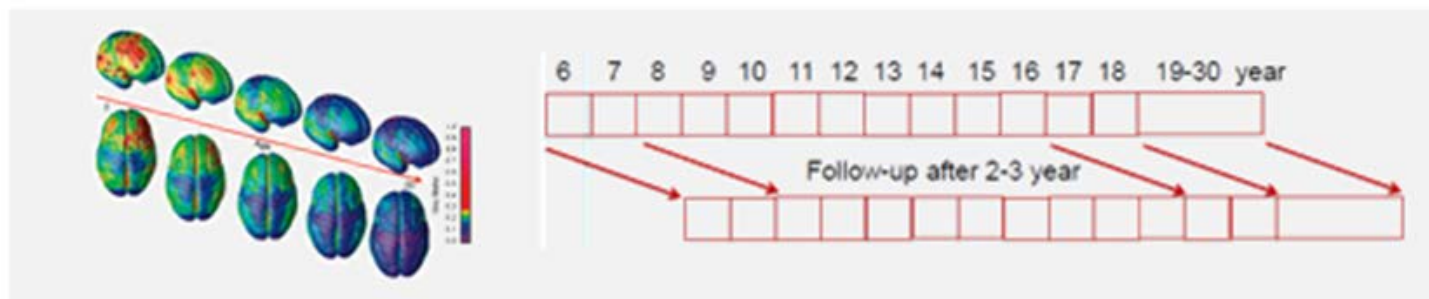
## *Naturalistic longitudinal observational study*

### EU AIMS WP4 activities

#### *Task 2: Accelerated longitudinal study*

#### Deep phenotypic longitudinal characterization of children/adults

- Subjects: **605** Total : N= 370 ASD individuals (6 - 30 y), 235 controls

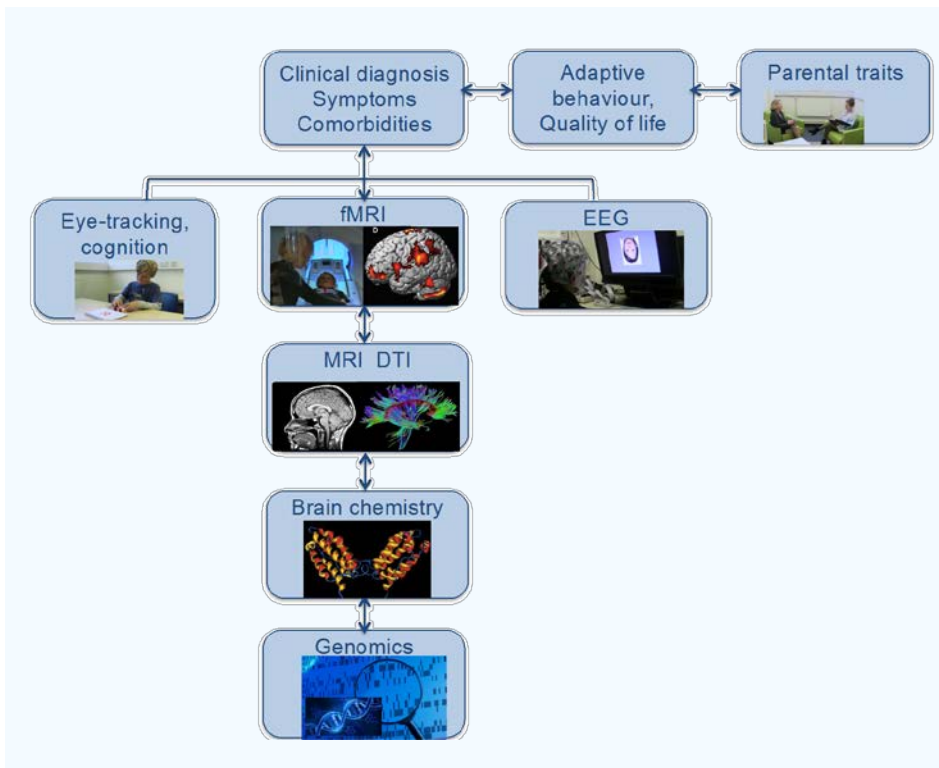


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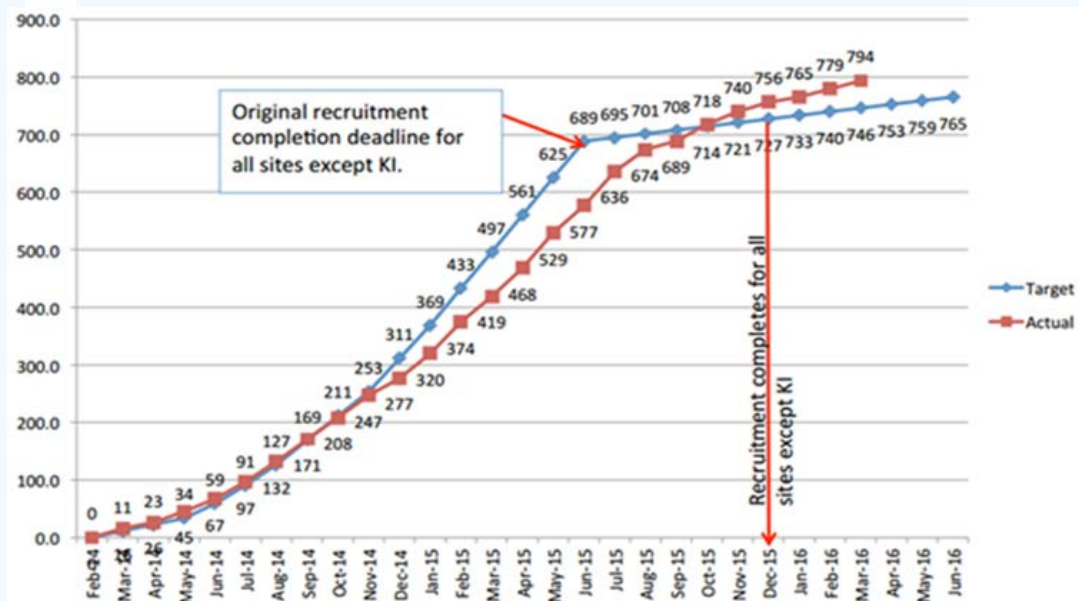
Clinical endpoints and biomarkers

# Unprecedented clinical study in autism patients

## Task 2: Deep phenotypic characterization



### EU-AIMS leap study recruitment

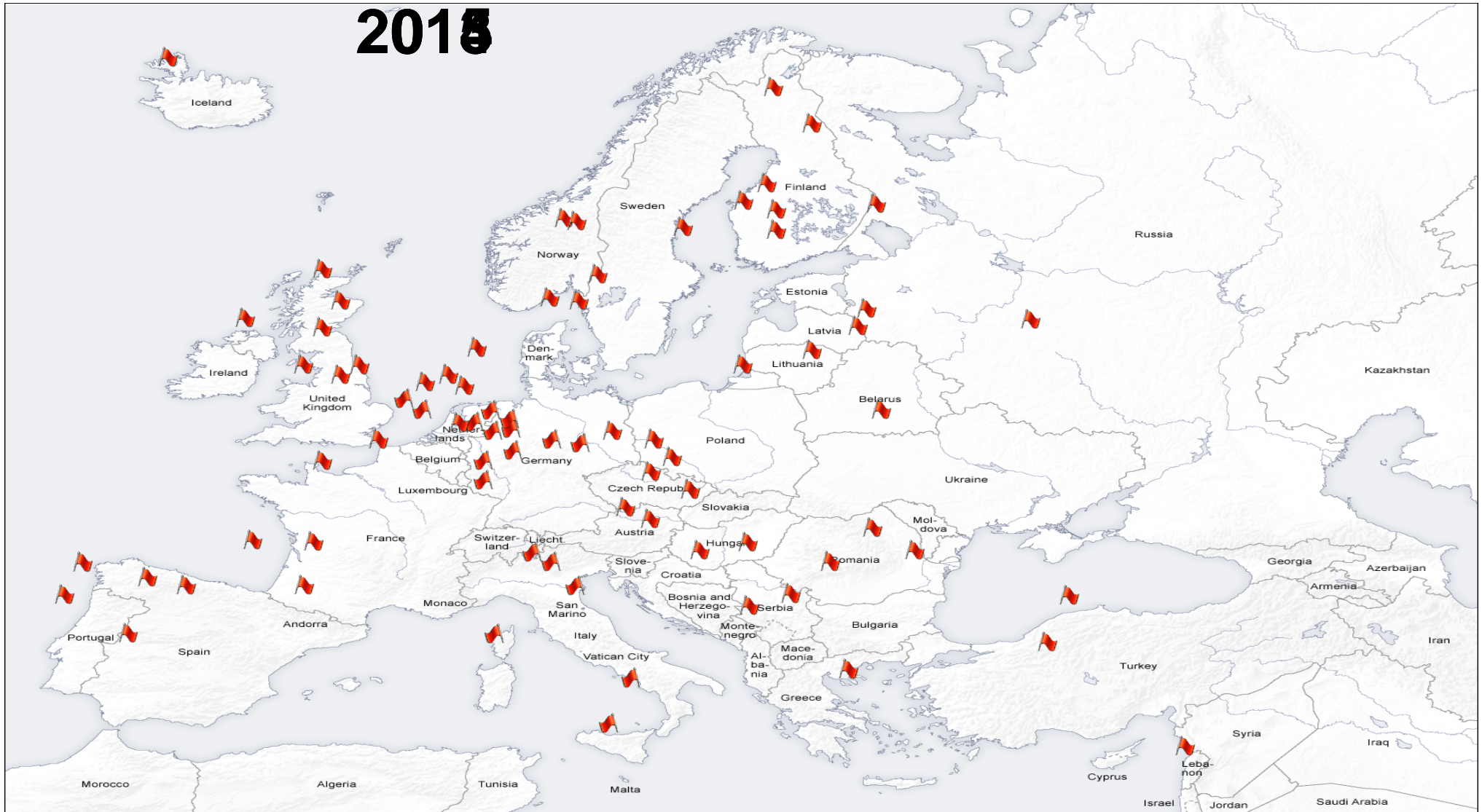


Clinical study run using industry GCP standardization



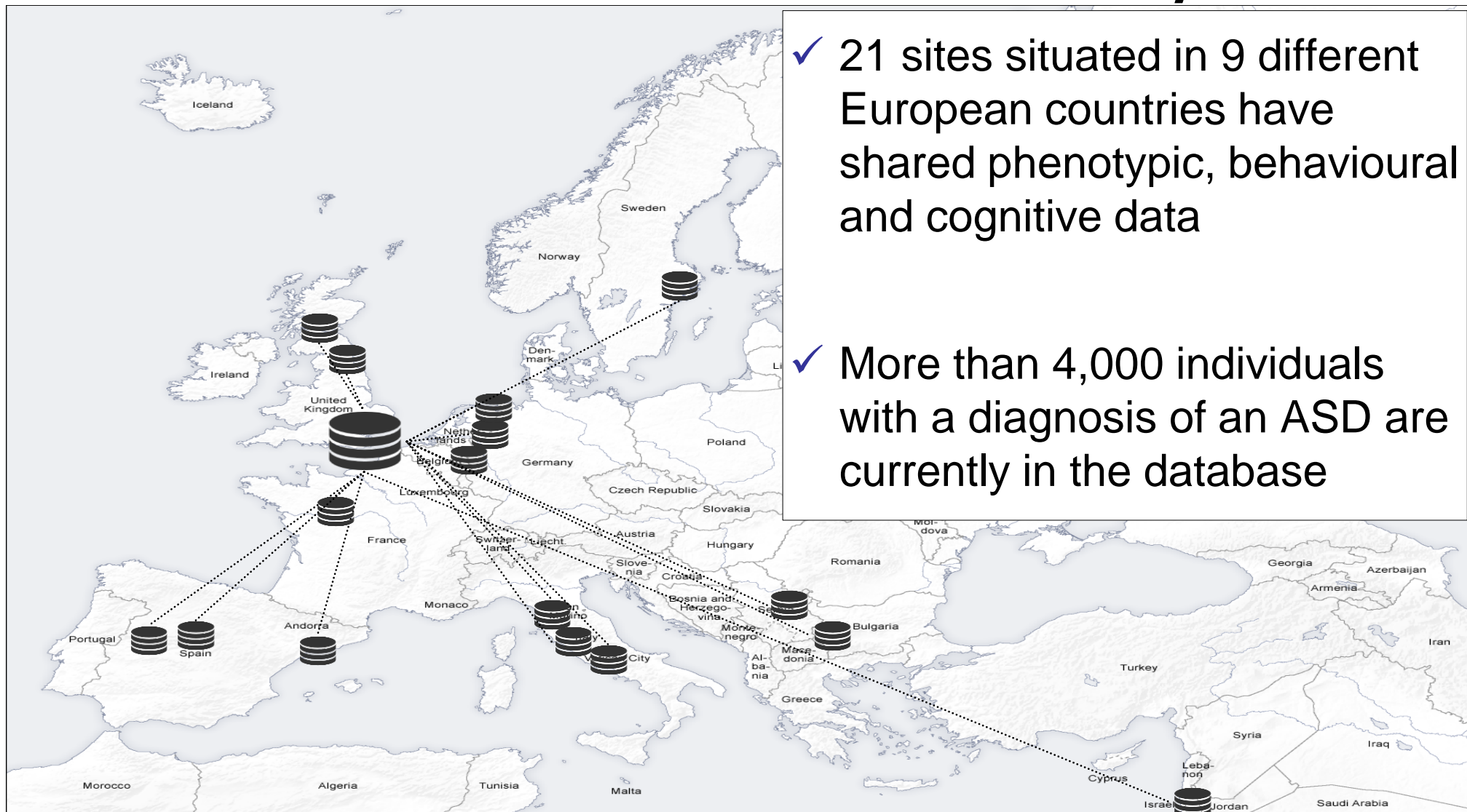
# Develop clinical capability for future studies

## *More than 90 sites in 36 countries*



# Build big data bases

## *Relevant clinical centers across Europe*

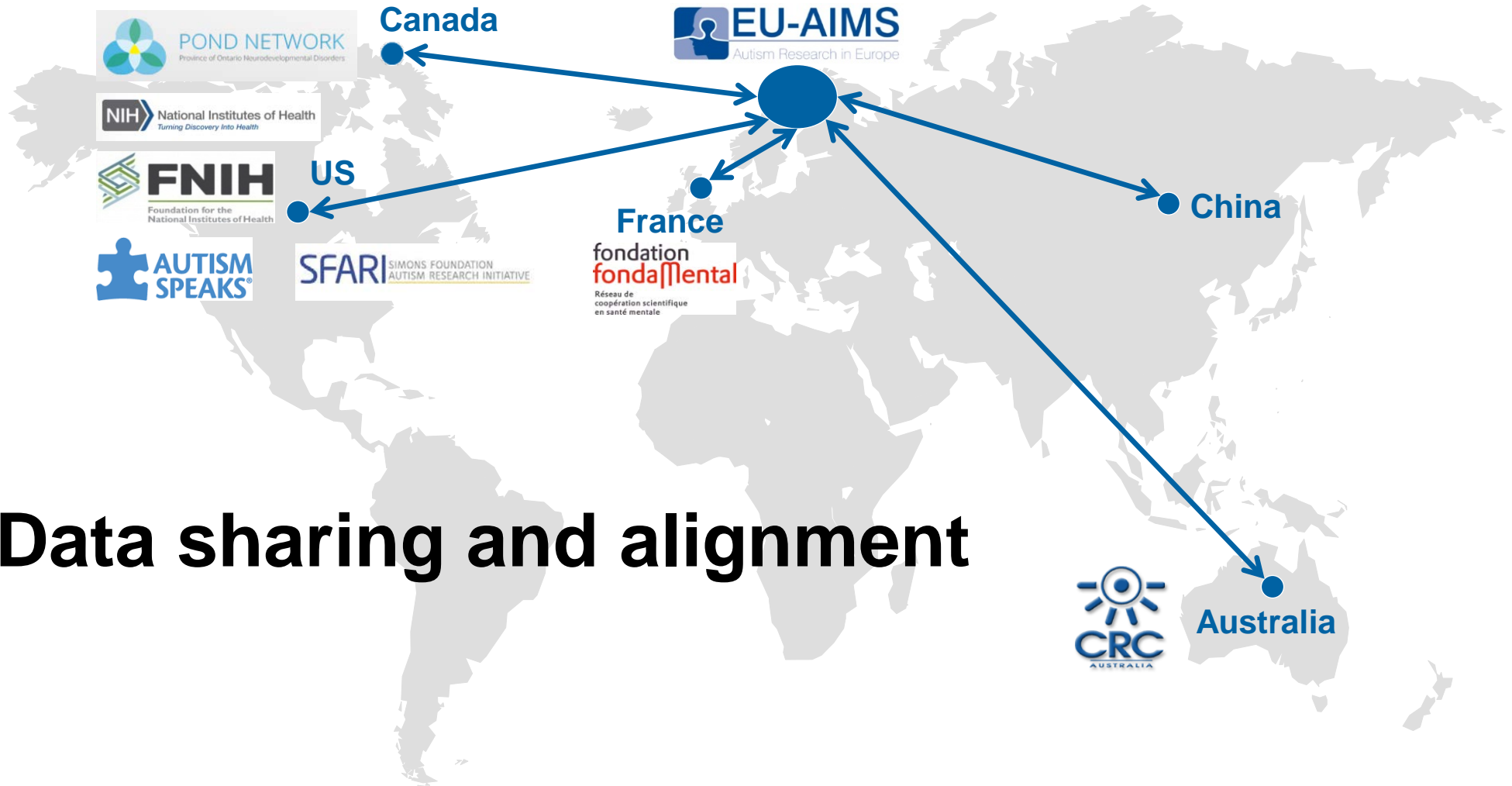


- ✓ 21 sites situated in 9 different European countries have shared phenotypic, behavioural and cognitive data
- ✓ More than 4,000 individuals with a diagnosis of an ASD are currently in the database

May indicate multiple sites in the same city/area

Map courtesy of San Jose, April 2006

# Scope and vision



# Data sharing and alignment



## IMI2 program, goals and focus

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## IMI-2 objectives

- Increase the success rate of clinical trials of new / re-purposed medicines
- Speed-up the drug development process and identify new treatments in areas of unmet medical need
- Develop new biological markers to diagnose diseases and assess treatments
- Improve the drug development infrastructure to better assess the efficacy, safety and quality of medicines



# Consortium Composition and budget

## Confirmed participation:

**F. Hoffmann-La Roche Ltd** (EFPIA)

UCB Biopharma (EFPIA)

Janssen (EFPIA)

Novartis (EFPIA)

TEVA (EFPIA)

Simon Foundation Autism Research Initiative (SFARI; Associated Partner)

Autism Speaks (Associated Partner)

National Institute of Mental Health (NIMH; Memorandum of Understanding)

**The indicative budget of EFPIA & Associated Partners is 55 Million EUR**

## Additional interest expressed to join consortium:

GSK (EFPIA)

Autistica (Associated Partner)

# Scope and vision (I)

- **Building on key pre-existing assets: ad 1-3 assessments/5 years**  
Baby-sibling study                      Leap study

## Identification of early predictive/diagnostic biomarkers for ASD

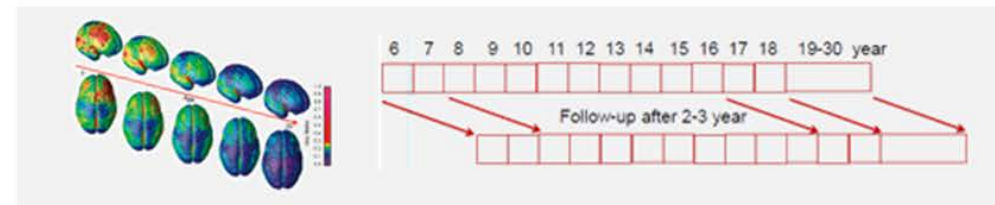
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## Deep phenotypic longitudinal characterization of children/adults

- Subjects: **605** Total : N= 370 ASD individuals  
(6 - 30 y), 235 controls



Clinical sites: London, Cambridge, Stockholm, Utrecht, Nijmegen

Risk factors and early diagnosis

Clinical endpoints and biomarkers

**Add 3-5 year profile data – mid term assessment**

# Scope and vision (II)

- **Building on key pre-existing assets: Clinical Trial Network**



- > 90 sites in 37 countries have been recruited into the Clinical Trial Network
- Regulatory framework established, first in the World; EMA QA

**Largest, most multi-national, autism network in the world**





# The key deliverables (1/2)



## Improve patient selection for stratification and clinical outcome.

- Validated risk factors, biomarkers and stratification markers across age and severity spectrum in ASD
- Initiate international 'big data' networks, linked to U.S and rest of the world
- Biological understanding of risk or protective factors for common co-morbidities.
- Digital biomarkers/smartphone apps

Fluid biomarkers, imaging, EEG/EMG, clinical endpoints, genomics/proteomics

Genetics/omics, other biomarkers (i.e., brain tissue banks)

Intellectual dysfunction, epilepsy, ADHD...



Development of unbiased clinical endpoints and biomarkers

# The key deliverables (2/2)



Improving research translation.

## Essential steps for successful trials

- EU wide clinical trials network trained to GCP standards
- EU registry of 'deeply phenotyped' clinical trials population for ASD
- Develop novel objective trial methodologies
- 
- **Run Europe's first GCP standard large scale multi-center drug study in ASD.**

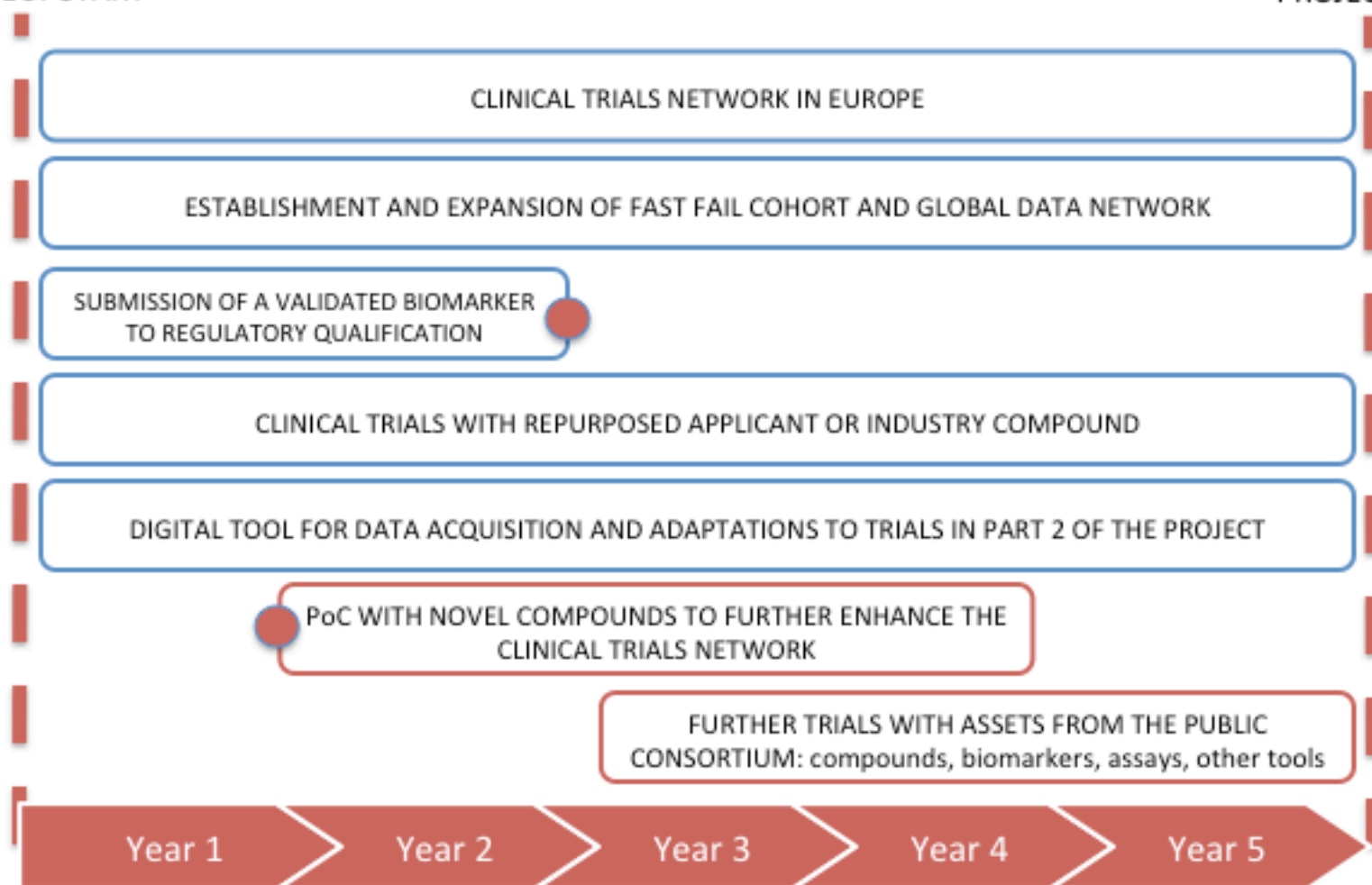
GCP standardization

Study ready and fast fail cohorts

- Select / replace treatment arms
- Reduce placebo response rates.

PROJECT START

PROJECT END



FIRST PART OF THE PROJECT

SECOND PART OF THE PROJECT



TRIGGER FOR REVIEW AND START OF PART 2 OF THE PROJECT

# Autism spectrum disorders

*Key deliverables – only through concerted efforts*

- ✓ major strategy defined within Europe
- ✓ major or concerted efforts in drug discovery
- ✓ pre-clinical network
- ✓ clinical trial network
- ✓ validated clinical endpoints
- ✓ regulatory strategy
- ✓ Late diagnosis and poor awareness (adults)
- ✓ Poor knowledge of patients needs across life-course
- ✓ Wide range in treatment strategy with no evidence of efficacy



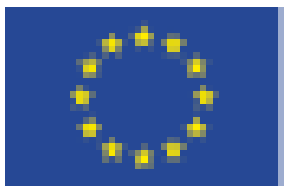
**Delivered**

**To be addressed**

# Scope and vision

Create a world leading clinical infrastructure for research and drug development in Autism Spectrum Disorders building on key pre-existing assets in Europe





**Thank You**

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