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 spending does not match economic cost*.

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

*REFERENCE REQUIRED

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

EU-AIMS

New evidence based treatments

Cellular assays
Animal models
Translational science
Clinical Research
Genomics

Biosource and data management

>200 scientist in 10 countries

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

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

Clinical endpoints and biomarkers
Unprecedented clinical study in autism patients

Task 2: Deep phenotypic characterization

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
- Prospective study of infants with older sibling with ASD
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- Subjects: 405 N = 305 (High-Risk infants; 4 – 36 months)
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Deep phenotypic longitudinal characterization of children/adults
- Subjects: 605 Total: N= 370 ASD individuals
  (6 – 30 y), 235 controls

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

CLINICAL TRIALS NETWORK IN EUROPE

ESTABLISHMENT AND EXPANSION OF FAST FAIL COHORT AND GLOBAL DATA NETWORK

SUBMISSION OF A VALIDATED BIOMARKER TO REGULATORY QUALIFICATION

CLINICAL TRIALS WITH REPURPOSED APPLICANT OR INDUSTRY COMPOUND

DIGITAL TOOL FOR DATA ACQUISITION AND ADAPTATIONS TO TRIALS IN PART 2 OF THE PROJECT

PoC WITH NOVEL COMPOUNDS TO FURTHER ENHANCE THE CLINICAL TRIALS NETWORK

FURTHER TRIALS WITH ASSETS FROM THE PUBLIC CONSORTIUM: compounds, biomarkers, assays, other tools

Year 1  Year 2  Year 3  Year 4  Year 5

FIRST PART OF THE PROJECT

TRIGGER FOR REVIEW AND START OF PART 2 OF THE PROJECT

SECOND PART 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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