European Rare Disease Overview

Irene Norstedt, 
DG Research and Innovation

Caroline Hager 
DG Health and Food Safety

European Commission
Rare diseases – orphan medicines a challenge too big to be mastered alone

- European Union population > 500 million citizens
- 5000-8000 diseases affecting 27-36 million EU citizens
- 128 orphan medicines authorized addressing 142 conditions (Dec 2016)
- 1805 orphan designations whereof 1464 still active (Dec 2016)
Rare diseases activities at EU level

Research and Innovation

Coordination of research

National plans, information, codification, patient registries, access to best care and knowledge
EU collaborative research on rare diseases

- Europe wide studies of natural history and pathophysiology: in vitro/in vivo models, registries & bio-banks, -omics of rare diseases, identification of biomarkers
- Development of diagnostic, therapeutic and preventive interventions including pharmacological, ATMPs, and innovative approaches

Overall EU contribution to rare diseases research over 800 M EUR since FP7*

Publication:
EU funded activities in rare diseases since 2007 available on: www.ec.europa.eu/research/health
Orphan designations

• Orphan designation has been a requirement for the Framework Programme funding since 2009

• > 50 % increase in submitted OMP applications and number of designations 2009-2015 compared with 2000-2008
• Orphanet consortium (currently supported by RD-ACTION)

• Information for patients and professionals

• Orphanet Rare Disease ontology & Orpha codes

• Regulation on Orphan Medicinal Products
European Commission awards EUR 6 million FP7 grant to support clinical development of NI-0501 to 'FIGHT HLH'

Novimmune’s NI-0501 Granted Breakthrough Therapy Designation by US FDA for Treatment of Patients with Primary Hemophagocytic Lymphohistiocytosis (HLH)

NI-0501 is the First Treatment Developed for HLH

Novimmune’s lead program, NI-0501, granted eligibility for PRIME scheme in Europe

Geneva — Novimmune, a Swiss biotech company focused on the discovery and development of antibody-based drugs, today announced that its lead program, NI-0501, has been declared eligible for PRIME (PRiority MEdicine) by the European Medicines Agency (EMA) for the treatment of primary Hemophagocytic Lymphohistiocytosis (HLH). The compound is currently in phase 2/3 of clinical development to treat HLH, a life-threatening disease of severe hyperinflammation which mainly occurs in children.
Clinical trial methodologies for small populations

- Innovative statistical design methodologies for clinical trials in small populations focusing on rare diseases
- 3 projects bringing together international experts in innovative clinical trial design methodology along with key stakeholders
- ASTERIX, IDEAL, INSPIRE
- IRDiRC-EMA joint workshop March 2016, report available on IRDiRC website, EMA workshop March 2017, publication submitted
An integrated platform connecting databases, registries, biobanks and clinical bioinformatics for rare disease research

The RD-Connect platform will accept data from IRDiRC research projects worldwide

http://rd-connect.eu
• Harmonisation, validation and standardisation in genetic testing
• Support professionals in achieving high quality in all aspects of genetic testing services
• Provide information on genetic testing to professionals and to the public
• Promote the implementation of novel technologies into current practice

www.eurogentest.org
Rare cancers: EU-wide impact

- Epidemiology, clinical registries
- World’s largest sarcoma biobank
- Phase I/II-III IDCTs: treatment and care,
- Predictive and prognostic markers
- Prognostic CINSARC sarcoma signature

INTEGRATION AND LONG-TERM COLLABORATION

- Virtual sarcoma biobank
- Translational research (pathology, gene expression, immunology, signalling)
- Translational biomarkers
- Early phase IDCTs
- ESMO clinical practice guidelines

- A first line treatment phase III IDCT to define standards of care for adjuvant chemotherapy (EuroEwing 2012)
- A second line treatment phase II/III IDCT which establishes a standard and will serve as a platform for testing new agents (rEECur)
- Companion studies - response, toxicity, biomarkers

Rare cancers: EU-wide impact

- 8 innovative investigator-driven clinical trials (phases I to III)
- Methods for histological and molecular diagnosis of sarcoma
- Translational research
- Patient involvement
Health, demographic change and wellbeing Challenge

Funding opportunities in 2017

Diagnostic characterisation of rare diseases (SC1-PM-03–2017) € 15 M
Deadline: 11 April 2017

New therapies for rare diseases (SC1-PM-08–2017) € 65 M
Deadlines: Stage-1: 04 October 2016, Stage-2: 11 April 2017

Full work programme available:
E-Rare-3: beyond Europe
26 partners in 18 countries
E-Rare: Joint Transnational calls

Since 2006, the number of countries participating in E-Rare funding activities constantly increases.
E-Rare: Joint Transnational calls

Molecular and pathophysiological studies
- Diagnostic studies
- Therapy Development (TD)
- Pre-clinical and validation studies
- Clinical trials

From bench ... ... ... ... ... ... ... ... to bedside

Number of projects:
- 28
- 1
- 8
- 1
- 3
- 7
- 6
- 7
- 16
- 9

Medical domains represented in the funded projects:
- Neurology
- Metabolic diseases
- Dermatology
- Others
- Musculoskeletal Diseases
- Rheumatology
- Pulmonary/Respiratory Diseases
- Hematology/Immunology
- Nephrology/Urology
- Cardiology/Vascular Diseases
- Ophthalmology
- Dysmorphology
- Endocrinology
- Psychiatry/Psychology

8 Joint Transnational Calls:
- 106 funded projects
- 92 M€ invested

Including 498 research partners funded
Pre-Announcement of E-Rare-3 Call for Proposals 2017

- Transnational projects for innovative therapeutic approaches for rare diseases focusing on pre-clinical development of therapeutic approaches in suitable existing animal or cell models
- Eligible countries: Austria, Belgium, Canada, Finland, France, Germany, Greece, Hungary, Israel, Italy, Japan, Latvia, Poland, Romania, Spain, Switzerland and Turkey
- Encouraged participation of Eastern European countries (Hungary, Latvia, Poland, Romania and Turkey)
- Use of existing European health research infrastructures or initiatives strongly encouraged when appropriate
- Patient organisations invited to participate where appropriate
- Excluded from call: Rare infectious diseases, rare cancers and rare adverse drug events in treatments of common diseases, clinical trials, set-up of new patient registries/databases, development of new cell or animal models, surgery or radiation therapies
- Indicative deadlines: Pre-proposal submission 1 February 2017; Full proposal submission 2 June 2017
Need for a coherent strategy – from bench to bedside

- More efficiently bring the results of research and innovation to the patient
- Programme to implement a research and innovation pipeline, from bench to bedside
- Integrative programme linking major EU and national initiatives – R&D, research infrastructures, registries
- Bridging to ERNs to help implementing research results and taking lessons learned from the clinic back to the bench

European Rare Disease Overview

- 23 EU Member States have national plans or strategies to tackle rare diseases
- European Commission expert group on rare diseases
- Patient Registries - *European Platform on Rare Diseases Registration*
The ERN

Networks of healthcare providers aiming at improving quality, and safety and access to highly specialised healthcare

- Patients affected by rare or low prevalence and complex diseases
- Added value at EU level
- Multidisciplinary approach (different specialities/areas of knowledge)
- Need of cooperation:
  - Scarcity knowledge
  - Need education
  - Complexity / high cost
  - Effectiveness in the use of resources

"The knowledge travels, not the patient"
ERN activities

23 European Reference Networks

26 COUNTRIES

300 HOSPITALS

900 HEALTHCARE UNITS

National Member of a ERN

Affiliated partner
<table>
<thead>
<tr>
<th>Network</th>
<th>Disease Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>BOND ERN</td>
<td>Bone Diseases</td>
</tr>
<tr>
<td>CRANIO</td>
<td>Craniofacial anomalies and ENT disorders</td>
</tr>
<tr>
<td>Endo-ERN</td>
<td>Endocrine Conditions</td>
</tr>
<tr>
<td>EpiCARE</td>
<td>Rare and Complex Epilepsies</td>
</tr>
<tr>
<td>ERKNet</td>
<td>Kidney Diseases</td>
</tr>
<tr>
<td>ERN GENTURIS</td>
<td>Genetic Tumour Risk Syndromes</td>
</tr>
<tr>
<td>ERN-EYE</td>
<td>Eye Diseases</td>
</tr>
<tr>
<td>ERNICA</td>
<td>inherited and congenital anomalies</td>
</tr>
<tr>
<td>ERN-LUNG</td>
<td>Respiratory Diseases</td>
</tr>
<tr>
<td>ERN-RND</td>
<td>Neurological Diseases</td>
</tr>
<tr>
<td>ERN-Skin</td>
<td>Skin Disorders</td>
</tr>
<tr>
<td>EURACAN</td>
<td>Solid Adult Cancers</td>
</tr>
<tr>
<td>EuroBloodNet</td>
<td>Onco-Hematological Diseases</td>
</tr>
<tr>
<td>EUROGEN</td>
<td>Urogenital Diseases</td>
</tr>
<tr>
<td>EURO-NMD</td>
<td>Neuromuscular Diseases</td>
</tr>
<tr>
<td>GUARD-HEART</td>
<td>Diseases of the Heart</td>
</tr>
<tr>
<td>ITHACA</td>
<td>Congenital Malformations and Intellectual Disability</td>
</tr>
<tr>
<td>MetabERN</td>
<td>Hereditary metabolic diseases</td>
</tr>
<tr>
<td>PaedCan-ERN</td>
<td>Paediatric Cancer</td>
</tr>
<tr>
<td>RARE-LIVER</td>
<td>Hepatological Diseases</td>
</tr>
<tr>
<td>ReCONNET</td>
<td>Connective Tissue and Musculoskeletal Diseases</td>
</tr>
<tr>
<td>RITA</td>
<td>Immunodeficiency, AutoInflammatory and Auto Immune Diseases</td>
</tr>
<tr>
<td>TRANSPLANTATION-CHILD</td>
<td>Transplantation in Children</td>
</tr>
<tr>
<td>VASCERN</td>
<td>Multisystemic Vascular Diseases</td>
</tr>
</tbody>
</table>
Share. Care. Cure.

Virtual care

Virtual clinical consultations
Remote monitoring and follow-up

PATIENTS
NATIONAL HEALTH-CARE PROVIDERS
SPECIFIC ERN

CLINICAL GUIDELINES
RESEARCH & INNOVATION KNOWLEDGE
GENERATION & SHARING
TRAINING & E-LEARNING
Research, innovation & knowledge generation
Key Elements

• A framework for structured cooperation to maximise cross-country expertise through joint research projects and clinical trials

• ERN provide an opportunity to build top level translational and basic research around shared strategies

• Dissemination of research results, education & training activities
Thank you for your attention!

Caroline.Hager@ec.europa.eu
Irene.Norstedt@ec.europa.eu

http://ec.europa.eu/research/health