INTERNATIONAL
RARE DISEASES RESEARCH
CONSORTIUM

Minutes of the 13th Consortium Assembly Meeting

December 6-7, 2018

IRDiRC

EXECUTIVE SUMMARY

The Consortium Assembly (CA) of the International Rare Diseases Research Consortium (IRDiRC) met on December 6-7, 2018 in Brussels, Belgium. It was attended by 45 participants in person and 2 via teleconference, representing 35 member organizations, the Scientific Committees (SCs) and the Scientific Secretariat (Sci Sec).

1. Welcome
   - IRDiRC Consortium Assembly (CA) members were welcomed to the 13th CA meeting in Brussels, Belgium.

2. Vice Chair Candidate presentation
   - Dr David Pearce, Executive Vice President of Innovation and Research of Sanford Health, presented himself as CA Vice Chair Candidate, prior to the closing of the vote.

3. CA Chair Updates (on activities since June 2018)
   - Several updates were provided on IRDiRC 2018 Roadmap Activities.
   - A Working Group on Goal 3 will be starting shortly.
   - Several CA meetings were planned, including the 13th in-person CA meeting.
   - Investigation of potential mechanisms for a "Voluntary Membership Fund" were performed.
   - The Governance was updated in the Summer on several aspects, most noticeably adding verbiage to encourage non-represented regions to join, clarifying inactive membership criteria, and adding updated membership criteria for patient advocacy groups.
   - One IRDiRC Recognized Resource, Exomiser, was approved.
   - Chair and Vice Chair elections were accomplished.
   - Two new members, WuXi NextCODE and the National Institute of Dental and Craniofacial Research, joined IRDiRC.
   - Several organizations had changes to their formal representative on the CA.

4. Sci Sec Update
   - The current Sci Sec provided an update on their activities from the past 7 months, including teleconferences, workshops and meeting organization, metrics tracking, and communication.
   - The Sci Sec presented an update on current publication efforts: 2 articles and 1 report were published; 4 other publications and 1 report are expected shortly.
   - The new Sci Sec team will start on January 1, 2019 based within the EJP-RD structure.

5. IRDiRC Priority Actions and Strategies
   - The IRDiRC Scientific Committees (SCs) provided updates on their current activities
     - Diagnostics Scientific Committee (DSC)
       - Currently working on 4 activities in different phases: Solving the Unsolved Task Force (workshop held; in finalization stages of drafting publication), Carrier

Screening (preparatory stages), Clinical Data Sharing (not yet started), Activity I: Indigenous Populations (was approved later in 13th CA meeting).

- Interdisciplinary Scientific Committee (ISC)
  - Currently working on 3 activities in different phases: Activity G: Clinical Research Networks for Rare Diseases (approved; not yet started) and the Model Consent Clauses Task Force (workshop held; in finalization stages of drafting publication), and Activity D: Facilitating the Conduct of Natural History Studies Related to Rare Diseases (was approved later in 13th CA meeting).
- Therapies Scientific Committee (TSC)
  - TF completed: Small Population Clinical Trials Task Force (paper published)
  - Currently working on 2 activities in different phases
    - Data-Mining and Repurposing Task Force (workshop held; in finalization stages of drafting publication), and the Orphan Drug Development Guidebook – Galaxy Guide Task Force (workshop will take place next week).

- The IRDiRC Constituent Committees (CCs) reported back from their breakout sessions, and presented updates on their current and proposed activities.
  - Companies Constituent Committee (CCC)
    - It is very important that companies are involved in different parts of IRDiRC, but are there specific topics that the CCC can work on? Existentialist question: is there an added value in the CCC?
    - Until there is a clear structure, CCC activities are on hold.
  - Funder Constituent Committee (FCC)
    - The FCC presented their progress on Activity A (*Global database and platform for RD funding analysis and collaboration)*, selection of a tool for the creation of a database of funded projects on rare diseases research, analysis of such data, and its preliminary results.
    - To work toward a future, potential collaboration for funding calls, the final results of an FCC questionnaire were discussed, in which it was clarified that the majority of funders have the possibility to establish a bilateral or multilateral collaboration. Two topics rose to the top, in particular: data sharing and IRDiRC Goal 3.
    - Ethical, Legal and Social Implications (ELSI) of rare diseases research funding were investigated via a short survey; the outcomes of the survey will form the basis for an article. In parallel, the E-Rare working group is setting up a strategic workshop in order to set up a funding call in 2020.
  - Patient Advocates Constituent Committee (PACC)
    - Activity B: *Identify barriers to patient participation in RD R&D and recommendations to remove them*
      - Now recommending TF do work in a two-step manner
        - Phase I – initial work & define methodology

        - Phase II —organizational survey in multiple languages to patient groups and other stakeholders
    - A publication is planned after both phases.
- Activity F: *Issue a position statement including specific recommendations on: (1) model for applying IRDiRC Goal 2 (1000 new therapies) internationally, and (2) model for inclusion of patients' perspectives in that therapy development*.
    - Initial, short statement has been drafted. It will be put into the public domain shortly (on IRDiRC website).
    - Full recommendations or position paper re: multi-stakeholder collaboration on regulatory and therapy development pathways will be developed once other IRDiRC Committees/TFs have developed recommendations and implementation strategies on related content (~early 2020)

- IRDiRC Work Plan for 2019 – updates and discussion
    - Two additional Task Force proposals, Activity D (*Facilitating the conduct of natural history studies related to rare diseases*) and Activity I (*Indigenous populations*).
    - MyScienceWorks, the group creating the tool for Activity A (*Global database and platform for RD funding analysis and collaboration)*, presented their progress. They are currently working on the data, testing and elaborating different curation models and workflows, and working on prototypes of the curation platform and the analytic tools.
    - 3 new DSC members and 2 DSC member renewals were approved.

6. Leadership Handover
    - The leadership was officially handed over from the outgoing to the incoming CA Chair, from Dr Christopher Austin to Dr Lucia Monaco; from the outgoing to the incoming CA Vice Chair, from Prof Hugh Dawkins to Dr David Pearce, and from the outgoing to the incoming Sci Sec Coordinator, from Dr Ana Rath to Dr Daria Julkowska.

7. New Member Presentations
    - Members were introduced to WuXi NextCODE.

8. Round Table
    - IRDiRC members presented the 2-3 key things that happened in the past six months at their respective organization relating to the new IRDiRC goals.

REPORT

1. Welcome

The Chair of the Consortium Assembly welcomed all participants to the Consortium Assembly (CA) meeting in Brussels, Belgium, and introduced the agenda of the meeting.

2. Vice Chair Candidate presentation

- Vision
  - Continue to build on what previous Chairs have set up, to help Lucia in her role as Chair
  - Listen to the different team members, as IRDiRC is not about one individual, but about many different groups and stakeholders
  - Look for synergies between different committees
  - Emphasize that we are in a whole new area of rare diseases research
  - Rare disease diagnoses has become a different chapter due to the development and availability of new techniques, such as WES and WGS
  - Gene therapy is a reality now in the world of therapies of rare diseases, not fully curing diseases but finally be able to really threat them
  - This requires a new set of data and natural history studies
  - Will bring up a discussion on how we pay for diagnosis and treatment
- Background
  - PhD in Biochemistry at the University of Bath
  - Started with an interest in one particular disease, Batten disease, and realized that if they wanted to set up a clinical trial, he needed natural history data and other datasets, and has been a strong supporter since for this kind of registries
  - Now at Sanford health, were he set up a research program, and incorporated a rare disease program into this
  - Precision medicine is the future of medicine, and this needs and can to learn from rare diseases, emphasizing the need for rare diseases research
  - Lot of experience building teams and working with different individuals
  - Will be able to contribute to all of IRDiRC missions based on his background
  - Worked with other researchers, pharma and patients

3. Chair Updates

3.1 OpComm activities: June-December 2018

The Chair presented an update on OpComm activities since the last face-to-face meeting:

- Actions for Roadmap 2018/2019 activities – (to be discussed in more detail later in the meeting):
  - Activity A – call for tenders/contractor discussed and awarded to MyScienceWorks
  - Activity B & C – TF initiated and ongoing

  - Activity G – proposal approved and leadership discussions ongoing
  - Activity H – work initiated and ongoing
  - Activity D: *Natural history and registries*
    - Proposal circulated; up for CA discussion and vote tomorrow
  - Activity I: *Indigenous populations*
    - Proposal circulated; up for CA discussion and vote tomorrow
- Initiated recruitment for several Committees and Task Forces
- Working Group on Goal 3
  - Given priority of the goal and expertise needed, short-term WG with external experts to identify the needs to Goal 3; *still in process*
- Planning of CA Q3-4 (Brussels) 2018 F2F Meeting
- Investigating potential mechanisms for "Voluntary Membership Fund"
- Governance updates
  - Membership criteria for patient advocacy groups updated (add research focus; encourage "lived experience" representation; update LOI/LOM accordingly)
  - Non-represented regions encouraged to join (for all of IRDiRC)
  - Inactive membership criteria clarified and codified
  - General verbiage updated for consistency
    - New version of Governance finalized and sent to all members
    - *Still working on: updating other LOI/LOMs to be consistent among committees*
- 2019 meeting schedule
  - Q1-2 CA/SC meeting – ZonMw to host; Leiden, The Netherlands
  - Q3-4 CA meeting – TBD
- IRDiRC Recognized Resources
  - 1 application approved (Exomiser); 1 currently under review (Cellosaurus)
- Chair and Vice Chair procedures and elections accomplished

3.2 IRDiRC membership changes: June-December 2018

- New members:
  - WuXi NextCODE
    - Christina Waters, SVP & GM of Global Rare Disease Program
  - National Institute of Dental and Craniofacial Research (NIDCR), NIH
    - Jason Wan, Director of Mineralized Tissue and Physiology Program
- Change of representation:
  - ISS – from Walter Ricciardi to Domenica Taruscio
  - NIAMS, NIH – from Steve Katz to Faye Chen
  - NHGRI, NIH – from Teri Manolio to Lisa Chadwick
  - NORD – from Peter Saltonstall to Vanessa Boulanger
  - Sanofi Genzyme – from Carlo Incerti to Daniel Gruskin

4. Sci Sec update

4.1 The Sci Sec in numbers: 2012-2018

- Coordinator Sci Sec: 2
- Project Manager: 4
- Assistant to the Chair: 2
- Communication Manager: 4
- Data Manager: 2
- Information Scientist: 1
- Assistant: 4

4.2 Activity updates: June-December 2018

The Project Manager of the Sci Sec updated members of activities from the past 7 months, including:

- Teleconferences: organization, document preparation, report writing (on average 1 per week)
- Fortnightly calls with the Chair of CA: exchange of updates and information on activities
- Workshops and meetings: venue and logistics, travel organization, document preparation, report writing, reimbursements
- Metrics tracking: therapies, new genes and diagnostic trackers
- Communication: updated standard slide decks, monthly newsletter, update IRDiRC website, prepare and submit posters, updated social media

4.3 Current publication efforts

- Articles published
  - Privacy-preserving record linkage TF policy recommendations published in October 2018
  - Small population clinical trials TF recommendations published in November 2018
- Reports
  - Model Consent Clauses TF Workshop report ready for internal use in October 2018
  - Orphan Drug Development Guidebook Task Force report will be available at the end of December
- Articles in preparation
  - Model Consent Clauses TF article will be submitted in December 2018
  - Solving the Unsolved TF State-of-the-Art article will be submitted in December 2018
  - Data-mining and repurposing TF article will be submitted in December 2018
  - Orphan Drugs US/EU: 2010-2018 analysis article will be submitted in January 2019

4.4 Future of the Sci Sec (2019-2024): European Joint Programme for Rare Diseases (EJP RD)

- Activities of Sci Sec are part of:
  - Coordination Office (WP1)
  - Transversal Activity: Strategy (WP2) → Task Forces

- Transversal Activity: Communication & Dissemination (WP5) → all IRDiRC related communication actions (website, publications, IRDiRC Conference)
- Pillar 2 WP11: Provision of RD analysis and data sharing capabilities through online resources (online DB and analysis)

- EJP RD builds its strategic research and innovation agenda and prioritization strategy in line with IRDiRC:
  - IRDiRC Chair & Vice Chair will be part of EJP RD policy board
  - There is no dedicated Scientific Committee(s) → EJP RD trusts in recommendations produced by IRDiRC SC
  - EJP RD will contribute to the Task Forces & mutual optimization of resources
- Positions in EJP/ IRDIRC Sci Sec
  - Senior Project Manager (2x): shared time (adaptable) for IRDiRC & EJP RD
  - Junior Project Manager (2x): shared time (adaptable) for IRDiRC & EJP RD
  - Data Manager: shared time (adaptable) for IRDiRC & EJP RD
  - Communication Officer: shared time (adaptable) for IRDiRC & EJP RD
  - Administrative Assistant: shared time (adaptable) for IRDiRC & EJP RD
  - Financial Officer: shared time (adaptable) for IRDiRC & EJP RD
- Other important information:
  - Budget dedicated to IRDiRC SciSec activities (excluding personnel costs): 1 000 000 € (direct costs) + 250 000 € (indirect costs)
  - Concise description of activities = more flexibility & adaptability based on the Annual Work Plans (AWP)
  - Alignment of planning dependent on the annual cycles (delivery of AWP in Sep every year; meeting of EJPRD Policy Board in June every year)
  - Annual IRDiRC Roadmaps are very important!

→The new Sci Sec will provide information and contact information of new Sci Sec members shortly.

5. IRDiRC Priority Actions and Strategies

5.1 Updates from Scientific Committees

Update from the Diagnostics Scientific Committee

- Currently 15 members, from every continent, with an improved gender balance
  - Some members will reach the end of their second term in early 2019, therefore some new candidates will be presented for vote later this meeting
  - Chair 2019-2022: Gareth Baynam
  - Vice Chair 2019-2022: Sarah Bowdin
- Currently different activities ongoing
  - Solving-the-Unsolved (STU) Task Force was held earlier this year
    - Outcomes of the STU Task Force will be published shortly in the American Journal of Medical Genetics (AMJG) and Cell
  - Carrier screening

        - Not yet a Task Force, but currently writing up a background/ state of play document on carrier screening initiatives worldwide
    - Clinical Data Sharing Task Force
        - Proposal is approved, but the Task Force will only get started after the Global Commission will have published their results, to prevent overlap
    - Activity I: Indigenous populations Task Force
        - Proposal is now fully developed, and will be presented for vote later this meeting

Updates from the Interdisciplinary Scientific Committee

- Currently 13 members
    - Some members will reach the end of their second term in early 2019, therefore the Committee is investigating new members
    - Identify external experts in HTA, payers/insurers, health economics, medical law
- Current different activities ongoing
    - Activity D: *Facilitating the conduct of natural history studies relating to rare diseases*
        - Proposal is now fully developed, and will be presented for vote later this meeting.
        - Should we somehow include biobanks? There is international biobank collaboration, and Teri Manolio is involved.
    - Activity G: *Clinical Research Networks for Rare Diseases*
        - Proposal was approved in June 2018
        - Call for nominations will be send out shortly
        - Task Force is expected to start in Q1 2019
    - Model Consent Clauses Task Force
        - Task Force workshop was held in September 2019
        - Paper is currently in preparation, to be published shortly.
    - Potential 2019-2020 activity
        - Focused on Goal 3

Updates from the Therapies Scientific Committee

- Currently 13 members
    - Some members will reach the end of their second term in early 2019, therefore the Committee is investigating new members, mostly from regulators, preferably outside Europe
- Previous & ongoing activities
        - Small Population Clinical Trials: published
        - Data Mining and Repurposing: will be submitted by December 31, 2018
- Current main activity -- Activity C: *The Galaxy Guide to drug development*
    - The current drug development model has been built for traditional pharma, based on clear guidelines and progressive de-risking
        - Model is not really suitable for orphan drug development, complex biotech products and does not suit the needs of new players (such as non-profit organizations and biotechs)

        - Single initiatives are working to define new tools for drug development, but a new model has not yet been defined
    - The scope of this project is therefore to create a guide for academic and industrial drug developers describing the available tools and initiatives specific for rare disease drug development and how to best use them
        - Galaxy Guide will be extremely helpful especially for education of junior investigators

          Will make people aware the next steps in drug development they have to prepare for, thereby avoiding to find out the wheel if the process is already in motion
    - Deliverables of this project are:
        - Fact sheet on new development tools (Building Blocks), that present pros and cons of each initiative, and practical tips. There are currently 110 building blocks.
            - Regulatory EU
            - Regulatory US
            - Regulatory Japan
            - HTA and reimbursement
            - Early access
            - Development opportunities
                - There is a list of research funder initiatives included with a large geographical scope
            - Development practices
            - Development resources
        - Roadmap with check-lists of “what to do” and “when to do it” for rare diseases
            - There is an educational component, a checklist, and possible trajectories how to organize the use of the different Building Blocks
        - Handbook
        - The Gameboard, starting at the patient’s need
            - Will be the basis to start the workshop
            - Opportunities in each stage to consider
            - Will be included to showcase several case studies
    - Workshop of this Task Force will take place next week, on December 12-13, 2018 in Dublin, Ireland
    - Overall reflections:
        - Alignment with Pillar 4 of the EJP RD is necessary, to exploit this initiative for further development.
        - There is reflection needed on the utility of such a resource to the different stakeholders and where to start the drug development pipeline from different stakeholder points of view.
        - How to organize the different elements.
        - How to make sure it is evergreen and doesn’t become outdated quickly.

5.2 Report back from Constituent Committee breakout sessions

Feedback from the Companies Constituent Committee

- Currently 14 members
- It is very important that companies are involved in different parts of IRDiRC, but are there specific topics that the CCC can work on?
    - Existentialist question: Is there a value in the CCC?
        - In the overall progress towards the IRDiRC goals, it is very important that companies are there and are part of IRDiRC
        - It is important to integrate company feedback in the different IRDiRC activities, but it is important to do so from the start
        - What are the unique topics and projects on which the CCC can add value?
    - Where academics think industry people are interested, and where industry people think is interesting is not necessarily aligned
        - Time to set up a bilateral interaction, for industry to be interested in the project, we need to have these elements, etc.
    - Might be time to revisit the dynamics of the CCC, without changing the structure
        - How do we reinvent the system, and how to build on progress that is in parallel, not sequential
- Until there is a clear structure, activities are on hold.

Feedback from the Funders Constituent Committee

- Activity A: *Global database and platform for RD funding analysis and collaboration*
    - MyScienceWorks (MSW) presentation later in the day
    - Data is collected from all funders, which is now curated and analyzed
- Funders needs:
    - Clarify how currently the data is collected and how MSW will be able to retrieve data (3 possibilities, API from the website, access to internal database, provided by excel sheet)
    - Language translation might be an issue
    - Add funders “identity card”
    - Add common denominators, for example number of inhabitants per country
    - If possible, tag intra- and extra-mural funding and projects
    - Separate tags for IRDiRC funders and other funders, if needed
- Future collaboration for funding calls: results questionnaire and next steps
    - Data on the process of setting up a funding opportunity and possibilities for collaboration were collected from almost all funders
    - Main outcome: the majority of the funders have the possibility to establish a bilateral or multilateral collaboration
    - Two main topics were identified as interest for now:
        - Data sharing standards, common data sets, use cases, promotion of awareness

        - IRDiRC Goal 3: rare diseases methodology development for health technology, assessment of health economics research to evaluate the burden and patient access to diagnosis and treatment
    - Next steps:
        - Go back to all FCC members to identify more details on their data sharing clauses
        - Propose a process for sharing of confidential information
        - Besides the bi-and multilateral collaborations, the possibility to focus on complimentary opportunities should be envisaged
        - Inform on a regular basis FCC members on the development and preparation of the EJP RD Call 2021, that might be aligned with Goal 3
- Ethical, legal and social implications (ELSI) of rare diseases research have recently received increased attention
    - Survey to investigate ELSI funding calls last year: A number of countries have funding calls on ELSI aspects
    - Opportunity to learn and see how this can be implemented in other counties, and opportunity to reduce redundancy
    - Working Group has drafted an outline for an article based on the survey
    - In parallel, the E-Rare working group is setting up a strategic workshop next year, in order to set up a future call for funding in 2020
- FCC roadmap
    - Continue working on Activity A to make the analysis tool live ASAP
    - Agree on a process of confidential sharing of strategic information for funding opportunities
    - Finalize the work on the ELSI paper → strategic workshop→ prepare the EJP RD funding opportunity for 2021, which will be a possibility of extended collaboration with IRDiRC FCC members (beyond scope of E-Rare members)
    - Work on facilitating data sharing (from FCC perspective) between countries
    - Participate actively in Activity D and G

Feedback from the Patient Advocacy Constituent Committee

- Currently 13 members
    - No new members joined last year.
    - Current members are from Asia, Australia, Africa, Europe and North-America.
- The discussion of the PACC breakout mostly focused on Activity B (*Identify barriers to patient participation in RD R&D and recommendations to remove them)* and on how to help shape this activity
    - Background:
        - Ultimate goal is to help advance Goal 2, serving therapies to patients with underserved rare diseases or those without treatment available; with the main question: how do we empower and enable patient participation in rare diseases research
    - Task Force aims to develop recommendations on:

        - Determining alignment of current efforts with need
        - Facilitating better patient engagement across geographic areas with shared resources
        - Determining strategic areas for new funding initiatives
        - Informing future activities of IRDiRC
    - Current Task Force membership
        - Task Force was put together after an internal and external call of interest, with both members from the PACC and external experts, with expertise on methodologies, surveys, and qualitative data analysis
    - Approach has been discussed with the TF over the last few months, and PACC recommended updating it further into two phases.
    - Phase I (2019)
        - Prepare for Phase II
            - Finalize Co-Chairs
            - Determine how to define 'research' and 'participation' to set up for Phase II
            - Determine exact methodology and create budget for Phase II (for submission to IRDiRC by April; to EJP RD by May)
            - Benchmarking and literature review of existing resources and surveys in this area
        - Gather initial feedback
            - From leadership of patient advocacy groups and other IRDiRC constituent representatives
            - Ask same set of questions on perceived barriers
        - Publication based on initial results, referencing that more inclusive data will be generated in 2020.
            - → feedback from TF/PACC: any knowledge that can be created and put in the public domain is useful
    - Phase II (2020)
        - Based on initial feedback from Phase I:
            - Finalize questions to be included in the questionnaire/survey, potentially with some tailored according to culture/lexicon (if deemed appropriate)
        - Conduct questionnaire/survey
            - Directly from the patients and stakeholders themselves
        - Publication based on full results, which will include the final recommendations
- Activity F: *Position statement with recommendations on a 1) model for applying Goal 2 internationally and 2) model for inclusion of patient's perspective in that therapy development*
    - The expected outcome is a recommendations or position paper re: multi-stakeholder collaboration on regulatory and therapy development pathways
    - A simplified statement has been drafted, and will be put in the public domain (i.e., IRDiRC website, as well as spreading through the different IRDiRC members) in a dynamic form.

- Areas of need/potential focus for the Consortium in the future
  - Data protection solutions to enable data sharing
  - Data protection regulation
  - Encourage and enable research funding in low income countries
  - Activities related to access

5.3 IRDiRC work plan for 2019

5.3.1 Activity D: *Facilitating the conduct of Natural History studies related to rare diseases* - Taskforce proposal

- Transversal proposal by ISC, TSC, FCC, PACC and CCC members, presented by Domenica, Dixie and Daria
- Objective of Task Force is:
  - To identify challenges in the existing ecosystem of resources, guidelines, and standards that impede real-world evidence data collection and the conduct of natural history studies;
  - To develop recommendations for funders in order to address these challenges
- The initiative will build on ongoing initiatives in the US, EU, Australia, Canada, Japan and other countries
  - Patient advocacy organizations are needed to provide input from all around the world
  - Information from Activity A is essential
  - Getting input from the CCC will also very important
- All CA members voted in favor of the proposal, and a request for nominations for Task Force members will be send out shortly

→ Send out a request for nominations for Task Force members

5.3.2 Activity I: *Indigenous populations* - Task Force proposal

- Transversal proposal by DSC, presented by Gareth
- Objective of Task Force is to identify the priorities and means, both existing and in need of development, to deliver equity and scale and in delivery against Goal 1; specifically, by focusing on underrepresented, including Indigenous populations.
- The majority of the world includes currently indigenous communities and that there are particular challenges and opportunities for people living in these countries, special efforts that address these are required for Goal 1 to be met.
- Indigenous populations are globally dispersed, may be in developed or developing countries, often reside in non-metropolitan and remote areas, and frequently experience health inequities, including in rare diseases diagnostics.
  - These inequities will be magnified unless and until concerted and coordinated initiatives address challenges that limit the equitable receipt of benefit from diagnostic innovation.
  - Until this is achieved, IRDiRC cannot achieve its goals.

- These challenges will require innovative, robust, and community engaged solutions. These solutions that are likely to translate more broadly, that is for impact for all people living with rare diseases.

→ Send out a request for nominations for Task Force members

5.3.3 DSC Nominations and renewals

- Renewals
  - Gareth Baynam
    - Contributed to various activities of the DSC, most noticeably participated in the STU Task Force and the development of newly approved Activity I (indigenous populations)
    - Recently elected as Chair of the DSC
  - Anthony Brookes
    - Contributed to various activities, for example the Automatable-Discovery and Access Task Force
- New nominations
  - Sergi Beltran Agulló
    - Spanish scientist, expert in Bioinformatics Analysis and high throughput sequencing data
    - Deals with the RD-Connect Genome-Phenome Analysis platform.
  - Clara van Karnebeek
    - Dutch pediatrician/ scientist/ genetic counselor, specialized in metabolics diseases
    - Specialized in the translation of multi-omics data in precise diagnosis and personalized treatments
  - Ruty Mehrian-Shai
    - Israeli scientist, specialized in identifying genes in the pathogenesis of multifactorial diseases, in particular in rare cancer.

All renewals and nominations were approved by the CA.

→Send out confirmation of acceptance to new DSC members.

5.3.4 Presentation MyScienceWorks

- Call for tenders
  - A call for tenders was launched in July to initiate the primary objectives of Activity A (*Global database and platform for RD funding analysis and collaboration*) through the creation of a comprehensive rare disease database and platform.
    - Aim is to systematically track and analyze global rare disease funding landscape, and coordinate that of all IRDiRC members.

        - Expectation is that this effort will provide a tool that allows for in-depth analysis of funded projects and the rare diseases research funding landscape at an international level – to enable better understanding, address the gaps in research, and provide a basis for further funding coordination.
    - MyScienceWorks was selected as the tender, and has started to set up the first analysis and tools.
        - Currently in a crucial phase, where input from all FCC members is important
        - Current input will provide the basis for further work for the next 5 years
- MyScienceWorks
    - Company founded in 2010, with the idea to help democratize science
        - 70 M research publications, 12 M patents
    - Data-driven solution to analyze scientific content, foster innovation, and drive strategic research decisions
        - Based on natural language processing and machine learning
- Proposed solution to analyze data:
    - 3 types of data sources
        - Current excel files provided by different IRDiRC funders
        - Orphanet-collected data
        - Direct capture at the funders website/database
            - Accurate analysis is only possible if everyone assists in the provision of accurate data in different formats
    - 3 steps of analysis:
        - Data capture
        - Structured metadata
        - Analytics
    - Analysis under different dimensions:
        - Time
        - Amount of funding
        - Geographic area
        - Classification (diseases, genes…)
        - Projects
        - …
- What is ongoing currently?
    - Data: cleaning, standardization
    - Testing different curation models
    - Elaborating the new curation workflow
    - Working on the prototype for the curation platform and interface
    - Working on the prototype for the analytics tool
- Currently, MyScienceWorks has started a number of technical tests of current proposed algorithms
    - Then a set of testers will be needed to set the analytical news
    - At the beginning of next year the testable prototypes will be in place

- In order to move forward, we need to be aware of the following elements:
  - We need to have the expected changes on the website content – how many calls results are foreseen to map how often the data will have to retrieved;
  - The info on the amount of funding is crucial and we will have to discuss it with funders: currency, funding per fiscal year, etc.
  - There is difficulty to calculate the intramural research; so maybe the extramural funding should be a start.

5.3.5 Current status of IRDiRC Roadmap

- IRDiRC Roadmap
  - 5 activities continued from previous Task Forces, before 2018 Roadmap planning:
    - 1 finalized (Small Populations Clinical Trials)
    - 3 soon to be finalized (Data-Mining and Repurposing, Solving the Unsolved, Model Consent Clauses)
    - 1 not yet started (Clinical Data Sharing), awaiting a different initiative
  - 3 new activities officially started in 2018, based on 2018 Roadmap planning:
    - Activity A (*Global database and platform for RD funding analysis and collaboration*),
    - Activity B (*Identify barriers to patient participation in RD R&D and recommendations to remove them),*
    - Activity C *(Orphan Drug Development Guidebook, aka Galaxy Guide)*
  - 2 approved, not yet started officially started:
    - Activity D (*Facilitating the conduct of natural history studies relating to rare diseases*)
    - Activity G (*Clinical Research Networks for Rare Diseases*)
    - Activity I (*Indigenous Populations*)
  - 3 not yet approved:
    - Activity E (*Support reframing of the current research agenda for RD for focused research efforts and funding*)
      - Will start after finalization Activity C
    - Activity F (*Position statement with recommendations on a 1) model for applying Goal 2 internationally and 2) model for inclusion of patient's perspective in that therapy development*)
      - Preliminary statement written, no further action planned at present
    - Activity H (*Penumbra Project)*
      - Might be abandoned altogether?

6. Leadership handover

The formal handover of IRDiRC chairmanship took place

- Dr Lucia Monaco, Head of the Research Impact and Strategic Analysis at Fondazione Telethon in Italy, has been formally presented as new IRDiRC Chair.

- Dr Monaco will follow the footsteps of Dr Christopher Austin, Director of the National Center for Advancing Translational Sciences (NCATS), USA.
- Dr Monaco's term will run from January 1, 2019 until December 31, 2021.

In addition to the handover of IRDiRC chairmanship, a new Vice Chair was also elected.

- Dr David Pearce, Executive Vice President of Innovation and Research of Sanford Health will replace Prof Hugh Dawkins, formerly Director of the Office of Population Health Genomics of Western Australia Department of Health and recently-appointed Chief Health Advisor of HBF Health Limited.
- Dr Pearce will work hand-in-hand with Dr Monaco to advance IRDiRC's vision and goals, and assist her through his experience in bringing teams together and working with multi-stakeholders in all aspects of rare diseases research.
- Dr Pearce's term will run from January 1, 2019 until December 31, 2021.

The coordination role of the IRDiRC Scientific Secretariat will also change hands:

- The coordination will go from Dr Ana Rath to Dr Daria Julkowska, under the framework of the European Joint Programme on Rare Diseases (EJP-RD).
- The new Scientific Secretariat will continue to support IRDiRC in its implementation of prioritized activities as determined by the IRDiRC Consortium Assembly, and ensure smooth running of the Committees and Task Forces to carry out their activities.
- Dr Julkowska will coordinate the Sci Sec from January 1, 2019 until December 31, 2023.

All leadership handovers are effective January 1, 2019.

7. New Member Presentations

Over the past six months, two new members have joined IRDiRC. The new member that was present at the meeting, WuXi NextCODE presented itself.

7.1 WuXi NextCODE, by Christina Waters

- WuXi NextCODE
  - Founded as deCODE genetics in Iceland, was set up to sequence the population of Iceland to discover genetic risk factors for dozens of diseases ranging from cardiovascular disease to cancer.
    - First time to have both genetic data and deep longitudinal phenotypic characterization for disease understanding
  - Then deCODE was purchased by AmGen, and then eventually merged with the WuXi group, to become WuXi NextCODE where it functions as independent company.
  - The core of WuXi NextCODE is the Genomically Ordered Relational Database (GORdb), a platform for genome and population health. The full platform exist of:

        - The GORdb, that provides a possibility of scalable data integration.
        - Sequencing on different kind of samples
        - Application suite, to analyze and mine the data, to do deep learning and to use artificial intelligence algorithms to discover new biological insights
        - A number of disease dataset, for both rare diseases, oncology and common diseases
            - Challenge of large population sequencing is the scale and the analyzing this large amount of data. This has been the strength of the GORdb, to do so in a systematic matter.
    - In addition, NextCode has a number of large datasets, in the US, in Iceland, Singapore, China, and other countries.
        - Example is their work together with Genomics Medicine Ireland, to create an Ireland population genome program, to sequence 400000 Irish (1/10 Irish), including patients with a range of rare and common diseases.

8. Round Table

Representative of each member organization was asked to present 2-3 key things which happened in the past six months that this group could benefit from knowing and relevant to the IRDiRC goals 2017-2027.

Iiro Eerola & Irene Norstedt, DG Research and Innovation, European Commission, EU

- Launch of the European Joint Programme on Rare Diseases (goal 1, 2, 3)
    - Subject to successful conclusion of the Grant Agreement Preparation, the European Joint Programme on Rare Diseases (EJP RD) is to start on 1 January 2019. EJP RD aims at implementing an integrative research and innovation program for rare diseases involving research funders, universities, research organizations, research infrastructures, hospitals and patient organizations to optimize the flow of information and knowledge on rare diseases ensuring rapid translation of research results into clinical applications and uptake in healthcare for the benefit of the patients.
    - EJP RD will bring together organizations from 35 countries including 27 EU Member States and 7 Countries Associated to Horizon 2020, as well as Canada with joint investment of over €100 M in which the European Commission will contribute €55 M from Horizon 2020.
- European Commission published the proposal for Horizon Europe, Next EU Framework Programme for research and innovation for 2021-2027 (goal 1, 2, 3)
    - In June 2018 the European Commission presented its proposal for Horizon Europe, the next EU Framework Programme for research and innovation, for the period 2021-2027. The Health Cluster of the proposed new programme includes six main intervention areas, one of which is focusing specifically on non-communicable and rare diseases. The Commission proposal is currently discussed by the co-legislators the European Parliament and the Council for the adoption before the launch of the Programme.
    - https://ec.europa.eu/info/designing-next-research-and-innovation-framework-programme/what-shapes-next-framework-programme_en

- Horizon 2020 Call: Innovation procurement topic to implement NGS in routine diagnosis (goal 1)
  - The current Horizon 2020 Call for proposals includes a topic for Innovation Procurement to implement next generation sequencing in routine diagnostics for personalized medicine and scale up demand-driven innovation for healthcare systems. The deadline for applications is April 16, 2019.
  - http://ec.europa.eu/research/participants/portal/desktop/en/opportunities/h2020/topics/sc1-bhc-10-2019.html

Christopher Austin, National Center for Advancing Translational Sciences (NCATS), NIH, US

- The current CA Chair, current Sci Sec, current coordinator of the Sci Sec and the DSC are working on an overview paper of rare disease diagnosis
  - How many rare diseases are there? Baseline question, but essential in order to encompass the entire rare disease problem
    - Gareth Baynam: "if we cannot count rare disease patients, rare disease patients do not count.
  - What accounts as a disease?
  - How many people get diagnosed at each stage: self-diagnosis; diagnosis by the physician; first, second and third specialist; undiagnosed diseases pipeline
  - What is missing in diagnosis numbers is the primary care (how many people enter the pipeline)? How can we measure the number of people who get diagnosis?
- NCATS published a paper last year on "A Dynamic Map for Learning, Communicating, Navigating and Improving Therapeutic Development." - https://www.nature.com/articles/nrd.2017.217
  - Paper on drug discovery, not rare disease specific, but it was to clarify and show different steps in drug discovery.
  - Used for educational purposes, under creative common licence.
  - Now being turned into an electronic, interactive version on the NCATS website, with a GPS to lead you through the map.
    - Red steps are bottlenecks

Daria Julkowska – E-Rare, Europe

- Granted a funding opportunity for multi-omics approaches for rare diseases (goal 1)
  - E-Rare Joint Transnational Call 2018: based on the IRDiRC recommendation on need on multi-omics approaches for RDs, was completed with 13 projects funded.
  - Initially 18 540 000€ were earmarked by 18 countries. At the end we invested 18 101 922 € from 16 countries.
- The E-Rare consortium took the decision to focus its next strategic workshop on social sciences in humanities.
  - The workshop will be organized in collaboration with the ELSI WG of FCC.
  - The goal is to define the topics for the future call (2021) of the EJP RD that should include/be aligned with the Goal 3 of IRDiRC.
- European Joint Programme on Rare Diseases will be launched on 01/01/2019.

- The whole program will follow IRDiRC recommendations and contribute to fulfill its goals. It includes 138 institutions from 35 countries.
- The member states contribution is estimated at 52 M€ minimum and will be complemented by 55 M€ of the EC.

- In the context of the EJP RD, the first JTC will be launched.
  - It will be broadly dedicated to RD diagnosis, natural history studies, registries, pathophysiology, etc. 31 funders from 23 countries will participate in this call. The total budget earmarked is of 27 M€ of the member states and about 5 M€ of the EC.

Jason Wan, National Institute of Dental and Cranial Research (NIDCR), NIH, USA

- NIDCR participated in writing and publishing a call; "Rare Diseases Clinical Research Consortia (RDCRC) for the Rare Diseases Clinical Research Network (RDCRN)" (goal 1,2,3)
  - The purpose of this FOA is to invite new and renewal applications for the Rare Diseases Clinical Research Consortia (RDCRC) that comprise the Rare Diseases Clinical Research Network (RDCRN)
  - Budgets of up to $1 million USD in direct costs per year were allowed for up to 5 years of support.
  - The due date for applications was October 9, 2018. Applications will undergo scientific merit review in February 2019.
- NIDCR awarded grant project titled "Regulation of the cancer stem cell phenotype in salivary gland cancers"
  - This two-year award, 1R03DE027433-01, to the University of Colorado Denver, Colorado, USA, studies rare salivary gland cancers that make up fewer than five percent of head and neck tumors. The goals of this study are to define the salivary gland cancer stem cell population across disease histotypes, and conduct gene expression and translation analysis to define enriched signaling profiles specific to cancer stem cells.
- NIDCR awarded support for conference grant titled "2018 Bones and Teeth Gordon Research Conference and Gordon Research Seminar"
  - This conference grant, 1R13DE027552-01, provided partial support for the meeting which was held in Galveston, Texas, USA.

Adam Hartman - National Institute of Neurological Disorders and Stroke (NINDS), US

- Participate and support RDCRNs (NINDS is the primary IC responsible for Autonomic Rare Diseases, Brain Vascular Malformation, Inherited Neuropathies, Lysosomal diseases, NAMDC, DSC, ALS, Frontotemporal Lobar Degeneration and PS for Dystonia Coalition and others) (goal 1, 3)
  - Directing the Undiagnosed Diseases Network, consulting for the NIH Intramural Undiagnosed Diseases Program
  - NINDS participated in crafting announcements for the next round of RDCRN funding.
- Funding trials in many rare diseases with neurological pathology, clinical trials for TSC, DMD, Rett syndrome, and Fragile X, to name a few (including our NeuroNEXT Clinical Trial network)." (goal 2)

- These activities are supported in both intramural and extramural programs.

- Cooperative funding mechanism for rare disease clinical trial planning (goal 2, 3)

Hugh Dawkins – Dept of Health Western Australia, Australia

- Australia will establish Australia's first National Rare Diseases Framework and Action Plan to support people with a rare disease, and Rare Voices Australia will develop the Action Plan with funding from the national government (goal 1, 2, 3).
- The WA Undiagnosed Diseases Program, that was already a pediatric only program, has transitioned to include patients up to 26 years old (goal 1).
  - Ran in parallel with a program specific for Aboriginals with the Aboriginal Australian Genomics Program.
- New program for rare cancers (both pediatric and adults) launched, comes under an Australian Cancer Medicines Program. (goal 1, 2).
  - To get a better cancer profile and to help identify new therapeutics, and understand the pathways to these diseases.
- There is a program developed for National Framework for Newborn bloodspot screening, to evaluate new targets for testing (goal 1).

Mathew Pletcher, Roche, Switzerland

- Progress in the Risdiplam program, a small molecule for the treatment of Spinal Muscular Atrophy, where there are three ongoing clinical trials and another one that will start shortly, in collaboration with PTC and the SMA foundation. (goal 2)
  - Trial in newborn babies for Type 1 SMA
  - Trial in patient from 2 to 25 years of age for Type 2 and 3 SMA
  - Exploratory study for safety for patients with Type 2 and 3 SMA, between 12 and 60 years old, who have previously been on a different SMA treatment
  - Another trial for Type 1, genetically diagnosed but pre-symptomatic patients will start soon
- Progress in the RG6042 drug development for Huntington disease, in collaboration with Ionis, a fatal neurodegenerative disease, with no effective treatment right now (goal 2)
  - Entering in a pivotal trial shortly
  - Phase I-II has shown that it lower the levels of the mutant HTT protein in the CSF, which is believed to be the underlying cause of Huntingon's disease
  - EMA PRIME designation obtained.
- Results from the phase I/II study for a drug targeting DMD, which lowers the levels of myostatin. (goal 2)
  - Careful monitoring for results on this drug.
- Roche is setting up its first gene therapy program, to be started next year, in collaboration with a 4DMT for an inherited retinal disorder, called choroideremia. (goal 2)
  - A new program in Angelman's syndrome is also being set up.

Sonja van Weely, ZonMw, The Netherlands

- ZonMw is the Joint Call Secretariat of the current E-Rare Joint Transnational Call JTC 2018 (goal 1)
  - Topic call: "Transnational research projects on hypothesis-driven use of multi-omic integrated approaches for discovery of disease causes and/or functional validation in the context of rare diseases"
  - Initially 18 540 000€ were earmarked by 18 countries. At the end we invested 18 101 922 € from 16 countries.
- ZonMw chairs the working group for the strategic workshop on social and human sciences
  - Goal is to set up a funding call dedicated to social and human sciences in rare diseases in 2020, after the workshop in mid-2019.
- There is a Dutch research group, commissioned by ZonMW and the Dutch Institute of Health, that will make in inventory in the Netherlands on several aspects of rare diseases
  - What is currently being done?
  - Where do we need more emphasis in the rare diseases research? Will be the basis for a further research agenda.

Ralph Schuster, Federal Ministry of Education and Research, Germany

- Participation in and preparation of first EJP RD call for "Transnational research projects to accelerate diagnosis and/or explore disease progression and mechanisms of rare diseases" (goal 1,2)
  - Call to be published mid December 2018, 31 Funders from 23 countries, EC cofounding, together about 35 M € available for call.
- Funding decision for national translational consortia for rare disease research (goal 1,2)
  - 11 national networks have been selected for funding with about 25 M. € for 3 years starting spring 2019;
  - Wide range of diseases including rare kidney, autoimmunity, mitochondrial, neurological and cancer predisposing diseases.

Manuel Posada, ISCII, Spain

- Spanish Undiagnosed Rare Diseases Program – SpainUDP (goal 1)
  - The Spanish Undiagnosed Rare Diseases Program (SpainUDP) is developed by the Institute of Rare Diseases Research, ISCIII at the National level.
  - At the end of 2018, more than 200 exomes (mainly trios) will be available in the RD-Connect GPAP and the corresponding phenotypic information collected in PhenoTips.
  - Some of them (n=29) are solved cases potentially useful to develop algorithms for further bioinformatics analysis that may help other researchers solve their cases. On the other hand, we also have unsolved cases (n=10) with strong candidate genes, which will be tested through functional analysis
- Advances therapies (goal 2)
  - A new strategy about Personalized Medicine and Advances therapies is now discussing in the Congress of Deputies of Spain. The ISCIII will coordinate this strategy. Several researchers groups are working in this topic. Some of these groups have reached new orphan designation in both the FDA and EMA.

- Registries, biobanks and new policies (goal 3)
  - The Spanish National RD Registry is ongoing. It is a global activity coordinated by the MoH in Spain together with all Spanish regions (Autonomous Communities). In parallel the patient registry for outcome research continues its activity collecting new collections of RD such as immunodeficiencies and also ophthalmological RD.
  - In addition, the coordination of Eurobiobank, the unique RD platform aimed to biobanks, is being promoting with a new strategic plan in collaboration with the BBMRI-ERIC European infrastructure.

Samantha Parker, Lysogene

- Two-year follow-up data for MPS IIIA natural history study as control group for gene therapy Phase 2-3 trial (goal 2).
  - To reinforce published data on the natural history of MPS IIIA and expand the geographic outreach, Lysogene launched an observational study in five countries (NCT02746341).
  - This study will function as a non-concurrent control for the Phase 2-3 gene therapy trial (NCT03612869).
  - The observational study also includes mixed methods research using face-to-face interviews, questionnaires, and digital health technology.
- FDA approval of IND Application to Initiate Phase 2-3 Clinical Trial in MPS IIIA (goal 2).
  - Lysogene's Phase 2-3 trial (NCT03612869) uses an optimized gene therapy construct (LYS-SAF302). The study is a single-arm, multicenter study of AAV serotype rh.10 carrying the human SGSH (AAVrh.10-SGSH) for the treatment of MPS IIIA. The study will include 20 patients.
  - The primary objective will be to assess the drug efficacy in improving or stabilizing the neurodevelopmental status of patients compared to the expected evolution based on natural history data.
- Initiation of an international immunogenicity working party to review and share immunogenicity findings from AAV clinical trials (goal 3).
  - Lysogene has initiated an immunogenicity working party to review and share immunogenicity findings from AAV clinical trials, which, viewed together, will allow the development of strategies for preventing, and managing host immune responses in AAV-mediated gene transfer for CNS disorders

Carolyn Hutter, National Human Genome Research Institute (NHGRI), US

- NIH Common Fund Undiagnosed Diseases Network (UDN) Phase II was funded (goal 1)
  - The Undiagnosed Diseases Network (UDN) is funded by the NIH Common Fund with the goal to improve and accelerate diagnosis of rare and undiagnosed conditions (aligns with IRDiRC goal 1).
    - Awards for Phase II of the UDN were made in September 2018, the total investment over the next four years will be ~$100M, pending availability of funds.
    - Phase II of the UDN is focused on sustainability of the UDN model.

        - A Phase I paper reporting on the first 1,519 applicants to the UDN was published in NEJM in October. For the 382 patients who had a complete evaluation, the diagnosis rate was 35%. PMID: 30304647; DOI: 10.1056/NEJMoa1714458
- NHGRI Centers for Mendelian Genomics (CMGs) (goal 1)
    - The Centers for Mendelian Genomics (CMGs) are funded by NHGRI (with co-funding from NHLBI and NEI) and focus on discovering "rare disease genes" to lay a foundation for diagnosing disease, understanding disease biology, and developing treatments (goal 1).
        - Since funding started in 2012, the CMGs have discovered over 3,500 disease-genes associations by conservative and more than 470 manuscripts directly acknowledge CMG support.
        - The CMGs have recently formed working groups and received supplemental funding to explore multiple approaches towards unsolved cases.
        - CMG investigators from the Broad Institute, and collaborators, published on a new open-source tool called "matchbox", which serves as a portable bridge for any given rare disease genomic center to participate in Matchmaker Exchange. PMC6250066; DOI: 10.1002/humu.23655

Durhane Wong Rieger, Canadian Organization of Rare Disorders (CORD), Canada

- After 15 years of advocacy with the Canadian government, and a new regulatory framework for regulatory review, that also includes for rare diseases (goal 1)
    - So far, there has also never been a definition for orphan drugs, so within this framework, a drug that has an orphan designation in Europe or the US is now accepted as Orphan Drug.
    - Bring together all guidelines and policies for rare diseases
- There is a consultation on a proposed process for complex and specialized drugs, including those for rare diseases, that focuses on four areas being evidence, pricing, access and communications. (goal 3)

Katherine Lambertson, Genetic Alliance, US

- Establishment of new partnership to enable broader data sharing by participants in PEER registry platform (goal 1)
    - Genetic Alliance has recently finalized a new partnership that will expand participants' options for data sharing in PEER, creating a place for participants to contribute their data to a variety of research potentially impacting any number of conditions. The partnership will be announced formally in January 2019.
- Addition of PEER registry platform to DiseaseInfosearch.org (goal 1)
    - IRB approval for the new DiseaseInfosearch.org (DIS) was received very recently. In addition to information about 10,000 diseases and their subtypes, we aggregate information on characteristics of the condition that will better help researchers and advocacy leadership prioritize research. The most exciting new feature in this release is the addition of PEER as a way for anyone visiting the site to join a registry.
- Hiring of executive director for Catalyst (goal 2)

- Catalyst is a project in collaboration with the University of North Carolina, the Structural Genomics Consortium, and Genetic Alliance. We've just hired an executive director for it.

Domenica Taruscio, Istituto Superiore di Sanità (ISS), Italy

- Organization of several rare diseases courses (goal 1, 2, 3)
  - International Course 6th International Summer School on Rare Disease and Orphan Drug Registries." ISS, September 10-14, 2018.
  - International Course "Clinical Practice Guidelines for Rare Diseases: development and quality assessment". ISS, October 9-10, 2018.
- Activity on drug development (goal 2)
  - ISS has a Full Member of Committee of Orphan Products COMP (EMA)
  - Activity on Orphan drugs at the Italian Drug Agency
- Co-founder and board member of the Undiagnosed Diseases International (UDNI) (goal 1)
  - Undiagnosed Diseases Network International (UDNI): Extension of the International Network, e.g. including new Countries.
  - Undiagnosed Diseases Network Italy (UDN-Italy): extension of the National Network, e.g. including new clinical sites.
  - Undiagnosed Diseases Network Italy Sud (UDN-Italy Sud): New project in order to better involve Italy Sud (e.g. Sicily)
  - Implementation on the entire National territory of the recent Italian Law on Newborn screening for 40 metabolic rare diseases.

Virginie Bros-Facer, EURORDIS-Rare Diseases Europe, France

- EURORDIS is partner in the Solve-RD project that started January 1, 2018 (goal 1)
  - In the framework of this project, EURORDIS organized the first annual Winter School in March 2018 and developed the Community Engagement Task Force which will be launched later this year (making links with parallel initiatives as the Patient Engagement Task Force in UDNI and the network of patient organizations for undiagnosed diseases, SWAN Europe)
- EURORDIS is partner in the Global Commission to End the Diagnostic Odyssey for Children with a Rare Disease (goal 1)
  - Joint initiative between Shire, Microsoft, EURORDIS
  - Following the Commission's deliberations over the next year, we plan to publish a report with recommendations and a roadmap to reduce diagnosis time in January 2019. The first face to face meeting took place in Boston in April 2017.
- EURORDIS is a partner in two new IMI projects (goal 2)
  - PARADIGM (started March 1, 2018) – set up to change ethical patient engagement in medicinal development processes
  - Connect 4 Children (C4C) (started May 1, 2018)
- Carried out a large quantitative and qualitative survey on perspectives of RD patients on Data sharing/data protection in research and healthcare via EURORDIS Rare Barometer Program (over

2000 respondents; currently analyzing results for forthcoming academic publication of results and recommendations) (goal 3)
    - We have now finished the analysis and are finalizing manuscript for publication of results and recommendations.
- EURORDIS is co-leader of Pillar 3 of the EJP RD (goal 3)
    - Comprising all training courses for clinicians, researchers and patient representatives in the field of RD research

Diego Ardigo, Chiesi Pharmaceutici, Italy

- Lamzede (velmanase alfa) post-approval progression (goal 2)
    - Lamzede® (INN: velmanase alfa; target disease: alpha mannosidosis): after EU approval in March 2018, a number of post-approval commitments are being progressed (registry set up, paediatric study progression, and quality related activities), as well as patient access activities and beyond EU development.
- Synthetic Surfactant phase 2 progression (goal 2)
    - Drug is being developed to treat lung problems in neonates, for babies born with a complete lack of lung surfactant
    - After end of phase 2 study in February, key results were delivered at end July, supporting the progression of the development.
- Holoclar post-approval progression (goal 2)
    - After Conditional Marketing Authorization in EU obtained in 2015, a post-approval confirmatory study (HOLOCORE) was started to confirm efficacy and safety in 65 patients, as well as a EU-wide registry (HOLOSIGHT).
    - Patient recruitment of the HOLOCORE study is now completed.

Dominique Dunon-Bluteau – ANR, France

- National general research call 2018 - ANR (goal 1, 2, 3)
    - The ANR National general research call 2018 has resulted in the funding of 30 research projects on rare diseases, with a total budget 13,4 M€
- Took part in setting up the third national plan for rare diseases in France 2018-2022 (goal 1, 2, 3)
    - Axes are Diagnostics, Data bases, New therapies, Treatment access
    - 23 networks, 107 Reference research center on RD (multisites =1800 centers), 220 Patient associations
- National priority on rare diseases in the 2019 ANR general research call "Translational research on rare diseases"
    - Estimated budget 1,5 M€
    - In addition to yearly funding (ie 13,4 M€ on 2018 see above)

En Kimura, AMED, Japan

- Progress on the Rare/Intractable Disease Project of Japan (goal 1, 2)
    - AMED conducted the Grant Calls for 2018 Rare/Intractable Disease Project of Japan (annual budget size 4,220 M yen = 38.7 M USD), and total 90 projects for orphan diseases

were selected and started in April 2018. Now, an additional 170 M Yen and 17 more projects were started. 2/3 of this budget was allocated to programs for discovery of clinical candidates and investigator-initiated clinical trials, and specific budget was allocated for neurological diseases

- "Rare/Intractable Disease Project of Japan" supports 24 projects under clinical development in 2017, which includes one project regulatory privileged as "SAKIGAKE"-designation

- Initiative on Rare and Undiagnosed Diseases (IRUD) and IRUD Beyond (goal 1, 2)
  - IRUD was launched in FY2015 and its diagnose network is currently consisting of 432 hospitals. The 1st phase of IRUD was terminated at the end of 2017, and the 2nd phase of IRUD was established through a grant call (budget size 666 M yen = 6.11 M USD in 2018). In this new system, the IRUD coordinating center was established to govern the whole IRUD network. In IRUD, at least 9,517 samples (3,416 proband samples) were analyzed by WES by the end of July 2018, 40% of them were given a definite diagnosis, and 19 new diseases were discovered.
  - The IRUD platform also became a node in MatchMaker Exchange in December 2017, and 9 patients were given a definite diagnosis through this collaboration so far.
- P Rare Disease Data Registry of Japan (RADDAR-J) (goal 1, 2)
  - AMED started research toward the construction of information infrastructure (Rare Disease Data Registry of Japan: RADDAR-J) (budget size 300 M yen = 2.7 M USD). Its objective is to facilitate the maximum effective utilization of information on rare diseases/intractable diseases that Rare/Intractable disease research groups in Japan obtained.

<u>David Pearce, Sanford Research, USA</u>

- Sanford Lorraine Cross Award (goal 2)
  - The Inaugural Sanford Lorraine Cross Award was awarded on Tuesday, December 4th. This award is to honour a researcher or innovator for pioneering the next breakthrough, innovation, or treatment to transform global health. The recipient received a $1 million prize for their work.
  - The award was given to Drs. Katherine High and Jean Bennett, who all contributed significantly to the application of gene therapy in inherited disease. As gene therapy has had a great significance on rare diseases, the impact of this award should raise the bar for gene therapy in rare diseases.
- Gene Therapy in CLN6 (goal 2)
  - In partnership with Nationwide Children's Hospital, Sanford Research helped develop and launch the first ever clinical trial that delivered gene therapy as a treatment option for CLN6-Batten Disease. Thus far, nine children have received this innovative new therapy that was initially approved by the FDA for six patients, and they have all tolerated the treatment well.
- CoRDS Registry (goal 2)

- Currently, the registry encompasses 943 different rare conditions across 6,000 participants. CoRDS has participants in all 50 states, and 63 countries around the world. We have partnered with nearly 40 advocacy organizations to create disease-specific questionnaires for their communities.
- So far in 2018, we have participated in 9 research studies sharing nearly 1,800 datasets with researchers and by notifying our participants of clinical studies that they may be interested in.

Ramaiah Muthyala – Indian Organization for Rare Diseases (IORD)

- Memorandum of understanding with Human Genetics FrigeHouse, Ahmadbad (goal 1)
  - Identified Gounder mutation for Morquio A in Gujarat people P77R is seen in nearly 50% of children affected with Morquio A. First report from India demonstrating molecular profile of children with NCVL1 and NCL2 related to batten disease.
- Memorandum of understanding with open Applications consulting Ltd (OpenApp) Ireland to create a registry platform that can be customized to hoist many registries (goal 1)
  - Hopefully will also help to get a better grasp on the number of rare disease patients in India.

Younjhin Ahn, Korea National Institute of Health, Korea

- Making a national list of rare diseases that will be supported (goal 1)
  - The Rare diseases Management Act came into force on the 30th of December 2016 in Korea. The term of "rare disease" is defined as a disease that affects fewer than 20,000 people or whose number is unknown because diagnosis of the disease is difficult.
  - Among diseases with fewer than 20,000 people, we selected the target diseases to care for and support. The patients with those diseases basically have supports of medical expenses.
- Expanded Undiagnosed diseases program (goal 1)
  - From 2013, KNIH has been running a genetic diagnosis-supporting program. From this year, KNIH expand the supporting diseases and, set a clinical center for UDP.
- Planning new projects (goal 1, 2)
  - KNIH is currently planning and preparing a new supporting program and research, which will start in early 2019.

Katherine Beaverson, Pfizer, USA

- Seng H. Cheng, PhD named SVP and CSO of Pfizer's Rare Disease Research Unit (goal 2)
  - Pfizer announced the appointment of Seng Hing Cheng, PhD as Senior Vice President and Chief Scientific Officer of the Rare Disease Research Unit (RDRU).
  - Seng H is well known to IRDiRC and will continue to be involved at the level of the Scientific Committees for Pfizer.
- Tafamidis Phase 3 Transthyretin Amyloid Cardiomyopathy (ATTR-ACT) (goal 2)
  - Pfizer released topline results for its Phase III trial (ATTR-ACT) testing Tafamidis for the treatment of transthyretin cardiomyopathy. In its study of 441 patients, Pfizer included

those who had the hereditary form of the disease, as well as the "wild-type form". Topline results showed that at 30 months the Pfizer drug caused a statistically significant reduction in mortality and disease-related hospitalization.
    - Also in March, the Ministry of Labour Health & Welfare in Japan granted SAGIGAKE designation to Tafamidis for the CM indication. In May, the FDA granted breakthrough therapy designation for Tafamidis for the treatment of patients with TTR CM.
- Newborn screening for sickle cell disease: Pfizer, The Hospital for Sick Children and Korle Bu Teaching Hospital in Ghana (goal 1, 3)
    - During Phase I, the screening program diagnosed more than 70 babies as testing positive for SCD and has led to nearly 60 percent of these children being enrolled at the newborn sickle cell clinic. At the clinic, these babies receive comprehensive follow-up care including penicillin prophylaxis in order to prevent life-threatening infections.
    - Phase II of the program, which has integrated the insights and learnings from Phase I, is already underway. In addition to screening almost all of the approximately 11,000 babies born at Korle Bu annually, it includes an increase in the number of community health workers, and an expansion of training for nurses and staff; all part of developing an infrastructure at Korle Bu to provide comprehensive care to SCD patients and their families.
- This year, the Project Hercules, a project in which Pfizer, together zith patient organizations, pharmaceutical companies, academics joined together to help build better evidence for DMD, won a NORD award.

James McArthur, Cydan II, USA

- One of Cydan's companies, Vtesse, has advanced a new therapy for a Niemann Pick type C that is in phase 3 development. This study is currently doing its phase 3 readout (goal 2)
- One of Cydan's companies, Imara, has advanced a therapy IMR-687 for sickle cell disease and beta-thalasemi into phase 2 clinical studies (goal 2)
- Cydan II has launched a new company, Tiburio (3rd Cydan spinout), that focuses on rare endocrine disorders (goal 2)

Christopher McMaster, Canadian Institute of Health Research (CIHR), Canada

- 2017 Large-Scale Applied Research Project Competition: Genomics and Precision Health (goal 1, 3)
    - Through this program, a total of 6 projects pertaining to rare diseases were jointly funded by CIHR and Genome Canada, for a total of $27 million Canadian dollars specifically towards rare diseases projects of a total of over $70 million Canadian dollars for the program overall.
- Research Catalyst Network: Rare Diseases 2 (goal 2)
    - This program, also jointly funded by Genome Canada and CIHR, represents a joint investment of $1,7 M CAD to support the ongoing activities of the Rare Diseases Models and Mechanism Network.

- The goal of the second launch of this program is to maintain Canada's leadership in enabling clinical geneticists who are identifying rare disease gene mutations to collaborate with model organism researchers with expertise in the cognate gene's function, and to develop the capacity to study genes for which no suitable models can be identified in Canada in other countries with similar networks.

- Participation in E-Rare3 JTC2018 (goal 2,3)
  - Focus on hypothesis-driven use of multi-omic integrated approaches for discovery of disease causes and/or on functional validation in the context of rare diseases.
  - A total of 5 projects with a Canadian component were jointly funded by CIHR, FRQS and Muscular Dystrophy Canada, representing a total investment of $1,8 M CAD.

Ritu Jane, Rare Diseases International, Singapore

- Growth of RDI (goal 1, 2, 3)
  - RDI has grown to it now represents 4 regional alliances, 32 national RD alliances, 14 disease specific federations.
- Participation in the Global Commission to end the Diagnostic Odyssey for children with rare diseases (goal 1)
  - RDI has been working with Eurordis, Shire and Microsoft on the Global Commission to End the Diag Odyssey for children with RD.
  - The commission focuses on solutions to core barriers preventing timely diagnosis for all rare diseases - with an emphasis on those affecting children.
- Report on RDI's activities in the Global South (goal 1,2)
  - RDI is official partner to The APEC (asia pac economic cooperation) Action Plan on RD which has, been endorsed by the APEC Life Sciences Innovation Forum at Papua NG during the APEC CEO summit on Nov 19th.
  - The Action Plan aims to define, diagnose and support rare disease patients through building capacity and aligning policies across the 21 APEC member economies.
  - It also aims to provide APEC Economies with a framework for policy action to tackle the challenges of rare disease. Among the 10 key areas outlined for action are: **a.** raising public awareness of rare diseases AND **b**. ensuring that patients are diagnosed and cared for in a timely manner. The Action Plan calls its 21-member economies to improve the economic and social inclusion of individuals living with rare diseases, with clear targets by 2025.
- In South America, RDI co-organiwed a conference (goal 1,2)
  - RDI together with the Latin American Alliance for Rare Diseases (Aliber) ALIBER who organized a conference on Nov 20-21 in Bogota, Colombia bringing together patient alliances or patient groups with presentation from Colombian Ministry of Health and updates on Colombia's Rare Disease Registry (data on patients affected overall by more than 1000 diseases) as well as their programs towards access to diagnosis and specialist care.

Lucia Monaco – Telethon Foundation, Italy

- Clinical trial for MPS I started (goal 2)
  - A new clinical trial with lentivirus-based gene therapy for mucopolysaccharidosis I has started at the San Raffaele-Telethon Institute for Gene Therapy (SR-Tiget) in Milan.
  - Overall, 95 patients affected by six different genetic diseases have received gene therapy treatments based on research developed by Fondazione Telethon at its Institutes.
- Venture capital partnership launched (goal 2)
  - A new partnership with the venture capital firm Sofinnova has been launched, aimed at creating 15-20 start-up companies for the development of rare genetic disease therapies stemming from Fondazione Telethon's research pipeline, with an initial capital of 80 M€. Fondazione Telethon's duty in the partnership regards the selection of the most promising projects to be developed, starting from the current research portfolio; a dedicated call for applications is envisaged at a second stage.
- Two calls for research /clinical projects being issued (goal 2)
  - Fondazione Telethon's research pipeline is soon going to be enriched with new research projects thanks to two new Calls for extramural research projects open to investigators in nonprofit Italian research institutes: the General Call on rare genetic diseases, and the Call for clinical projects on rare genetic neuromuscular diseases.
  - Both calls are planned to open on December 12.

Weiling Wang, BGI, China

- Rare disease sample collection (goal 1)
  - Till Dec. 2018, BGI has collected more than 22,288 samples of rare disease patients. We found about 1,189 novel causative variants and 114 novel causative genes in total to push more patients getting a clear molecular diagnosis result.
- WES pipeline (goal 1)
  - BGI has developed a pipeline based on WES for genetic testing of rare disease patients. Till now, we have finished about 3,700 samples sequencing and issued reports

Katherine Needleman – US Food and Drug Administration (FDA), Washington, DC

- Grants (goal 1, 2)
  - OOPD held a call for its clinical trials resubmission grants and received 28 applications in October 2018.
  - OOPD revised and reissued the RFAs for both the clinical trials and natural history programs taking into account lessons learned and making improvements to better meet our goals.
    - NH grant submission date is January 10, 2019. https://grants.nih.gov/grants/guide/rfa-files/RFA-FD-19-001.html
    - CT grant submission date is June 2019. https://grants.nih.gov/grants/guide/rfa-files/RFA-FD-20-001.html
  - OOPD completed the 2018 receipt date cycle for the Pediatric Device Consortia (PDC) Grant Program and funded 5 consortia.

https://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/PediatricDeviceConsortiaGrantsProgram/ucm337850.htm

Nicole Boice, Global Genes, USA

- 2018 RARE Patient Advocacy Symposium (now the RARE Drug Development Symposium) (goal 2)
  - Global Genes, in partnership with the Penn Medicine Orphan Disease Center, organizes and hosts this annual Symposium. The 2018 event had about 130 participants and featured speakers from leading patient advocacy organizations conducting research, pharmaceutical and biotech companies, and regulatory agencies.
- 2018 RARE Patient Advocacy Summit (with Entrepreneurial Readiness Bootcamp and RARE Global Advocacy Leadership Summit) (goal 1,2)
  - This year, Global Genes organized and hosted the 7th annual RARE Patient Advocacy Summit. There were more than 800 participants at the Summit.
  - The Global Genes RARE Patient Advocacy Summit includes dedicated session tracks focused on patients as partners and drivers in research and science and technology innovations for rare disease.
- David R. Cox Scholarship for Rare Compassion (goal 1)
  - Global Genes is presenting the third year of the David R. Cox Scholarship for Rare Compassion
  - This scholarship program is an opportunity for emerging medical students to connect to the rare disease community with the goal of developing and understanding compassion for the challenges and lifestyles that patients diagnosed with a rare disease are faced with every day
  - The winning submissions for 2018 can be found at https://globalgenes.org/2018-david-r-cox-scholarship-for-rare-compassion-recipients/.

Actions and deliverables

- Sci Sec
  - Send out contact information for new Sci Sec
  - Send out call for nominations for Task Forces
  - Send out confirmation of acceptance to new DSC members

Document history

Version 1. Report drafted by Anneliene Jonker, December 31, 2018
Circulated to Chair of the CA, January 2, 2019
Version 2. Report edited by Christine Cutillo, January 22, 2019
Circulated to members of the CA, January xx, 2019

Annex - List of participants

Members	**Representative**
National Center for Advancing Translational Sciences (NCATS), USA	Christopher Austin (Chair)
Western Australian Department of Health, Australia	Hugh Dawkins (Vice Chair)
Canadian Institutes of Health Research (CIHR), Canada	Christopher McMaster
Canadian Organization for Rare Disorders, Canada	Durhane Wong-Rieger
BGI, China	Weilin Wang
WuXi Next Code Ltd., China	Christina Waters
E-Rare Consortium, Europe	Daria Julkowska, Florence Guillot
European Commission, DG Research and Innovation, Europe	Iiro Eerola, Carmen Laplaza, Irene Norstedt
European Commission, DG Sante, Europe	Nicoline Tamsma
Agence Nationale de la Recherche	Dominique Dunon-Bluteau
EURORDIS-Rare Diseases Europe, France	Virginie Bros-Facer
French Foundation for Rare Diseases, France	Daniel Scherman
Lysogene, France	Samantha Parker
Federal Ministry of Education and Research, Germany	Ralph Schuster
Indian Organization for Rare Diseases, India/USA	Ramaiah Muthyala
Chiesi Farmaceutici S.p.A, Italy	Diego Ardigo
Istituto Superiore di Sanità, Italy	Domenica Taruscio
Telethon Foundation, Italy	Lucia Monaco
Advocacy Service for Rare and Intractable Diseases' multi-stakeholders in Japan (ASrid), Japan	Yukiko Nishimura
Japan Agency for Medical Research and Development (AMED), Japan	En Kimura, Makoto Suematsu
The Netherlands Organisation for Health Research and Development, the Netherlands	Sonja van Weely
Rare Diseases International, Singapore	Ritu Jain
National Institute of Health Carlos III, Spain	Manuel Posada
Korea National Institute of Health, South Korea	Younjhin Ahn
Roche, Switzerland	Mathew Pletcher
Cydan II, USA	James McArthur
Food and Drug Administration, Office of Orphan Products Development (FDA/OOPD)	Katherine Needleman (teleconference)
Genetic Alliance, USA	Katherine Lambertson
Global Genes, USA	Nathalie Douglas

National Human Genome Research Institute (NHGRI), USA	Carolyn Hutter
National Institute of Neurological Disorders and Stroke (NINDS), USA	Adam Hartman (teleconference)
National Institute of Dental and Craniofacial Research (NIDCR), USA	Jason Wan
Pfizer, USA	Katherine Beaverson
Recursion Pharmaceuticals Inc, USA	Tim Considine
Sanford Research, USA	David Pearce

Scientific Committees	
Diagnostics	Gareth Baynam
Interdisciplinary	Dixie Baker, Domenica Taruscio
Therapies	Diego Ardigò, Virginie Hivert

IRDIRC Scientific Secretariat	
SUPPORT-IRDIRC Project	Marlene Jagut, Anneliene Jonker, Anne-Laure Pham Hung d'Alexandry d'Orengiani, Ana Rath
NIH/NCATS	Christine Cutillo, Lilian Lau

Apologies

Members	**Representative**
Rare Voices Australia, Australia	Nicole Millis
European Organisation for Treatment & Research on Cancer, Belgium	Denis Lacombe
Botswana Organization for Rare Diseases (BORDIS), Botswana	Eda Selebasto
Genome Canada, Canada	Cindy Bell
Chinese Organization for Rare Disorders, China	Qi Sun
WuXi AppTec Co. Ltd., China	James Wu
Academy of Finland, Finland	Heikki Vilen
French Muscular Dystrophy Association, AFM-Téléthon, France	Marie-Christine Ouillade
Children's New Hospitals Management Group, Georgia	Oleg Kvlividze
Organization for Rare Diseases India (ORD-I)	Prasanna Kumar Shirol
Shire Pharmaceuticals, Ireland	Madhu Natarajan
National Institutes of Biomedical Innovation, Health and Nutrition (NIBIOHN), Japan	Yoshihiro Yoneda

Saudi Human Genome Project, Saudi Arabia	Sultan Turki AlSedairy
Rare Diseases South Africa, South Africa	Kelly du Plessis
Ultragenyx, Switzerland	Tom Pulles
Loulou Foundation, UK	Daniel Lavery
National Institute for Health Research (NIHR), UK	Willem Ouwehand
Genzyme, USA	Daniel Gruskin
Ionis Pharmaceuticals, USA	Brett Monia
National Cancer Institute (NCI), USA	Jack Welch
National Eye Institute (NEI), USA	Santa Tumminia
National Institute of Child Health and Human Development (NICHD), USA	Melissa Parisi
National Institute of Arthritis and Musculoskeletal and Skin Diseases, (NIAMS), USA	Faye Chen
National Organization for Rare Diseases (NORD), USA	Vanessa Boulanger
NKT Therapeutics, USA	Robert Mashal
PTC Therapeutics, USA	Ellen Welch

IRDiRC

INTERNATIONAL
RARE DISEASES RESEARCH
CONSORTIUM