

Meeting report series

Report of the 4th Companies Constituent Committee Meeting

Vienna, Austria

May 15-16, 2018

Participants

Dr Christopher Austin, NIH/NCATS, USA – Acting Chair

Ms Katherine Beaverson, Pfizer, USA

Dr Tim Considine, Recursion Pharmaceuticals, USA

Dr Shiyin Foo, Cydan II, USA – May 15

Dr Christina Waters, WuXi NextCODE, USA – Observer, May 16

Dr Virginie Hivert, Therapies Scientific Committee, France – May 15

Dr Lilian Lau, Scientific Secretariat, France

Dr Anne-Laure Pham Hung d’Alexandry d’Orengiani, Scientific Secretariat, France

Apologies

Dr Mathew Pletcher, Roche, Switzerland – Chair

Dr Madhu Natarajan, Shire, USA – Vice Chair

Ms Karen Aiach, Lysogene, France

Dr Andrea Chiesi, Chiesi Farmaceutici, Italy

Dr Carlo Incerti, Genzyme, USA

Dr Ning Li, BGI, China

Dr Robert Mashal, NKT Therapeutics, USA

Dr Brett Monia, Ionis Pharmaceuticals, USA

Dr Tom Pulles, Ultragenyx, Switzerland

Dr Ellen Welch, PTC Therapeutics, USA

Dr James Wu, WuXi AppTec, China

Agenda

1. Welcome and introduction of participants
2. Activity D 2018: Natural history and registry (NH/R) platform for use in real world evidence (RWE) data collection
3. Activity H 2018: Background internal work on common knowledge base to drive rare diseases research
4. CCC membership: Current and potential new members

REPORT

1. Welcome and introduction

The Acting Chair of the Companies Constituent Committee (CCC) welcomed the meeting participants, who each introduced themselves.

- ▶ **Christopher Austin** is the Director of the National Center for Advancing Translational Sciences at the NIH and Acting Chair for this meeting.
- ▶ **Katherine Beaverson** is the Patient Advocacy Director of the Rare Disease Research Unit at Pfizer.
- ▶ **Tim Considine** is the Senior Vice President of the Strategic Development Unit at Recursion Pharmaceuticals.
- ▶ **Shiyin Foo** is the Chief Medical Officer of Cydan.
- ▶ **Christina Waters** is the Senior Vice President and General Manager of the Global Rare Disease Program at WuXi NextCODE; she was attending as an observer, pending an application of WuXi NextCODE to become an IRDiRC member organization.

The Acting Chair summarized some key points:

- ▶ The major goals of the CCC are to:
 - Identify common roadblocks to efficient rare disease research in the company space
 - Develop solutions and contribute towards the IRDiRC goals
 - May be through time-limited, task-specific Task Forces, with support of the Scientific Secretariat (Sci Sec) to set up meetings, prepare documents, etc
 - May be through coordinated actions by CCC and/or IRDiRC members
 - Promote concerted effort and collaborations on pre-competitive aspects of R&D
- ▶ IRDiRC Goals for 2017-2027
 - Goal 1: All patients coming to medical attention with a suspected rare disease will be diagnosed within one year if their disorder is known in the medical literature; all currently undiagnosable individuals will enter a globally coordinated diagnostic and research pipeline
 - Goal 2: 1000 new therapies for rare diseases will be approved, the majority of which will focus on diseases without approved options
 - Goal 3: Methodologies will be developed to assess the impact of diagnoses and therapies on rare disease patient

The CCC positions itself to focus on the therapeutic side, i.e. Goal 2, while still contribute towards Goals 1 and 3, with the following principles in mind:

- ▶ Reimagining and transforming science to accelerate clinical development
- ▶ Making environment for therapeutic development more permissive for success
- ▶ Translating innovation into sustainable access to medicines

The CCC should also use the IRDiRC “bully pulpit” (e.g. position papers) to make new approaches with potential for log improvement viewed as less risky/more acceptable.

2. Activity D 2018: Natural history and registry (NH/R) platform for use in real world evidence (RWE) data collection

The key reason of clinical trial failures is the lack of natural history (NH) to better understand disease progression, identify biomarkers and clinical endpoints, and target the right patient population for a given candidate therapy. Moreover, if done right, NH is increasingly used as control dataset.

Background to Activity D

- ▶ The Therapies Scientific Committee (TSC) carried out a brainstorming exercise in 2017 to identify its strategic action plan
- ▶ The resulting Theme 3 was to support the definition of standards for use of data collected in healthcare practice for RWE generation for disease understanding and treatment monitoring
- ▶ With multiple projects on hand, the TSC brought this topic to the attention of the CCC, which has also identified the need for high quality NH studies and RWE data collection
- ▶ The Funders Constituent Committee (FCC) has also recognized the need to identify and fund innovative schemes to perform NH studies
- ▶ The converging points led to the CCC being requested to lead this activity, with active input of the TSC and FCC
- ▶ At the Scientific Committees meeting in Vienna, given the involvement of the Interdisciplinary Scientific Committee (ISC) in works regarding data standards, NH and registries, the ISC has been tasked to take on the lead of Activity D, supported by the CCC, TSC and FCC

Points to take into consideration:

- ▶ Standards-based data collection: guidelines to conduct NH studies, data collection, improving accuracy (and not just be vigorous)
- ▶ Need to capture data elements that satisfy the requirements of patients, regulators, and payers
 - Involve these stakeholders when considering endpoints
- ▶ Need not collect every little detail
 - Plan ahead and determine the type of data to collect
 - Design collection with the end goal in mind
 - Consider what can be used to show interim results during clinical study phases: a good strategy to show value in the study and attract investment
- ▶ Need to also build infrastructure with sustainability in mind
- ▶ Potentially to start by listing challenges in building a solid, sustainable NH/R platform

Notes regarding European Reference Networks (ERNs):

- ▶ An extensive virtual network in Europe, currently covering 24 medical areas and linking about 1,000 hospitals in the European Union
- ▶ ERN can potentially be used to help therapeutic development through data collection and patient recruitment for clinical studies
- ▶ However, system currently not built to engage with industry
 - Companies also cannot proactively design NH dataset that the ERNs may use
 - Might need a different engagement model, e.g. emulate IMI-style partnership?

➔ *Support the development of Activity D proposal led by the ISC, together with the TSC and FCC*

Notes: please also refer to the Tokyo November 2017 meeting and March 2018 teleconference reports for previous discussion points.

3. Activity H 2018: Background internal work on common knowledge base to drive rare diseases research

Activity H of the IRDiRC 2018 roadmap, also known as the “Penumbra Project”

- ▶ Proposed and led by the CCC
 - Initially will be the work of CCC members
 - To better organize and share knowledge and tools thus enable therapy development
 - To define characteristics that makes a rare disease acceptable to a company with various risk tolerances
- ▶ The idea: to generate knowledge beyond the core 15-20 diseases that pharmas are working on thus find the next tranche of 100 diseases or so for therapeutic development and move them from the periphery into the core set
- ▶ Barriers/gaps on common knowledge base to act on:
 - What are the rare diseases: establish a list of diseases and subtypes of a disease
 - How to identify them: need to move categorization by name to by biology and pathway
 - Define some common vocabulary and process, e.g.
 - What is a rare disease, and how to identify and characterize a rare disease?
 - What is a therapeutic target?
 - What is RWE? (In industry it relates to incidents in clinical setting, but for layperson, it’s used around wearables and apps to monitor health conditions)
 - What is a control population?
 - What is a clinical endpoint, and how to measure it?
 - Common repository of what is being studied by whom and how much investment to generate knowledge has there been
 - What is the disease prevalence
 - Define common standards to facilitate interoperability of dataset
- ▶ Additional considerations
 - Knowledge database should be accessible by all albeit through permission-controlled system so all users are identifiable
 - Tools to enable multiplex sharing of genotype and phenotype data
 - Potential partnership with cloud computing facilities, e.g. Google, Amazon, Microsoft
 - Note: data ownership not transferred to these infrastructures
 - Inbuilt capability to connect partners for collaborations
 - To subsequently identify methods to de-risk projects and encourage investment

➔ *Develop the Activity H proposal and submit to the Consortium Assembly for feedback and approval*

Notes: please also refer to the Tokyo November 2017 meeting and March 2018 teleconference reports for previous discussion points.

4. CCC membership: Current and potential new members

4.1 Current members

There are currently 14 organizations that are members of IRDiRC, therefore of the CCC. Members will be contacted shortly to clarify their commitment to advance IRDiRC's Vision and Goals together.

4.2 Membership criteria

To date, membership criteria is based on spending in rare diseases research, i.e. \$10 million over 5 years, and pledge to align with IRDiRC's objectives, policies and guidelines, and governance structure. Moving forward, companies may be asked to demonstrate active engagement – how will they contribute to IRDiRC's Vision and Goals – and community spirit, by nominating representatives who are actively engaged to make a difference, be it from within the structure or through actions with IRDiRC.

4.3 Potential new members

Given the ambitious Goal 2, IRDiRC seeks players who are investing in innovation and not just on revenue generation, and those who push to disrupt the current system for a paradigm shift in orphan drug development process.

- ➔ *Identify and inform the Chair and the Sci Sec of any potential new members with innovative approach and community spirit*
- ➔ *Potentially directly contact the organizations to gauge interest in becoming a part of IRDiRC*

Main action points

- ▶ Support the development of proposal for Activity D
- ▶ Develop the proposal for Activity H
- ▶ Identify potential new members and send names to Chair, Sci Sec