

Meeting report series

Report of the 2nd Companies Constituent Committee Meeting

Tokyo, Japan

11 November 2017

Participants

Dr Mathew Pletcher, Roche, Switzerland (Interim Chair)

Dr Diego Ardigo, Chiesi Farmaceutici, Italy (Chair of the Therapies Scientific Committee)

Dr Andrea Chiesi, Chiesi Farmaceutici, Italy

Dr Tim Considine, Recursion Pharmaceuticals, USA

Dr Sabine Gilliam, Pfizer, Japan

Mr Nicolas Li, BGI, Japan

Dr Lilian Lau, Scientific Secretariat (Sci Sec), France

Dr Noriaki Imanishi, Japan Agency for Medical Research and Development (AMED), Japan

Apologies

Ms Karian Aiach, Lysogene, France

Dr Bryan Goodwin, Shire, USA

Dr Carlo Incerti, Genzyme, USA

Dr Robert Mashal, NKT Therapeutics, USA

Dr Brett Monia, Ionis Pharmaceuticals, USA

Dr Ellen Welch, PTC Therapeutics, USA

Dr James Wu, WuXi AppTec Co., Ltd., China

Agenda

1. Welcome and Introduction
2. Common roadblocks to efficient research for drug development
3. Focus areas and actions to address roadblocks
4. Potential new IRDiRC industry members

REPORT

1. Welcome and introduction

The Interim Chair of the Companies Constituent Committee (CCC) welcomed the meeting participants, who each introduced themselves. The Interim Chair solicited ideas of focus areas and concrete actions for implementation collectively by company members as a group within IRDiRC.

Among the main goals of the CCC:

- ▶ Identify common roadblocks of efficient research in company space that IRDiRC should address
- ▶ Identify overlaps and gaps in company priorities, and potential common ways to address them
- ▶ Recommend concerted efforts in pre-competitive space to advance rare diseases research

2. Common roadblocks to efficient research for drug development

Among the common roadblocks identified:

- ▶ Limited experience and only for a handful few diseases
- ▶ Need the establishment of common ground truth about disease state
- ▶ Lack of registries and natural history studies, and best practices around them
- ▶ Lack of (placebo) control population data
- ▶ Barriers to data sharing including data standards, ethical-legal concerns, and ownership issues
- ▶ Need of adapted drug development process and post-approval data collection
- ▶ Need to cope with mid-study protocol changes, with additional clinical works
- ▶ Need of appropriate proxies to measure clinically relevant and patient-centered outcomes
- ▶ Different (meaningful) outcome expectations and/or requirements from different stakeholders
- ▶ Lack of expertise and funding to bridge translational gaps
- ▶ Lack of guidelines to fruitful collaborations with external networks of patients and clinicians
- ▶ Limited patient recruitment ability thus delaying development and trials
- ▶ Limited number of patients to participate in clinical studies
- ▶ Smaller sub-population of patients due to genetic variability and/or reactivity to therapies
- ▶ Patients enrolled in multiple studies, preventing accurate evaluation of therapy efficacy
- ▶ Financial risk given uncertainty of obtaining payments from governments, payers and insurers
- ▶ Lack of industry alignment on the issue of methods of payments
- ▶ Competitive nature among industry members to get products to the market and patients
- ▶ Varying political environment and governmental priorities
- ▶ Lack of education to familiarize patients and patient advocates with rare diseases research

Four emerging broad themes tie in with all aspects of IRDiRC, giving rise to potential activities involving:

- ▶ Natural history studies, registries and (failed) clinical trials data

- ▶ Common infrastructure to drive rare diseases research
- ▶ Patient-centered endpoints
- ▶ Restructuration of drug development process and payers model

3. Focus areas and actions to address roadblocks

3.1 Natural history studies and registries, and (failed) clinical trials data

Recurring issues:

- ▶ Lack of standards-based data collection
 - Lack of experience to conduct such studies
 - Lack of standards to guide data collection
 - Lack of platform to adequately record data
 - Lack of best practices in engaging patients for (long term) data collection
- ▶ Data collected during studies but not shared
 - Data collected are not interoperable across platforms
 - Data collected are not guided by recommended standards
 - Data collected are restricted from sharing due to consent and ownership issues
- ▶ Silos of data from stopped developments and/or unsuccessful trials
 - Data can be used for collective learning on why studies failed
 - Data can be used as potential placebo control due to connection to natural history
- ▶ Competition among companies
 - Companies urged to work together to set up placebo group
 - Companies should collaborate on “zero”/pre-competitive aspects of development, e.g.:
 - Best practices in patient engagement for research and development
 - Natural history gaps
 - New standards to guide data collection
 - Roadmap to improve work flow and drug development for rare diseases

Build universal, broad-based platform for use by everyone

- ▶ Establish best practices: identify patient groups to pilot project
- ▶ Define standards: for collection of high-quality and interoperable data
- ▶ Ideally based on existing case studies, covering different technologies and therapeutic areas
- ▶ Focus on building knowledge of diseases currently without available therapies

Proposal of a 2-day workshop

- ▶ Pre-workshop
 - Identify 4-5 real cases used in development
 - How were they used
 - Ensure minimum requirements met
- ▶ Workshop

- Build and discuss simulated cases
- Output: recommendations on how to build an ideal system for use in the real world
- Output: recommendations of standards and best practices in data collection
- Eventual, for long-term use: craft the infrastructure
 - This will require substantial resource to build and maintain
- ▶ Considerations
 - How to capture natural history data, e.g. social media monitoring
 - Big data approach likely, but cautions raised re standards and compliance
- ▶ Multi-stakeholder involvement
 - Companies already working on building such infrastructure
 - Organizations providing research infrastructure
 - Patients and caregiver-centricity aspect important
 - Payers and regulators to be included
 - Contract research organizations (CROs) adopting new ways of trialing

Clinical trials data

- ▶ Central repository to submit clinical trials data, including failed investigations
- ▶ Potential use as placebo or control dataset

3.2 Common infrastructure to drive rare diseases research

To rethink drug discovery process, which “traditionally”

- ▶ Obtain disease list from Orphanet and OMIM = about 7,000 diseases
- ▶ Apply prevalence filter to diseases = narrow down to about 100 diseases
- ▶ Ascertain what other companies are developing = down to the “safe” 10-15 diseases
- ▶ Need to move away from these 10-15 core diseases everyone is working on and address the 6,950 diseases without activities
- ▶ Unless more knowledge is generated, companies reluctant to move into new disease space

Essential to establish common ground truth about disease state

- ▶ Orphanet is a good starting point and should strive for more complete information
 - Establish a list of all rare diseases, including subtypes of a disease
 - Provide support to frequently cited statistics, e.g. number of diseases
 - Currently still based on outdated diagnostics categorization
 - Certain diseases (e.g. retinitis pigmentosa) affected by many genetic mutations, each representing unique biological diseases, but categorized as a broad “single” disease
 - Would like definitive list of diseases by gene as a starting point
 - Monogenetically-defined diseases have best chance in terms of drug discovery and development
 - Build a “genomepedia”
- ▶ Then add knowledge of disease

- Include disease prevalence, genetic variants, tissues affected, gene expression, epigenetics, quality of life (QoL)
- Identify key leaders or researchers, their locations and their disease expertise
- ▶ System will enable new drug discovery
 - Highlight the next level of diseases with high potential for development
 - Academia can de-risk some studies, improving attractiveness for development

Information on areas of focus for research

- ▶ Three broad categories of investment landscape:
 - “Built”: many players investing in the disease domain, competition is high
 - “Developing”: less developed, science-driven domain with strategic visibility to pursue
 - “Desert”: needs research programs to build knowledge in order to attract investment
- ▶ Data-driven information is needed to guide informed decision on investments
 - Address gaps of research funding in “deserts” to push into “developing” stage
 - Funders Constituent Committee (FCC) is looking into the question of where research funding gaps are and how to address these gaps
 - Academic knowledge helps de-risking investment decisions by industry players
 - E.g. the use of a Growth/Market Share (aka BCG) Matrix based on technology availability and prevalence information to guide development choice

3.3 Patient-centered endpoints

Focus on patients, their families and caregivers

- ▶ Clinical endpoints should be patient-centered
 - Question to pose: what outcomes do patients want and find meaningful?
 - How to align these to scientific and regulatory requirements?
- ▶ Mitigation of caregiving burden should also be taken into account during clinical development
 - Caregivers not usually economically-efficient, representing cost to the society

Post-marketing surveillance

- ▶ In Japan, mandatory surveillance:
 - Every patient receiving a new drug is registered
 - First follow-up: 2 weeks after the first prescription – capture immediate adverse effects
 - Subsequent follow-up may run for 12 months, 24 months or 36 months
 - Real world data systematically captured to inform safety and efficacy
 - PMDA reassessment based on data collected
- ▶ Question: how to enable the setup of a similar surveillance system in other countries?
 - Need to strike a balance against the workload of healthcare providers
 - Need to account for the cost to collect and analyze data
 - Need to identify approach to ensure patient compliance and attendance to follow-ups

3.4 Restructuration of drug development process and payers model

Financing translational gaps

- ▶ Gap between basic science and clinical development: funding and expertise under-represented
- ▶ Traditionally, research funders support basic science while industry finances clinical works
- ▶ To rethink different sources of translational funding
 - Is there a way to bring in VC philanthropy?
 - Is public-private partnership a good way forward?

Financing clinical development

- ▶ Huge financial risk undertaken by industry therefore some play it “safe” in overcrowded space of developing therapies for a handful few diseases
- ▶ Payers and HTAs should be involved right from the start
 - Inform clinical developers of conditions for approval to access
 - Pro-active engagement in addition to reactive assessment after approvals
- ▶ Proposal of a new model: R&D cost be partly defrayed at early access stage?
 - Reducing the financial risk of the company
 - Enabling early access of therapy for patients
 - Enabling parallel collection of real world evidence data
 - Lowering of final price in return
- ▶ Cynicism against industry limits its capability to affect paradigm shift
 - Can patient advocates be effective lobby for access to research and therapies?
 - Can regulators adapt to improve access for patients while protecting public health?
 - How to build consensus between companies, regulators, payers and patients in order to translation innovation into sustainable access to medicines?

Payers model

- ▶ Different therapy type necessitates remodeling the payment system
 - E.g. once-off vs long-term treatment: high cost of once-off treatment likely to have a cap and be cheaper compared to total cost of long-term treatment
 - Cost of once-off treatment may be paid in instalments
- ▶ As more therapies become available, how much of the cost can be budgeted by the payers?
 - Real world evidence important for monitoring studies and post-marketing surveillance
 - Data can be used to establish value-based contracts, i.e. payment per performance
 - Payers can better manage budget for new treatments
 - Companies can assign prices more accurately reflecting product value

4. Potential new IRDiRC industry members

Several companies can potentially be approached and invited to be part of IRDiRC to participate in the discussion of the CCC and act together to advance rare diseases therapeutics development.

Considerations prior to issuing invitations to apply as members:

- ▶ Careful deliberation based on the type of change IRDiRC wants to bring about
- ▶ Large companies have regulatory capabilities and connections
- ▶ New biotech companies tend to be more innovative and are change drivers
- ▶ Smaller companies cultivate closer relationships with patients
- ▶ A combination of above helps build different approaches and way of thinking things