Recommendations to speed up the R&D process in the field of orphan drugs

Gert-Jan van Ommen

Leiden University Medical Centre

IRDiRC Therapies Scientific Committee

IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

IX Annual meeting of ICORD

Ede, 9 October 2014

IRDiRC's Objectives for 2020

200 new therapies for rare diseases

Means to diagnose most rare diseases

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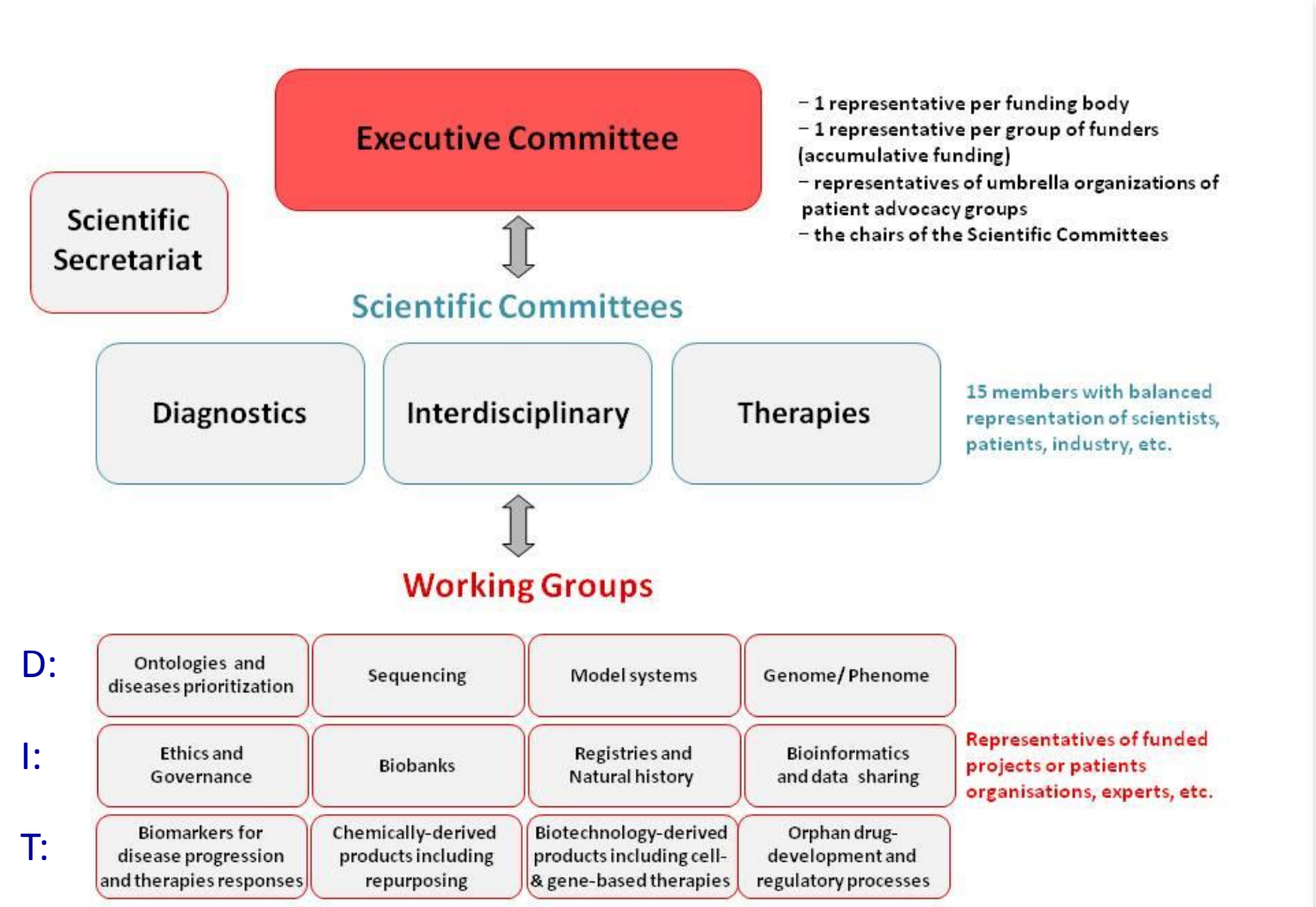
IRDiRC governance structure



IRDiRC Therapies Scientific Committee (TSC)

Yann Le Cam (chair)
•EURORDIS (France)

Gert-Jan Van Ommen
•Leiden University Medical Centre (Netherlands)

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•Prosensa Therapeutics (Netherlands)

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•Rare Diseases Science Genzyme Corporation (USA)

Shuling Guo
•Isis Pharmaceuticals (USA)

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•Genethon (France)

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•University Medical Centre (Netherlands)

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•NKT Therapeutics (USA)

Josep Torrent i Farnell
•Spanish Medicines Agency (Spain)

Ellen Welsh
•PTC Therapeutics (USA)

Anne Zajicek
•NICHD (USA)

Working Groups:

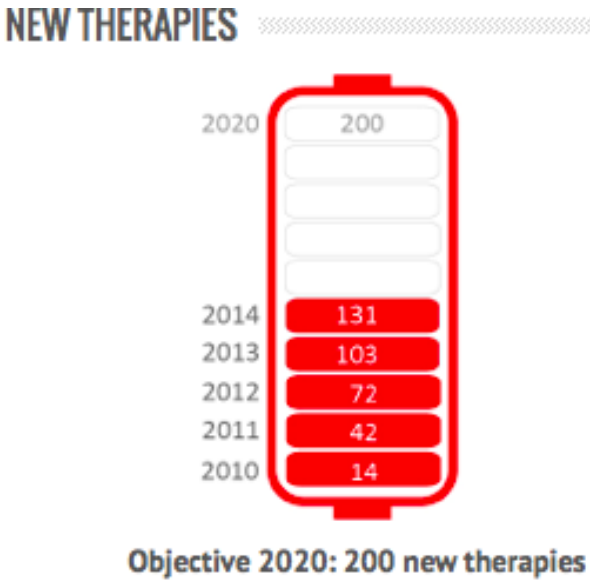
- Biomarkers for Disease Progression and Therapy Response
- Biotechnology-derived Products including Cell- & Gene- therapies
- Chemically-derived Products including Repurposing
- Orphan Drug-development and Regulatory Processes

Former members:

- Maria Mavris (Eurordis)
- Marc Walton (FDA)
- Jack Welch (NIH NCI)

IRDiRC's Objectives for 2020

200 new therapies for rare diseases



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TSC recommendations

- *Recommendations for IRDiRC funding organisations*
  - *Strategic recommendations*
  - *Criteria for research funding*
  - *Priorities for research funding*
  - *Priorities for gap analysis funding*
- *Recommendations related to regulatory processes*
- *TSC milestones for the next 3 years*

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Criteria of selection for recommendations

- Essential actions defined for their highest leverage effect to unlock the potential of rare disease therapy development
- Well-targeted actions with potential to produce results before or by 2020
- Actions identified for their international relevance
- Clarity and flexibility of the actions recommended
- Overall consistency of the set of actions

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Recommendations for IRDiRC funding organisations

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Strategic recommendations

- Prioritization of international collaborative rare disease research and orphan medicine development programmes:
  - Using unique expertise and availability of special resources.
  - With alignment of themes and coordination of the process for calls for proposals in order to optimise funding of collaborative research projects by agencies from several countries.
  - With commitment to sharing and integration of data into existing platforms.

Criteria for research funding: clinical trials

Mandatory criteria recommended when funding clinical trials:

- Excellence of the scientific rationale, proof-of-concept and development plan
- Preferentially selecting products (not exclusive, preferred / IRDiRC objective of 200 approved therapies in 2020):
  - with an orphan designation from FDA and/or EMA
  - for which the sponsor has received Scientific Guidance from both or either Regulatory Agency
  - For which the sponsor adheres to the guidelines of Good Practice (i.e., GXP).

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Criteria for research funding: Non-clinical research

Non-clinical work should:

- be highly supported with an adjusted level of funding,
- without the requirement of orphan designation or scientific guidance from regulatory agencies at the time of grant application,
- but with an explicit commitment from the grant applicant to apply for orphan designation in both EMA and FDA or either, and to seek scientific guidance from regulatory agencies in due time.

Products at clinical stage with orphan status (EU ± US)

Already received scientific guidance (and follow up as necessary)

Not yet having sought scientific guidance but committed to applying for it within a defined timeline

Receive funding from IRDiRC members
(support achievement of 2020 objectives)

Products at non-clinical stage

Data from appropriate preclinical animal models/preliminary clinical data

Receive adjusted funding from IRDiRC members
Proof of concept (as per Policy #13) to support plausibility and rationale to seek orphan designation
(support an active pipeline)

Priorities for research funding

- New **methodological and statistical approaches** for clinical development in small populations.
- Biomarkers and outcomes measures:
  - **Identification and timely development** of new and more effective biomarkers and outcome measures with sufficient lead-time in the R&D process.
  - Development and use of **optimized and standardized technologies** and **assays** for biomarkers to further accelerate overall development.
- Identification of **mechanisms of action** for medicinal products with potential for development and identify how they are linked to rare clinical conditions.
- **Repurposing/repositioning** of medicinal products for their potential in rare indications.

Priorities for gap analysis funding

- **Gap analysis of unmet medical needs** that could potentially be addressed by 2020
- **Identification of regulatory hurdles**
- Analysis of **outcomes from previously funded projects** in order to understand the reasons of success or failure.
- Assessment of **off-label use** of current therapies that may be of relevance for the patient needs.
- Survey **biomarker and natural history** project leaders in order to perform a gap analysis, identify potential clusters of biomarkers by disease and find information on biomarkers used in failed clinical trials.
- Perform a review of the currently funded IRDiRC projects to identify **'clusters' of compounds** of the same therapeutic class or by conditions, and to identify gaps that may deserve further discussion.

Recommendations related to regulatory processes

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Recommendations related to regulatory processes (1)

- Encourage, support and establish **early and continuous dialogue on clinical development strategy and wide evidence generation** with all relevant stakeholders.
- Further **develop information, training, dialogue and support among regulatory agencies and sponsors**.
- Within the limits of the regional/national laws, develop **more guidelines for clinical development of medicinal products for RD**.
- Strongly support **scientific guidance** by regulatory agencies, and encourage more joint scientific advice by regulators.

Recommendations related to regulatory processes (2)

- Encourage flexibility of regulatory to enable **earlier and progressive patient access** to medicinal products for those severe diseases without any treatment options.
- Encourage greater **harmonization of national/regional regulations** in order to ease the burden of rare disease clinical development.
- Encourage, support and develop **patient focused/relevant outcomes**.
- Encourage better **coding/health record** search ability as a way to accelerate therapy development and help identifying rapidly and accurately patients/potential trial participants with a particular disease.

TSC milestones for the next 3 years

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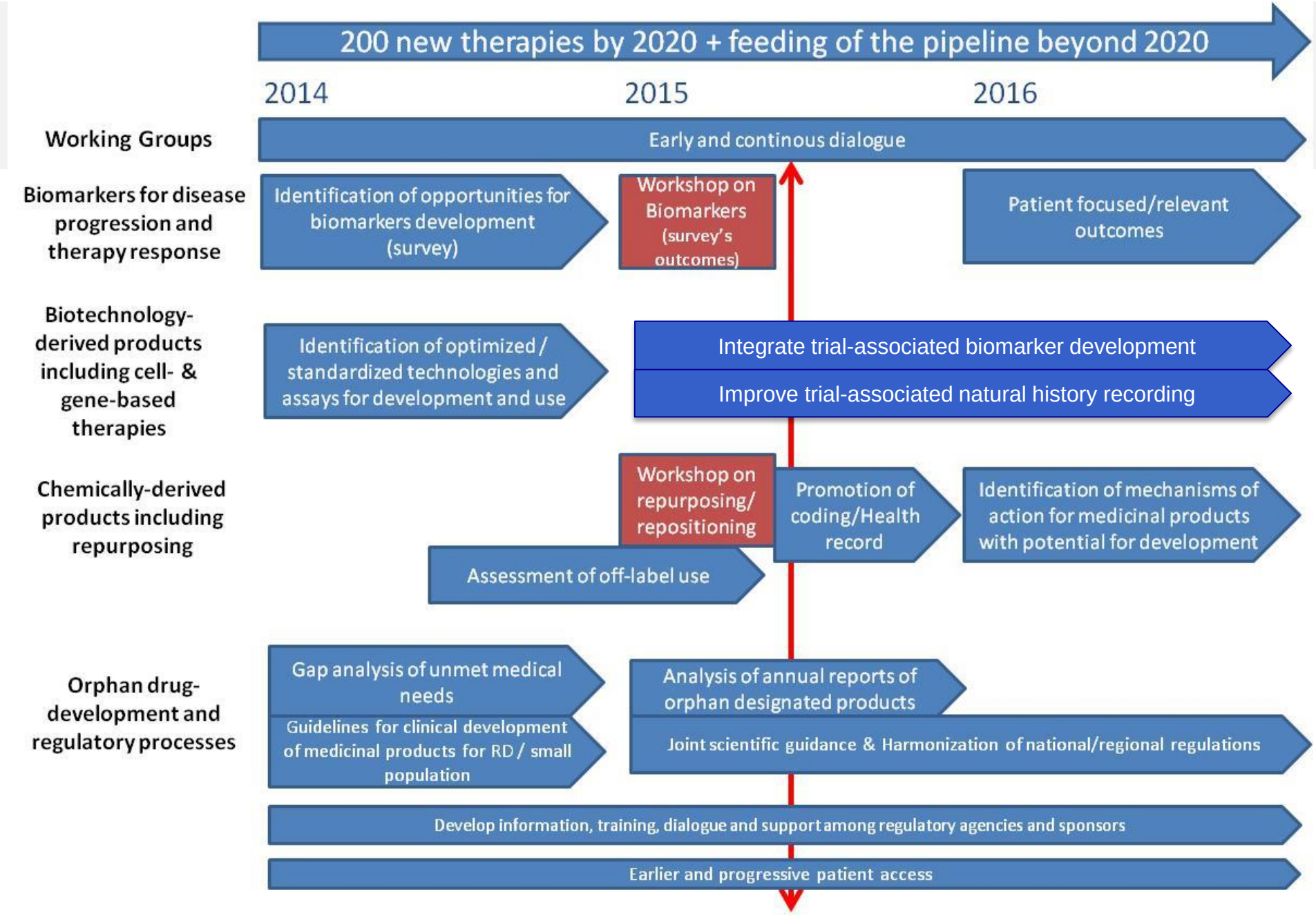
200 new therapies by 2020 + feeding of the pipeline beyond 2020
2014
2015
2016
Working Groups
Early and continous dialogue
Biomarkers for disease progression and therapy response
Identification of opportunities for biomarkers development (survey)
Workshop on Biomarkers (survey's outcomes)
Patient focused/relevant outcomes
Biotechnology-derived products including cell- & gene-based therapies
Identification of optimized / standardized technologies and assays for development and use
Integrate trial-associated biomarker development
Improve trial-associated natural history recording
Chemically-derived products including repurposing
Workshop on repurposing/ repositioning
Promotion of coding/Health record
Identification of mechanisms of action for medicinal products with potential for development
Assessment of off-label use
Orphan drug-development and regulatory processes
Gap analysis of unmet medical needs
Analysis of annual reports of orphan designated products
Guidelines for clinical development of medicinal products for RD / small population
Joint scientific guidance & Harmonization of national/regional regulations
Develop information, training, dialogue and support among regulatory agencies and sponsors
Earlier and progressive patient access