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INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

Meeting report series

Report of the 2nd Meeting of the Working Group on Chemically-derived products including repurposing

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Organization

Organized by: Scientific Secretariat
Teleconference

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REPORT

Data generation – How to generate leads for repurposing

Generating leads for repurposing would necessitate finding the link between the drug and the clinical condition, i.e., to identify which drug could be useful for which disease by examining properties of the drugs, history of the diseases and by expanding knowledge on connections between drugs and new indications, before going to the clinical trials step.

In order to accelerate the process for repurposing, eliminating the initial discovery phase would be a good option.

Several strategies can be used to find candidates for repurposing:

- Rescuing drugs by looking at previous projects to find drugs that were developed for rare diseases but failed. It is necessary to determine the origin of the failure (an insufficient number of participants in the trial, problem in the trial design, etc.).
- Buying library of drugs to test them through an assay to determine which drugs have a potential for repurposing, or fund the organizations that have the compound library or develop partnerships.
- Contact patient support group to inquire if they have any candidate for repurposing but no possibility to develop them.
- Compare gene expression profile of molecules and diseases (through cell or animal models) or between molecules to find match. This technique can give hints to identify potential molecules but necessitates cell- or animal models of the disease.

Members of the WGs agreed to start with available data to find candidates.
Possible sources of information:

- Regulatory agencies databases (designated, approved and rejected drugs). It would be interesting to explore the possibility to have access to other databases than the ones from the FDA and EMA (Japan, etc.). Focusing on designation older than 4-5 years (or more) to ease the IP situation?
- NCATS resources.
- Patient association.
- Outcomes of previous projects funded to develop products (FP6, FP7, E-Rare, NIH, etc.). To possibly cross-check with data from regulatory agencies to increase the probability to find good candidates and solve part of the IP issues?
- Information provided by industries.

The next step would be to release a list of couples (molecules & disease); the organization interested in moving on would contact the Orphan designated sponsor to harvest the data available and discuss IP whenever required.

Funding of analysis for rationale is necessary for the development of candidate drugs for repurposing once discovered.

Since the last teleconference, internal EMA discussions regarding the following resources: existing orphan medicines annual reports, previous orphan sponsor surveys, and possible SME office resources, considered these sources as important for drawing conclusions on general development related issues, but not particularly fit for the purpose of identifying specific leads at this point in time.

How to accelerate the development of repurposing drug?

- By limiting the difficulties related to IP, particularly when there is collaboration between several partners. Is there a way to simplify the IP situation?
- Encourage the use of protocol assistance to avoid problems in clinical designs and quality issues, (particularly for academics and SMEs). Early dialogue with regulatory agencies increase the success rate for marketing authorization and this should be an incentive for sponsor to use protocol assistance.
- Major hurdles are at identifying clinical candidates.
- Academic researchers should be encouraged to identify the science behind off-label use.

Recommendations to accelerate repurposing

To find candidate for repurposing

- Launch a communication campaign to RD alliances in each country to ask them to send an email to all their patient groups asking if there is any treatment that they believe could be developed for their disease or treatment whose development have been stopped.
- Analyze the outcomes of FP6, FP7 and E-Rare funded projects and of projects funded by NIH or FDA.
- Develop a repository of potential drug for repurposing and/or facilitate communication between existing library to find compounds if know of a biomarker for a disease for example. Publicizing available information would also be useful.
- Biomarkers for the diseases, natural history, pharmacological properties of drugs may be made available to interested parties

To help the development of repurposing drugs

- Fund projects working on the development of assay, cell- and animal models of disease, etc.
- Encourage early dialogue with regulatory agencies.
- Promote international collaborations for identifying problems.
- Facilitate partnership between any organization/individual and biotech/pharma to accelerate development of candidate drugs.