More than 400 million people worldwide have a rare disease.

~80% of rare diseases are of genetic origin.

~80% of rare diseases are children.

6,000 – 8,000 diseases are classified as rare.

~80% considered ultra-rare.

~60% are serious and disabling.

~50% are life threatening.

500 drugs have reached the market.

5% of rare diseases have an approved treatment.

700-800 treatments in development.
TREMENDOUS UNMET MEDICAL NEED

IRDiRC’s GOAL

1000 new rare disease treatments by 2027

At the current rate of drug development (40-50 new therapies developed per year), it would take 500 years to get a treatment for all rare conditions! Therefore a better means to repurposing drugs for rare diseases is needed.

A patient focused guidebook that describes the available tools, incentives, resources and practices for drug repurposing for rare diseases and how to best use them. It can be used by academic, non-profit organizations, small and larger (innovative) biotechs and patient-driven drug developers.
DRG — PROJECT AT-A-GLANCE

- 1 Workshop with 27 drug repurposing & RD experts and stakeholders
- 44 Building Blocks (BBs)
- 3 Case Scenarios
- Use of building blocks across the different phases and milestones of drug development
- Roadmap Check-lists of “what to do” and “when to do it”
TECHNICAL EXPERTS AFFILIATIONS
DRG - FRAMEWORK

Patient’s NEED

Disease knowledge  Target  Product discovery  Nonclinical PoP  FiH ready  Human PoC  Pivotal data  MAA NDA/BLA  Market Access  Patient care

Traditional regulatory activities

- EMA Pre-submission meeting
- FDA End of Phase III meeting
- FDA Pre-NDA/BLA

- EMA-SA
- PMDA - consultations
- Pre-IND
- FDA End of Phase II meeting
- PIP
DRG – Building Blocks (BBs) Classification

For each BB it was created a factsheet describing its relevance to rare disease drug development, availability, scope of use, output, pros and cons of usage, best time to apply, duration and costs.

44 BBs were identified consisting of:

- **Regulatory** - pathways, designations and incentives for ODD in EU, US and Japan
- **HTA and reimbursement** - practices and procedures to support the economic value proposition and assessment, mainly focused on EU
- **Development practices** - best-practice established by developers in the field of rare diseases, to improve orphan drug development in terms of speed, quality or efficiency
- **Development resources** - physical or practical existing accessible resource, to support drug developers in the orphan space

![Building Blocks Graph]
DRG – HOW DO YOU START THE DEVELOPMENT OF YOUR PRODUCT?

- S
  - Stakeholders mapping
- T
  - Available information on the disease
- A
  - Financial Resources
- R
  - Target Patient Value Profile
**KEY TAKEAWAYS:**

- Missing info on the disease need to be generated ASAP
- Create or build-out a solid network of stakeholders and KOL
- Collect info on the drug such as IP, data inside and outside the public domain and the regulatory background
**DRG – ENGAGEMENT**

### Traditional regulatory activities

- **Pre-IND**
- **End of Phase II meeting**
- **Pre-NDA/BLA**

### Engagement with MA

- **Public-private collaboration**
- **Pre-competitive space working**

### Contact with TTO and patents

- **Search & use IP & legal db**
- **Patent framework DR**
- **TTOs**
- **Literature archive**

### Patient and KOL engagement

- **Patient and KOL engagement**
- **EU, US and Japanese CRN**
- **EURORDIS’ CAB**

### Funding

- **Funding resources for DR**
- **Public funding**
- **Private funding**

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**Figure 1**

- **Patient’s NEED**
  - Disease knowledge
  - Target
  - Product discovery
  - Nonclinical Pop
  - FIH ready
  - Human PoC
  - Pivotal data
  - MAA NDA/BLA
  - Market Access
  - Patient care

- **Engagement with MA**

- **Contact with TTO and patents**

- **Patient and KOL engagement**

- **Funding**

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**EMA-MA**

- **Traditional regulatory activities**
- **End of Phase III meeting**
- **Pre-IND**
- **End of Phase II meeting**
- **Pre-NDA/BLA**
- **Anticipate Market Authorisation**

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**Traditional regulatory activities**

- **Pre-IND**
- **End of Phase II meeting**
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- **Private funding**
# DRG – Regulatory & Access

## Patient's NEED
- Disease knowledge
- Target
- Product discovery
- Nonclinical Pop
- FIH ready
- Human PoC
- Pivotal data
- MAA NDA/BLA
- Market Access
- Patient care

### Clinical development, including extrapolation of efficacy and safety data
- Dose finding
- Extrapolation
- Safety data across indications
- Combinations of drugs
- Clinical trial db
- PKPD modelling in children
- New formulations of drugs

### Orphan Drug Development
- ODD

### Regulatory and HTA engagement
- JointEMA-HTA SA
- PUMA
- ILAP
- EMA Pilot to support academia
- STAMP
- Initiative updating old labels
- STARS
- Engaging with HTA
- Pricing models

### Design trials for DR
- Alternative designs for SPCT

## Figure 1
- Patient's NEED
- Disease knowledge
- Target
- Product discovery
- Nonclinical Pop
- FIH ready
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DRG – TOOLS AND DATA

Availability of data
- Data outside pd
- Prevalence data
- NH studies
- Cure ID
- Off-label use
- CDRC
- DARWIN EU
- Generics

Compound and network databases and tools to use them
- Chemical compound db
- Network db
- EU Open Screen
- In Silico - VPH
- Machine Learning & DM
- Competitive intelligence
- Drug Prio analysis

Supporting tools
- EATRIS
- REMEDI4ALL
- Newfound initiative
- Remedi
- REPO4EU
- Drug Discovery Platform
- ROADMAP
- Drug Databases
- LifeArc
DRG – Take Home Messages

**Regulatory advice is essential and should be requested as early as possible.**

Collect info on the drug such as IP, data inside and outside the public domain and the regulatory background.

Start with the engagement of KOL, the current and future MAH and patients.

Starts with Patient’s NEED rather than idea.

All available non-clinical, clinical trial and real-world data (including off-label use), prevalence and natural history data must be exploited for the development plan.

Think about a sustainable market access plan.

Ends with Patient’s NEED rather than patient care.

REGULATORY ADVICE IS ESSENTIAL AND SHOULD BE REQUESTED AS EARLY AS POSSIBLE.

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