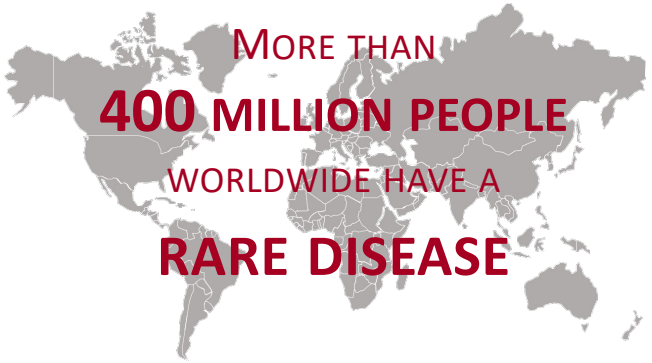
IRDiRC

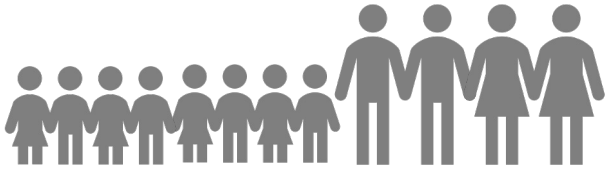
INTERNATIONAL
RARE DISEASES RESEARCH
CONSORTIUM

Drug Repurposing Guidebook

Rare Diseases landscape and Drug Repurposing Trends



More than
400 million people
worldwide have a
rare disease



70-80% are Children

6,000 – 8,000
Diseases are classified as Rare

~80% considered Ultra-rare
~60% are serious and disabling
~50% are life threatening

~80% of Rare Diseases are of genetic origin

500 Drugs have reached the market
5% of rare diseases have an approved treatment
700-800 treatments in development

World Health Organization. Background paper 6.19 Rare Diseases. (2013); Orphanet; RARE Facts. Global Genes.

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

Austin CP, et al., Future of Rare Diseases Research 2017-2027: An IRDiRC Perspective. Clin Transl Sci. 2018 Jan;11(1):21-27

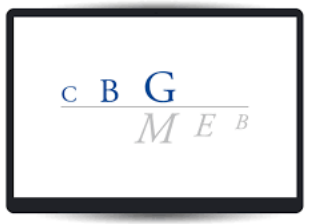
DRUG REPURPOSING GUIDEBOOK

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.

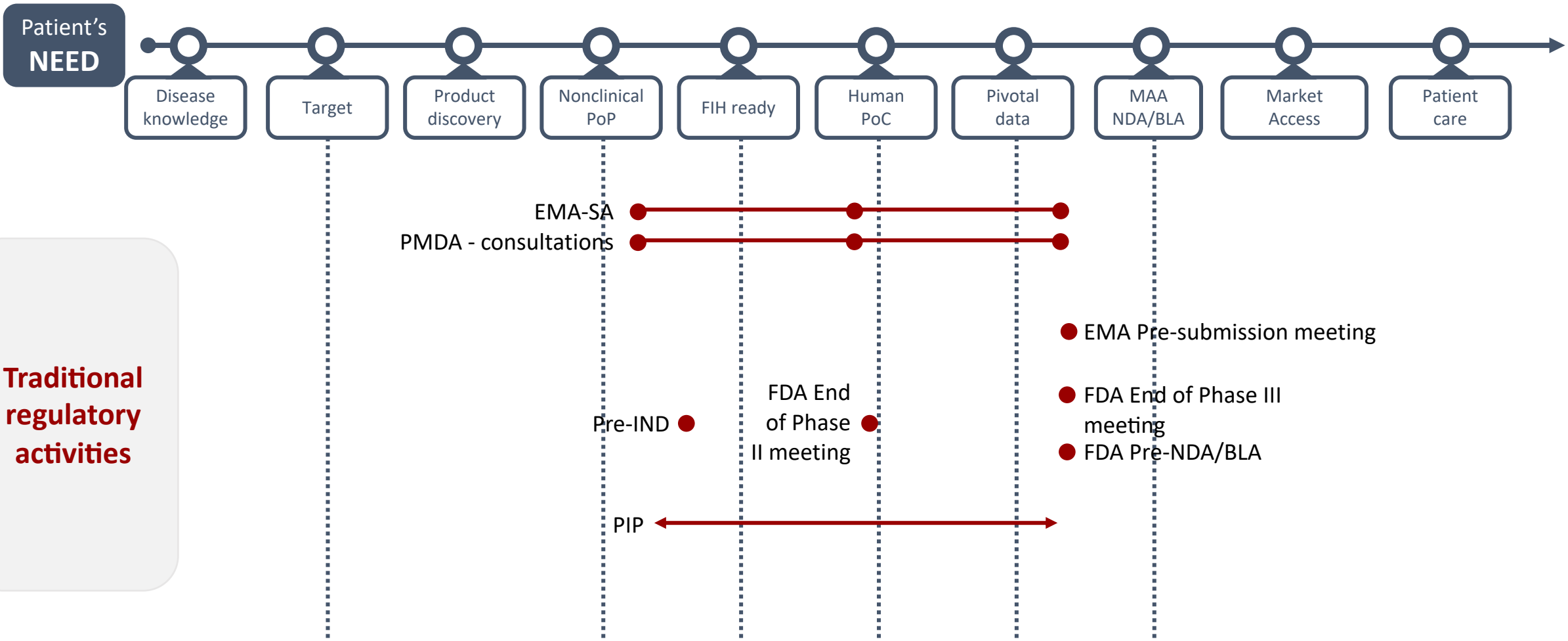
DRG – PROJECT AT-A-GLANCE

- 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



Traditional regulatory activities

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

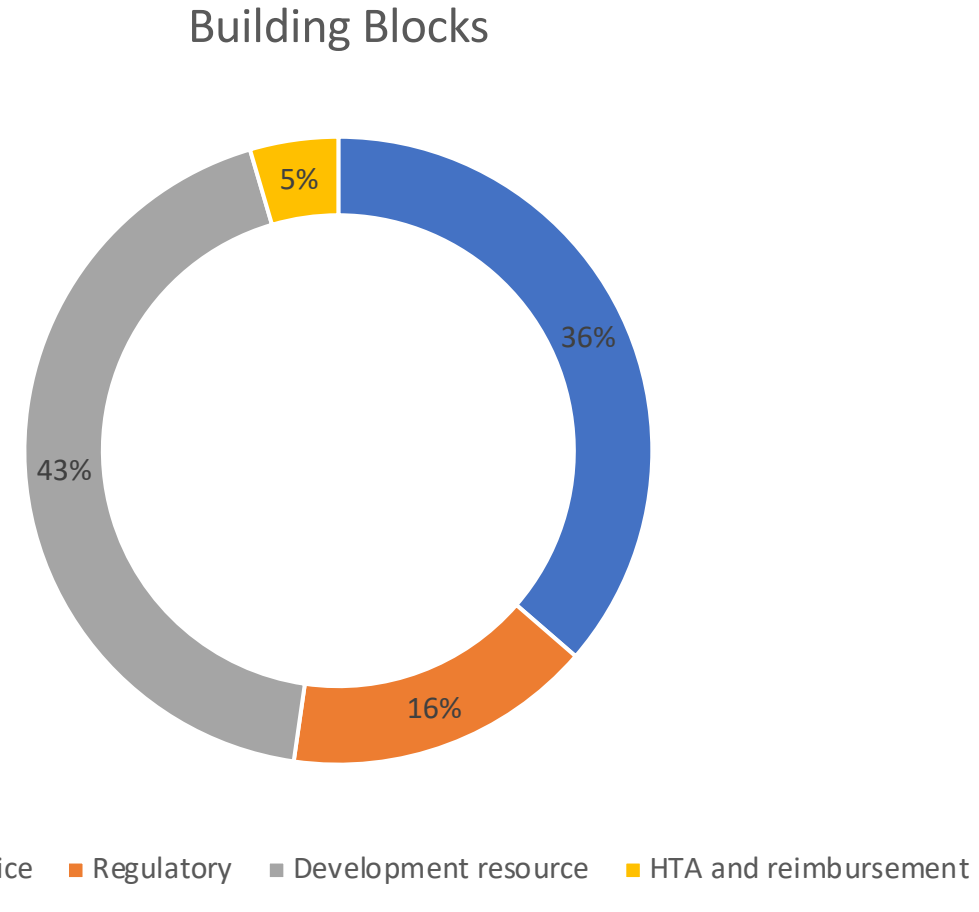
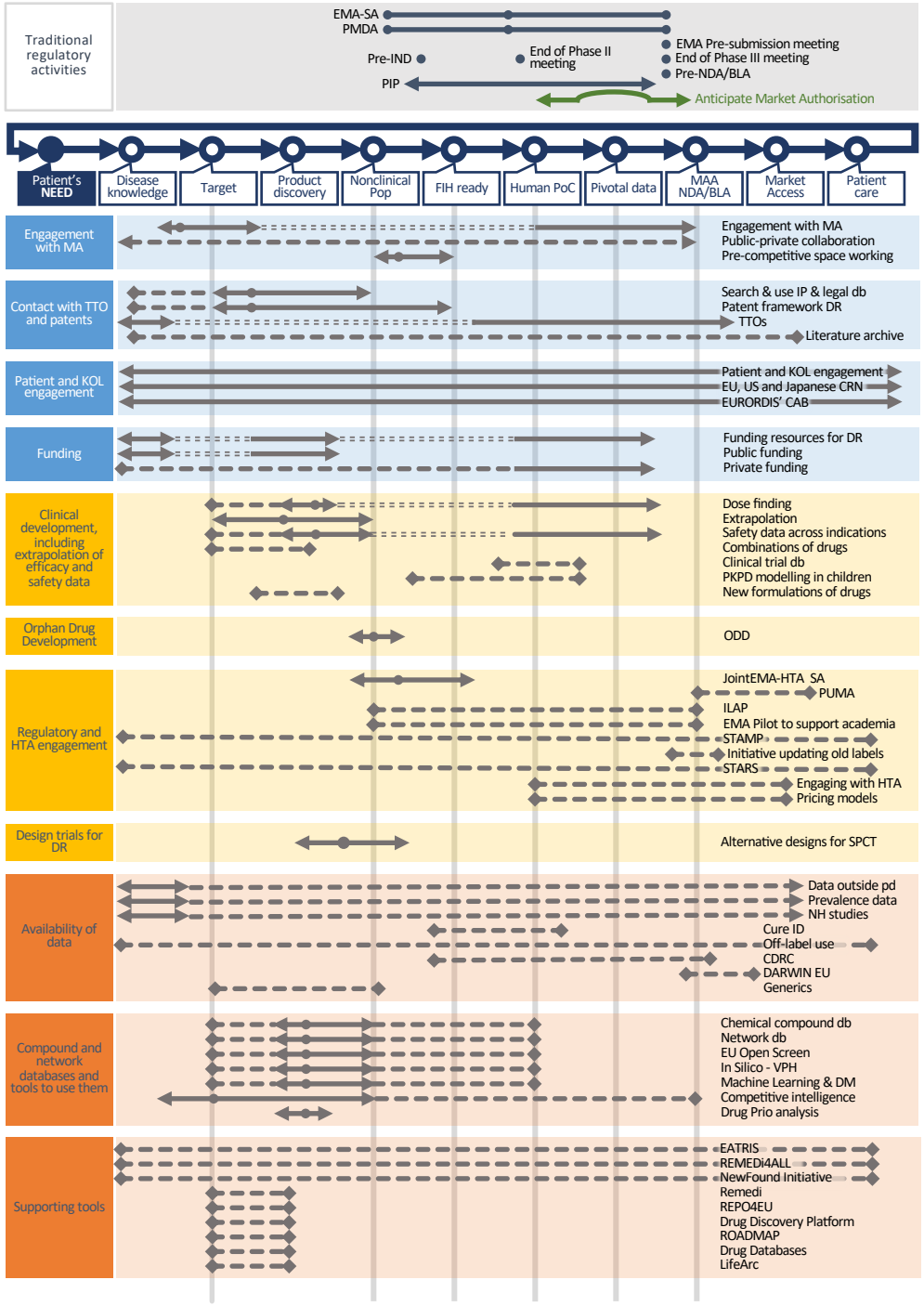
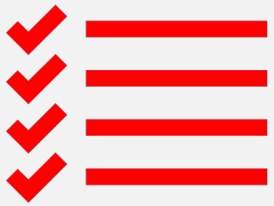


Figure 1


Traditional regulatory activities
EMA-SA
PMDA
Pre-IND
End of Phase II meeting
PIP
EMA Pre-submission meeting
End of Phase III meeting
Pre-NDA/BLA
Anticipate Market Authorisation
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
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
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
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 – How do you start the development of your product?



S

T

STakeholders mapping

A

Available information on the disease

R

Financial **R**esources

T

Target Patient Value Profile

START

STAKEHOLDERS MAPPING

- Are there patient organizations?
- Are there community advisory boards?
  - CAB's
- Are there stakeholder networks?
  - ERNs
  - CRNs
  - AMED-IRUD
- Are there general development support platforms and infrastructures ?
  - Compound and network databases
  - Supporting tools for drug repurposing
- Contact with TTOs?
- Engagement with current and/ or future Marketing Authorization Holder?

AVAILABLE INFORMATION ON THE DISEASE & DRUG

- Natural History Studies & prevalence data
- Diagnostic Tools
- PCOMs
- Biomarkers
- Coding of Rare Diseases
- IP and legal framework
- Patent framework
- Data inside and outside the public domain

FINANCIAL RESOURCES

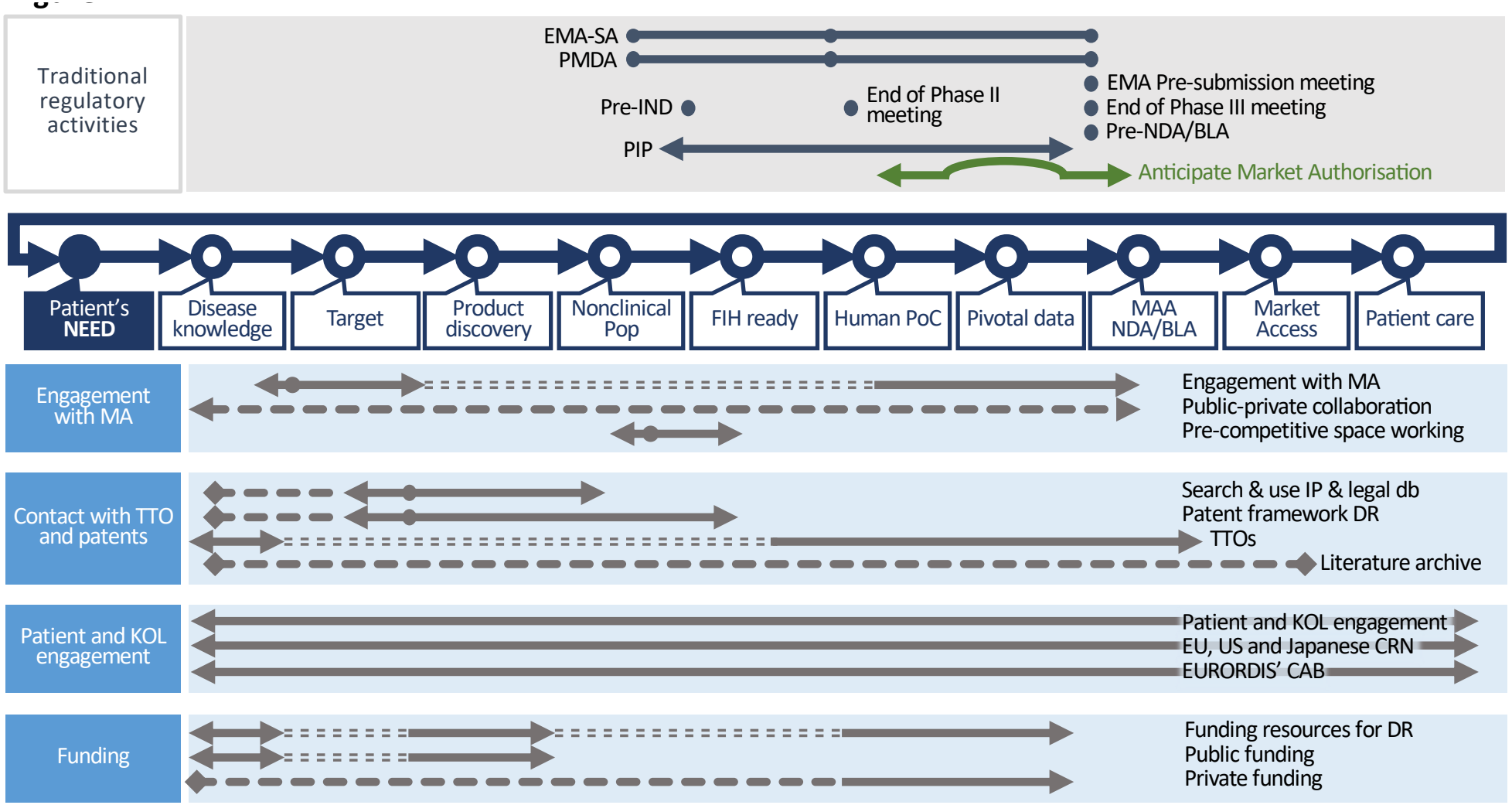
- Public Funding
- Repurposing specific funding
- Private Funding

TARGET PATIENT VALUE PROFILE

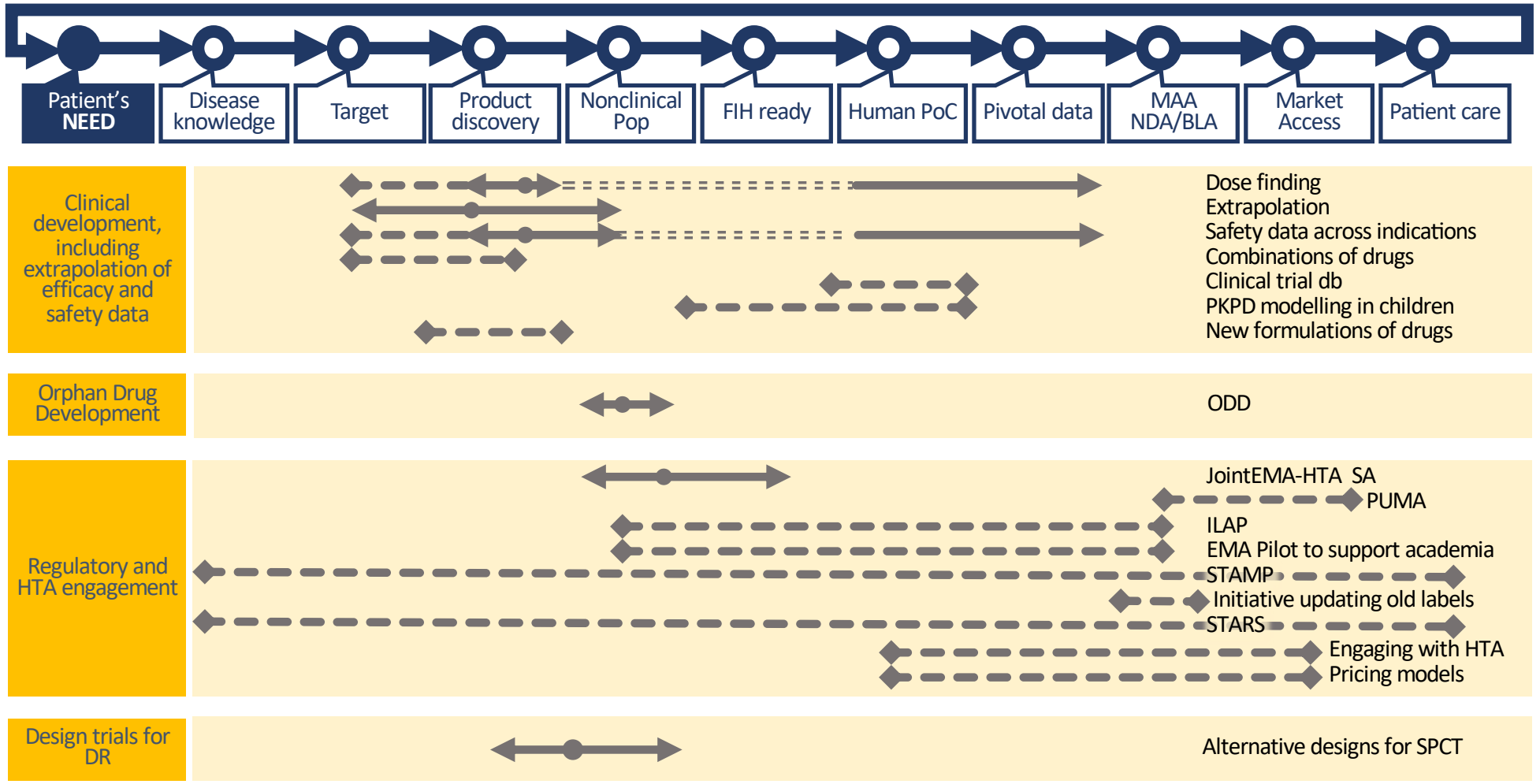
KEY TAKE AWAYS:

- 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

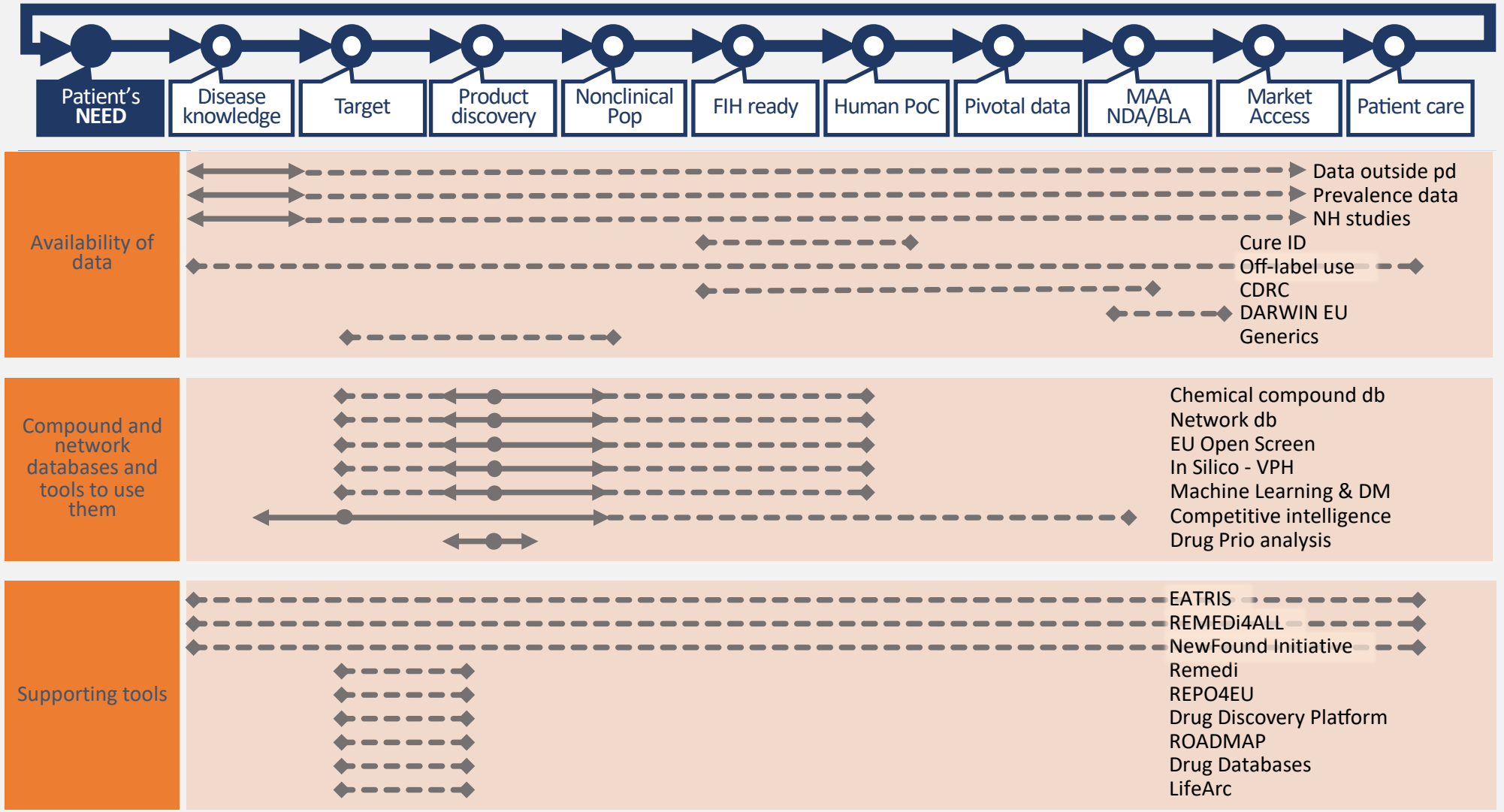
DRG – ENGAGEMENT



DRG – Regulatory & Access



DRG – TOOLS AND DATA



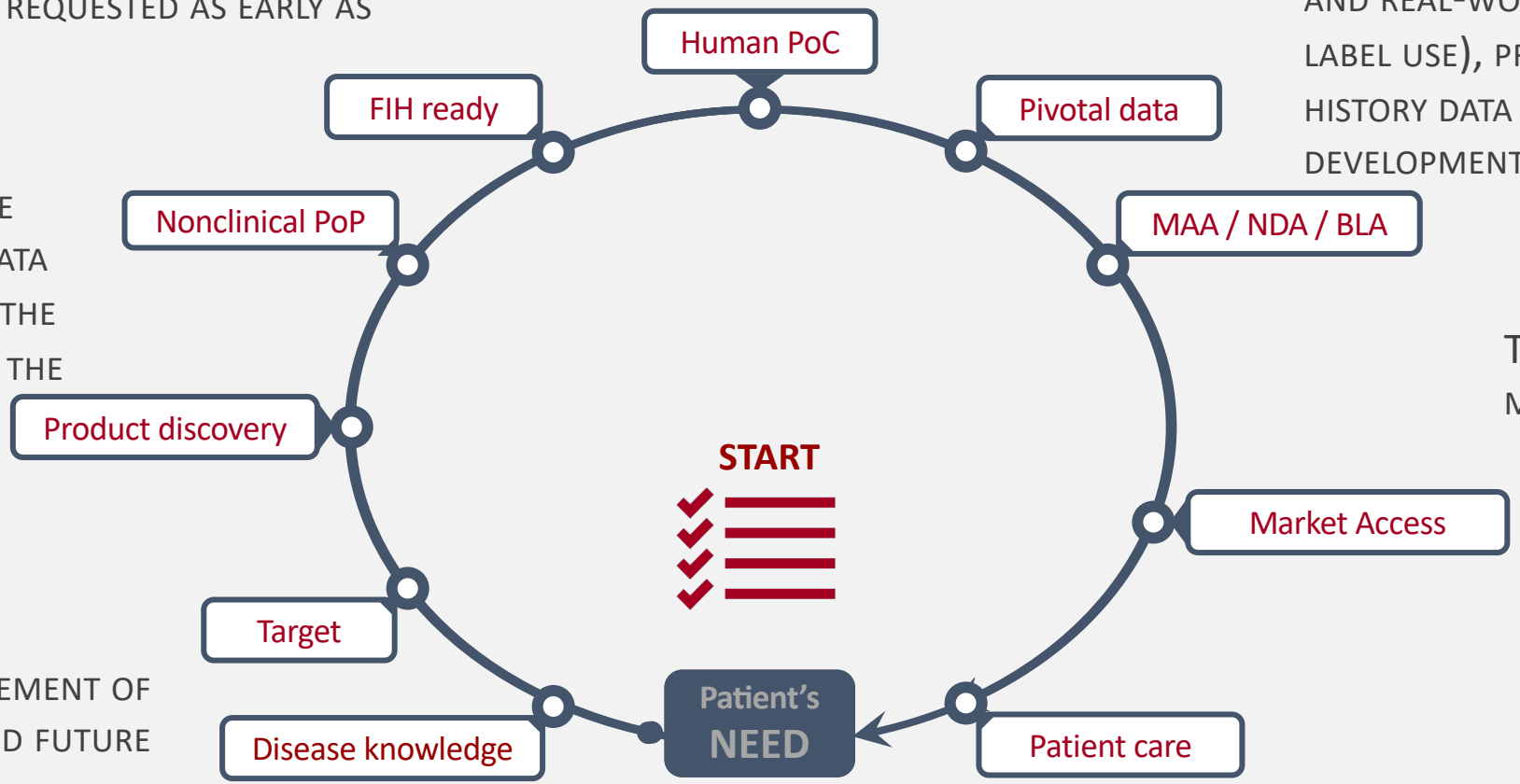
DRG – Take Home Messages

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

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

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

Think about a sustainable market access plan



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

Starts with Patient's NEED rather than Idea

Ends with Patient's NEED rather than Patient Care