C-Path in Europe: Moving Global Regulatory Science Forward

20 April 2022

CRITICAL PATH INSTITUTE

Please be advised this Webinar is being recorded

Welcome

Critical Path Institute is a catalyst for innovation that accelerates the path to a healthier world.








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Agenda

1. Welcome Remarks
2. C-Path Overview
3. Alignment with EMA Regulatory Science Strategy to 2025
4. Panel Discussion

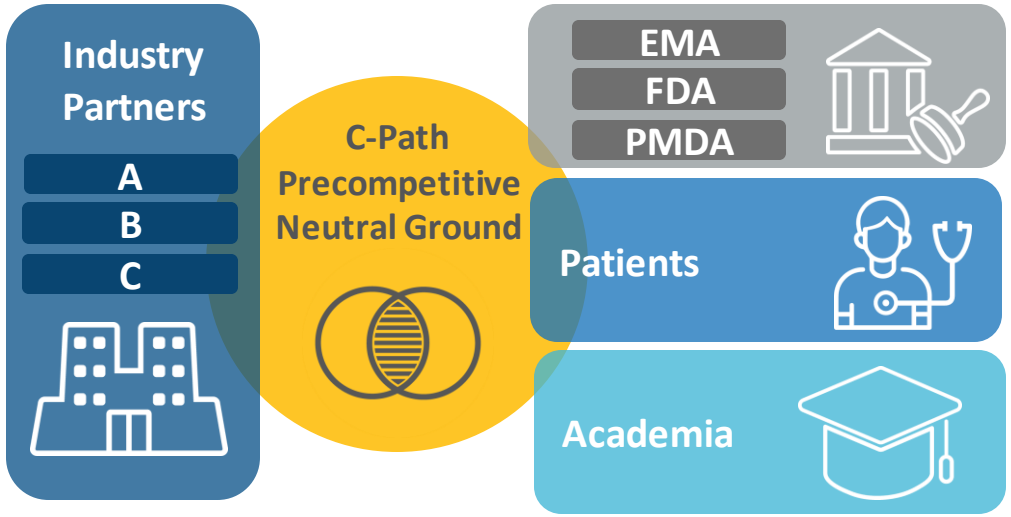
What We Do

- Foster development of new evaluation tools to inform medical product development and regulatory decision-making
- Convene scientific consortia of industry, academia, and government for sharing of data/expertise

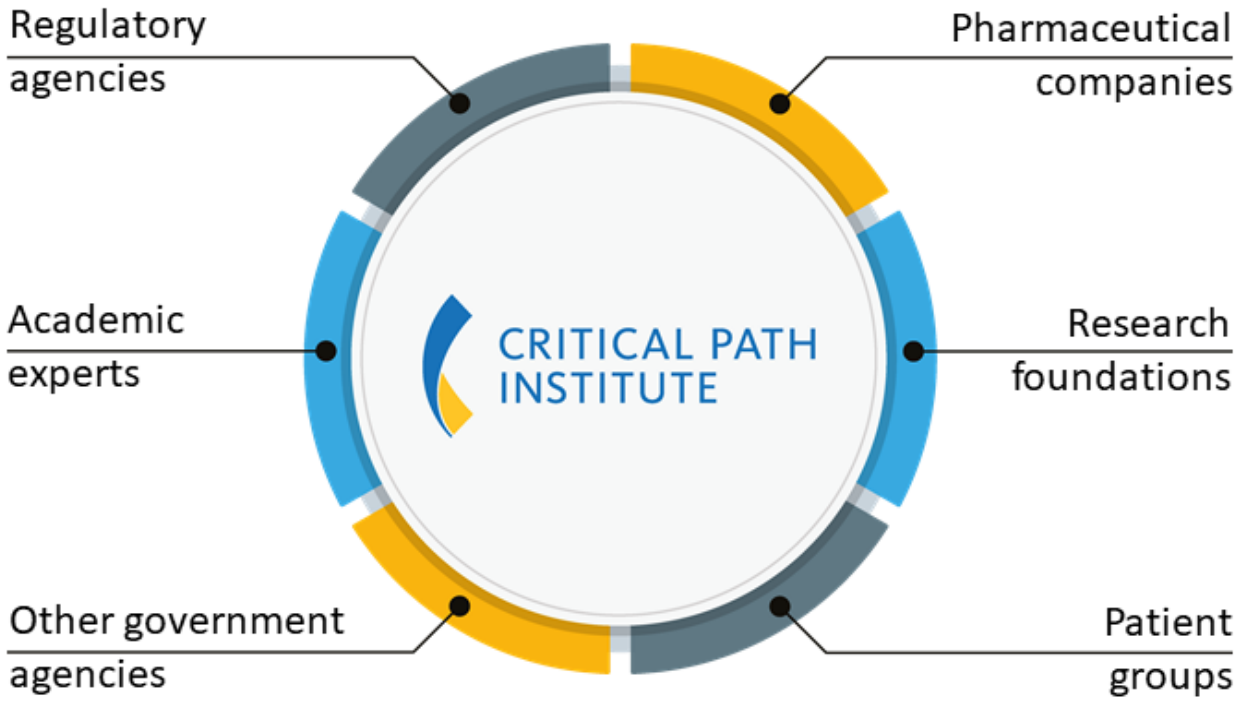
The best science

- ✓ The broadest experience
- ✓ Active consensus building
- ✓ Shared risks and costs

- Enable iterative EMA/FDA/PMDA participation in developing new methods to assess the safety and efficacy of medical products
- Obtain official regulatory endorsement of novel methodologies and drug development tools



Global Partners and Collaborators



Active C-Path Consortia & Programs

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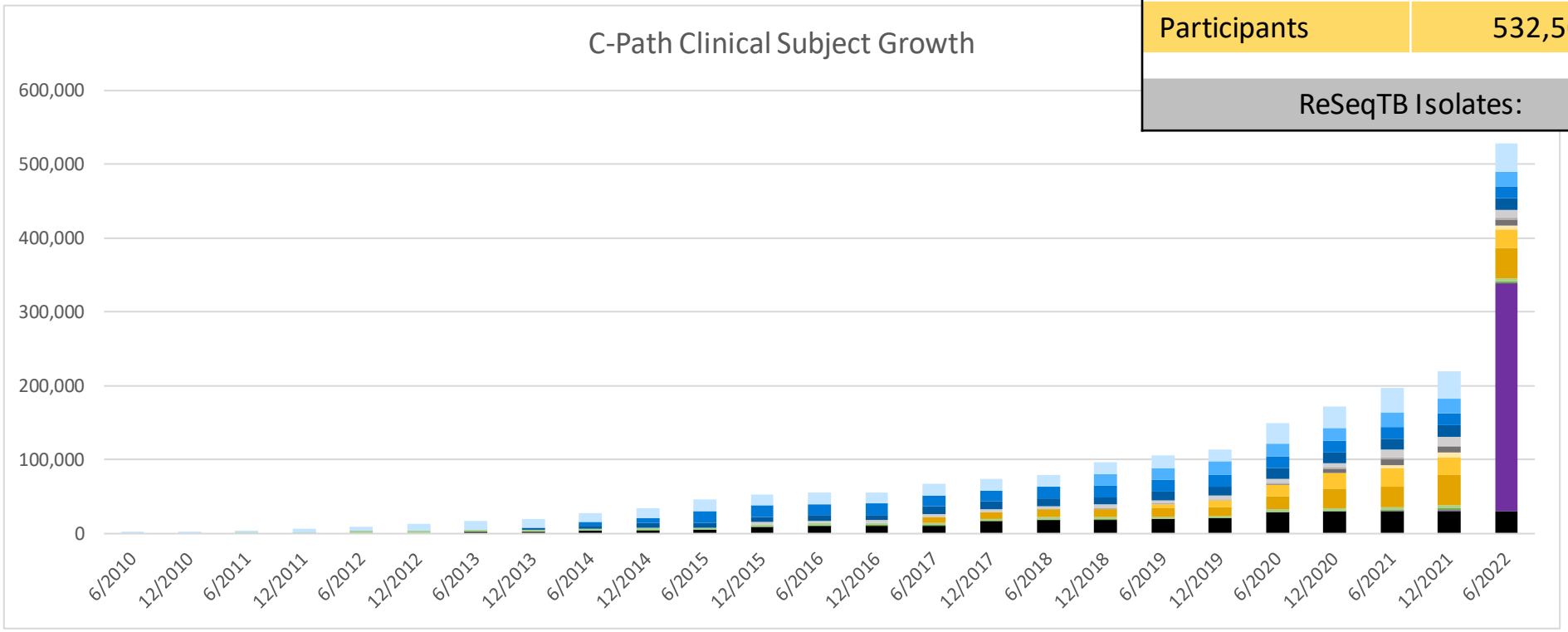
Active Consortia/Programs

BmDR	Biomarker Data Repository	**ERA4TB**	European Regimen Accelerator for Tuberculosis*	**RD-COAC**	Rare Disease Clinical Outcome Assessment Consortium
CDRC	Cure Drug Repurposing Collaboratory	**HD-RSC**	Huntington's Disease Regulatory Science Consortium	**T1D**	Type 1 Diabetes Consortium
CPAD	Critical Path for Alzheimer's Disease	**INC**	International Neonatal Consortium	**TOMI-T1D**	Trial Outcome Markers Initiative in T1D Consortium
CPP	Critical Path for Parkinson's Disease	**MSOAC**	Multiple Sclerosis Outcome Assessment Consortium	**TTC**	Transplant Therapeutics Consortium
CPTA	Critical Path to Therapeutics for the Ataxias	**PKDOC**	Polycystic Kidney Disease Outcomes Consortium	**UNITE4TB**	Worldwide Accelerator for Tuberculosis*
CPTR	Critical Path to TB Drug Regimens	**PredicTox KE**	PredicTox Knowledge Environment		
CP-SCD	Critical Path for Sickle Cell Disease	**PRO Consortium**	Patient-Reported Outcome Consortium		
DCC	Data Collaboration Center	**PSTC**	Predictive Safety Testing Consortium		
D-RSC	Duchenne Regulatory Science Consortium	**QuantMed**	Quantitative Medicine		
eCOA Consortium	Electronic Clinical Outcome Assessment Consortium	**RDCA-DAP**	Rare Disease Cures Accelerator- Data and Analytics Platform		

* C-Path Ltd.

Data Sharing and Aggregation by Area

	Clinical Data	Nonclinical Data
Studies	354	148
Participants	532,504	11,084
ReSeqTB Isolates:		9,215



Neuro	
Alzheimer's Disease	38,890
Huntington's Disease	19,903
Multiple Sclerosis	15,626
Parkinson's Disease	15,885

Rare	
Duchenne's Muscular Dystrophy	11,442
Friedreich's Ataxia	1,572
Rare Diseases	8,087

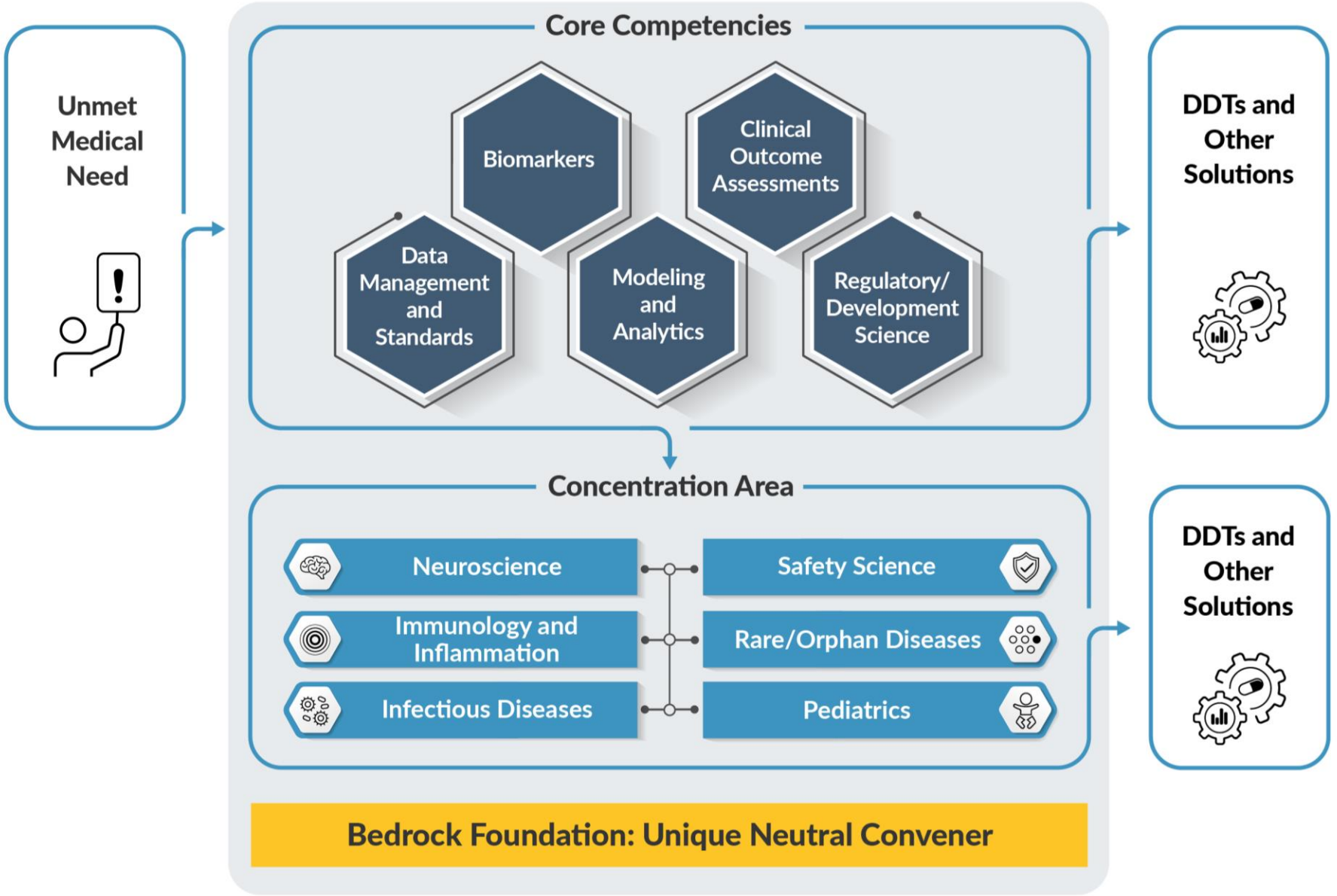
IHP	
Sickle Cell Disease	6,240
Transplant Therapeutics	24,688
Type 1 Diabetes	41,096

TSSP	
Polycystic Kidney Disease	4,422
Safety Testing	2,274

Neonatal	308,672

Tuberculosis	29,630

C-Path Core Competencies



Funding Models for Multi-Stakeholder Collaborations

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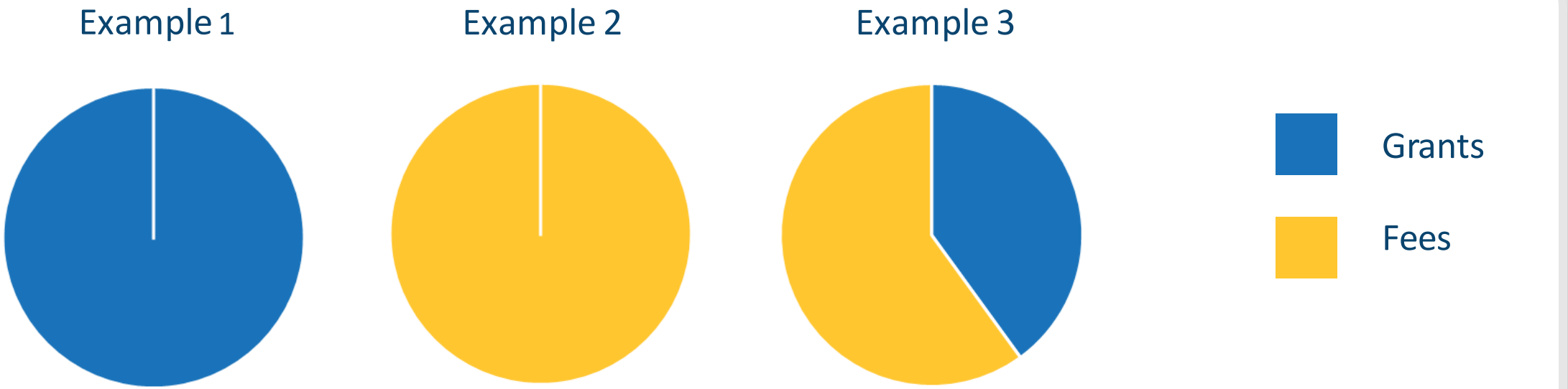

Key Milestones of Collaboration in Europe

Agenda

1. Welcome Remarks
2. C-Path Overview
3. Alignment with EMA Regulatory Science Strategy to 2025
4. Panel Discussion

C-Path in Amsterdam

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Mission

- Leveraging and developing C-Path US and European activities in a complementary operational setting to facilitate global collaboration and harmonisation
- Strengthen C-Path relationship with EMA and EU Member States
- Strengthen and develop collaboration with European key stakeholders in the DDT, Data Management and Standards, and Regulatory Science

C-Path Operational Model - Impact

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C-Path Unmet needs Horizon Scanning

Decision Point

Pre-PPP Assessment
~12-18 months

Decision Point

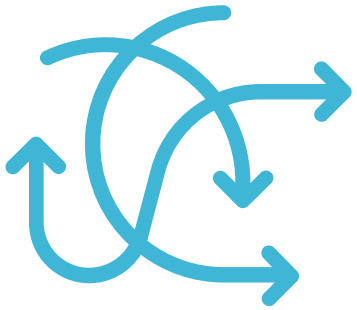
Operational Consortium

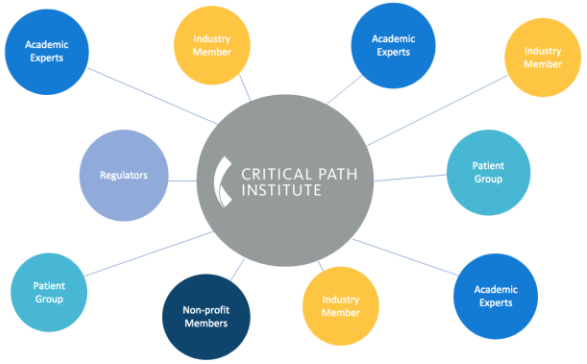
Impact

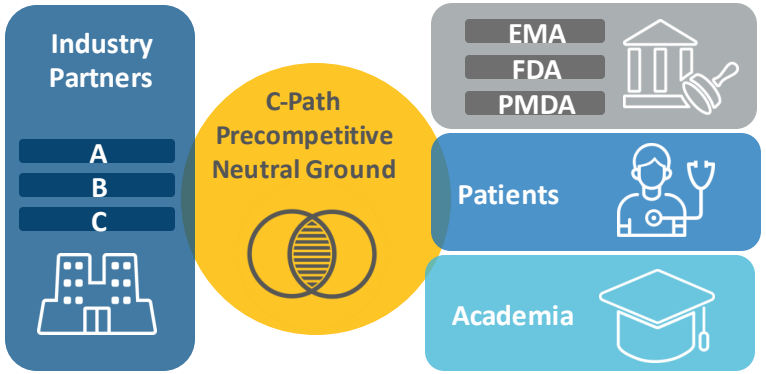
1. Synergies with EMA RSS 2025
2. EMA x C-Path webinars & workshops
3. Education and trainings

1. EU contribution beyond individual capacity
2. Focused contribution and optimized resource input
3. EU goals integrated in a global strategy

1. EU fit for purpose DDTs
2. Global data strategy
3. Sharing knowledge and learnings with the EU network







C-Path Alignment with EMA RSS to 2025

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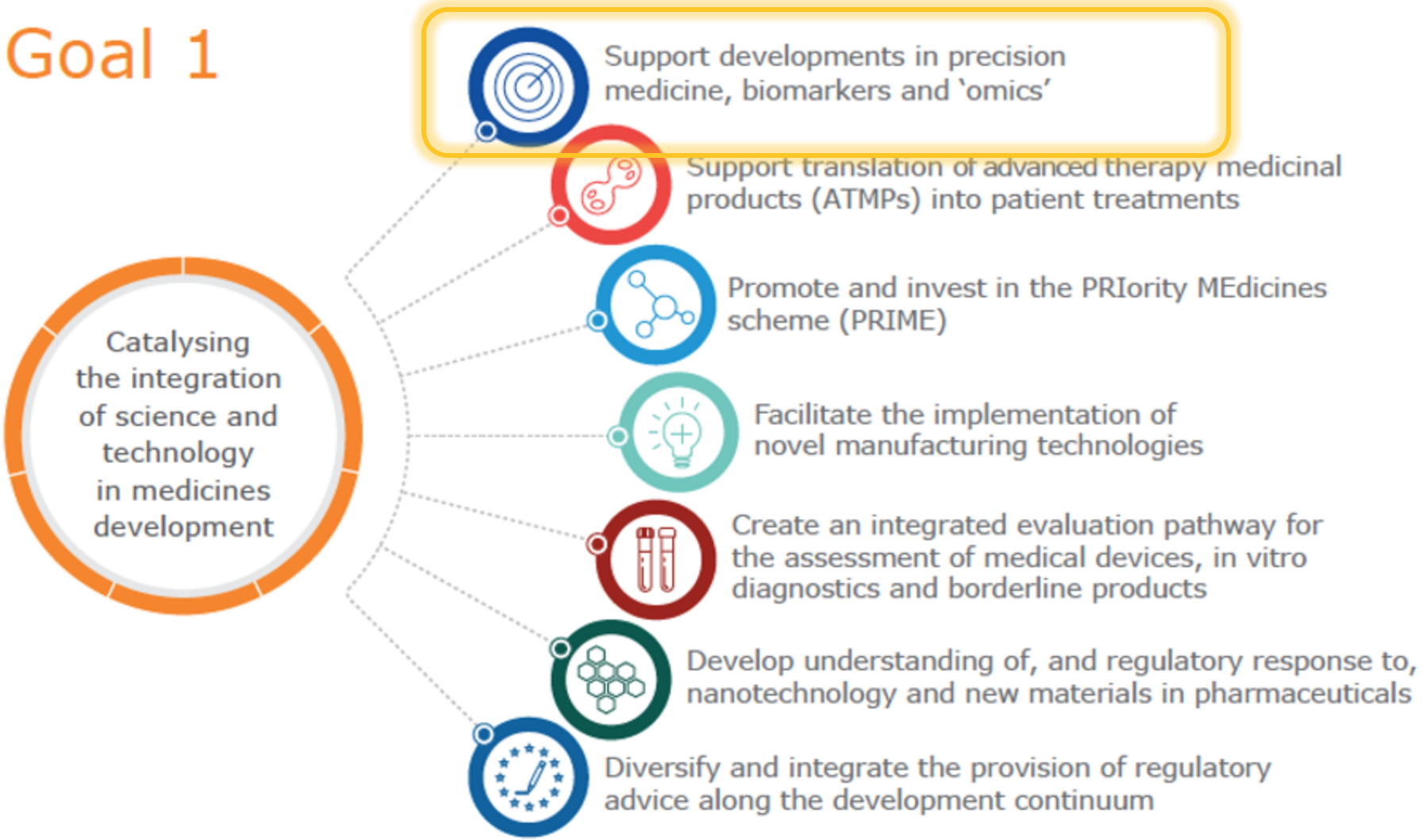
EMA RSS Goals	Example C-Path efforts
Goal 1: Catalyze integration of science and technology in drug development	Drug Development Tools
Goal 2: Collaborative evidence to improve decision-making	Complex Clinical Trials and Modeling
Goal 3: Patient-centered access to medicines	Real-world data/Real-world evidence
Goal 4: Emerging Health Threats	Repurposed Drugs
Goal 5: Research and innovation in regulatory science	Academic Partnerships in Regulatory Science

C-Path Alignment to EMA RSS H1 Goals



Regulatory Successes in Drug Development Tools

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FDA

- 7 Qualification Decisions
- 7 Letters of Support
- 1 Fit-For-Purpose Endorsement

EMA

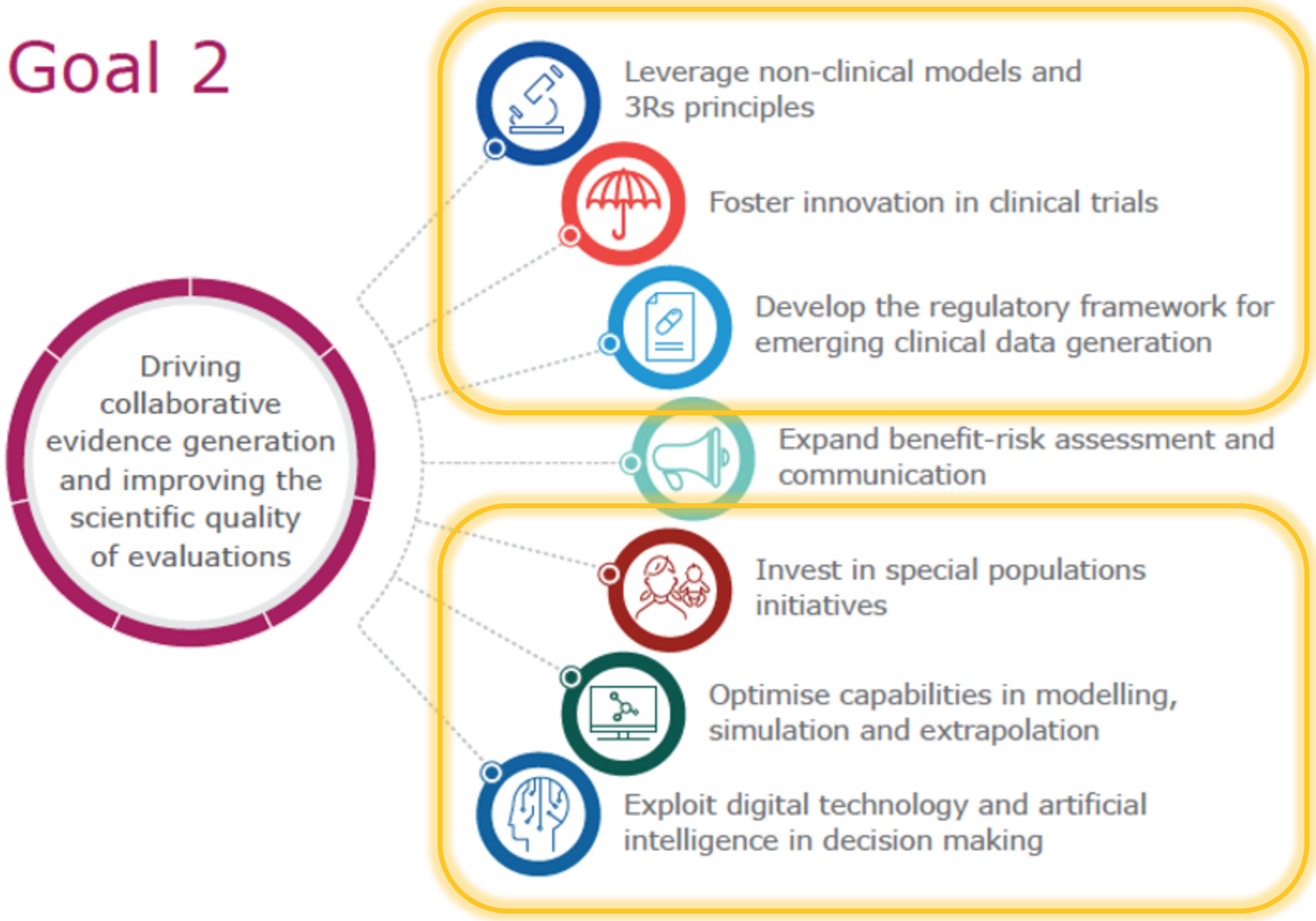
- 8 Qualification Opinions
- 8 Letters of Support

PMDA

- 1 Qualification Decisions

Global endorsement of actionable solutions accelerates and de-risks medical product development.

C-Path Alignment to EMA RSS H2 Goals



Advancing Drug Development in Rare Disease

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Examples of modelling in Duchenne muscular dystrophy (DMD) from C-Path's Duchenne Regulatory Science Consortium (D-RSC)

DMD Progression Models and Building CTS Tools

Data and Quantitative Model-Based Drug Development Approach to Clinical Trial Simulation (CTS) Tools

GLDH Qualification as Safety Biomarker for DMD Clinical Trials

Collaboration with C-Path's Predictive Safety Testing Consortium (PSTC) on Safety Biomarker Qualification for Glutamate Dehydrogenase (GLDH)

Master Protocol for Duchenne Adaptive Platform Trial

Complex Clinical Trial Design in Rare Diseases

Impact

- Learnings from the DMD CTS platform have been used by industry sponsors in trial design for new therapeutic candidates.

Clinical trial simulation (CTS) platform for DMD

- First-ever comprehensive collection of models for five clinically meaningful outcome measures across the continuum of DMD.

Development of Novel Digital Measures for Clinical Trials in PD

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- **Need:** Better outcome measures for assessment of progression of Parkinson's disease (PD)
- **Solution:** Critical Path for Parkinson's (CPP) Digital Drug Development Tools (3DT) initiative

FDA Critical Path Innovation Meeting (**CPIM**)

2019 - 3DT launched → 2020 to today → Future Vision - digital measure(s) for use in clinical trials

EMA Innovation Task Force (**ITF**) Meeting

COMMENT · 12 MAY 2020

Digital technologies for medicines: shaping a framework for success

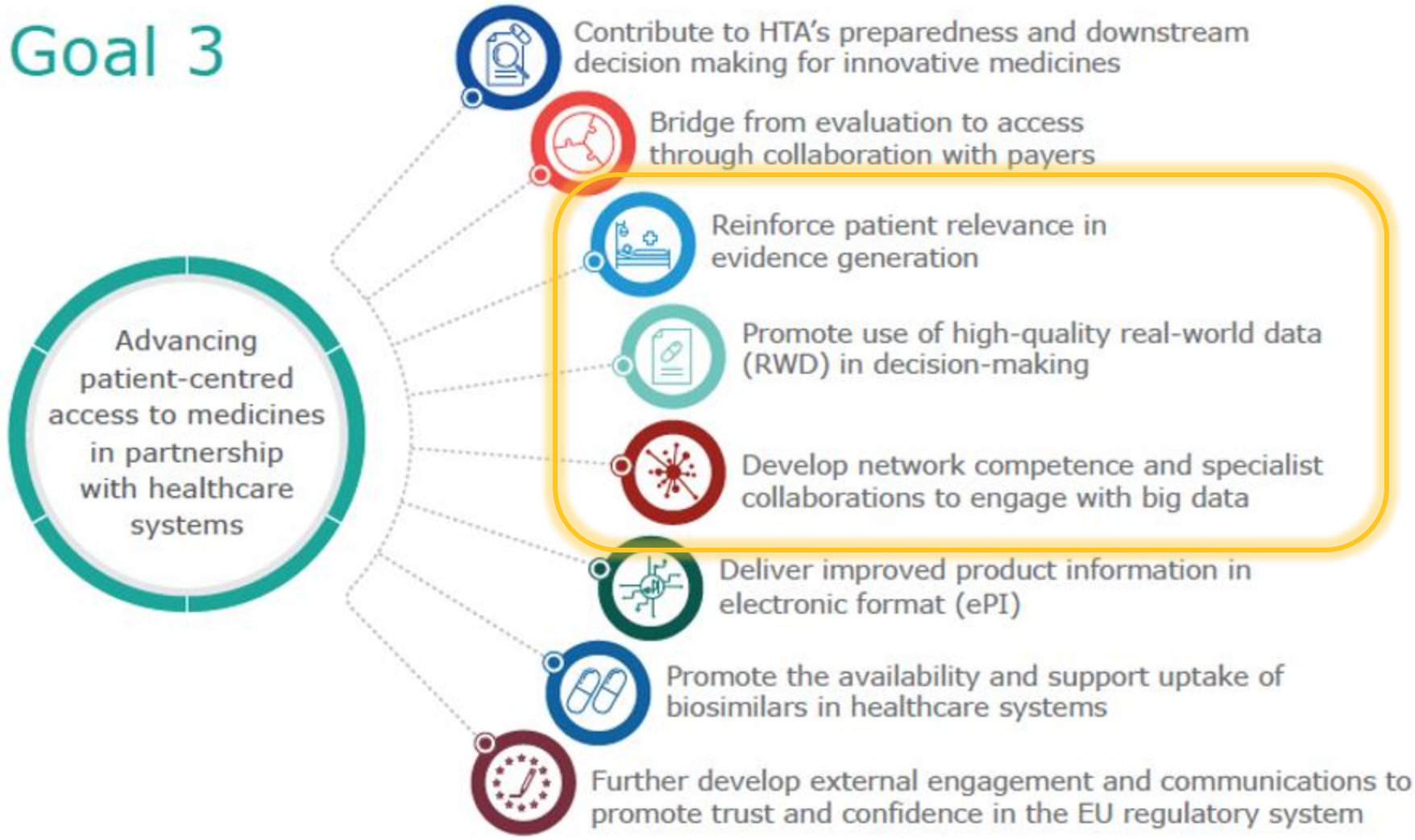
Regulatory agencies can provide advice to support developers of digital technologies for medicines use, but what are the best strategies to maximise the chance of a successful regulatory interaction? Here, EMA and industry representatives comment on the experience so far.

Francesca Cerreta ✉, Armin Ritzhaupt, Thomas Metcalfe, Scott Askin, João Duarte, Michael Berntgen & Spiros Vamvakas

Nat Rev Drug Discovery 19(9): 573-574, 2020

(**W**earable **A**ssessments in **T**he **C**linic and **H**ome in **PD**)

C-Path Alignment to EMA RSS H3 Goals



Patient-Centric Drug Development

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Chronic Heart Failure (CHF) Working Group (WG) in the Patient-Reported Outcome (PRO) Consortium

- WG objective: Qualification by FDA of an activity monitor-based endpoint measure for use in assessing clinical benefit in CHF treatment trials
- Project goal: Identify variables obtainable via activity monitors that can be used to derive efficacy endpoints that adequately reflect meaningful aspects of day-to-day physical activity for persons with CHF

Conducted Concept Elicitation Interviews

- Generated qualitative evidence of important day-to-day physical activities and performance dimensions
  - **Light/moderate physical activities**: cleaning, cooking, laundry, self-care, gardening
  - **Walking:** shopping, appointments, exercise
  - **Dimensions:** duration, frequency, intensity, distance

Convened an Advisory Panel

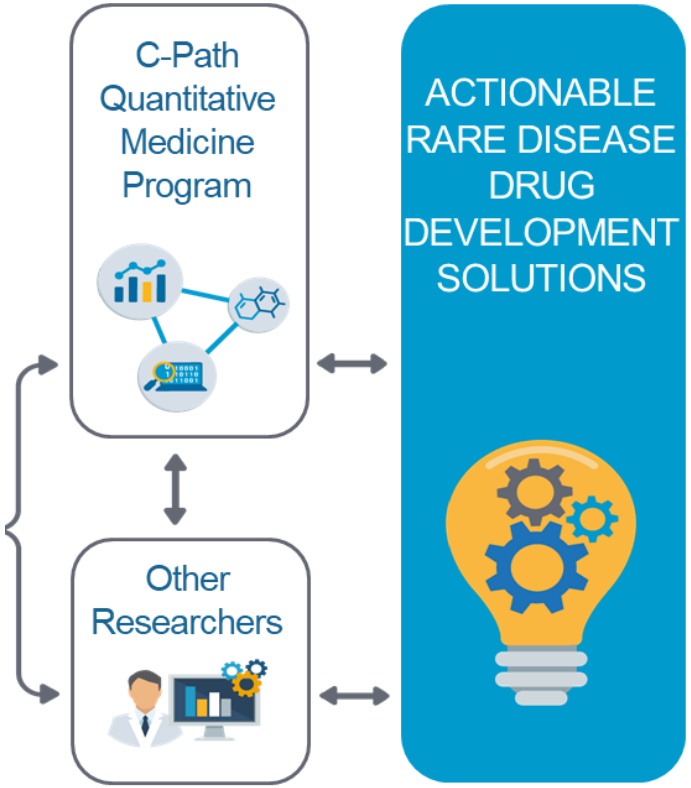
- Advisory panel meetings (1 Dec 2021 and 16 Mar 2022)
- Built on WG's study results, other research, and literature
- Identified candidate metrics for assessing clinical benefit and deriving endpoints
  - Step counts (walking)
  - Activity counts (general activities)

Future Vision

- Alignment among WG sponsors, C-Path, and FDA on specific metric(s) to move forward for Qualification Plan submission to FDA

Pilot Studies: Drug Development Tools from RDCA-DAP

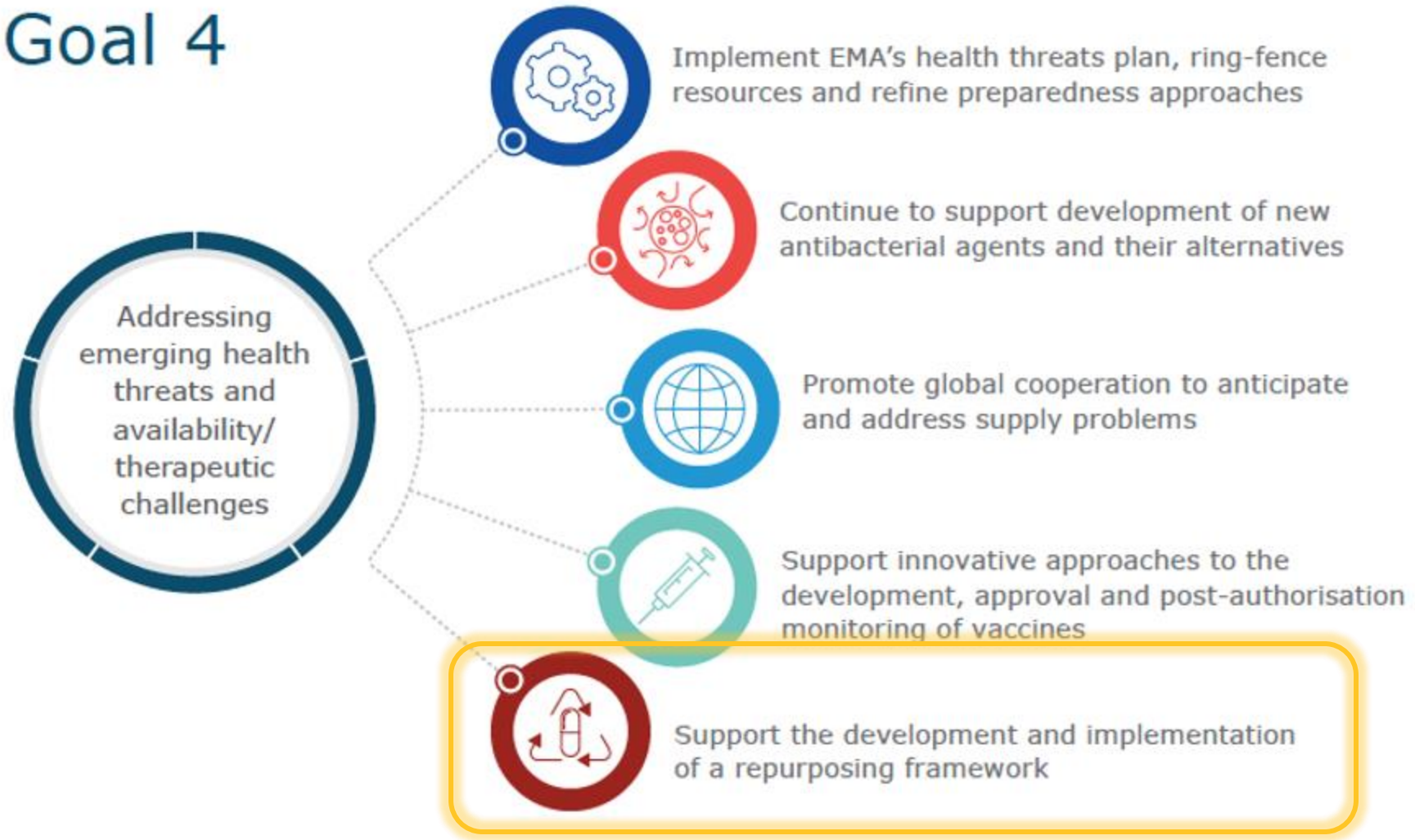
(GDPR compliant)



- **Metabolic disorders**
  - Analysis of baseline characteristics of patients in the PKU registry from NPKUA
  - Evaluation of the Foundation of Prader-Willi Research data from hyperphagia questionnaires
- **Genetic disorders**
  - Exploration of GNE myopathy cross diseases discovery potential
- **Neurodegenerative disorders**
  - Progressive Supranuclear Palsy (TBD)
  - Dynamics of the modified Friedreich's Ataxia Rating Scale: population variance, placebo affect and clinical meaningfulness

RDCA-DAP is an initiative led by Critical Path Institute in collaboration with FDA and NORD

C-Path Alignment to EMA RSS H4 Goals



Global Partnerships to Address Global Health Threats

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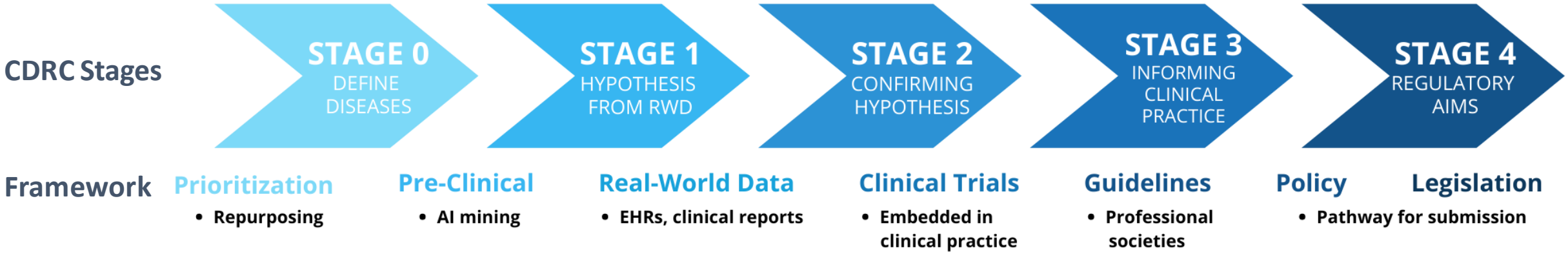
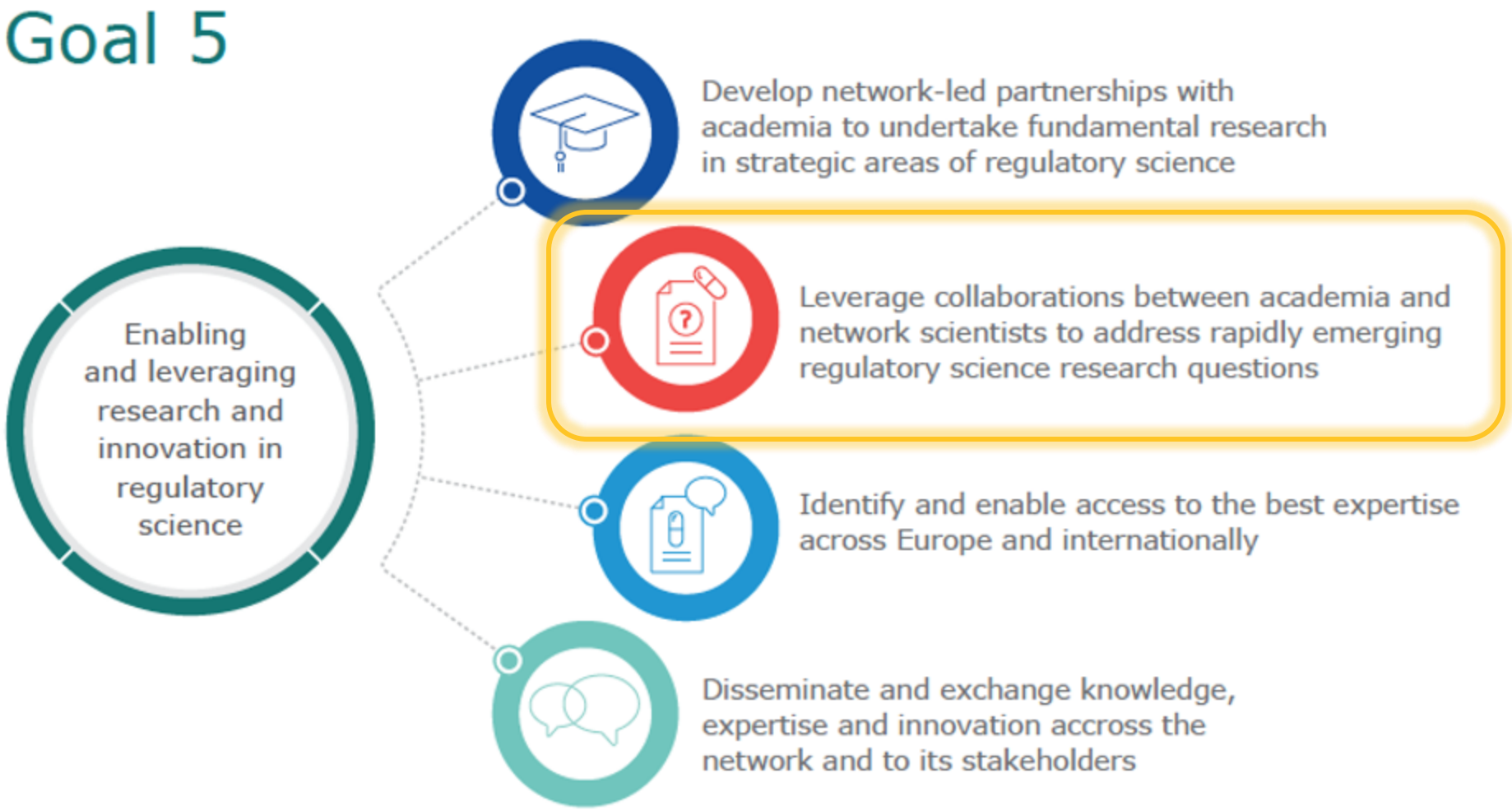


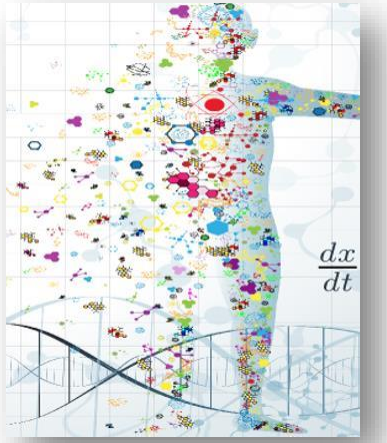
- **Challenges to repurposing drugs**
  - No financial incentives to expand drug labels
  - Labeling changes must be initiated by drug sponsor
  - Intellectual property/patent protections

- **Changing the landscape**
  - Maximize use of existing medicines
  - New incentivizes for expanded use of existing generic drugs
  - Establish a new pathway for non-industry drug sponsors
  - Affect policy changes

C-Path Alignment to EMA RSS H5 Goals



C-Path and Regulatory Science Training



1. **Model-informed Drug Development training courses**
   - 8 modules with focus areas in:
     - Introduction to drug development and regulatory science
     - Foundation of MIDD
     - Model-informed decision making in drug development
     - Future Considerations including Digital Health, RWD/RWE, and AI/ML
     - E-learning environment, web-based learning management system (LMS)

James E. Rogers College of Law

2. **Regulatory Science Graduate Certificate program**
   - 9 courses total (3 of which are led by C-Path scientists)
     - Drug Discovery, Development, and in the Market
     - Development and Innovation: Biologics, Devices, and Diagnostics
     - Regulatory Science Case Study Project

STARS
STRENGTHENING REGULATORY SCIENCE

3. **Strengthening Training of Academia in Regulatory Science (STARS) Global Conference – 19 May 2022**
   - Session on “Excellence in Regulatory Science”

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Acknowledgements – Regulatory Science team

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Kimberly Ward Barowicz

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Project Coordinator

Panel Discussion

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Dimitrios Athanasiou, MBA

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Member in World Duchenne Organization,

European Patients Forum Greek Patient Association

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Klaus Romero, MD, MS

Chief Science Officer

Executive Director of Clinical Pharmacology

Cécile Ollivier, MS

EU Regulatory Science Advisor (US)

Board of Directors (Netherlands)

Tomas Salmonson, PhD, MSc

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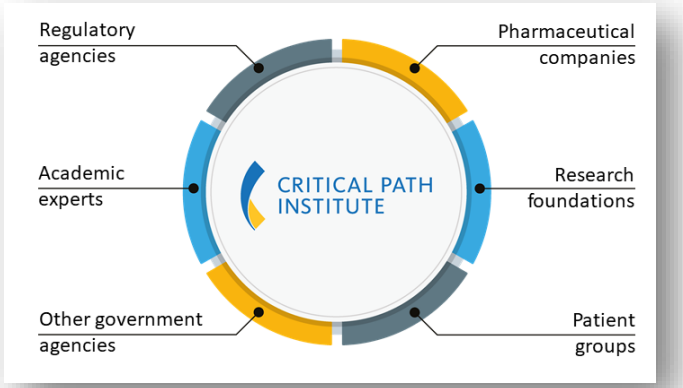
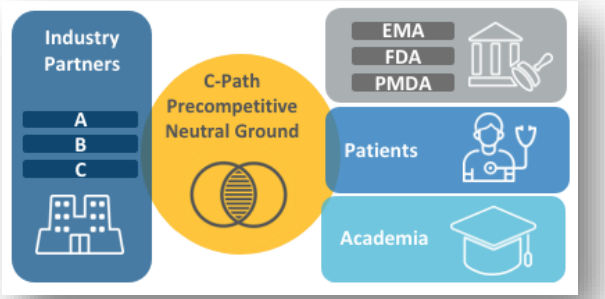
Closing Remarks

- Timely global compatibility can only be achieved through collaboration



- Regional multistakeholders platforms need appropriate regional fundings to be able to develop global consensus

- C-Path is a neutral convener committed to moving Regulatory Science forward and will focus for the next 5 years on developing such global platform in areas with great impact for the patients



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