Critical Path for Lysosomal Diseases

A Public Private Partnership to Accelerate Drug Development in Lysosomal Diseases

Kanwaljit Singh, MD MPH (Executive Director of CPLD)

Understanding Public Private Partnerships

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Definition of Public Private Partnership (PPP):

- A PPP is a collaborative agreement between public sector entities and private sector companies.
- This model leverages the strengths of both sectors to achieve common goals.

Key Characteristics of PPPs:

- Shared Resources: Combines public oversight and private sector efficiency.
- De-risking: Reduces bottlenecks associated with drug development process.
- Mutual Benefits: Aims for outcomes that benefit both the public interest and private sector profitability.

The Role of Critical Path Institute's PPP Model:

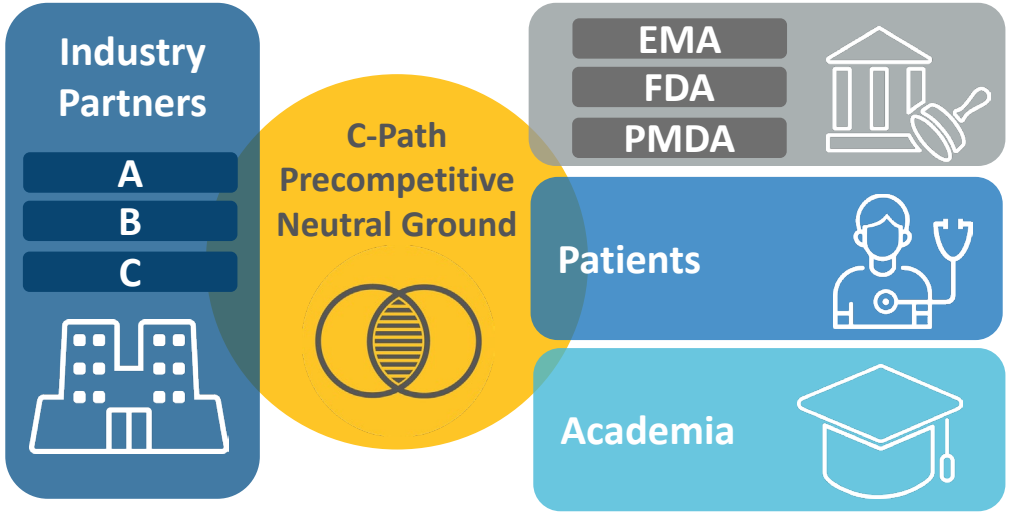
- C-Path's PPPs bring together pharmaceutical industry, academic researchers, patient groups, and regulators to serve as a platforms to advance medical product development through shared innovation and knowledge.

Why Engage with PPPs:

- **For Industry:** Engage with cutting-edge scientific research and gain regulatory insights to ensure compliance.
- **For Academia:** Directly translate research into actionable medical practice.
- **For Regulators:** Access innovative methodologies for drug safety and efficacy, and actively participate in the development of forward-thinking drug development tools.
- **For Patients:** Contribute to the drug development process, ensuring patient-centric product innovation and the possibility of accelerating development of new therapies.

C-Path's Public-Private Partnership Model

- Act as neutral, third party
- Foster development of new evaluation tools to inform medical product development and regulatory decision-making
- Convene scientific consortia of industry, academia, patient groups, 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



FDA: US Food and Drug Administration
EMA: European Medicines Agency
PMDA: Japanese Pharmaceuticals and Medical Devices Agency

C-Path's North Star

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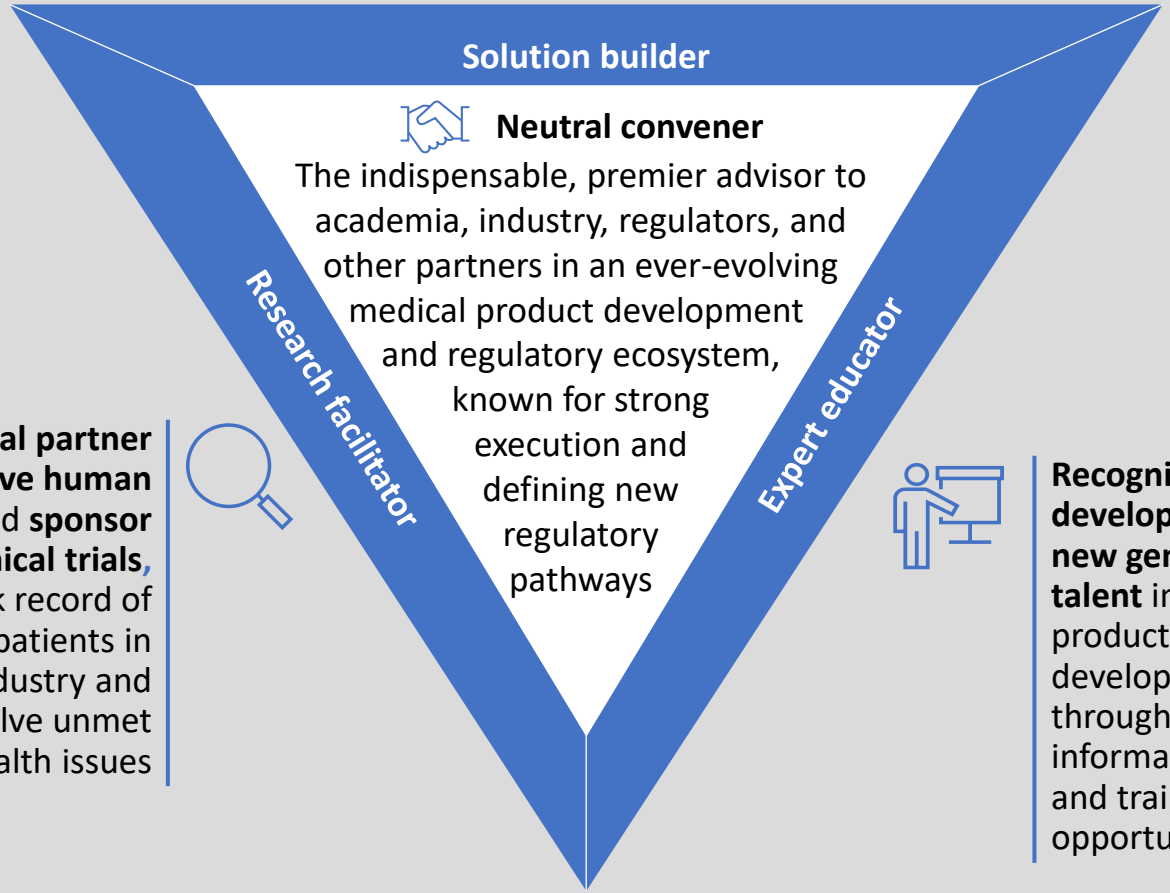
Leading **provider of precompetitive data analysis services and generator of solutions** for industry, academia and regulators, known for leveraging data assets and quantitative, biomarker, and clinical outcome assessment (COA) expertise to advance medical product development (e.g., clinical trial data integration, advanced analytics, as well as modeling and simulation)



Results-oriented **global partner for pre-competitive human subjects research** and **sponsor for collaborative clinical trials**, with a proven track record of engaging patients in partnership with industry and academia to solve unmet public health issues

Recognized chief developer of the new generation of talent in medical product development science through formal and informal educational and training opportunities

C-Path's Active PPPs*

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Active Consortia/Programs

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

* C-Path Europe

**C-Path's active PPPs include programs on diseases with high unmet needs, adult and pediatric conditions, rare and non-rare diseases*

Pathway to establishing a Public Private Partnership at C-Path

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For Patient Organizations (and for other stakeholders also):

- **Inquire**: Reach out with your condition's profile and partnership vision
- **Discuss**: Collaborate with us on objectives, impact potential, and partnership scope

Selecting Topics/Conditions:

- **Impact & Opportunity**: Prioritize conditions with high unmet needs and the potential for scientific breakthroughs
- **Community Readiness**: Evaluate existing research and active community engagement
- **Strategic Fit**: Selection aligns with our goals and resource capabilities
- **Strategic Decision**: Choices made to maximize impact within our mission scope

Engage with Us:

- Join our mission to empower patient-centric healthcare initiatives!
- For general C-Path enquiries, please visit our website https://c-path.org or contact us at info@c-path.org

The Road to Critical Path for Lysosomal Diseases (CPLD)

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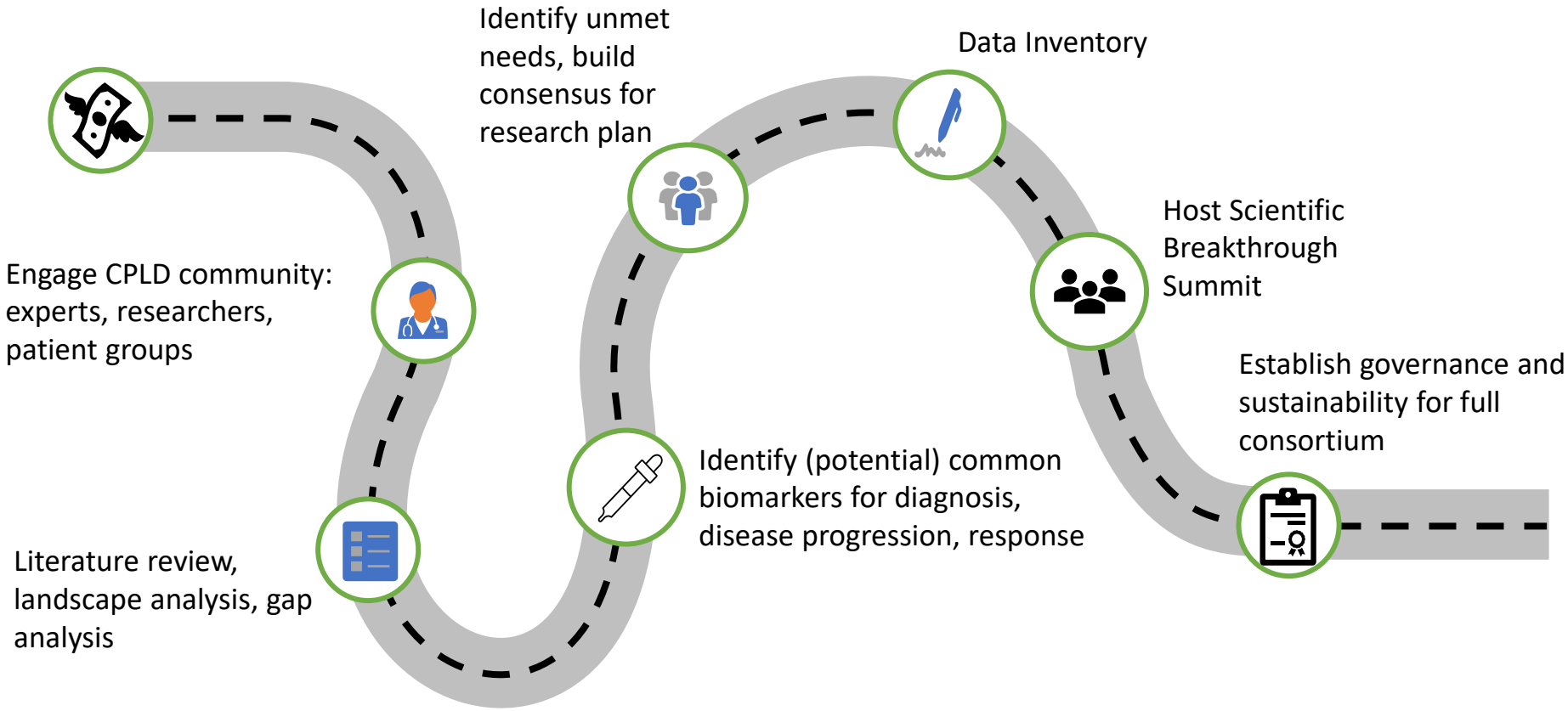

Developing a roadmap for CPLD – A Public Private Partnership to Advance LD Drug Development

CPLD Achievements Thus Far

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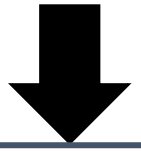
Meticulous landscape analysis to develop pathophysiological rationale for working groups and 3-year research plan. This led to the establishment of a common platform to interrogate a solutions-based physiological strategy for solutions specific to neuronopathic Lysosomal Diseases (LDs) and work closely with regulatory agencies to accelerate solutions (drug development, medical device, gene therapy) to address unmet needs.

Aggregated evidence from existing clinical trials and publications informing selection of neuroimaging as a proposed biomarker. Using a hypothesis-driven approach to assess the potential of structural imaging for accurate depiction of atrophic changes, detecting signal abnormalities, observing neuronal loss, and monitoring brain region water content and volume. Advancements in technology will lead to CPLD discovering novel biomarkers, potentially revolutionizing LD diagnosis, monitoring, and management.

Selected NfL as a biomarker based on aggregated clinical evidence showing elevated "blood" NfL levels reflecting acute axonal damage, disease severity (white and grey matter atrophy), and potential for assessing treatment response and disability progression. Hypothesis-driven assessment for early diagnosis, disease progression, and treatment response.

Created a Unified Data Strategy: Performed a comprehensive data inventory, which will lead to establishment of a comprehensive longitudinal database by aggregating imaging and fluidic CNS markers from diverse sources, including industry-sponsored trials, government-funded studies, international trials, and registries. Addressing the crucial need for biomarker validation by developing standardized methods and consensus protocols, potentially including MRI guidelines and NfL assessment, to enhance LD clinical trials.



Launching of CPLD as a consortium of regulatory, industry, and academic stakeholders with the mission to create drug development tools to fulfil unmet drug development needs of patients with LDs

CPLD Consortium Objectives

Lysosomal disorders (LDs) involve intricate pathological mechanisms that impact both white and grey matter structures across the central nervous system (CNS). The substantial diversity within LDs contributes to variations among patients and even within LD subtypes. In response to the unmet needs in LD management, CPLD is forging a consortium that brings together key stakeholders from the pharmaceutical industry, academia, patient groups, and regulatory authorities. This consortium is dedicated to charting a path guided by innovative solutions for the identification, screening, diagnosis, and development of novel therapies addressing CNS pathologies within LDs.

CPLD Consortium Objectives:

- **Advancing Drug Development in LDs**: Our primary goal is to pioneer actionable solutions for LD drug development. Initially, this includes the identification of biomarkers, followed by other solutions like clinical trial endpoints, clinical outcome assessments, and simulation tools. These solutions will be presented for regulatory endorsement to facilitate progress in LD drug development.

- **Comprehensive Data Repository**: We aim to create a comprehensive database, encompassing various data sources such as longitudinal interventional study data, registries, observational research, and Real World Data (RWD) as appropriate. This repository will serve to expand our knowledge and provide ongoing research support within the Consortium. Additionally, we are exploring the possibility of data-sharing among consortium members through a data platform with storage and management capabilities.

Challenges and Potential Solutions with gaining support for biomarker identification

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Challenges

- Standardize sample collection and assay methods to align across multiple testing sites
- Lack of standardized, normative database in LD patients
- Undetermined predictive value of biomarkers for progression across multiple LDs
- Fragmented data sharing/repository LD ecosystem

Potential Solutions

- RDCA-DAP* harmonization integration and access to maximize utility
- Prospective standardization and assay methods
- Longitudinal validation in early and advanced CNS involvement

RDCA-DAP: C-Path's Rare Diseases Cures Accelerator Data And Analytics Platform

Emerging CPLD Workstreams

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Address challenges and needs that may not be met by neuroimaging and fluidic biomarker workstreams

Evaluate opportunities related to additional workstreams

Patient experience	Clinical Trial Optimization	Disease specific workstreams

Exploring cell and gene therapies for LDs

Patient Experience Data for LD Drug Development

- FDA CDER Patient-Focused Drug Development Initiative
  - Disease symptoms, daily impacts
  - Current approaches to treating LD
- Dec 2016, 21st Century Cures Act, section 3004:

  …FDA to report on the use of patient experience data in regulatory decision-making, especially focusing on the review of patient experience data and information on Patient-Focused Drug Development tools as part of applications approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(c)) or section 351(a) of the Public Health Service Act (42 U.S.C. 262(a)).[1]
- PED data can inform:
  - Clinical trial design
  - Endpoint development/selection
  - Benefit/Risk assessments

CDER Patient-Focused Drug Development

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What is Patient-Focused Drug Development?

Patient-focused drug development (PFDD) is a systematic approach to help ensure that patients' experiences, perspectives, needs, and priorities are captured and meaningfully incorporated into drug development and evaluation. As experts in what it is like to live with their condition, patients are uniquely positioned to inform the understanding of the therapeutic context for drug development and evaluation.

The primary goal of patient-focused drug development is to better incorporate the patient's voice in drug development and evaluation, including but not limited to:

- Facilitating and advancing use of systematic approaches to collecting and utilizing robust and meaningful patient and caregiver input to more consistently inform drug development and regulatory decision-making
- Encouraging identification and use of approaches and best practices to facilitate patient enrollment and minimizing the burden of patient participation in clinical trials
- Enhancing understanding and appropriate use of methods to capture information on patient preferences and the potential acceptability of tradeoffs between treatment benefit and risk outcomes
- Identifying the information that is most important to patients related to treatment benefits, risks, and burden, and how to best communicate the information to support their decision making.

[1] Assessment of the Use of Patient Experience Data in Regulatory Decision-Making | FDA, 29Jun2021

Next Steps for CPLD Progress

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CPLD Value Proposition: CPLD consortium is established to tackle to tackle complex LD drug development challenges beyond the scope of any single entity.

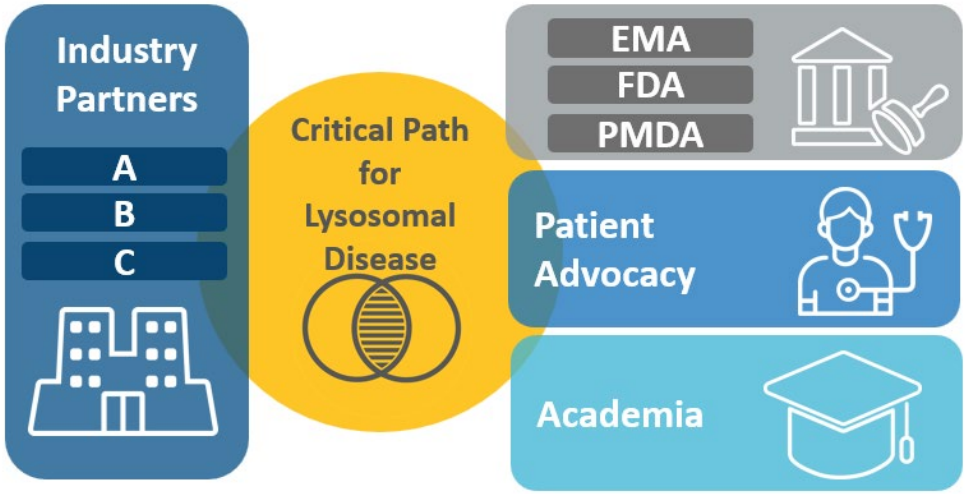
Engagement Optimization: CPLD will focus on bridging scientific gaps in LD drug development and fulfilling unmet regulatory needs. Establishing and enhancing partnerships with diverse stakeholders will be pivotal for the dissemination and application of regulatory science outcomes and biomarker discoveries.

Comprehensive Data Repository: Establish a central database for lysosomal diseases, merging study data, registries, and RWD. Aimed at enriching our knowledge and facilitating research within the Consortium. Includes initiating a data platform for efficient data exchange and management among members.

Strategic Discussions: Continue to identify and implement synergistic solutions that align with our unified mission and leverage CPLD's unique capabilities..

CPLD Value Proposition

- **Stakeholder Engagement**: Building strategic alliances through a collaborative framework
- **Regulatory Collaboration**: Fostering open dialogue and cooperative relationships with regulatory bodies, including FDA DRDMG, with aspirations to include EMA partnerships
- **Leveraging Influence**: Utilizing C-Path's historical impact and strategic positioning
- **Knowledge Sharing**: Facilitating cross-pollination of insights across disciplines
- **Investigative Research**: Pioneering exploratory studies on emerging topics
- **Scientific Synchrony**: Aligning expertise with current scientific trends and needs



CPLD and Precision Medicine: Shaping the future of lysosomal disease drug development

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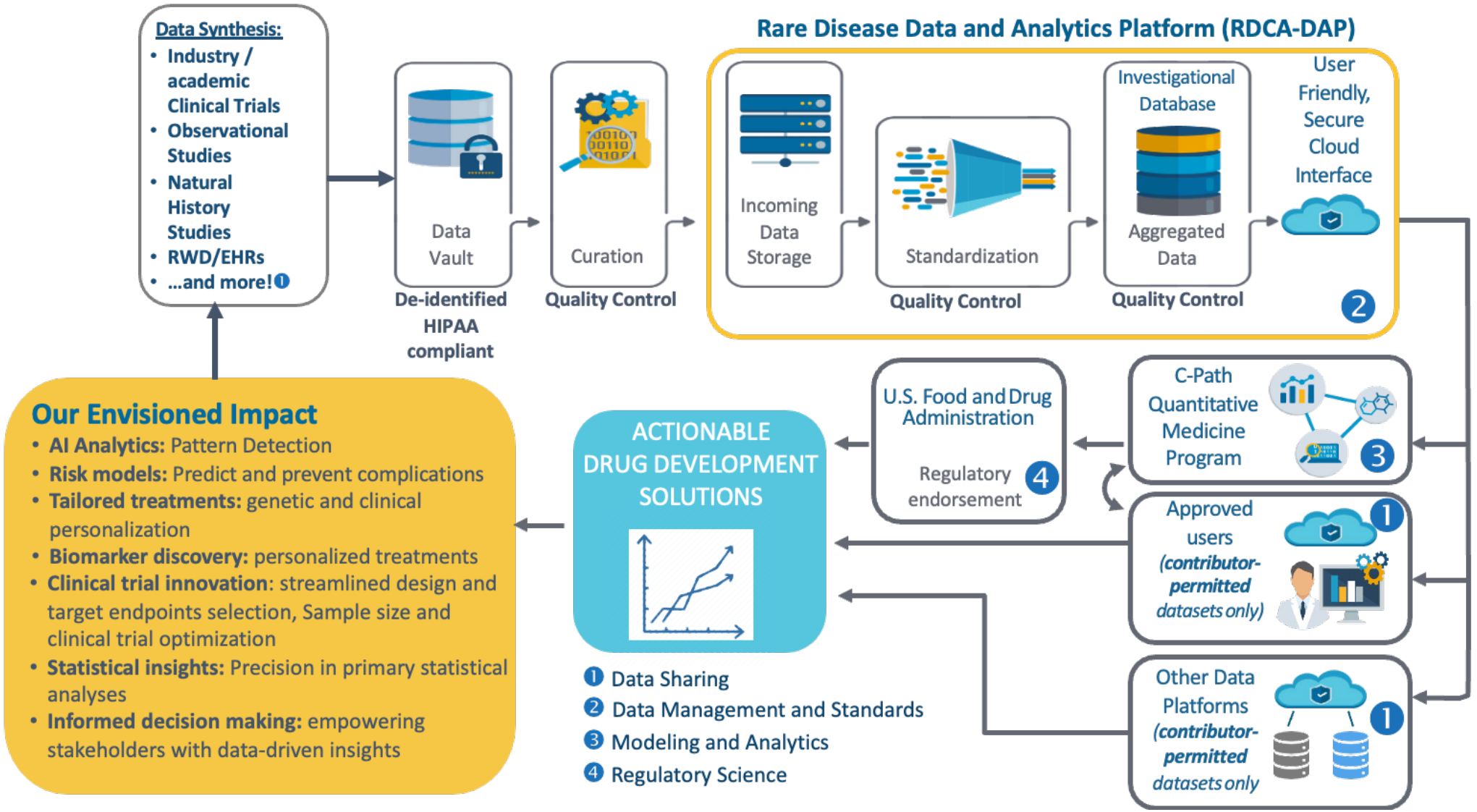

Thank you! Questions?

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For general C-Path enquiries, please contact us at:

info@c-path.org

https://c-path.org

For CPLD enquiries, please contact us at:

cpld@c-path.org

https://c-path.org/programs/cpld/

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