



Advancing Drug Development. Improving Lives. Together.

April 9, 2024

Rare and Orphan Diseases - Quarterly Newsletter

Welcome to the Rare and Orphan Diseases quarterly newsletter. In between major announcements, webinars and meetings, this communication serves to update you on the latest developments within the platform and overall initiative. None of ROD's advancements are possible without the participation of our supporters and data contributors. Thank you.

Introduction

Welcome to the first edition of the Rare and Orphan Diseases Quarterly Newsletter!

You might notice the change from the RDCA-DAP to the Rare and Orphan Disease Newsletter. RDCA-DAP remains central to the success of C-Path's Rare and Orphan Disease Program, but the hope of this communication is to convey the broader efforts at Critical Path Institute's ROD Programs in which RDCA-DAP is actively involved. We strongly believe in the Rare Disease Community and its ability to learn from each other. We hope that this change in scope inspires new ideas and forges new collaborations as you work with C-Path to address unmet needs in drug development. This newsletter will continue to be released in between major announcements, webinars and meetings, this communication serves to update you on the latest developments within the platform and overall initiative. None of ROD's advancements are possible without the participation of our supporters and data contributors. Thank you.

RDCA-DAP Updates

The platform continues to expand since going live in September 2021, containing data for over 33 different rare diseases. More data will be accessible throughout 2024 as outreach efforts continue.

RDCA-DAP currently contains data for the following diseases:

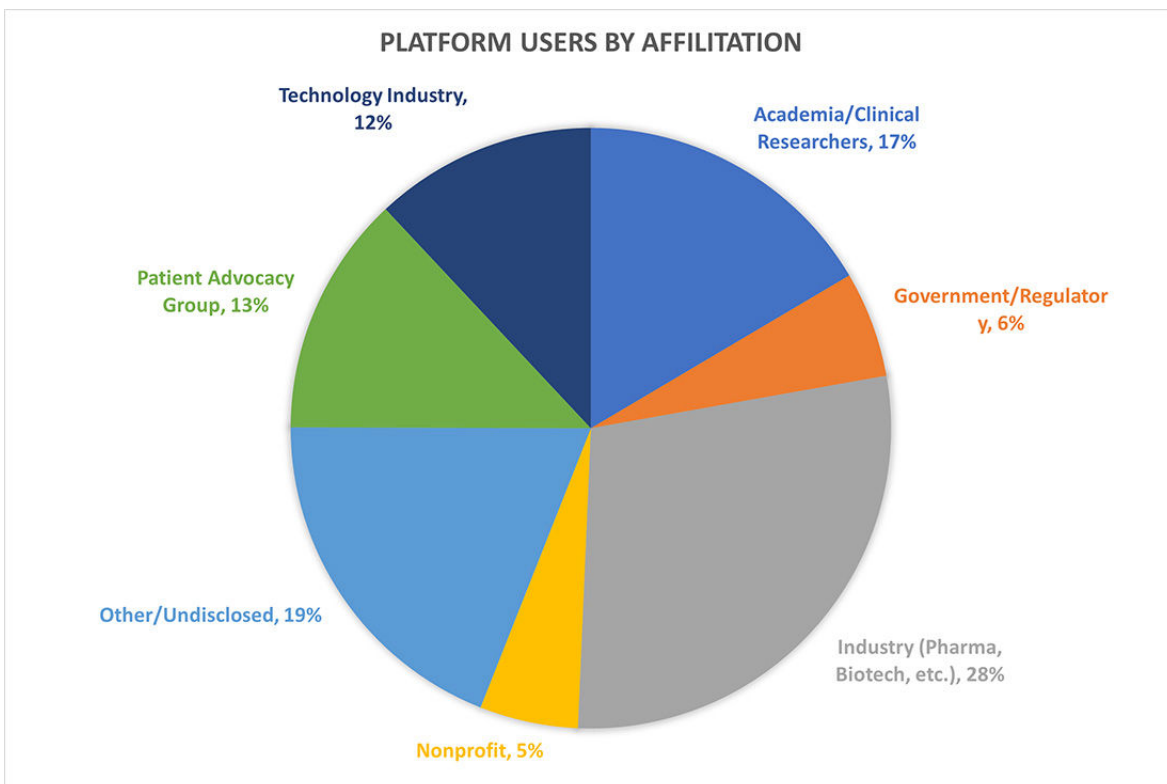
Angelman Syndrome*	Mucopolysaccharidoses (MPS)
CACNA1*	Myotubular or centronuclear myopathy*
Charcot-Marie-Tooth disease	Necrotizing Enterocolitis*
COL6-related dystrophies*	Niemann-Pick Disease
Congenital Hyperinsulinism*	Ocular Melanoma

Desmoid Tumor*	Pemphigus & Pemphigoid*
Duchenne Muscular Dystrophy*	Phenylketonuria (PKU)*
Facioscapulohumeral muscular dystrophy (FSHD)*	Polycystic Kidney Disease
Fibrous Dysplasia disorders*	Prader-Willi Syndrome*
Friedreich's Ataxia*	Progressive Supranuclear Palsy*
GNE Myopathy*	Rare Epilepsies*
Kidney Transplant	Ryanodine Receptor-1 (RYR-1) Related Myopathies*
KIF1A Associated Neurological Disorder (KAND)*	Spinal Muscle Atrophy with Respiratory Distress*
Kleefstra Syndrome	Spinocerebellar ataxias type 1, 2, 3, 6 ,7, 8 & 10
Leigh Syndrome and other mitochondrial disorders*	Sturge-Weber Syndrome*
Lennox-Gastaut Syndrome*	Tuberous Sclerosis*
Mitochondrial Disease*	

*Indicates disease with datasets that are currently discoverable on the platform

Engagement to date:

- 494 approved platform requests
- 29 approved workspaces for external users/research



Task Force Update

Task forces are new initiatives within C-Path intended to work on a focused deliverable that will address a key unmet need and/or bottleneck in drug development. Each task force deliverable will be specific to the respective drug development area, but with a scalable strategy to integrate learnings for other drug development areas and are developed through iterative discussion with Patient Advocacy Groups (PAGs), industry partners and regulators. We anticipate task forces to run for no longer than two years, but timing will fluctuate depending on specific deliverables. At the completion of the deliverable, task forces may cease or move forward focused on a new deliverable. They may also jump-start bigger activities and provide the framework to build a public-private partnership.

ACTIVE TASK FORCES

Progressive Supranuclear Palsy (PSP)

- [Launched](#) December 2023
- Members: Novartis, Cure PSP, The Association for Frontotemporal Degeneration (AFTD), Rainwater Charitable Foundation (RCF), Key opinion leaders
- Database: Natural History and multiple trials (active and placebo arms)
- Deliverable: Drug Development Tool (early Disease Progression Model and Clinical Trial Simulation Tool obtained)

Rare Mitochondrial and Inherited Metabolic Diseases

- [Launched](#) January 2024
- Members: Astellas Pharma, 9+ Patient advocate groups, Key opinion leaders
- Database: Registry, Digital app PRO
- Deliverable: Data aggregation to inform data standardization and collection across diseases

Spotlight – Polycystic Kidney Disease Outcomes Consortium

Founded in 2010, C-Path's **Polycystic Kidney Disease (PKD) Outcomes Consortium** is a collaborative partnership whose research leads to discovery of treatments for PKD. PKDOC brings together key experts and stakeholders from regulators, industry, academia, and patient advocacy to address challenges associated with PKD drug development.

PKD is a genetic disorder that causes clusters of fluid-filled cysts to grow in the kidneys causing them to enlarge and lose function over time. PKD can also cause cysts to develop in the liver and elsewhere in the body and lead to serious complications including high blood pressure and kidney failure. There are two main types of PKD: **Autosomal Dominant PKD (ADPKD) and Autosomal Recessive PKD (ARPKD)**.

Autosomal Dominant PKD (ADPKD) affects more than 600,000 Americans and 12 million people worldwide. Currently, only one FDA-approved drug (Tolvaptan) exists for ADPKD but given its mechanism of action and side effects profile (liver toxicity, polyuria), the need for an improved therapy remains a priority. The clinical course of kidney disease in ADPKD is typically marked by a long period of stable glomerular filtration rate (GFR) due to hyperfiltration despite the continuous expansion of height-adjusted total kidney

volume (htTKV) due to the growth of cysts. Due to the observed stability or slow decrease of GFR even in the presence of ~5-fold change in kidney volume in many patients, clinical trial design in ADPKD is challenging, especially for earlier disease stages.

PKDOC's drug disease trial models, done in conjunction with the PKD Foundation, academic, industry, and regulatory stakeholders, were used to support the regulatory qualification of baseline Total Kidney Volume, or TKV, with or without age inclusion. These efforts create a prognostic enrichment biomarker for ADPKD, to predict a 30% decrease in estimated glomerular filtration rate.

PKDOC has successfully qualified TKV as a prognostic enrichment biomarker with both the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA). Furthermore, the FDA designated TKV as a reasonably likely surrogate marker for disease progression in ADPKD. This marker could serve as an endpoint under an accelerated approval pathway followed by a post-marketing confirmation trial showing an effect on the loss of kidney function.

PKDOC also supports its own database that consists of de-identified data from three ADPKD longitudinal observational patient registries. These data have been standardized and aggregated into a common format using a Clinical Data Interchange Standards Consortium (CDISC) Standard Data Tabulation Model (SDTM) structure. This enables analyses to be performed on a larger expanded dataset. The data covers approximately seven decades of patient visits from the University of Colorado — Denver, Mayo Clinic, and Emory University. In addition, several randomized controlled trial (RCT) datasets (HALT, TAME, ALADIN1) have been ingested.

Autosomal Recessive PKD (ARPKD) is a rare genetic disorder that occurs in about one in 20,000 births, with an estimated 1,500 children and young adults living with ARPKD in the United States.¹ ARPKD can be caused by many different gene variants. The majority of patients with ARPKD have variations in the PKHD1 gene, which encodes the fibrocystin protein, but variants in other genes can also be involved as well. ARPKD is a progressive disease that affects the kidneys as well as the liver. The severity of both liver and kidney symptoms are highly variable and there is not a clear relationship between the severity of kidney and liver disease. Current ARPKD treatments only manage disease symptoms and cannot prevent or stop the declining kidney and liver function. The development of targeted therapies for this disease are limited by ARPKD's rare disease status and clinical variability.¹

Most recently, PKDOC and the PKD Foundation held the first-ever Externally-Led Patient Focused Drug Development (EL-PFDD) meeting on ARPKD with the objective of connecting the ARPKD community with FDA to provide for a collaborative dialogue to identify specific unmet needs from the perspectives of patients, families, caregivers, and patient advocates. This dialogue is a key factor in envisioning the specific drug development tools that could accelerate drug development for ARPKD.

Currently, PKDOC is continuing its efforts in three areas of focus including: 1) novel biomarker development (prognostic and response biomarkers including pharmacodynamic and surrogate biomarkers) in ADPKD, 2) disease progression models and clinical trial simulator (CTS) tools for ADPKD, and 3) patient-reported outcomes (PRO) tools for ARPKD. A series of publications describing the current regulatory concepts and avenues being pursued in the space were recently published by PKDOC stakeholders and can be found here:

[Drug Development for Cystic Kidney Diseases : Clinical Journal of the American Society](#)

[of Nephrology \(lww.com\)](#)

[Perspectives on Drug Development in Autosomal Recessive Polycystic Kidney Disease : Clinical Journal of the American Society of Nephrology \(lww.com\)](#)

[Perspectives on Drug Development in Early ADPKD : Clinical Journal of the American Society of Nephrology \(lww.com\)](#)

[Current Challenges and Perspectives on Developing a Clinical Trial Design for ADPKD : Clinical Journal of the American Society of Nephrology \(lww.com\)](#)

[Polycystic Kidney Disease Drug Development: A Conference Report - Kidney Medicine \(kidneymedicinejournal.org\)](#)

[¹Voice of the Patient Report - Externally-led Patient-Focused Drug Development Meeting \(EL-PFDD\)](#)

For more information about PKDOC please [click here](#) to see our webpage.

Or feel free to contact:

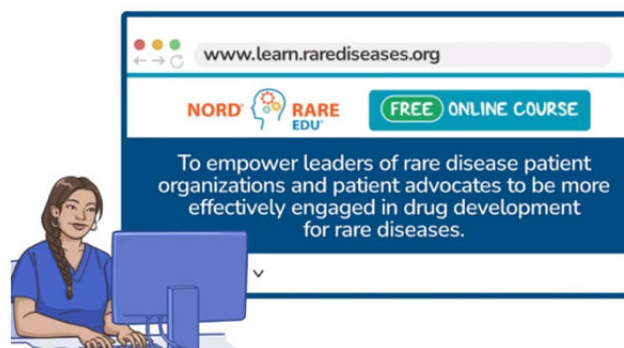
Sorin Fedeles, PhD, MBA, Executive Director, PKDOC sfedeles@c-path.org
Wendy Vanasco, Senior Project Manager, PKDOC wvanasco@c-path.org

NORD Corner



NORD[®]
National Organization
for Rare Disorders

Did you know drug development begins long before the first patient enrolls in a clinical trial? Learn about the drug development process through NORD's free online course series, "Rare Disease Drug Development: What Patients and Advocates Need to Know," available in both English and Spanish! This course is free and open to all and can be completed at your own pace, even on your mobile device.



Part One: Foundations and Pre-Clinical Research focuses on the importance of the pre-clinical period and how patients can participate. Visit learn.rarediseases.org to start learning today and work toward your certificate of completion!



The National Organization for Rare Disorders (NORD) is bringing its beloved Living Rare, Living Stronger Patient and Family Forum to the West Coast! Taking place in Los Angeles and virtually this June 7-8, the Living Rare Forum is an opportunity for people living with rare diseases and their families to come together, often for the first time, to gain practical knowledge on how to manage their health and live their best rare lives. Attendance is free for patients and caregivers, and childcare will be offered on premises. **View the event agenda and register to attend at livingrare.org.**



The National Organization for Rare Disorders (NORD) invites you to the 2024 Rare Impact Awards, coming to Universal Studios, Hollywood on June 8! This annual gala celebrates and honors the individuals and organizations driving progress and pioneering advancements in rare disease treatment and care. **Tickets to this event are on sale**

now – reserve your table today at rareimpact.org.

Announcements and Consortium News

March 28 - [C-Path Launches Clinical Trial Simulator for Duchenne Muscular Dystrophy Research](#)

March 25 – [C-Path to Spearhead New Task Force Dedicated to Accelerating Drug Development for Progressive Supranuclear Palsy](#)

March 8 – [Rare Neurodegenerative Disease Efforts Under the Act for ALS](#)

February 1 – [In a significant step to enhance research efforts for SCN2A-related autism and epilepsy, Critical Path Institute \(C-Path\) and FamilieSCN2A are pleased to announce a new data sharing agreement.](#)

January 11, 2024 – [Critical Path Institute \(C-Path\) today announced the launch of a task force focused on accelerating drug development for mitochondrial and inherited metabolic diseases](#)

January 9, 2024 – [Critical Path Institute \(C-Path\) today announced that Klaus Romero, M.D., M.S., FCP, has been named its new Chief Executive Officer.](#)

December 12, 2023 – [C-Path \(Critical Path Institute\) is thrilled to announce a significant addition to its Rare Disease Cures Accelerator-Data and Analytics Platform \(RDCA-DAP®\). Children’s Hospital of Orange County \(CHOC\) has generously contributed clinical trial data related to mucopolysaccharidosis \(MPS\), reinforcing the power of collaboration in advancing rare disease research.](#)

December 12, 2023 – [Critical Path Institute \(C-Path\), a leader in advancing rare disease research, is pleased to announce a data collaboration with PicnicHealth, a patient-centered healthcare evidence generation company.](#)

Webinar Series 2024

RARE AND ORPHAN DISEASE PROGRAMS
CRITICAL PATH INSTITUTE

RDCA-DAP®
Rare Disease Cures Accelerator
Data and Analytics Platform

WEBINAR SERIES

**The Use and Development of DHTs
with Patient Advocacy Groups**

Thurs | May 23
10 AM ET

REGISTER NOW

Laurent Servais, MD, PhD
University of Oxford, UK, and University of Liège, Belgium

Dr. Laurent Servais, Oxford University, will provide an overview of Actimyo and relevant learnings from use cases across rare disorders spanning different degrees of complexity and readiness.

PAG leaders will speak to their experience based on stage of development and the ability of Actimyo to assess individuals with a neuromuscular disorder or non-NMDs (e.g., DMD,

Angelman Syndrome, and CTNNB1).

March 14th: [Improving Data Collection for Rare Epilepsies: Case example from the TSC Natural History Database](#)

This webinar discussed how better standardization of data and data collection is needed in rare epilepsies.

February 15th: [Understanding disease progression models: What are they, why are they useful, and how are they applied? A high-level overview](#)

Summary: Disease progression modeling synthesizes statistics with disease knowledge and data to inform predictions and understanding of disease course in populations and subpopulations and is commonly used in model-informed drug development. This webinar looks to break down the high-level ideas behind disease progression models, exploring what they are, what they do, and why they are useful

***You can now view all 2023 RDCA-DAP Webinars on demand [here](#)**

For more information about Rare and Orphan Diseases, visit: <https://c-path.org/area-of-focus/rare-and-orphan-diseases/>

Help support our mission.

MAKE A GIFT TODAY



1840 E River Rd, Suite 100 | Tucson, AZ 85718 | (520) 547-3440 | info@c-path.org
c-path.org



[FDA Acknowledgment](#)

This email was sent to [email address suppressed]. If you are no longer interested you can [unsubscribe instantly](#).