Advancing Drug Development. Improving Lives. Together.

March 31, 2025

RARE/ORPHAN AND PEDIATRIC DISEASE PROGRAMS: QUARTERLY NEWSLETTER

Welcome to the Rare/Orphan and Pediatrics Disease Programs quarterly newsletter. In between major announcements, webinars and meetings, this communication serves to update you on the latest developments within C-Path's rare/orphan and pediatrics disease programs and the RDCA-DAP platform. None of C-Path's advancements are possible without the participation of our members, collaborators and data contributors. Thank you.

Introduction

As spring blossoms and conference season kicks off in earnest, we are excited to share updates from our team. February is marked as Rare Disease Month, with February 28 designated as Rare Disease Day. The month provided a time to spotlight the voices and experiences of more than 300 million people, and their loved ones, worldwide living with a rare disease. C-Path is proud of the important work we do leading collaborations that accelerate drug development for those living with rare diseases.

In March, we are celebrating National Kidney Month, new team members and upcoming webinars and conferences. We're looking forward to the opportunities ahead and the upcoming events that will bring us closer as C-Path celebrates 20 years of impact 2025. Read on to catch up on our latest developments and what's in store for the months ahead.

SPOTLIGHT: National Kidney Month

PKDOC: Advancing Research and Innovation in Kidney Disease

March marks National Kidney Month, a time to raise awareness about kidney health and highlight the groundbreaking efforts in kidney disease research and treatment. The Polycystic Kidney Disease Outcomes Consortium (PKDOC) continues to lead initiatives that drive progress in understanding and treating Autosomal Dominant Polycystic Kidney Disease (ADPKD) and Autosomal Recessive Polycystic Kidney Disease (ARPKD).

Accelerating Research in ADPKD

PKDOC has long been at the forefront of ADPKD research, playing a pivotal role in the qualification of Total Kidney Volume (TKV) by the U.S. Food and Drug Administration (FDA) as a prognostic enrichment biomarker, followed by its designation as a reasonably

likely surrogate marker. Furthermore, TKV received a positive Qualification Opinion from the European Medicines Agency. These successes have set the stage for continued advancements in biomarker validation and clinical trial optimization.

One of PKDOC's key initiatives is advancing the Fit-for-Purpose pathway to obtain FDA endorsement for a model-based clinical trial simulation platform for ADPKD. This platform is designed to track the progression of estimated glomerular filtration rate and TKV over time in ADPKD patients by facilitating an ongoing global participant-level data sharing initiative to integrate data from relevant longitudinal observational studies, natural history studies, and clinical trials.

In addition, PKDOC is investigating urinary monocyte chemoattractant protein-1 as a potential prognostic biomarker for ADPKD and conducting a systematic review of fluid biomarkers to evaluate markers found in blood, urine, and other bodily fluids. These initiatives are paving the way for improved disease monitoring and therapeutic development.

Amplifying the Patient Voice in ARPKD Research

A significant milestone in PKDOC's mission was the Externally-led Patient-Focused Drug Development meeting on ARPKD, hosted in collaboration with the PKD Foundation in late 2023 and continuing into 2024. This landmark event united ARPKD patients, caregivers, researchers, and FDA representatives to document patient experiences, highlight unmet medical needs, and shape the future of ARPKD drug development. Insights from this meeting will play a key role in continued efforts to develop PRO tools and instruments that can enhance clinical trial design, ensuring patient voices remain central to therapeutic advancements.

Expanding Beyond PKD – A New Focus on ADTKD

PKDOC has recently launched a collaborative project with Wake Forest University to advance drug development tools for Autosomal Dominant Tubulointerstitial Kidney Disease (ADTKD), a rare genetic kidney disorder that leads to progressive kidney failure due to mutations affecting tubulointerstitial cells. Unlike other kidney diseases that primarily cause cysts or glomerular damage, ADTKD predominantly affects the tubules and interstitial tissue, leading to chronic kidney disease and, in many cases, end-stage renal disease in adulthood.

Since ADTKD is often misdiagnosed, genetic testing is essential for accurate identification. Currently, no targeted treatments exist, but through Wake Forest's expertise in ADTKD research and patient registry and C-Path's expertise in model-informed drug development and biomarker qualification, this collaboration aims to accelerate the discovery and potential regulatory qualification of ADTKD biomarkers through engagement with the FDA and other regulatory bodies.

For more information on PKDOC's initiatives, visit C-Path's website.

RDCA-DAP UPDATES

The platform currently contains data for over 41 different rare diseases. More data will be accessible throughout 2025 as outreach efforts continue.

RDCA-DAP data includes:

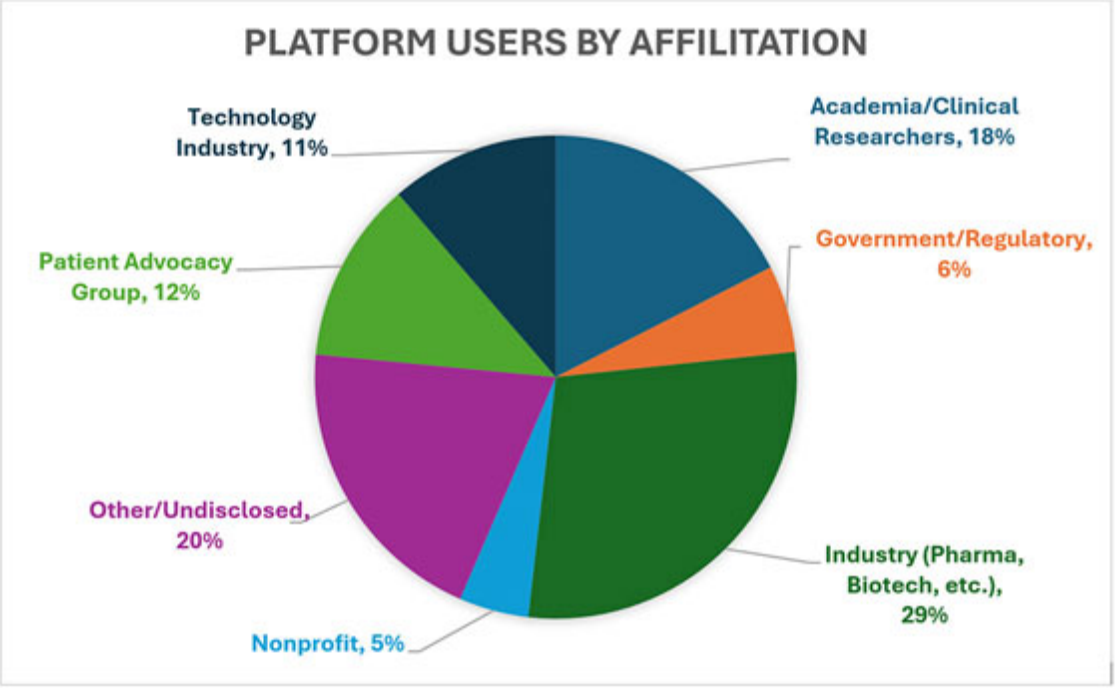
Disease	
Amyotrophic Lateral Sclerosis*	Angelman Syndrome*
CACNA1*	Charcot-Marie-Tooth disease*

Choroideremia	COL6-related dystrophies*
Congenital Hyperinsulinism*	Cystic Fibrosis
Desmoid Tumor*	Duchenne Muscular Dystrophy*
Facioscapulohumeral muscular dystrophy*	Fibrous Dysplasia Disorders*
Friedreich's Ataxia*	GNE Myopathy*
hnRNPH2-related disorders*	Kidney Transplant
KIF1A Associated Neurological Disorder*	Kleefstra Syndrome*
Leigh Syndrome and other mitochondrial disorders*	Lennox-Gastaut Syndrome*
Limb-Girdle Muscular Dystrophy	Malan Syndrome
Mitochondrial Disease*	Mucopolysaccharidoses*
Myhre Syndrome	Myotubular or centronuclear myopathy*
Necrotizing Enterocolitis*	Niemann-Pick Disease
Ocular Melanoma*	Pemphigus & Pemphigoid*
Phenylketonuria*	Polycystic Kidney Disease*
Prader-Willi Syndrome*	Progressive Supranuclear Palsy*
Rare Epilepsies*	Ryanodine Receptor 1 Related Myopathies*
SCN2A-related disorders	Spinal Muscle Atrophy with Respiratory Distress*
Spinocerebellar ataxia types 1, 2, 3, 6, 7, 8 & 10	Sturge-Weber Syndrome*
Tuberous Sclerosis*	VCP Disease

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

Engagement to date:

- 669 approved platform requests
- 49 active workspaces for external users/research



NORD CORNER

NORD Breakthrough Summit® Research Poster Applications Open

The 2025 NORD Rare Diseases + Orphan Products Breakthrough Summit® will be held in **Washington, D.C., October 20-21, 2025.** This event brings together thought leaders in the biopharma industry, academia, patient advocacy, and government for the latest updates on rare disease diagnosis, drug development, research, patient engagement, public policy, and market accessibility of orphan products.

NORD is accepting poster abstracts featuring innovative rare disease research. **Submit your research poster abstract by Friday, July 18. Click here to review the Abstract Submission Guidelines and submit** your proposal.

Introducing NORD® Claim Your Care

After an initial debut in November 2024, focusing on insurance open enrollment, the NORD® Claim Your Care program will now provide comprehensive resources on different health insurance options, how they work, and step-by-step guidance on filing appeals. These expanded materials will help ensure patients and caregivers have the tools they need to navigate their health care coverage with confidence.

Available to the public and to NORD Member organizations, the NORD Claim Your Care program was created to help empower you to better advocate for patients, reduce barriers to care, and provide direct support to those in need. More exciting developments are on the horizon, but in the meantime, we encourage you to explore the program at ClaimYourCare.org and share it with your community to ensure individuals living with rare diseases and chronic conditions receive the support they deserve.

ANNOUNCEMENTS AND CONSORTIUM NEWS

Welcome Sheryl Denker, CPA-1 Scientific Director

Sheryl is grateful to bring her passions for scientific innovation, strategic communications, and stakeholder engagement to C-Path's' Rare/Orphan Disease Programs. With a foundation in cell biology and a career spanning the biomedical sciences ecosystem – from academia to industry to publishing – she is ready to tackle the challenge! When not asking fellow C-Path colleagues questions that start with where, how, or who, she can be found walking her dog in Golden Gate Park or in a dance studio.

Save the Date, C-Path's Global Impact Conference is set for Sept. 9-11, in Washington, D.C.

February 26: Transforming Data into Breakthroughs: 5 Years of RDCA-DAP Journey and Impact

February 20: Vivli and RDCA-DAP: Data Platform Partnerships to Promote Rare Disease Data Sharing

February 18: C-Path's CPA-1 Consortium Welcomes Newest Members Kamada, Sanofi

February 17: CP-RND ALS Public-Private Partnership Public Forum

Webinar Series 2025

Thursday, April 17, noon ET | Register now for our upcoming webinar, 'ACE Inhibitors as a Cardioprotective Treatment in Dystrophinopathies.'

View Now: Vivli and RDCA-DAP: Data Platform Partnerships to promote Rare Disease Data Sharing

C-Path collaborator Julie Wood, Chief Operating Officer at Vivli, led this webinar, highlighting Vivli's mission as an independent nonprofit dedicated to global data sharing and analytics. She explored how Vivli and RDCA-DAP are working together to advance data sharing in rare diseases. Following her presentation, panelists from Vivli and C-Path engaged in a dynamic discussion on platform-to-platform collaboration and strategies to enhance data accessibility, concluding with a live Q&A. C-Path participants included Richard Liwski, Alexandre Bétourné, and Ramona Walls.

**You can view all 2024 ROD Webinars on demand here.*

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

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FDA Acknowledgment