Critical Path Institute Annual Report FY 2023

CRITICAL PATH INSTITUTE

ANNUAL REPORT 2023

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Our Mission

"C-Path leads collaborations that accelerate drug development, advancing better treatments for people worldwide."

A Letter From Our Leadership

Klaus Romero, MD, MS, FCP

Dear Friends and C-Path Supporters,

It is with great pride that we reflect on the significant milestones C-Path has realized this past year in advancing drug development worldwide, a journey marked by dedicated collaboration and inspirational work. Our concerted efforts have shaped innovative scientific and regulatory pathways, significantly accelerating the development for therapies to those in need.

C-Path's dynamic growth is driven by pioneering leadership, diverse stakeholders, and a strong spirit of unwavering commitment. Together, we have addressed formidable barriers in the development of therapies, which have resulted in remarkable process improvements and groundbreaking achievements worldwide.

Our collaborative efforts, which bring together experts from regulatory agencies, research institutions, advocacy groups, and the pharmaceutical industry, have been a crucible for innovation.

This year, in partnership with the pharmaceutical industry and FDA, our collaborations drove crucial progress in drug development for Alzheimer's disease, which now benefits from the regulatory approval of the first two disease modifying medications.

Similarly, the transformation of data into actionable solutions led to the first-ever endorsement of a quantitative drug development tool by the European Medicines Agency (EMA) for Parkinson's disease. This tool allows researchers to run computer simulations of multiple trial design options for drug candidates to treat this condition, prior to clinical trial dosing.

This year we also celebrated an EMA endorsement of the first-ever composite biomarker endpoint ("iBox scoring system") for kidney transplant trials, while novel safety biomarkers addressing the early detection of acute drug-induced pancreatic injury also received a positive FDA response.

2023 also marked a new peak in our data integration efforts, now representing close to 700,000 individual records. Notably, C-Path hosts the world's largest standardized real-world database in Friedreich's ataxia, which directly fueled the first-ever treatment for this rare neurodegenerative condition in March.

Moreover, in April, C-Path's Cure Drug Repurposing Collaboratory (CDRC) deployed Edge Tool for the purpose of standardizing electronic health record data for specific applications in COVID-19 and sepsis and is further scalable to many more indications.

In 2023, we also launched the Rare Disease Clinical Outcome Assessment Resource (RD-COAR), a searchable database that simplifies COA selection for use in rare disease drug development.

Continuing the strategic impact of our activities in Europe, we expanded the footprint of our nonprofit operations in Amsterdam, furthering our global mission to impact and innovate in public health. This key development not only enhances our activity across Europe but also broadens the reach of our global operations.

Our journey continues with unwavering dedication. C-Path's future goals include strengthening our existing core competencies to embrace exciting frontiers in gene and cell-based therapies, translational sciences, digital health technologies, decentralized trials and artificial intelligence.

We extend our deepest gratitude to you, our partners and friends. Your expertise, support, and advocacy are not just the foundation of our past achievements but also the pillars of our collaborative endeavors. Together, we are not only envisioning an innovative future in medical solutions but actively constructing it.

Thank you for joining us on this exceptional journey.

With our sincerest appreciation,
Klaus Romero, MD, MS, FCP
Chief Executive Officer

Our Impact

It takes too long and it costs too much to take a discovery from the lab through the development process to demonstrate efficacy and safety, and achieve a regulatory-approved therapy.

C-Path forms collaborations comprised to generate tools and solutions that help address specific bottlenecks in the drug development process.

Our solutions have contributed to the achievement of major healthcare advancements, including the first new tuberculosis treatment in 50 years, the first-ever disease modifying drugs for conditions like Alzheimer's, polycystic kidney disease and Friedreich's ataxia, as well as the first-ever product to delay the onset of type 1 diabetes.

C-Path is responsible for the first-ever regulatory-endorsed clinical trial simulators, first-in-class biomarkers, transformative patient-centric endpoints, and the largest integrated individual-level databases in both rare and non-rare diseases. We are currently working on these types of solutions and resources for over 20 therapeutic areas.

A T1D Consortium Impact Story: Ryan Eberwine

Ryan Eberwine, a Drug Development Scientist at IGM Biosciences, has been living with type 1 diabetes for 24 years, dedicating his career to advancing treatments for autoimmune diseases. His personal journey with T1D began with a regimen of multiple daily insulin injections and frequent blood sugar checks, a routine marked by constant uncertainty. Over the years, Ryan has not only witnessed but also contributed to the transformative advancements in T1D management. These include the evolution from basic insulin pumps to cutting-edge technologies like the Dexcom G6 continuous glucose monitoring system, integrated with Tandem insulin pumps. This progress represents a significant leap, moving from manual glucose monitoring to hybrid closed-loop systems that automatically adjust insulin doses.

In his professional role, Ryan's involvement with C-Path's T1D Consortium exemplifies his commitment to collaborative drug development. T1DC, a unique public-private partnership, brings together various stakeholders in the T1D community, fostering noncompetitive dialogue and unified efforts to advance treatment options. Ryan's experience as both a scientist and a patient provides him with a unique perspective, enabling him to effectively translate complex scientific data into actionable strategies. He believes that the methodologies developed in T1D research can serve as a blueprint for tackling other autoimmune diseases, focusing on early intervention strategies. Ryan's story is not just about personal resilience in the face of a chronic condition but also highlights the significant impact individuals can have in the realms of medical research and advocacy, driving progress in the treatment and understanding of autoimmune diseases.

Ryan Eberwine

Ryan Russell

Colin Werth

A Duchenne Regulatory Science Consortium Impact Story: Ryan Russell and Colin Werth

Ryan Russell and Colin Werth are not just individuals living with Duchenne muscular dystrophy; they are pivotal figures in the advocacy and support community for the condition. Besides their active roles in C-Path's Duchenne Regulatory Science Consortium, both serve on the Adult Advisory Committee of Parent Project Muscular Dystrophy, with Colin as its President. Additionally, Ryan contributes as a Senator for Patients Rising Now, is the Founder of Life on Positivity, and an Ambassador for the Jett Foundation. Their careers are equally dynamic, with Colin thriving in IT and Ryan as a Life Coach, armed with a Ph.D. in psychology. Embracing life to its fullest, Ryan has even taken up skiing and looking forward to conquering the mountains this winter.

However, their most impactful roles lie in being advocates and mentors for others with DMD, a condition characterized by challenges like muscle stiffness, altered gait, and a shortened life expectancy. Ryan, who initially struggled to accept his diagnosis, now uses his experiences to guide the younger generation and parents within the Duchenne community, helping them navigate a path he once found daunting. His efforts to connect with other organizations post-Ph.D. have amplified his voice, transforming his personal journey into a beacon of hope and possibility.

Similarly, Colin's advocacy extends into ensuring that the pharmaceutical industry hears the voices of those living with DMD. His active participation in patient sessions and dialogues with drug developers and researchers is pivotal in shaping more effective clinical trials and treatments. Both Ryan and Colin's recent involvement with C-Path's D-RSC program as advisors further cements their dedication to improving the landscape of DMD treatment, spotlighting the importance of collaborative research and data analysis in tackling the disease's complexities. Their commitment to the cause is unwavering, with hopes that D-RSC's work will lead to a future where DMD is a thing of the past, and until then, they continue to inspire and motivate others to join in making a tangible difference.

FY23 Year in Review

As C-Path enters its 18th year, we are proud to announce that we have surpassed our previous milestones in terms of innovation and impact. Our active programs and consortia have continued to grow in number, encompassing an even wider network of collaborators, members, and organizations. This expansion is a testament to our unwavering dedication to produce real-world, actionable outcomes. Our unique model of collaboration continues to unite industry leaders, scientists, academic researchers, regulatory bodies, and patient groups, driving forward groundbreaking advancements in medical research and treatment development.

A snapshot of our achievements this year, includes:

.01

TRxA Awarded $750,000 for Groundbreaking Drug Development Projects

C-Path's Translational Therapeutics Accelerator (TRxA) proudly announced research grants, totaling $750,000, to advance its first novel drug development projects. Initiated in June 2022, TRxA is a global initiative dedicated to supporting academic scientists in the crucial transition of new therapies from lab to clinic. These grants mark a significant milestone in TRxA's journey, embodying C-Path's commitment to accelerating the path from innovative research to clinical care.

.02

PSTC's New Biomarkers for Pancreatic Injury Receive FDA Support

C-Path's Predictive Safety Testing Consortium (PSTC) achieved a major milestone with the FDA's support for four new pancreatic injury biomarkers. These biomarkers, identified by PSTC's Pancreatic Injury Working Group, are crucial for detecting drug-induced pancreatic injury in phase 1 clinical trials. The FDA's endorsement reflects a significant advancement in enhancing drug safety and efficacy during the early stages of clinical development, reinforcing C-Path's dedication to improving clinical care and drug development processes.

.03

EMA Supports C-Path's Duchenne Clinical Trial Simulation Platform

The European Medicines Agency (EMA) issued a Letter of Support for C-Path's Duchenne Regulatory Science Consortium's (D-RSC) Clinical Trial Simulation Platform for Duchenne muscular dystrophy (DMD). This endorsement recognized C-Path's innovative approach to enhancing clinical trial designs in DMD. The EMA's support underlines the platform's potential in accelerating drug development for this rare, debilitating disorder. This significant achievement reinforces C-Path's commitment to advancing patient care through collaborative and scientific leadership in the Duchenne community.

.04

TTC's iBox Scoring System Gains EMA Qualification for Kidney Transplant Trials

The EMA qualified C-Path's Transplant Therapeutics Consortium's (TTC) iBox Scoring System as a novel secondary endpoint for kidney transplant clinical trials. This qualification, a first in transplant indications, enables the use of iBox for evaluating novel immunosuppressive treatments and improving long-term graft survival. This milestone by TTC represents a significant advancement in kidney transplant research and underscores C-Path's dedication to innovative drug development.

.05

C-Path's Parkinson's Disease Trial Platform Receives EMA Support

C-Path's Critical Path for Parkinson's (CPP) Consortium received a Letter of Support from the EMA for its Model-based Clinical Trial Simulation Platform for Parkinson's disease (PD) studies. This endorsement encourages industry collaboration in data sharing for enhancing drug development methodologies. The platform, a key tool in optimizing the design of PD efficacy studies, marks a significant advancement in the pursuit of new PD therapies.

.06

FDA Boosts C-Path CDRC Initiative for Automated EHR Data Extraction

C-Path's CURE Drug Repurposing Collaboratory (CDRC) received enhanced FDA support through a new Health and Human Services grant to expand CDRC's capabilities to automate data collection from electronic healthcare records for hospitalized COVID-19 patients. Key institutional partners, including Emory School of Medicine, Johns Hopkins University, the Society of Critical Care Medicine and others, collaborated on this initiative.

The project streamlined data extraction pipelines for acute and critical care conditions, providing valuable insights into effectiveness of already FDA-approved drugs against COVID-19 and other infectious diseases, thereby advancing individual-centered research and accelerating the development of effective therapies of existing drugs for new indications.

.07 C-Path Initiates Pre-Consortium for Alpha-1 Antitrypsin Deficiency Development

C-Path launched a pre-consortium collaboration with the FDA's Center for Biologics Evaluation and Research and Center for Drug Evaluation and Research, focusing on accelerating medical product development for alpha-1 antitrypsin deficiency (AATD). Named Critical Path for Alpha-1 Antitrypsin Deficiency (CPA-1), this initiative collaborates with stakeholders to identify and address unmet needs in AATD drug development. Leveraging C-Path's expertise in regulatory science, data management, and individual-focused solutions, CPA-1 aims to foster advancements in treatment options for AATD, a condition linked to liver disease and COPD.

.08 C-Path Launches CP-RND with FDA Grant for Rare Neurodegenerative Diseases

As a result of the Accelerating Access to Clinical Therapies for ALS ACT and the FDA's Action Plan for Rare Neurodegenerative Disease, C-Path was awarded an FDA grant to establish the Critical Path for Rare Neurodegenerative Diseases (CP-RND), a public-private partnership aimed at advancing treatments for rare neurodegenerative diseases. This initiative, supported by both the FDA and NIH, utilizes C-Path's expertise in data integration, biomarkers, clinical outcome assessments, digital health technologies and regulatory science to accelerate drug development in this field. CP-RND represents a significant step forward in collaborative efforts to improve therapies for conditions like amyotrophic lateral sclerosis (ALS), leveraging cutting-edge science and diverse stakeholder engagement to address the urgent needs of patients and families affected by these diseases. Additional drug development efforts in Huntington's disease and inherited ataxias are also supported by two consortia within CP-RND: the Huntington's Disease Regulatory Science Consortium (HD-RSC) and Critical Path to Therapeutics for the Ataxias (CPTA) Consortium, respectively. HD-RSC is focused on developing and validating clinical endpoints in early disease stages and CPTA is working to develop a biology based integrated staging system for spinocerebellar ataxias.

C-Path in Europe

In the past year, C-Path has significantly expanded its global reach and proudly celebrates a series of significant achievements that highlight its pivotal role in advancing regulatory science and accelerating global health solutions.

With a focused nonprofit European base, C-Path is now better equipped to initiate and lead international collaborations, drawing on diverse expertise and resources to a accelerate the pace of medical innovation. Our strategic expansion and global integration efforts underscore our unwavering dedication to advancing healthcare solutions.

Showcasing strategic partnerships, regulatory excellence, and a key operational integration, the following stand out as significant achievements for C-Path's work in Europe in FY23:

A Year of Milestones in Global Drug Development

C-Path Europe achieved notable successes this year, receiving two EMA Qualification Opinions and two Letters of Support for vital drug development initiatives. These accomplishments in T1D, kidney transplant, Parkinson's, and Duchenne muscular dystrophy trials underscore C-Path's influence in enhancing regulatory science and accelerating global health solutions.

C-Path Unifies European Operations to Enhance Global Health Initiatives

C-Path completed the integration of its Dublin office into the Amsterdam-based nonprofit, marking a strategic expansion in Europe. This unification boosts C-Path's ability to influence global public health positively by consolidating expertise, data, and resources. The integration signifies C-Path's commitment to fostering worldwide consensus and advancing regulatory science. This move not only strengthens C-Path's presence in Europe but also bolsters its global operations, ensuring greater efficiency and effectiveness in developing medical solutions. Through this enhanced European platform, C-Path continues to lead in collaborative efforts for improved global health outcomes and accelerated drug development.

C-Path Partners with WHO to Advance Paediatric Medicine Development

C-Path joined forces with the World Health Organization's Global Accelerator for Paediatric Formulations (GAP-f) to address the critical shortage of paediatric medicines. This partnership marks a significant step in C-Path's commitment to improving global health, particularly for children. Through this

collaboration, C-Path will contribute to the Clinical Research Working Group and the GAP-f Paediatric Data Hub, leveraging its expertise in regulatory science to enhance access to essential medicines for children. This initiative aligns with C-Path's mission to expedite drug development, to ensure that paediatric needs are prioritized and met with effective, safe, and tailored treatments.

C-Path Joined 'Rare Disease Moonshot' to Accelerate Research in Rare Diseases

C-Path teamed up with six other organizations in the 'Rare Disease Moonshot' initiative, launched at the European Health Summit. This collaborative effort aims to revolutionize research and development for rare and paediatric diseases. By pooling resources and expertise, the coalition is committed to breaking down research barriers and fostering collaborations to enhance treatment options for rare diseases. The initiative aligns with C-Path's dedication to improving individual care and expediting drug development, focusing on diseases with significant unmet medical needs and no existing therapies.

As C-Path continues to expand, our European team is established in a pivotal role across all C-Path programs and consortia and is well-integrated into the overarching framework of C-Path. These efforts contribute significantly to our global mission to foster innovative health solutions and transformative medical research.





By the Numbers

30 dedicated pre-competitive **collaborations** that collectively accelerate drug development in areas of unmet need

Combined **36 Qualifications, Endorsements** and **Letters of Support** from FDA, EMA and PMDA

Tuberculosis

C-Path solutions were key in approvals of new drugs and regimens, reigniting this **$2B** market

Polycystic Kidney Disease

FDA-endorsed surrogate imaging endpoint

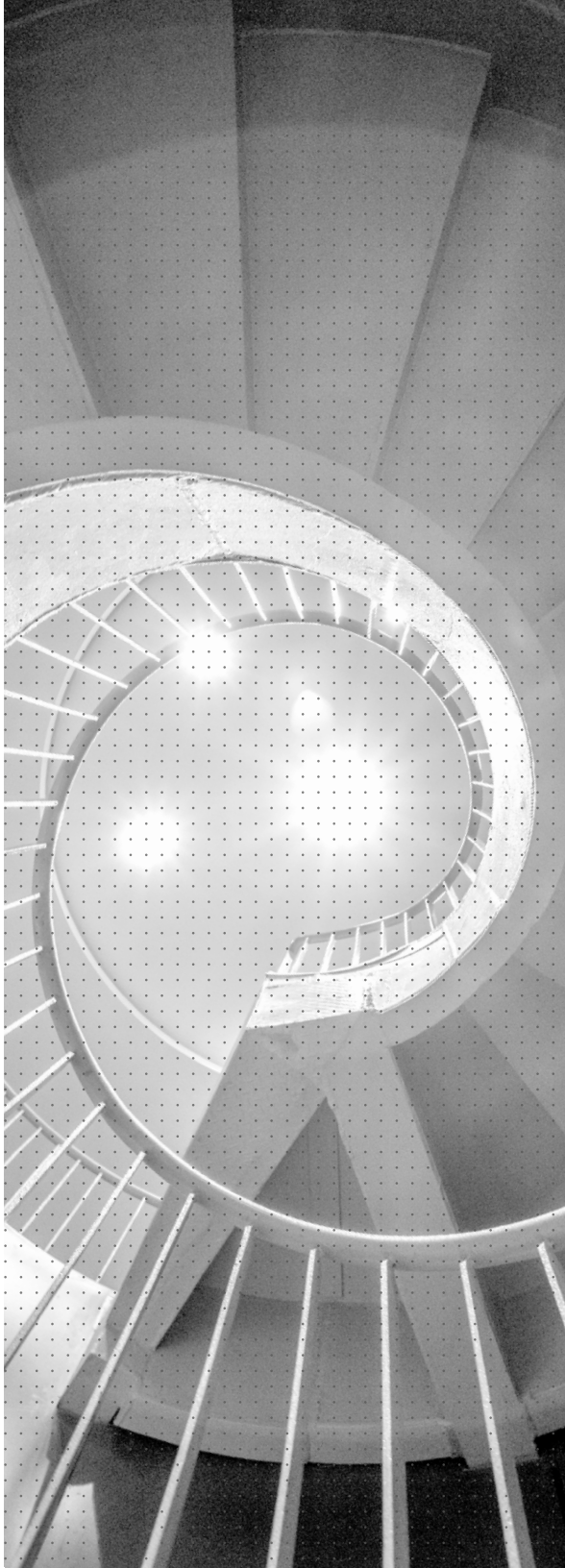
FDA-qualified prognostic biomarker for use in clinical trial patient selection

Roadmap to approval of novel drugs addressing the PKD market of **$450+ million**

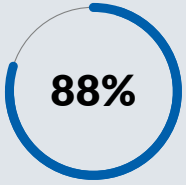
Alzheimer's Disease

Transformative disease modeling tools endorsed by FDA and EMA, allowing companies to successfully address a **$5B** market

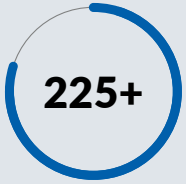
Agency letters of support for exploratory prognostic biomarkers to assist with clinical trial patient selection



C-Path Expertise



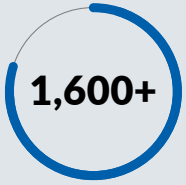
of C-Path directors hold doctorate degrees



public presentations each year

peer-reviewed publications

of combined experience working at regulatory agencies



science and data contributors

400+ Strategic Partnerships

AbbVie	NORD
Alzheimer's Association	Novartis
Duke University	Novo Nordisk
EMA	Oxford University
FDA	Parkinson's UK
JDRF	Pfizer
Johns Hopkins University	Roche
Johnson & Johnson	Sanofi
Janssen	Takeda
Merck & Co.	Tufts University
The Michael J. Fox Foundation for Parkinson's Research	University of Arizona
Newcastle University	University of Florida

Find a full list of strategic partners at c-path.org/c-path-collaborators.

Core Excellence

C-Path's commitment to fostering collaborative solutions in drug development is rooted in the sharing of information and data within a neutral environment. Established in 2005, the Institute has significantly expanded its expertise and achieved excellence in five key areas:

Data Management and Standards

Developing and implementing cutting-edge data management practices and universal standards.

Biomarker Research

Identifying and validating biomarkers to enhance drug development efficiency.

Modeling and Analytics

Utilizing state-of-the-art modeling techniques and analytical tools for more precise predictions and evaluations.

Clinical Outcome Assessments

Crafting and refining tools for accurate and meaningful measurement of clinical outcomes.

Regulatory Science

Advancing the field of regulatory science to streamline the review and approval processes.

These core competencies lay the groundwork for C-Path's mission to facilitate informed decision-making in drug development and regulatory review. With a primary focus on neuroscience, immunology and inflammation, infectious diseases, translational and drug safety sciences, pediatrics, and rare and orphan diseases, C-Path continues to drive innovation and progress in the quest for more effective and safer medical solutions.

Financials

ASSETS

Cash and Cash Equivalents	$	20,311,435
Certificates of Deposit	$	—
Accounts Receivable	$	4,391,846
Property and Equipment, Net	$	41,740
Other	$	2,197,871
Total Assets	**$**	**26,942,892**

LIABILITIES AND NET ASSETS

LIABILITIES

Accounts Payable	$	1,326,792
Accrued Expenses	$	1,266,463
Deferred Revenue*	$	6,978,466
Deferred Rent	$	2,105,301
Total Liabilities	**$**	**11,677,022**

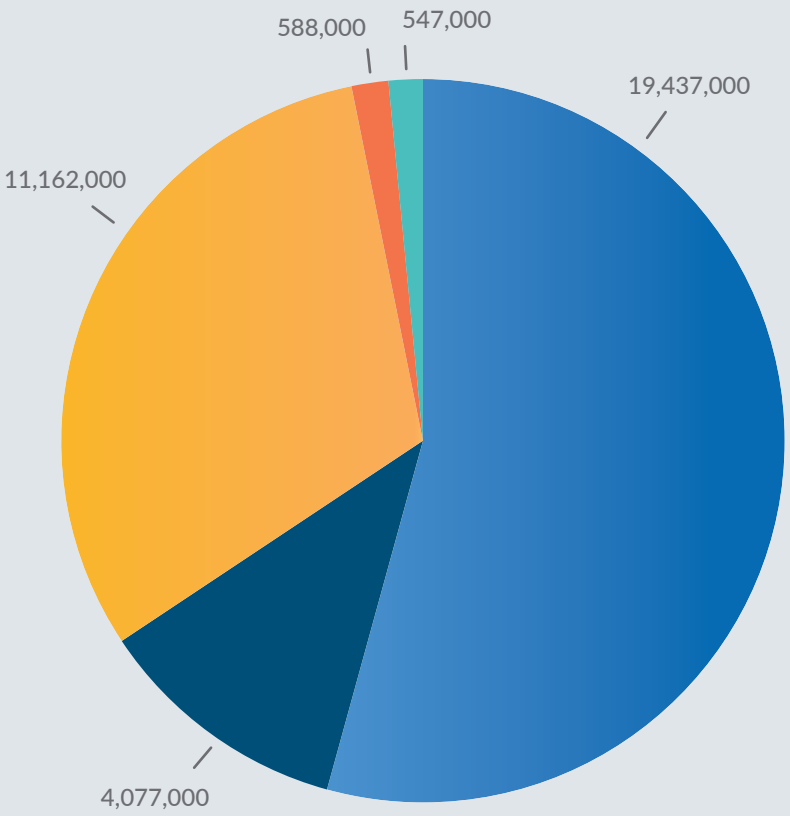
NET ASSETS

Undesignated	$	4,096,742
Board Designated**	$	4,045,065
Coordinating committee designated	$	2,770,723
Property and Equipment	$	41,740
Donor Restricted	$	4,311,600
Total Net Assets	**$**	**15,265,870**
Total Liabilities and Net Assets	**$**	**26,942,892**

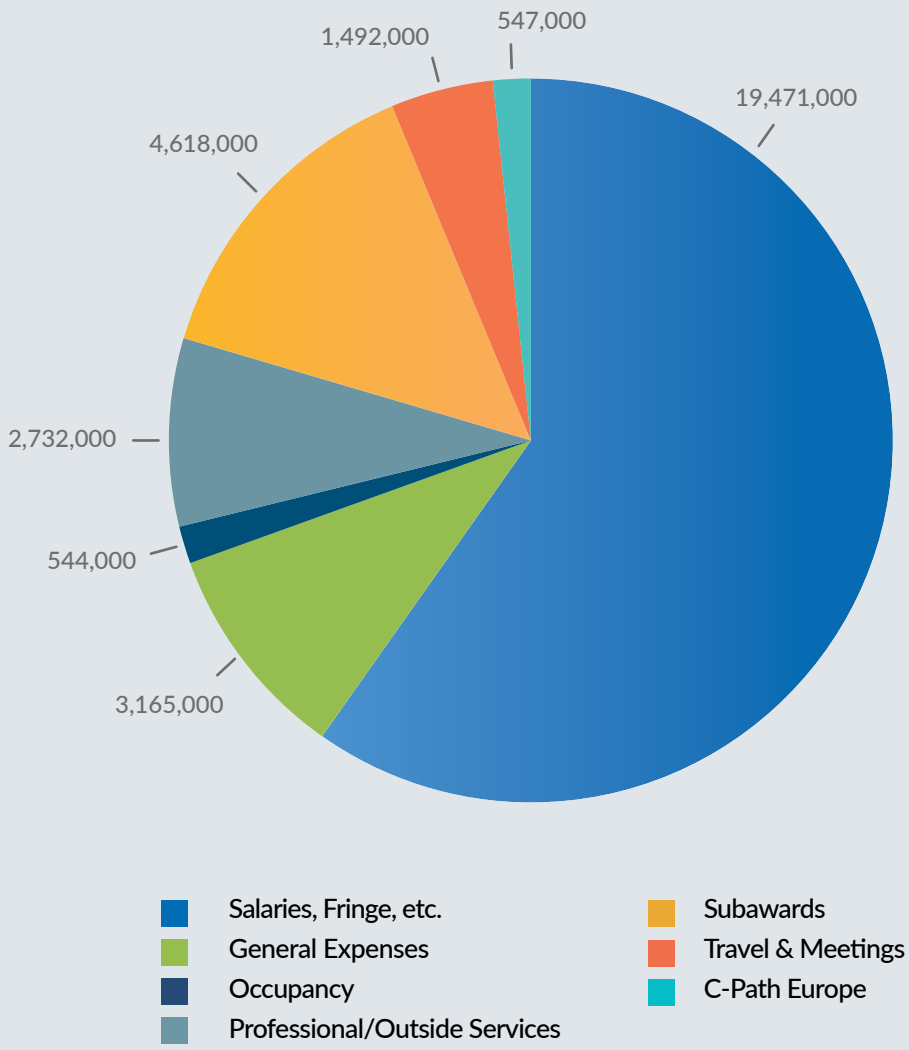
* Pre-awarded funds received for grants and consortia

** Consortia fees managed by C-Path to support consortia activities

C-PATH 2023 FISCAL YEAR REVENUE: $ 35,810,000



C-PATH 2023 FISCAL YEAR EXPENSES: $ 32,569,000



Our Collaborators

Scientists

By addressing broad process inefficiencies, C-Path enables industry and academic scientists to focus on their true goal: developing therapies and medical products that will improve human health and well-being.

Patients and Patient Advocacy Groups

C-Path relies on insights from patients with lived experience, their care partners and advocacy groups that support them around the world, to help make the process of developing cures, therapies, and medical products more efficient.

Regulatory Agencies

Regulatory agencies play a critical role as stewards of public health, and regulators share valuable non-competitive insights at every stage of the C-Path process.

Donor and Philanthropic Community

C-Path's work to accelerate the development of products and therapies that can benefit patients whose conditions lack safe and effective treatments would not be possible without the support from donors and Foundations.

Drug Development Industry

By increasing process efficiencies, C-Path helps industry stakeholders focus on their organizations' goals and meet their investor milestones.

For a full list of our collaborators, visit c-path.org/c-path-collaborators.

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Forward Focus

C-Path stands at the forefront of transformative healthcare solutions, continually evolving from our foundational mission to enhance global health. Our journey has been marked by relentless perseverance and innovative breakthroughs, demonstrating our unwavering commitment to addressing complex health challenges.

C-Path's achievements are a testament to the power of collaboration. We extend our heartfelt gratitude to our global community of supporters, and we deeply value our partnership with the individuals and families who bring lived experience in the diseases we aim to find treatments for. Their insights and contributions are vital to our work, informing and enriching our endeavors every step of the way.

Each milestone reached, and every individual who has benefited from our initiatives, fuels our resolve to forge new pathways in healthcare innovation. As we navigate the future, our focus remains steadfast on pioneering groundbreaking initiatives and strengthening our global partnerships, especially by engaging and working closely with those directly affected by these diseases. The road ahead is filled with possibilities, and we are excited to explore them together, continuing our shared mission to create a healthier world for all.

Advancing Drug Development. Improving Lives. Together.

CRITICAL PATH INSTITUTE

To help support C-Path's mission, visit **c-path.org** or scan the QR Code:

Acknowledgement of Federal Funding Support