CRITICAL PATH INSTITUTE

2018
ANNUAL
REPORT

for fiscal year ending
June 30, 2018

ACCELERATING THE PATH
TO A HEALTHIER WORLD

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Mission

Critical Path Institute is a catalyst in the development of new approaches to advance medical innovation and regulatory science. We achieve this by leading teams that share data, knowledge, and expertise, resulting in sound, consensus-based science.

Vision

Accelerating the path to a healthier world.

Values

As an independent and trusted partner, we value integrity, innovation, and teamwork.

FROM THE CEO

Dear friends and supporters,

In the day-to-day work of C-Path's mission to advance medical innovation and regulatory science, it's easy to sometimes lose sight of the bigger picture — that is, the fact that our efforts are enabling a pathway for patients to receive the safest, most effective, cutting-edge treatments possible.

As I look back on the past fiscal year, I am excited to share some new developments that demonstrate our enduring commitment to creating a healthier world and that propel us toward the future as we continue to engage in this all-important work. And I will also say this: After five years at C-Path, I am just as motivated and impassioned to lead this organization as I was the day I started in 2013.

I was able to share that sentiment with a reporter from the *Arizona Daily Star* — a reporter who, in his profile of C-Path, wrote that we are "one of the most important emerging drug-research organizations in the nation, if not the world." And while the reporter also noted that we have no laboratories, drug chemists, or patent lawyers, it is important to highlight what we do have: an amazing team of talented and passionate people working tirelessly each day.

I am happy to welcome a new member to the C-Path family, Kay Holcombe, who joined our Board of Directors in January 2018. Recently retired as Senior Vice President for Science Policy at the Biotechnology Innovation Organization (BIO), Ms. Holcombe brings to the Board her extensive experience in health care and regulatory policy, a history of collaboration with U.S. regulatory agencies, and broad knowledge of government initiatives that affect the biotechnology and pharmaceutical industries.

Other highlights from the past fiscal year include the announcement of the second clinical outcome assessment (COA) qualification from the U.S. Food and Drug Administration (FDA) for C-Path's Patient-Reported Outcome (PRO) Consortium. The qualification of the Non-Small Cell Lung Cancer Symptom Assessment Questionnaire (NSCLC-SAQ) represents another major milestone for the PRO Consortium and, specifically, for the NSCLC Working Group.

While acknowledging our successes, I must emphasize the fact that we cannot — and do not — do this work alone, it does take a community to collaborate; so I thank the external partners whose support enables us to do what we do.

In March, we announced the official launch of C-Path's Huntington's Disease Regulatory Science Consortium (HD-RSC), in partnership with the CHDI Foundation, Inc. (CHDI). In addition to C-Path and CHDI, the consortium includes more than 20 different member organizations, including industry partners, academic institutions, and nonprofit societies. HD-RSC members will work to advance innovation in regulatory science methods, enabling novel approaches to expedite development and regulatory review of Huntington's disease (HD) therapeutics.

Along with The World Health Organization (WHO) and the Foundation for Innovative New Diagnostics (FIND), we announced that the **Relational Sequencing TB Data Platform (ReSeqTB)**, a global TB knowledge base for predicting TB drug resistance, will be adopted as the WHO bioinformatics platform for surveillance of drug-resistant TB (DR-TB). ReSeqTB will also serve as a resource for the development of global policies on new TB diagnostics and can be utilized in the future to support clinical management of DR-TB.
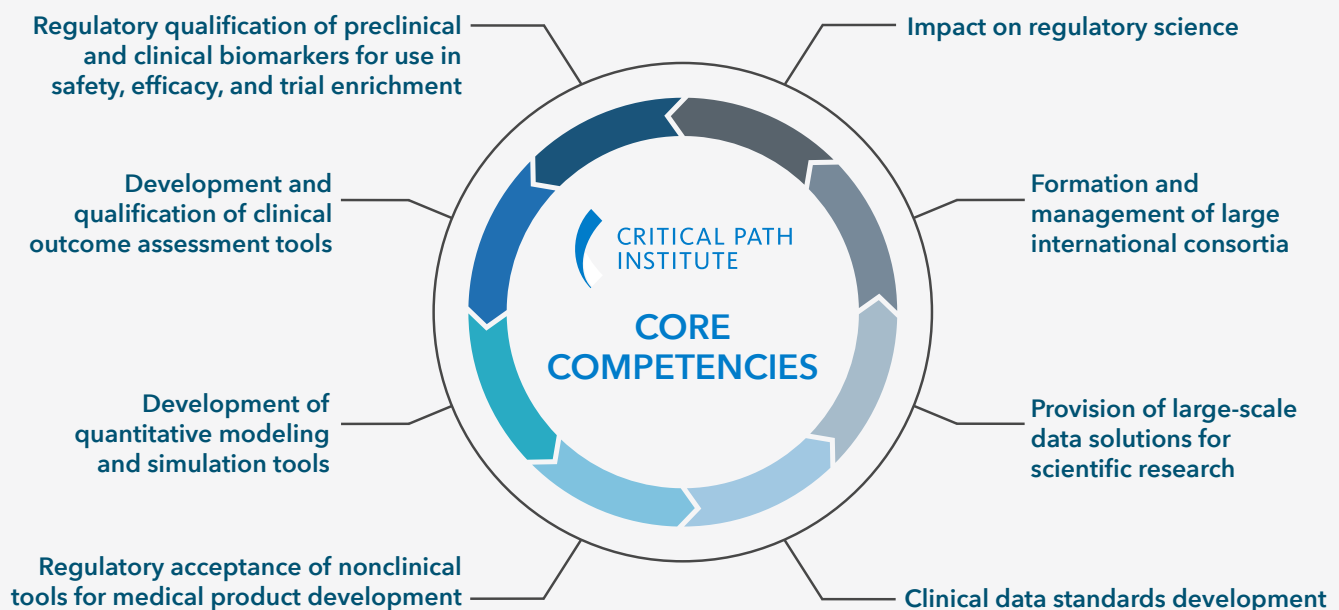
This development is critically important, as TB continues to be the world's deadliest infectious disease. In 2016 alone, 10.4 million people fell ill with TB, and 1.7 million died from the disease, with 240,000 of those deaths occurring as a result of DR-TB.

I am honored to have had the opportunity to contribute to these achievements. There is still so much work to be done, but I know that with the continued backing of our multiple partners, including patients, donors, foundations, board members, pharmaceutical and academic members, regulatory agency advisors, and the community at large, we will continue to make progress and have an even greater impact on global health. The future is looking bright for innovation in drug development.

Sincerely,
Martha A. Brumfield, Ph.D.

CORE COMPETENCIES

C-Path serves as a neutral third party to enable multiple stakeholders across the spectrum of medical product development to work together in a pre-competitive consortium model to drive the creation of innovative tools and methods that help to de-risk decision making in the development and regulatory review process. This makes C-Path a unique source of expertise working to achieve many of the objectives outlined in the sixth installment of the Prescription Drug User Fee Act (PDUFAVI), the 21st Century Cures Act and the Regulatory Science to 2025 initiative of the European Medicines Agency.

Regulatory qualification of preclinical and clinical biomarkers for use in safety, efficacy, and trial enrichment

Impact on regulatory science

Development and qualification of clinical outcome assessment tools

Formation and management of large international consortia

CRITICAL PATH INSTITUTE

CORE COMPETENCIES

Development of quantitative modeling and simulation tools

Provision of large-scale data solutions for scientific research

Regulatory acceptance of nonclinical tools for medical product development

Clinical data standards development

1   Regulatory qualification of preclinical and clinical biomarkers and novel methodologies for safety, efficacy, and trial enrichment

C-Path leads the way in regulatory qualification of biomarkers. C-Path was the first organization to qualify biomarkers with the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA), and Japan's Pharmaceutical and Medical Devices Agency (PMDA). The following C-Path consortia have successfully qualified biomarkers with regulatory agencies;

- The Predictive Safety Testing Consortium (PSTC): FDA, EMA, and PMDA qualified six nonclinical urinary biomarkers for the detection of acute drug-induced nephrotoxicity.

- The Critical Path for Alzheimer's Disease (CPAD) Consortium: EMA qualified the baseline measurement of low hippocampal volume (atrophy) by MRI to predict whether such patients are likely to evolve to Alzheimer's disease-type dementia during the course of an Alzheimer's disease clinical trial.
- The Polycystic Kidney Disease (PKD) Outcomes Consortium: FDA and EMA qualified Total Kidney Volume as a prognostic biomarker for enrichment of clinical trials in Autosomal Dominant Polycystic Kidney Disease.
- The Predictive Safety Testing Consortium (PSTC): FDA qualified a panel of six clinical urinary biomarkers for the detection of acute drug-induced nephrotoxicity in Phase 1 trials.
- The Critical Path for Parkinson's Disease (CPP): EMA qualified dopamine transport imaging as an enrichment biomarker for use in clinical trials in Parkinson's disease.

2 Development and qualification of clinical outcome assessment tools

By working with multiple stakeholders (e.g., patients, regulators, clinical advisors, industry scientists, measurement experts) in the U.S. and around the globe, C-Path has established itself as a leader in the development and qualification of patient-reported outcome measures and other clinical outcome assessment (COA) instruments. C-Path's Patient-Reported Outcome (PRO) Consortium provides a collaborative framework for the qualification of COA tools that can be used to support medical product labeling claims. The Electronic Patient-Reported Outcome (ePRO) Consortium works closely with the PRO Consortium to make the PRO instruments emerging from its therapeutic area working groups available for multiple modes of data collection. While other COA tools are in development or other stages of qualification, the following PRO measures have obtained FDA qualification:

- *Symptoms of Major Depressive Disorder Scale (SMDDS)*
- *Non-Small Cell Lung Cancer Symptom Assessment Questionnaire (NSCLC-SAQ)*

3 Development of quantitative modeling and simulation tools

The discipline of modeling and simulation has been a key area of expertise for C-Path since its inception. The vision of C-Path's Quantitative Medicine team is to transform drug development through methodological innovation and Model-Informed Drug Discovery and Development (MID3). C-Path's Quantitative Medicine team also works to drive innovation in MID3 through partnerships with leading groups and organizations in the field, and through collaborations with societies such as the International Society of Pharmacometrics. The development of these tools is possible thanks to the standardized integration of clinical and data analytical knowledge to solve bottlenecks in the drug development process. C-Path collaborated with scientists in industry to develop the first FDA- and EMA-endorsed quantitative drug development platform. Diseases benefiting from C-Path's work in modeling include:

- Alzheimer's disease
- Tuberculosis
- Polycystic kidney disease

C-Path's Quantitative Medicine team directly led the development of the disease progression model that supported the qualification of dopamine transporter imaging as an enrichment biomarker for trials in early motor Parkinson's disease. Currently, the team is developing disease progression models for Parkinson's disease, Duchenne muscular dystrophy, and mild cognitive impairment (a pre-dementia stage in Alzheimer's disease), as well as several new quantitative drug development tools for tuberculosis, and the model-based biomarker qualification of four auto-antibodies as prognostic biomarkers for trials in type-1 diabetes.

4 Regulatory acceptance of nonclinical tools for medical product development

C-Path also has demonstrated capability in developing and providing evidence packages to regulators for *in vitro* tools and other atypical (or non-traditional) tools. *In vitro* tools are critically important in earlier phases of drug development to facilitate decision making regarding compound, dose, combination regimen selection, and more. *In vitro* tools can also be utilized in clinical diagnosis and pathogen detection. Surveillance of pathogen resistance is another application with which C-Path has expertise.

- C-Path's Critical Path to TB Drug Regimens Initiative (CPTR): EMA qualified the *in vitro* Hollow Fiber System of Tuberculosis to inform selection of dose and treatment regimen, including combination of two or more anti-Mycobacterium tuberculosis drugs, to maximize bactericidal effects and minimize emergence of drug resistance.
- CPTR has developed a Relational Sequencing TB Knowledge Base (ReSeqTB) as a knowledge platform integrating genotypic, phenotypic, and clinical data to aid in surveillance of TB drug resistance, support clinical decision making for TB patient management, and inform development of new diagnostics and treatment regimens.

5 Clinical data standards development

C-Path works together with our partner, the Clinical Data Interchange Standards Consortium (CDISC), to develop industry and regulatory accepted standards for collecting, storing, and transmitting clinical data. C-Path's core competency in clinical data standards development enables the effective aggregation of large datasets and helps expedite the regulatory review process. CDISC is a recognized standards-setting organization and CDISC standards are required for new NDA and IND submissions to the FDA. C-Path worked with CDISC to develop the first therapeutic area data standard which was for Alzheimer's disease. Since then, C-Path led efforts in many other disease areas, including Parkinson's disease, polycystic kidney disease, tuberculosis, multiple sclerosis, Duchenne muscular dystrophy, and others. Approved data standards are published for use by the scientific research community on CDISC's website.

6 Provision of large-scale data solutions for scientific research

C-Path's Data Collaboration Center (DCC) was instituted to provide large-scale data solutions for scientific research. Our DCC team has more than a decade of experience in data standards

development, platform development, platform hosting, data curation, stewardship of patient-level data privacy, data security, and access control methodologies. C-Path has developed and continues to maintain databases for Alzheimer's disease, Parkinson's disease, polycystic kidney disease, tuberculosis, Duchenne muscular dystrophy, kidney safety biomarkers, multiple sclerosis, and other disease areas. Information about the C-Path-developed databases is available on the DCC Projects site: https://c-path.org/programs/dcc/.

7 Formation and management of large international consortia

C-Path is an expert in pre-competitive collaboration and is a trusted, neutral entity in regulatory science that excels in forming, managing, and facilitating large international consortia. Stakeholders include industry, regulatory and other governmental agencies, non-governmental organizations, patient groups, and academia around the world.

C-Path's ability to drive toward focused goals is key to its extraordinary competence in overseeing large consortia through technical, scientific, legal, regulatory, and project management expertise enabling the achievement of regulatory acceptance of drug development tools and novel methodologies. Each consortium collaborator is encouraged to share data that promotes the advancement of a wide variety of cross-cutting and disease-specific drug development tools and innovative methodologies.

8 Impact on regulatory science

C-Path focuses on the advancement of regulatory science through multiple avenues beyond qualification. This includes the development of points to consider white papers representing consensus among experts and stakeholders within a consortium. These papers serve to provide input to regulatory authorities as they work to develop regulatory guidance documents. Furthermore, C-Path has provided public feedback on numerous draft guidance documents and notices released for comment by both FDA and EMA.

C-Path has been instrumental in leading the movement within the scientific community to more clearly articulate the level of evidence necessary to achieve qualification, one of the most challenging issues in the drug development tool qualification process. In April 2016, key stakeholders including FDA CDER, C-Path, and the Foundation for the National Institutes of Health Biomarkers Consortium (FNIH BC) held a workshop to develop an evidentiary criteria framework for safety biomarker qualification. The resulting white paper delineated a proposed framework and provided specific examples of its applicability to clinical safety biomarkers. In June 2017, C-Path and the Duke Margolis Center for Health Policy held a public conference to bring together key stakeholders to discuss a draft framework outlining criteria and best practices for biomarker assay performance expectations and validation. A draft white paper was prepared in advance of the public forum, and input was solicited after the conference. Currently, the framework is being utilized by biomarker qualification stakeholders to evaluate assay acceptability in ongoing and planned biomarker qualification projects.

C-PATH'S NEW CONSORTIA

Huntington's Disease Regulatory Science Consortium

In March 2018, C-Path and the CHDI Foundation officially launched the Huntington's Disease Regulatory Science Consortium (HD-RSC) with the focus of accelerating development of Huntington's disease (HD) therapeutics. The consortium, along with its more than 20 different member organizations, including industry partners, academic institutions, and nonprofit organizations, strives to advance innovation in regulatory science and to expedite development, regulatory review, and approval of HD therapeutics. "C-Path has an established record of success in leading precompetitive consortia whose members collaborate to advance innovation in addressing the regulatory science needs of drug development," said Martha Brumfield, Ph.D., President and CEO of C-Path. "We value this new partnership with CHDI, an organization that also embraces collaboration as a mechanism to more quickly and efficiently reach a common goal."

Charles Sabine, an HD patient-advocate, emphasized the need to move forward with purpose in HD drug development. "We have hope," he said. "Hope can only be built on the trust that everyone is working as fast as they can in the same direction," something C-Path has a track record of nurturing.

Critical Path for Alzheimer's Disease: A Fresh Start for the Coalition Against Major Diseases

Since February 2008, Critical Path for Alzheimer's Disease (CPAD), formerly Coalition Against Major Diseases (CAMD), has been doing notable work in the areas of data sharing, disease modeling, and biomarkers. This year brought about another notable milestone — a complete rebrand of the consortium. What was formerly named the Coalition Against Major Diseases is now known as the Critical Path for Alzheimer's Disease, or CPAD. The consortium has a highly refined focus on Alzheimer's disease (AD), the most prevalent and devastating dementia, as well as dementias sharing similar characteristics.

CPAD's partnership with the Global Alzheimer's Association Interactive Network (GAAIN), also plays a key role in treatment development, as it allows for an open-access data resource portal that provides scientists with rapid access to Alzheimer's research data.

"Data sharing is the cornerstone for enabling advances in regulatory sciences that provide a gateway to new, innovative treatments for patients with dementias related to AD," said Stephen Arnerić, Ph.D., executive director of CPAD. "We are very proud of all that the CPAD consortium has accomplished. We are also excited to continue our work in AD, in collaboration with our members and regulators, to pave the way for early diagnosis, treatments, and better quality of life for those affected."

Transplant Therapeutics Consortium

In the United States there are approximately 680,000 patients receiving dialysis each year, with more than 105,000 patients on the kidney transplant waiting list and approximately 160,000 patients living with kidney transplants. In 2016, there were approximately 19,000 kidney transplants (from a deceased organ donor) performed in the U.S, and the failure rates for kidney transplants at one, five, and 10 years were 8 percent, 27 percent, and 53 percent, respectively. These five- and 10-year failure rates result in patients returning to dialysis, with a significant decrease in quality of life and a significant increase in cost.

The reality of these statistics is precisely why, in spring 2017, the Transplant Therapeutics Consortium (TTC) was founded by C-Path, the American Society of Transplantation (AST), and the American Society of Transplant Surgeons (ASTS).

The TTC convenes diverse stakeholders (industry, academia, and government agencies) to support collaborative development and regulatory endorsement of new drug development tools for transplantation which, in turn, may help to shorten the time needed to develop and deliver safe, effective therapies for transplantation patients.

"As demonstrated in other therapeutic areas of unmet need, the use of standardized datasets from a broad number of stakeholders informs the development of biomarkers, outcome assessment measures, and other novel tools that regulatory authorities may endorse," said C-Path President and CEO Martha Brumfield, PhD. "Ultimately, the incorporation of these new methods and tools into drug development programs will increase the likelihood of success in getting safe and effective therapies to those living with a transplanted kidney."

Through the TTC, members share expertise, resources, and data in a neutral, precompetitive, confidential environment. TTC's goal is to define and prioritize the areas of unmet need and provide tools to address these needs and accelerate the transplant drug development process by:

- Acquisition and aggregation of key patient-level clinical datasets
- Development of tools capable of optimizing clinical trial design for novel transplant therapeutics, considering both efficacy and safety/tolerability of novel therapies
- Endorsement of novel drug development tools by FDA and EMA so these tools can be used with confidence that they will be accepted by regulatory agencies.

The sharing of knowledge, expertise, and data will be critical to the success of each of these TTC endeavors.

Crohn's Disease Biomarker Pre-Consortium

In April 2018, it was announced that Critical Path Institute was the recipient of a Leona M. and Harry B. Helmsley Charitable Trust grant to support a Crohn's disease biomarker pre-consortium. The pre-consortium identifies unmet needs for the use of biomarkers in developing new treatments for people with Crohn's disease. Additionally, the pre-consortium focuses on identifying Crohn's disease biomarkers and laying the groundwork for future regulatory endorsement with a long-term objective to obtain regulatory qualification of biomarkers, which will enable drug developers and the broader Crohn's disease community of clinicians and researchers to accelerate the development and approval of treatments for those living with this disease.

"The partnership and support from Helmsley will allow us to define the most effective approach to forming a Crohn's Disease Biomarker Consortium to take forward the best biomarkers into regulatory qualification," said C-Path Biomarker Program Officer John-Michael Sauer, Ph.D.

Garabet Yeretssian, Ph.D., director of the Helmsley Charitable Trust's Crohn's Disease Program, said, "C-Path's initiative to identify and position Crohn's disease-specific biomarkers for regulatory endorsement is a pivotal step in getting improved therapies into the hands of people living with Crohn's disease more quickly than currently possible."

C-PATH'S CRITICAL MILESTONES

CPAD — CRITICAL PATH INSTITUTE

CPP — CRITICAL PATH INSTITUTE

CFAST

CPTR

- AD clinical trial database
- AD clinical trial simulation tool
- EMA qualified AD biomarker
- FDA letters of support - MCI model
- FDA letters of support - AD biomarkers

- FDA letter of support - PD biomarker
- EMA qualified PD biomarker

- 21 therapeutic area users guides to supplement CDISC foundational standard

- EMA qualified Hollow Fiber System for Tuberculosis
- ReSeqTB data platform
- LAM biomarker
- PB/PK Model for lung penetration
- TB-PACTS data platform

PRO Consortium Achievements Make Meaningful Impact to Patients

C-Path's Patient-Reported Outcome (PRO) Consortium was formed in late 2008 by the Critical Path Institute (C-Path) in cooperation with the U.S. Food and Drug Administration's (FDA) Center for Drug Evaluation and Research and the pharmaceutical industry. Formally launched in March 2009, the PRO Consortium's membership is comprised of pharmaceutical companies, along with C-Path as the managing member. Patients, clinicians, measurement consultants, and representatives from the FDA and National Institutes of Health (NIH) provide critical advice and assistance to the PRO Consortium's Coordinating Committee and working groups.

This year brought two major milestones for the PRO Consortium. In December 2017, C-Path received clinical outcome assessment qualification from the FDA for exploratory use of the Symptoms of Major Depressive Disorder Scale (SMDDS), a 16-item, patient-reported outcome (PRO) measure developed to capture the core symptoms of major depressive disorder (MDD) that matter most to patients.

PKD
CONSORTIUM
CRITICAL PATH INSTITUTE

PRO
CONSORTIUM
CRITICAL PATH INSTITUTE

PSTC
CRITICAL PATH INSTITUTE

- ▶ EMA & FDA qualified Total Kidney Volume (TKV) imaging biomarker
- ▶ FDA letter of support - TKV imaging biomarker
- ▶ PKD clinical database

- ▶ FDA clinical outcome assessment qualification:
  - Symptoms of Major Depressive Disorder Scale (SMDDS)
  - Non-Small Cell Lung Cancer Symptom Assessment Questionnaire (NSCLC-SAQ)

- ▶ EMA/FDA/PMDA qualified non-clinical kidney safety biomarkers
- ▶ FDA qualification of a panel of six clinical kidney safety biomarkers for use in Phase 1
- ▶ FDA & EMA letters of support:
  - kidney biomarkers
  - skeletal muscle injury biomarkers
  - liver biomarkers

"The qualification of the SMDDS is an incredibly important achievement for the PRO Consortium," said Stephen Joel Coons, Ph.D., the PRO Consortium's executive director. "It is the result of a tremendous amount of time and effort invested by C-Path, our industry partners, clinical and measurement consultants, FDA, and the patients who volunteered to help us with this worthwhile project. The SMDDS has the potential to change the current measurement paradigm for assessing treatment benefit in MDD clinical trials."

Additionally, in May 2018, C-Path had received a clinical outcome assessment (COA) qualification from the FDA for the exploratory use of Non-Small Cell Lung Cancer Symptom Assessment Questionnaire (NSCLC-SAQ), a seven-item, patient-reported outcome measure. The NSCLC-SAQ is an important advance in PRO measurement in patients with NSCLC. It is also further evidence of the FDA's commitment to patient-focused drug development through qualification of COAs that provide valid and reliable information that is meaningful to patients. Stephen Joel Coons stated, "The qualification of the NSCLC-SAQ is another important achievement for C-Path, the PRO Consortium, and the many collaborators involved."
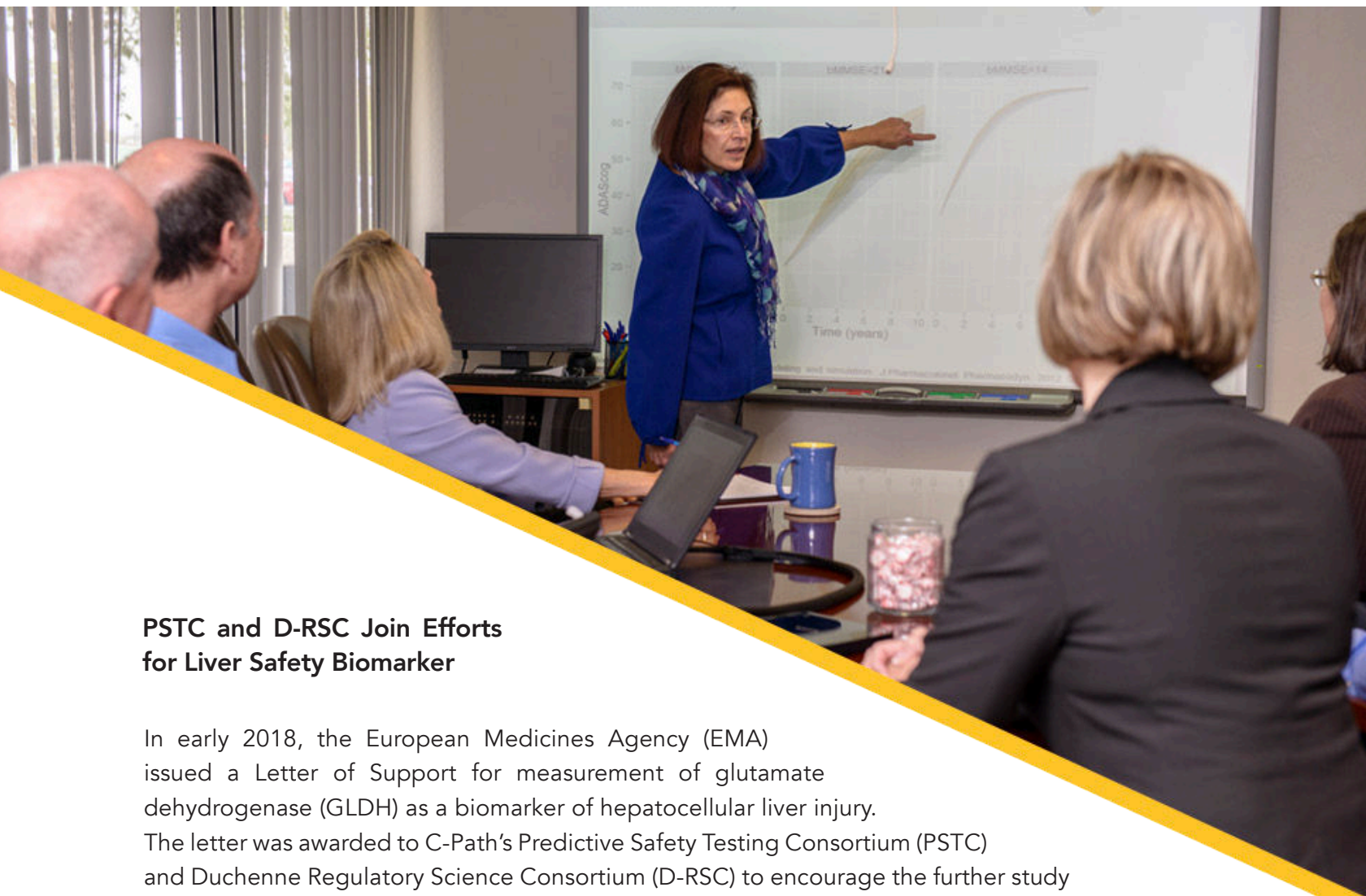
PSTC and D-RSC Join Efforts for Liver Safety Biomarker

In early 2018, the European Medicines Agency (EMA) issued a Letter of Support for measurement of glutamate dehydrogenase (GLDH) as a biomarker of hepatocellular liver injury. The letter was awarded to C-Path's Predictive Safety Testing Consortium (PSTC) and Duchenne Regulatory Science Consortium (D-RSC) to encourage the further study of serum GLDH for monitoring hepatocellular liver injury.

The letter — in response to data submitted by the PSTC Hepatotoxicity Working Group (HWG) and D-RSC — described EMA's thoughts on the value of GLDH and supports further evaluation. In it, EMA encouraged PSTC and D-RSC to investigate "the voluntary and complementary use of serum GLDH, in conjunction with currently used biomarkers of liver injury, as a clinical biomarker of liver injury." EMA also supported PSTC's generation of additional clinical safety data and plans for further clinical studies to potentially enable formal qualification of GLDH in the future.

"Many of the proteins currently monitored to evaluate liver safety are also found in muscle tissue," said D-RSC Executive Director Jane Larkindale, Ph.D. "In situations where a patient has underlying muscle injury, such as muscular dystrophies, levels of these enzymes may be high in the absence of liver injury. Monitoring of GLDH levels may allow liver injury caused by novel drugs to be detected in this population of patients."

LOOKING AHEAD

C-Path's competencies are in demand; it is expanding into new areas and continuing to grow. C-Path is engaging in more collaborations in the U.S. and around the world — its global profile is expanding. By the end of 2018, a new C-Path entity in Europe was created in Ireland, enabling the organization to increase its activity in the European Union and broaden its global operations as it works to accelerate the development of therapies in a wide range of diseases and medical conditions.

Many C-Path grantors, like the Bill & Melinda Gates Foundation and the Leona M. and Harry B. Helmsley Charitable Trust, continue to fund projects over time, which shows continued confidence and trust in C-Path. The organization also secured a new agreement with Doris Duke Charitable Foundation to begin looking at drug development tools for sickle cell disease and potentially form a new consortium. All of this is evidence that organizations continue to seek out C-Path to help solve difficult drug development problems.

As a leader in the technical aspects of curating and aggregating clinical trial data, C-Path has become a meaningful catalyst in drug development. The organization is known and respected among regulators, foundations, nonprofits, and industry for initiating collaboration on some of the world's most pressing health challenges.

There is still much work to be done, but with the continued support from patients, donors, foundations, board members, pharmaceutical and academic members, regulatory agency advisors, and the community at large, C-Path will continue to make progress and have an even greater impact on global health, advancing its mission to accelerate the path to a healthier world.

FINANCIAL UPDATE

C-Path maintains a strong financial position at the close of this fiscal year. The U.S. Food and Drug Administration (FDA), patient organizations, and industry leaders in the pharmaceutical and biotech industries continue to find value in the collaborations C-Path manages and the innovative drug development tools and methods the consortia work together to create. Organizations that historically have funded basic research increasingly are coming to the realization that in order to enable the development of new therapies to help patients, a lot of work remains to be accomplished in the areas of translational and regulatory science. As a result, C-Path continues to grow at a steady rate and expand into new areas.
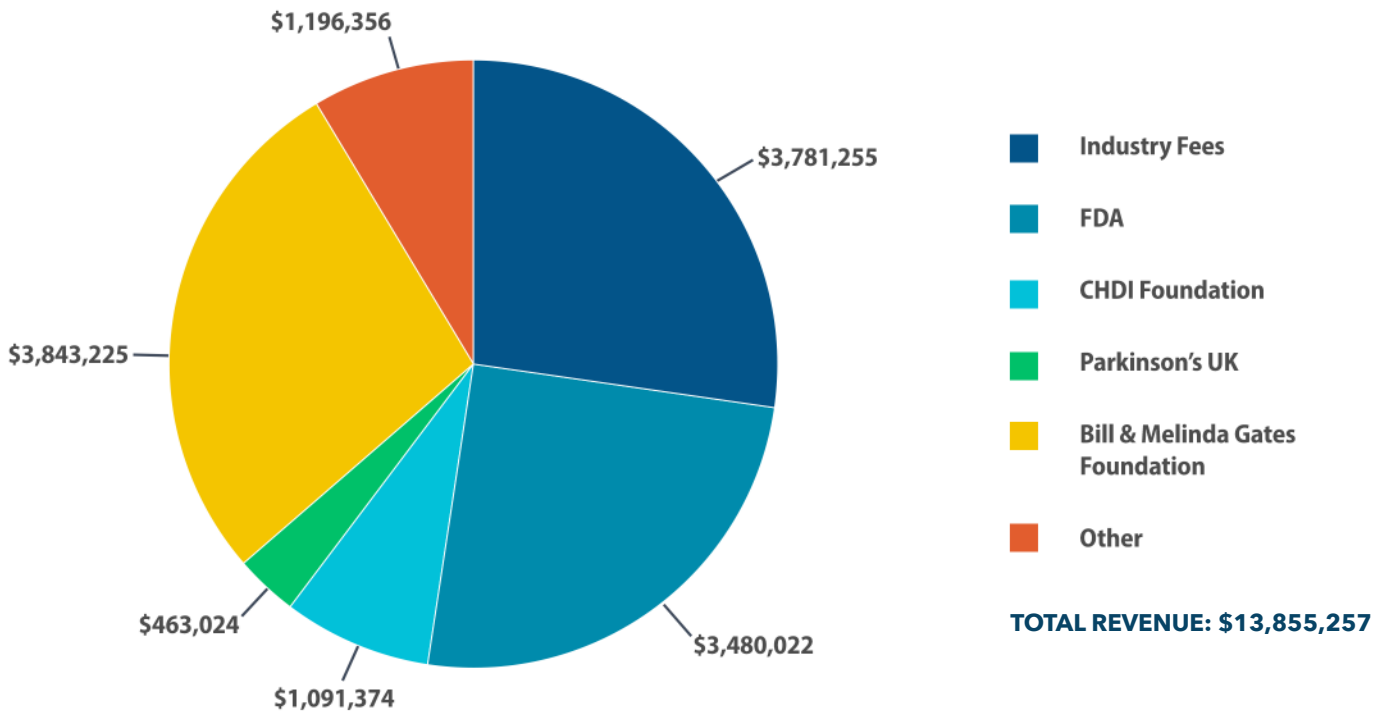
With the new entity, Critical Path Institute, Ltd. opening in Ireland, C-Path will be able to broaden its global operations. After an initial startup phase, it anticipates increased activities in the European Union.

C-Path is dedicated to helping organizations provide safe and effective therapies to individuals living with disease. While the work to fulfill this commitment requires rigorous scientific methods, significant quantities of high-quality data, along with robust analytical and statistical procedures, and the management of collaboration platforms, C-Path continues to achieve success in its efforts to develop and receive regulatory endorsements for biomarkers, clinical outcome assessment instruments, quantitative models, and other tools. There is no doubt it will continue to do so going forward.
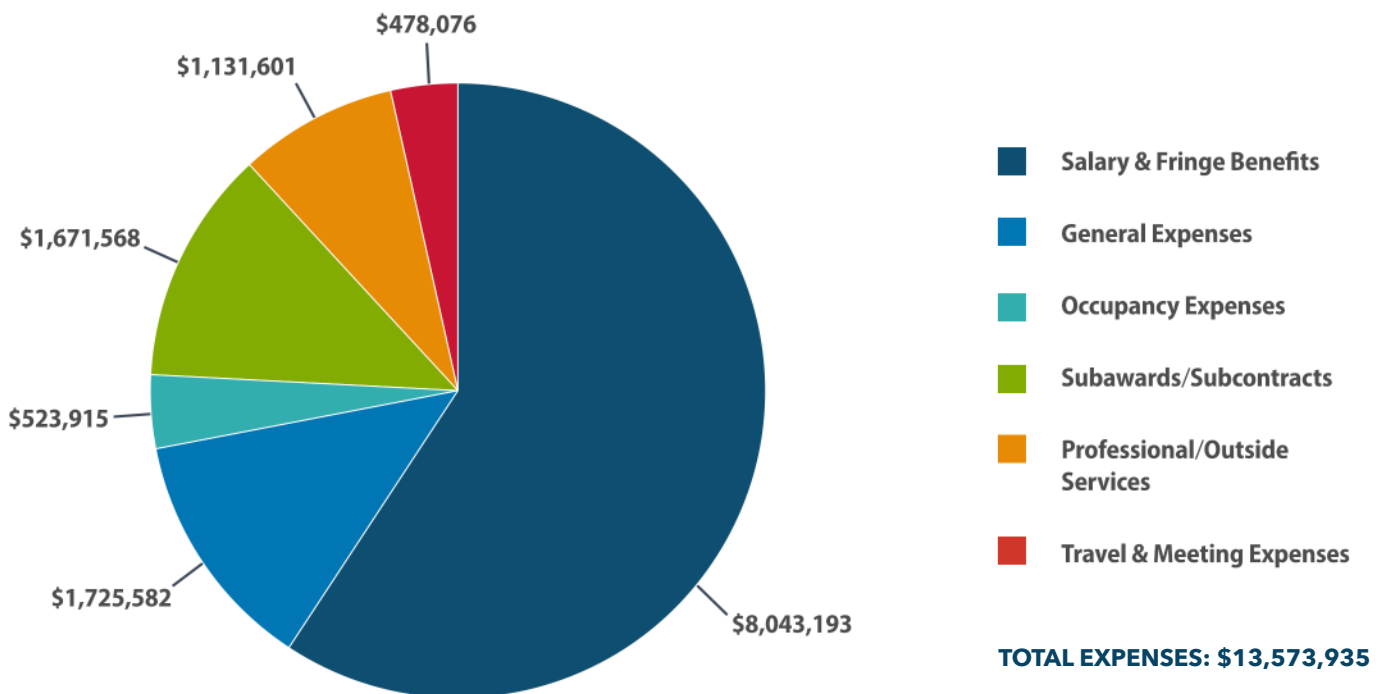
Significant financial news this year includes:

- **The Critical Path to TB drug Regimens (CPTR) received three new grants from the Bill & Melinda Gates Foundation.**

- **The Huntington's Disease Regulatory Sciences Consortium (HD-RSC), sponsored by the CHDI Foundation, formally launched.**

- **The FDA awarded additional funding to enable C-Path to assist other organizations in their attempts to develop qualifying drug development tools when they are referred by the FDA.**

- **New or increased funding has been awarded for work in Alzheimer's disease, Parkinson's disease, and Duchenne muscular dystrophy.**

- **C-Path received grants to fund planning efforts to begin new work on Crohn's disease and sickle cell disease.**

C-PATH 2018 FISCAL YEAR REVENUE

$1,196,356

$3,781,255

$3,843,225

$463,024

$1,091,374

$3,480,022

- Industry Fees
- FDA
- CHDI Foundation
- Parkinson's UK
- Bill & Melinda Gates Foundation
- Other

TOTAL REVENUE: $13,855,257

C-PATH 2018 FISCAL YEAR EXPENSES

$478,076

$1,131,601

$1,671,568

$523,915

$1,725,582

$8,043,193

- Salary & Fringe Benefits
- General Expenses
- Occupancy Expenses
- Subawards/Subcontracts
- Professional/Outside Services
- Travel & Meeting Expenses

TOTAL EXPENSES: $13,573,935

C-PATH INITIATIVES

The Biomarker Data Repository (BmDR), launched by C-Path's Predictive Safety Testing Consortium (PSTC), is a repository for data on novel translational safety biomarkers from drug development programs. Masked, de-identified data from multiple sponsors is collected and stored in a secured repository, and that data is then made available to C-Path and FDA staff to support research that leads to additional evidence to support potential qualification of novel safety biomarkers for new Contexts of Use (CoUs), as well as to modify and possibly expand existing CoUs to identify appropriate exploratory biomarkers to advance drug development in the future. The initial pilot focuses on kidney safety biomarkers, and the main goal of the BmDR is to provide industry with new drug development tools. Existing biomarker data could be used to significantly advance and accelerate understanding of the utility of novel biomarkers as drug development tools.

The Coalition For Accelerating Standards and Therapies (CFAST), a joint initiative of C-Path and CDISC, was founded to advance clinical research and medical product development by creating and maintaining data standards, tools, and methods for conducting research in therapeutic areas that are important to public health. C-Path led the development of the first CDISC Therapeutic Area (TA) Data Standards, in order to advance the data aggregation needs of specific C-Path consortia. This was done in collaboration with CDISC. To date, in partnership with CDISC and the U.S. Food and Drug Administration, the National Cancer Institute Enterprise Vocabulary Services (NCI EVS), TransCelerate BioPharma, the European Medicines Agency (EMA), the Innovative Medicines Initiative (IMI), and the Association of Clinical Research Organizations (ACRO), 31 CDISC therapeutic area standards have been published, and C-Path has led or supported the work on 16 of these projects.

The Critical Path For Alzheimer's Disease (CPAD) was founded to create new tools and methods that can be applied to increase the efficiency of the development process of new treatments for Alzheimer's disease (AD) and related neurodegenerative disorders characterized by impaired cognition and function. CPAD focuses on sharing precompetitive patient-level data from the control arms of legacy clinical trials, developing new tools to be submitted to the regulatory agencies, and developing consensus data standards, all with the goal of accelerating therapeutic treatment development for patients with chronic neurodegenerative disease.

The Critical Path for Parkinson's Consortium (CPP) was created in partnership with Parkinson's UK, one of the world's largest charity funders of Parkinson's (PD) research. Parkinson's has traditionally been viewed as a disorder in which individuals don't have enough dopamine, because specific nerve cells inside the brain have died. Current research, however, indicates that the processes leading to dopamine deficit start decades earlier than previously thought, increasing the need to understand the early stages of PD progression. CPP brings together pharmaceutical companies and academic partners working toward a common goal of developing modeling tools to establish best practices and more efficient protocols for planning and designing clinical trials in early PD, which will improve the clinical trial process and deliver better treatments faster.

The Critical Path to TB Drug Regimens (CPTR) facilitates the accelerated development of novel drug regimens and provides access to a platform of resistance data which can support rapid drug susceptibility diagnostics for TB. Tuberculosis is a disease that still impacts one-third of the world's population, which is in desperate need of a safer, shorter-duration, and more effective drug regimen. Much of this critical work is enabled by a global data-sharing initiative, funded by the Bill & Melinda Gates Foundation and led by C-Path and partner organizations, which include WHO, TB Alliance, and multiple data contributors representing industry, academia, and government agencies.

The Data Collaboration Center (DCC), which built and oversees C-Path's Online Data Repository (CODR), has the goal to enable multiple organizations to work together to share clinical data, in order to optimize its value in creating new insights and tools that accelerate drug development in areas with unmet medical needs. The DCC supports data-sharing projects aligned with specific C-Path consortia, as well as data-sharing initiatives that are independent of C-Path consortia. All of DCC's work takes place in a neutral, precompetitive environment, utilizing appropriate CDISC standards. The DCC possesses the technical and scientific subject matter and project management expertise necessary to support advanced research efforts.

The Duchenne Regulatory Science Consortium (D-RSC) was formed in partnership with Parent Project Muscular Dystrophy (PPMD) to aggregate data and develop a disease progression model to accelerate the development of new therapies for Duchenne muscular dystrophy, which is an urgent unmet medical need. Duchenne is a genetic disease that causes progressive loss of muscle, resulting in the inability to walk, breathing and cardiac issues, and premature death. D-RSC aims to improve trial protocol development and reduce the number of patients needed to demonstrate the effect of new therapies, thereby accelerating the development of the therapies themselves.

The Electronic Patient-Reported Outcome (ePRO) **Consortium** was established to advance the science surrounding electronic collection of PRO endpoints in clinical trials. The ePRO Consortium provides a pre-competitive environment in which a critical mass of experts collaborates to support and conduct research, design and deliver educational opportunities, and develop and disseminate best practice recommendations for electronic collection of clinical outcome data.

The Huntington's Disease Regulatory Science Consortium (HD-RSC) was created in partnership with the CHDI Foundation, a privately-funded, not-for-profit biomedical research organization devoted solely to Huntington's disease. With the goal of improving the efficiency of development, review, and approval of emerging therapeutics for Huntington's disease, this global initiative aims to facilitate collaboration among the bio-pharmaceutical industry partners, technology industry partners, academic institutions, government agencies, and patient-advocacy associations. HD-RSC fosters consensus and data-driven research to increase efficiency, safety, and speed in developing new therapies.

The International Neonatal Consortium (INC) is a global collaboration forging a more predictable regulatory path to evaluate the safety and effectiveness of therapies for neonates. The consortium engages the global neonatal community — families, neonatal nurses, academic scientists, regulators, pharmaceutical investigators, advocacy organizations, clinicians, and funders — to focus on the needs of the neonate. Through teams that share data, knowledge, and expertise, INC advances medical innovation and regulatory science for this underserved population.


The Multiple Sclerosis Outcome Assessments Consortium (MSOAC) collects, standardizes, and analyzes data about MS that have been generated over several decades, with the goal of qualifying a new measure of disability as a primary or secondary endpoint for future trials of MS therapies. MSOAC has brought together members from academia and industry, regulatory authorities, patient advocacy groups, and persons living with multiple sclerosis. MSOAC is working to speed the development of new therapeutic options by developing better measures of outcomes.

The Polycystic Kidney Disease Outcomes Consortium (PKDOC) brings together leading nephrologists and other scientists from academia, industry, and government to spur the development of new therapies for patients with this debilitating disease. PKDOC's mission is to develop drug development tools and methods to promote research that will lead to the development of treatments for PKD and improve the lives of all it affects. PKDOC has developed CDISC data standards for PKD and aggregated clinical data from Autosomal Dominant Polycystic Kidney Disease (ADPKD) patients collected over many years in patient registries and observational studies. These data enabled the development of a disease-biomarker model that provided the support necessary for FDA and EMA to qualify an imaging biomarker, Total Kidney Volume (TKV), for use as an enrichment strategy in drug development trials. PKDOC continues to work on alternative endpoints and clinical trial designs.
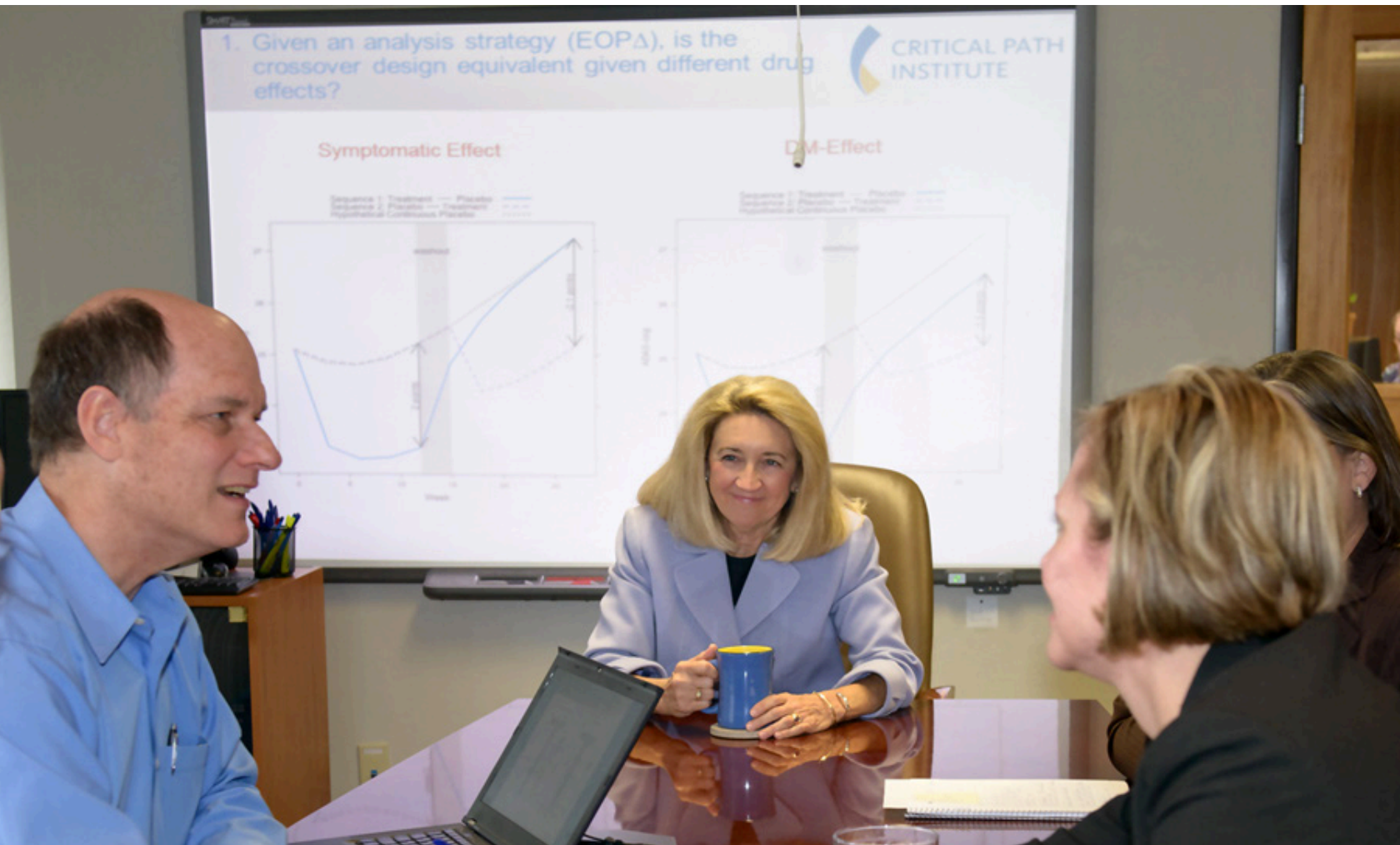
The Patient-Reported Outcome (PRO) **Consortium** brings together drug developers, measurement scientists, patients, clinicians, and regulators to collaborate on effectively incorporating the voice of the patient into the drug development process. Its primary goal is to obtain regulatory qualification of patient-reported outcome measures and other clinical outcome assessment (COA) tools for use in clinical trials where COA tools can, and should, be used to evaluate patient-focused treatment benefit.

Despite considerable advances in medicine and technology, many of the tests used to evaluate drug safety have not changed in decades. The mission of the **Predictive Safety Testing Consortium** (PSTC) is to bring together pharmaceutical companies to share and validate innovative safety testing methods to accelerate drug development under advisement of the FDA, EMA, and PMDA. PSTC does this by developing and implementing scientific research strategies in a neutral, pre-competitive environment, thereby allowing members to share expertise, resources, data, and internally developed approaches, which improves both the speed and precision of the drug development process. PSTC's efforts are intended to develop drug development tools that assist pharmaceutical companies and regulatory agencies in making better-informed decisions, all of which ultimately benefits patients. Currently, PSTC is engaged in the qualification of novel nonclinical and clinical safety biomarkers across several organ systems for application in the development of drugs.

The aim of the **Pediatric Trials Consortium** (PTC) was to develop a business model and the infrastructure required to launch a new, independent nonprofit organization whose mission is to facilitate clinical trials in children. PTC launched a new, independent legal entity (the Institute for Advanced Clinical Trials for Children [I-ACT for Children]) that provides the sustainable global infrastructure needed to plan, start up, conduct, and complete pediatric studies. I-ACT for Children spans subspecialties, study types, phases, and sponsor types (such as industry, academia, and nonprofits). I-ACT for Children will accelerate the availability of innovative, safe, and effective medicines for children, improving health and wellness globally.

The Type 1 Diabetes Consortium (T1D) is a public-private partnership initiated by C-Path, JDRF, the Leona M. and Harry B. Helmsley Charitable Trust, Sanofi, and Janssen Research & Development LLC. Membership also comprises pharmaceutical companies, academic partners, and advisors from the National Institutes of Health (NIH). The goal of the T1D Consortium is to initiate a qualification program for biomarkers of islet autoimmunity for use in the development of therapies for the treatment of T1D. The objective of this consortium is to understand the scientific basis for the use of these biomarkers as well as the regulatory expectations associated with their use as susceptibility/risk biomarkers that could identify individuals who are likely to develop a clinical diagnosis of T1D. The islet autoantibodies of interest include insulin autoantibodies (IAA), glutamic acid decarboxylase 65 (GADA), insulinoma antigen-2 (IA-2), and zinc transporter 8 (ZnT8) autoantibodies, and will be evaluated per data availability.

The TB-PACTS data platform is designed to catalyze and accelerate tuberculosis (TB) research by curating and standardizing Phase III TB clinical trial data and making this data available to qualified researchers. A robust body of knowledge, TB-PACTS allows members of the TB research community to pursue research that would otherwise be prohibitively expensive or not feasible with their data alone and helps them make better-informed decisions relating to their research. It's a one-stop data source for clinical metadata on Mtb, which is otherwise currently scattered across numerous public and private repositories. The TB-PACTS data platform currently includes data from 17 TB clinical trials and more than 12,000 subjects.

The Transplant Therapeutics Consortium (TTC) convenes diverse stakeholders (industry, academia, and government agencies) to support collaborative development and regulatory endorsement of new drug development tools for solid organ transplantation, which, in turn, may help to shorten the time needed to deliver safe, effective therapies for transplantation patients. There are a number of barriers to developing new therapies for transplantation, and there is a need for experts in the field to work collaboratively to prioritize and resolve them. The TTC brings together key stakeholders in the transplant community with the primary goal of identifying and addressing the regulatory challenges that impact the development and approval of new therapies in transplantation.

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- Brigham and Womens Hospital
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- .assisTek
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