I-ACT
INSTITUTE FOR ADVANCED CLINICAL TRIALS
FOR CHILDREN

Advancing Pediatric Clinical Trial Innovation

2022 ANNUAL REPORT

IN SERVICE OF CHILDREN

Our Mission

To serve the pediatric community as an independent and connected organization to accelerate the clinical development of innovative therapeutic solutions to improve health outcomes in children.

Our Vision

To be the pediatric clinical development powerhouse, enabling timely access to the best therapy for every child with a medical need.

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From the Chairwoman

Elizabeth Garofalo
Chairwoman

FROM THE CHAIRWOMAN:

This 2022 edition of the Annual Report for the Institute for Advanced Clinical Trials for Children represents a summary of the Institute's accomplishments and progress to date. We are grateful for all the support, engagement, and feedback from our members and all stakeholders who have helped develop the Institute to build up a unique collaborative and global site network, growing consulting capabilities and successfully managing innovation forums to help advance drug development for children. This year was a year of change to adapt the organization to the needs of a more demanding environment to improve the performance of pediatric research.

Since 2017, we had been tasked by our founders to build up a pediatric clinical trial infrastructure capable of completing the quality trials needed to support regulatory approval and labelling in a timely manner. Five years later, we are proud to report that we have met this objective. We have built a robust global pediatric research site network, with 80 sites of which 70 are in the United States. Moreover, we have established efficient collaborations with other pediatric networks such as conect4children ("C4C") via the Belgium Pediatric Research Network in Europe to provide coordinated access to their sites. Our relationships with dedicated "site points of contacts and site champions" at each of our sites contributed to accelerated site identification for trials and we also efficiently supported contracting, enrollment, and early study engagement as well as progressing on our proprietary quality improvement program named "PICTR" ®. We have completed several critical pre-competitive projects that address unmet needs and align with key regulatory priorities.

In 2022 the Institute focused on strengthening connections to medical and scientific expertise in the pediatric drug development community. Over 2022, while the Institute continued to benefit from the committed support of our biopharmaceutical members and from the FDA that awarded us a grant to support PICTR, we have been able to generate $ 1,043,000 from our "fee-for services" revenue stream. To continue to grow, we have launched a national fundraising campaign to promote advocacy and pediatric drug development awareness with a broader public audience. Numerous events associated with this effort are scheduled in 2023.

On behalf of the Board of Directors, I want to recognize the commitment and hard work of the Institute's leadership and staff during this time of development and want to thank the whole organization for this year 's accomplishments and solid progress.

More than ever, our goal is to continue to adapt our capabilities to today's context and needs from the pediatric community to improve our ability to make an impact and fulfill our mission for the children and their families we serve.

Elizabeth Garofalo

Elizabeth Garofalo, MD
Chairwoman of the Board

MAKING AN IMPACT

Key 2022 Achievements

ACT
ACCELERATE
ACHIEVE
More Efficient Pediatric Clinical Development

Creating an Efficient, Sustainable Infrastructure

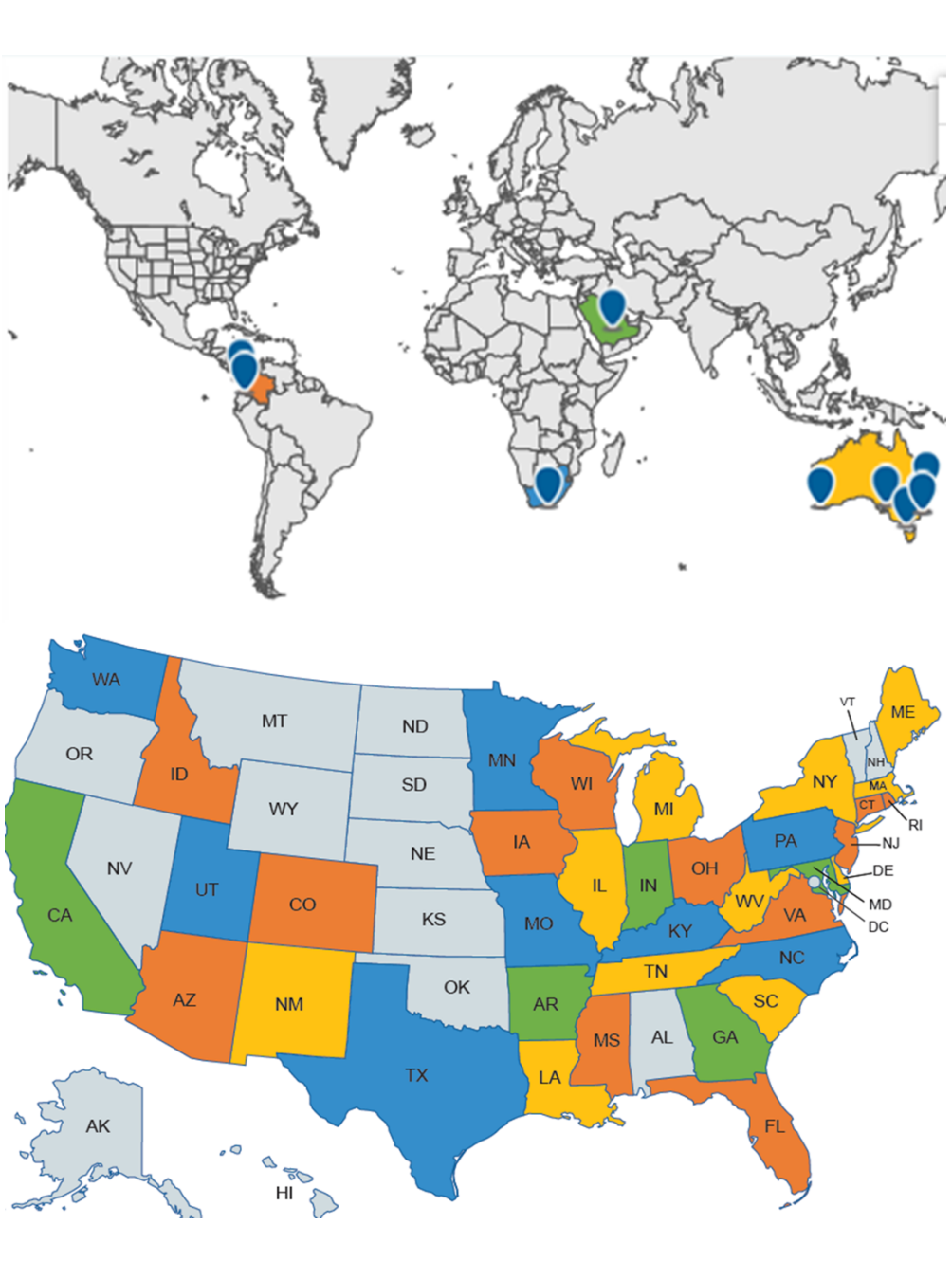
Advancing Innovation in Clinical Trial Design

Thought Leadership

Supporting Our Global Site Network

In the past 5 years, we have built a robust global pediatric research site network, with 80 sites of which 70 are in the United States.

In parallel and notably, we have established efficient collaborations with other pediatric networks i.e., conect4children ("c4c") via the Belgium Pediatric Research Network in Europe and the Maternal Infant Child and Youth Research Network (MICYRN) in Canada to provide coordinated access to their sites. Our relationships with dedicated "site points of contacts and site champions" at each of our sites contributed to accelerated site identification for trials and we also efficiently supported contracting, enrollment, and early study engagement as well as progressing on our proprietary quality improvement program named "PICTR".® To strengthen their skills and competencies, we eventually have provided 3 education sessions to investigating sites and other interested individuals and groups.



Top Map: 10 international sites located in Australia, Columbia, Panama, South Africa and Saudi Arabia.

Bottom Map: 70 US Sites in all states except those indicated in grey.

In 2022, several key metrics for the Site Network Team:

- Time range to complete an Early Engagement Site Interest Survey 9-16 business days
- Our average site outreach response rate is 77%
- Ninety-two sites were identified for sponsors across 4 broad therapeutic areas
- Twenty-nine face-to-face site visits were completed in 2022 with very positive and enthusiastic responses from our sites

Other Core Site Network Activities

Quarterly Site Network Calls

Amended the content for 2022

Invited speakers

Well attended, reviewed and received by our sites

Site Educational Teleconferences

Topics in 2022:

Recruitment and Retention of Clinical Research Staff

Decentralized Trials

Improving the Site Start-up Process

Site Mentorship Program

22 Mentor/Mentee pairs in 2022

Approaching 30 Mentor/Mentee pairs in 2023

Very popular and needed program with the shortages of clinical research staff experienced by the sites

Site Educational Award Program

Competitive Program-application required

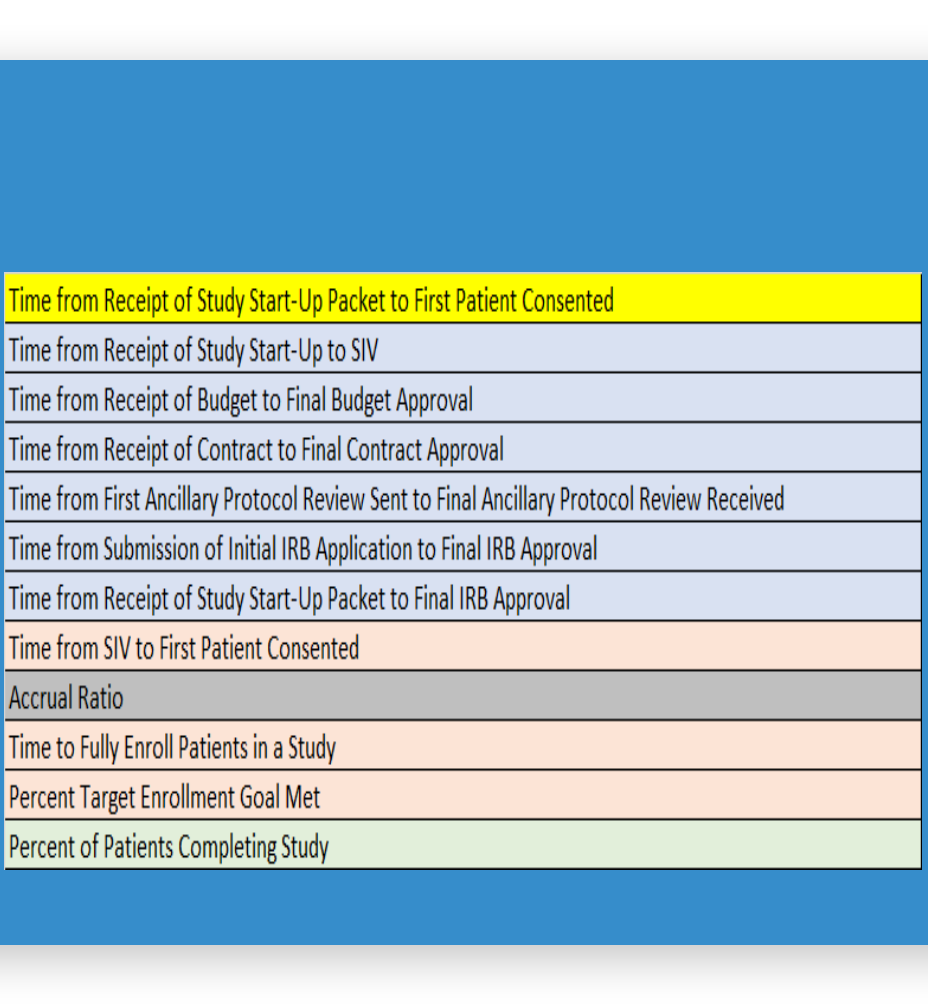
Two awardees of 2K/each to attend a scientific/research symposium

Following January 2021 launch of our proprietary Pediatric Improvement Collaborative for Clinical Trials & Research (PICTR®) initiative, a quality improvement program to measure and enhance the efficiency of our site network. We are proud to be partnering on this important initiative with Peter Margolis, MD, and his team at the James M. Anderson Center for Health Systems Excellence. In 2022, we have collected baseline measures from all participating sites and incorporate QI change packages within a select subset of "trailblazer" sites, so that we can make and measure improvements as rapidly as possible. This work was supported by FDA Grant U18FD006297

Some overall 2022 PICTR highlights include:

- 278 studies entered into our database contained at least 2 data points
- The database collection was simplified
- 6 Trailblazer Sites actively worked on quality improvement
- 2 Learning Sessions were held to educate sites on methods for quality improvement
- 1:1 Quality Improvement Coaching sessions were held
- Poster presentation at the DIA annual meeting
- Quarterly site dashboards were sent to all sites entering clinical trial data

Data Points collected were:



Time from Receipt of Study Start-Up Packet to First Patient Consented
Time from Receipt of Study Start-Up to SIV
Time from Receipt of Budget to Final Budget Approval
Time from Receipt of Contract to Final Contract Approval
Time from First Ancillary Protocol Review Sent to Final Ancillary Protocol Review Received
Time from Submission of Initial IRB Application to Final IRB Approval
Time from Receipt of Study Start-Up Packet to Final IRB Approval
Time from SIV to First Patient Consented
Accrual Ratio
Time to Fully Enroll Patients in a Study
Percent Target Enrollment Goal Met
Percent of Patients Completing Study

Additional PICTR Data collected:

- 25% of studies ready to enroll at time of SIV
- 55% of studies open to enrollment
- 44% of studies consented first patient
- 11% of studies stopped prior to completion
- 16 COVID Studies

The size of this database of pediatric clinical trials and the rigor applied in defining these time points makes this data extremely useful to identify areas of improvement at individual sites. In addition, the aggregate data can be used to inform other stakeholders with information capable of being used to plan a clinical development program. The data will provide accurate site-level data from a large number of sites and across a variety of therapeutic areas.

Advancing Innovation in Pediatric Clinical Trial Design

Advancing methodologies for more efficient pediatric product development is a high priority for both regulators and sponsors. I-ACT for Children leveraged our strength in convening stakeholders in a pre-competitive environment to follow-up and complete several important projects in 2022 that focus on innovative approaches to improving pediatric trial speed and efficiency.

1) Real-World Data

We contributed, in partnership with the Critical Path Institute and the International Neonatal Consortium, to the development of a neonatal real-world database and our hosting meetings aimed at advancing pathways for more efficient development of products for use by children.

2) Inflammatory Bowel Disease webinar

In March 2022 I-ACT for Children conducted the final webinar which was part of a four-part series of half-day webinars addressing the challenges being faced in development of innovative products for treatment of children with Inflammatory Bowel Disease.

3) Antimicrobial Resistance Webinar

In early 2022 I-ACT for Children began development of a project aimed at defining and addressing the challenges of antibacterial drug development for infants and children. A webinar series that will bring together experts to discuss these challenges and make recommendations on how we can best meet the needs of children that are evolving from antimicrobial drug resistance is planned for in early 2023.

Other Accomplishments of Note

REGULATORY AFFAIRS PANEL

A Pediatric Regulatory expert panel was established in early 2022. Members of the panel, Stephen P. Spielberg, MD, PhD, Hari C. Sachs, MD and Andrew Mulberg MD each have held leadership positions at the US Food and Drug Administration FDA in addition to having extensive experience in developing innovative products for use in infants and children. Sponsors are encouraged to meet with the panel to discuss regulatory development strategies.

DIVERSITY PANEL

Established in 2019 the panel is available to discuss strategies aimed at ensuring diverse patient populations of children are enrolled in clinical trials that involve the I-ACT for Children trial network. The panel includes Tamera Coyne-Beasley, MD, MPH, Jamie Fergie, MD and Robert Nobles, DrPH, MPH.

Thought Leadership

An important part of our mission is to raise awareness unmet needs in pediatric clinical research and advocate for addressing the medical needs of children urgently. In 2022, this advocacy included publishing manuscripts and presenting at prominent conferences.

Publications authored by I-ACT for Children staff in 2022 included the following:

Mulberg AE, Conklin LS, Croft NM et al.. Pediatric Extrapolation of Adult Efficacy to Children Is Critical for Efficient and Successful Drug Development. Gastroenterology. 2022 July;163(1):77-83. PubMed PMID: 35288113; DOI: 10.1053/j.gastro.2022.03.018.

Coppes MJ, Jackson C, Connor EM. I-ACT for Children: helping close the gap in drug approval for adults and children. Pediatric research. 2022 October 21. PubMed PMID: 36271160; PubMed Central PMCID: PMC9589790; DOI: 10.1038/s41390-022-02349-5.

Greenberg RG, McCune S, Attar S, Hovinga C, Stewart B, Lacaze-Masmonteil T. Pediatric Clinical Research Networks: Role in Accelerating Development of Therapeutics in Children. Therapeutic innovation & regulatory science. 2022 November;56(6):934-947. PubMed PMID: 36085251; PubMed Central PMCID: PMC9462608; DOI: 10.1007/s43441-022-00453-6.

Williams PC, Qazi SA, Agarwal R, Velaphi S, Bielicki JA, Nambiar S, Giaquinto C, Bradley J, Noel GJ, Ellis S, O'Brien S, Balasegaram M, Sharland M. Antibiotics needed to treat multi drug resistant infections in neonates. Bulletin of the World Health Organization. 2022 December 1;100(12):797-807. PubMed PMID: 36466207; PubMed Central PMCID: PMC9706347; DOI: 10.2471/BLT.22.288623.

In June 2022, I-ACT for Children Drs Mc Neeley and Noel presented analyses related to the development of new antibacterial agents for use in children at the American Society for Microbiology Microbe meeting at a Symposium entitled "Preterm and Pediatric Infections: How to Prevent and How to Treat."
Neely D, Noel G, Bradley J, Nambiar S. The Need for Continued Vigilance to Ensure that Children of All Ages Are Appropriately Prioritized in the Development of New Antibacterial Agents. American Society of Microbiology, Annual Meeting, Washington, DC. Platform/Abstract 4982.

Hovinga C, Neely D, Bradley J, Nambiar S, Noel G. Characterization of Published Information Available for Informing Treatment of Children with Serious Infections with Antibacterials Approved for Use in Adults But Have Not Yet Been Labeled for Use in Children. American Society of Microbiology, Annual Meeting, Washington, DC. Platform/Abstract 4311.

ADVANCING INNOVATION TOGETHER

Our I-ACT for Children Members

We work closely with our biopharmaceutical members to help them plan and execute their pediatric trials of innovative medicines and to advance pre-competitive initiatives that address unmet pediatric research needs. Our Sustaining Members hold five-year memberships, while our Annual Members hold one-year memberships. Each of our members shares our commitment to accelerating pediatric research and ensuring that children have access to medicines that have been proven safe and effective for them.

Sustaining Members

Johnson & Johnson
Lilly
NOVARTIS

Annual Members

BAYER
Chiesi

EMBRACING OPPORTUNITY

Looking Forward

The coming year continues to hold much promise for I-ACT for Children and for pediatric clinical research at large. We look forward to welcoming additional clinical trials into our I-ACT for Children Pediatric Clinical Trial Site Network, seeking new opportunities to optimize the design and feasibility of these trials from their inception and advancing pre-competitive projects that address ongoing critical needs within the pediatric research community.

We will continue to build the site network infrastructure, continually increasing its efficiency and interoperability. Thanks to the incredible efforts from our Site Network Team and based on the positive feedback from attendees and its impact, we will strengthen our educational efforts with all sites.

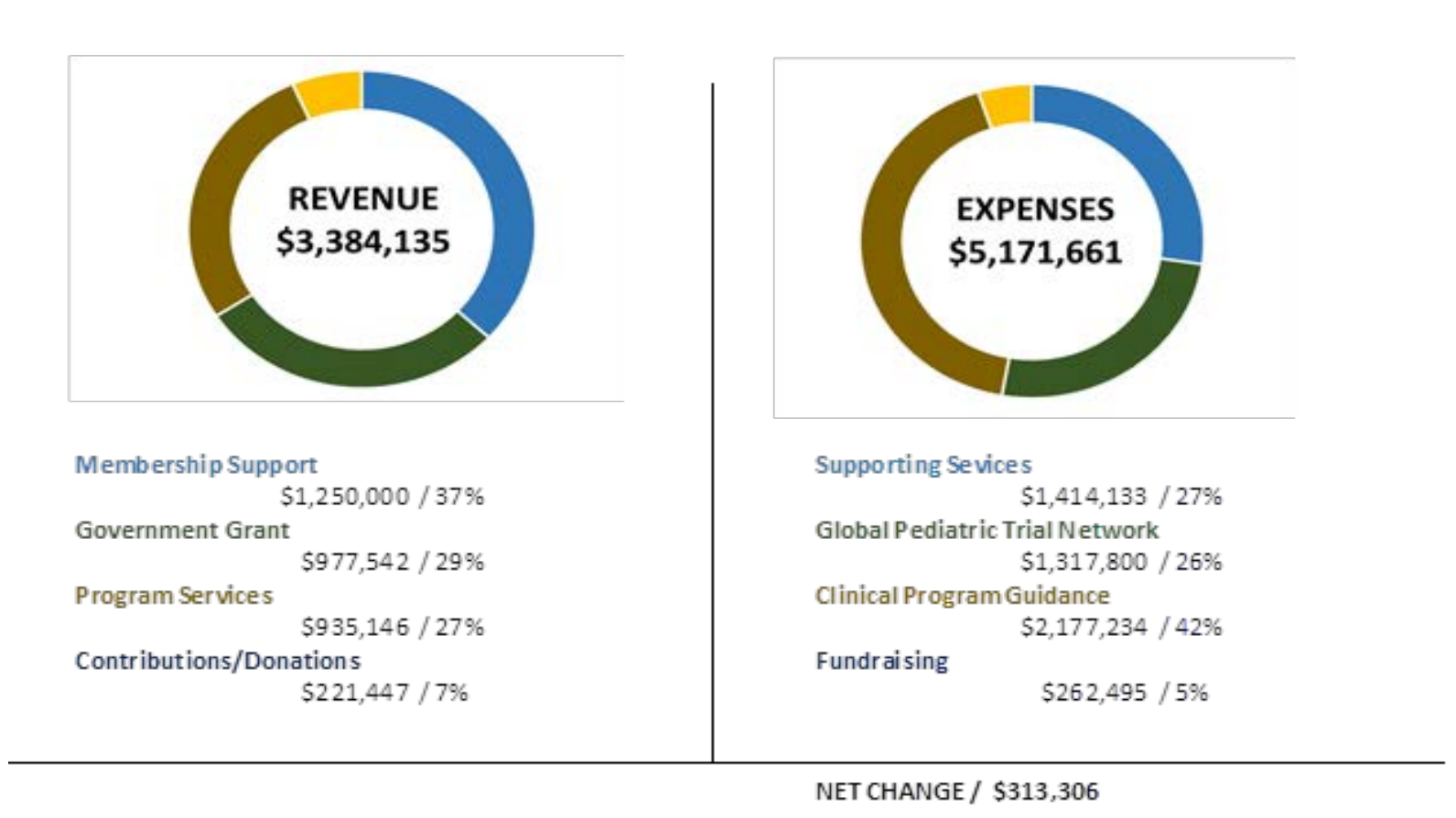
From a strategic perspective, we will continue to account for our members and all stakeholders from the pediatric community's feedback to better align with their needs. Since the pandemic, the clinical trial enterprise has changed.

We must manage expectations to accelerate clinical research and development pathways in children. From a financial standpoint, this year has been a challenging one. We had a decreasing number of projects from pharmaceutical sponsors in context of the impact of the pandemic and rationalization or attrition of drugs' portfolios in 2022. This loss of revenues was paralleled by an increase in the "cost to operate" our organization that worsens because of the inflation rate and we had to rapidly adapt to improve our budget outlook. Because of our public health mission, we have decided to launch a targeted fundraising campaign mid-2022 with the support of an experienced consulting firm to accelerate its implementation and results. We anticipate holding a series of fundraising events in 2023 to support our organization and mission. In parallel, we have begun seeking government support of our Pediatric Site Network. We believe that we will create the conditions improving our budget and secure growth and sustainability by the end of 2023.

In a post-pandemic era, we remain determined for our work to make an impact on pediatric drug development and children to have rapid access to innovation. With the continued support of the pediatric community and public at large, let's not make our children wait any longer.

2022 Financial Report

I-ACT for Children's 2022 Fiscal Year Financial Activities



REVENUE $3,384,135		EXPENSES $5,171,661	
Membership Support	$1,250,000 / 37%	Supporting Sevices	$1,414,133 / 27%
Government Grant	$977,542 / 29%	Global Pediatric Trial Network	$1,317,800 / 26%
Program Services	$935,146 / 27%	Clinical Program Guidance	$2,177,234 / 42%
Contributions/Donations	$221,447 / 7%	Fundraising	$262,495 / 5%

NET ASSETS

NET CHANGE / $313,306
NET AT DEC 31, 2021 / $7,199,967
NET AT DEC 31, 2022 / $6,886,661

The Institute for Advanced Clinical Trials (I-ACT) for Children is tax exempt under section 501(c)(3) of the Internal Revenue Code. Contributions to I-ACT for Children are tax deductible. Calendar year 12/31/2022 amounts, estimated and unaudited. The 990 is available through www.guidestar.org and upon request.

I-ACT for Children Leadership Team & Board of Directors

Leadership team

- Cindy Jackson, D.O., F.A.A.P, Chief Operating Officer
- Gary Noel, MD, FPIDS, Chief Medical Officer
- Laura Lopez, VP, Head of Finance
- Holly Huntington, VP, Head Clinical Site Network Operations
- Callie Heaton, Director, Project Management

Board of Directors

- Elizabeth Garofalo, MD (Chair)
- Edward Connor, MD, MBE, FAAP (Founding Member)
- Robert Ward, MD, FAAP (Founding Member and Vice chair)
- Martha Brumfield, PhD (Founding Member and Secretary-Treasurer and Chair, Governance & Nominating Committee)
- James Pomfret, ChFC,® CLU,® AIF® (Chair, Audit & Compensation Committee)
- Barry Brooks, JD
- Max Coppes, MD, MBA
- Jeff Barrett PhD

I-ACT for Children Collaborators

External Advisory Committee:
John Bradley, MD, Rady Children's Hospital; Jonathan Davis, MD, Tufts Children's Hospital; William Smoyer, MD, Nationwide Children's Hospital, Kathleen Neville, MD, Vice President, Clinical Development, C4 Therapeutics Inc.

DMD Platform Trial Consortium:
Pat Furlong, Parent Project Muscular Dystrophy; Abby Bronson, MBA, Edgewise Therapeutics; Richard Finkel, MD, St. Jude Children's Research Hospital; and Craig McDonald, MD, UC Davis Health (Scientific Co-Chairs)

International Pediatric Network Leaders:
Mark Turner, BSc, PhD, MBChB, DRCOG MRCP(UK), FRCPCH, FFPM(Hon), University of Liverpool, c4c; Thierry Lacaze-Masmonteil, MD, PhD; Alberta Children's Hospital Research Institute, MICYRN; and Hidefumi Nakamura, MD, PhD, National Center for Child Health and Development (Tokyo, Japan)

Other Acknowledgments:
Pharmaceutical Research and Manufacturers Association (PhRMA), Shionogi and Pfizer for their unrestricted grant support of I-ACT for Children programs in 2022.

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