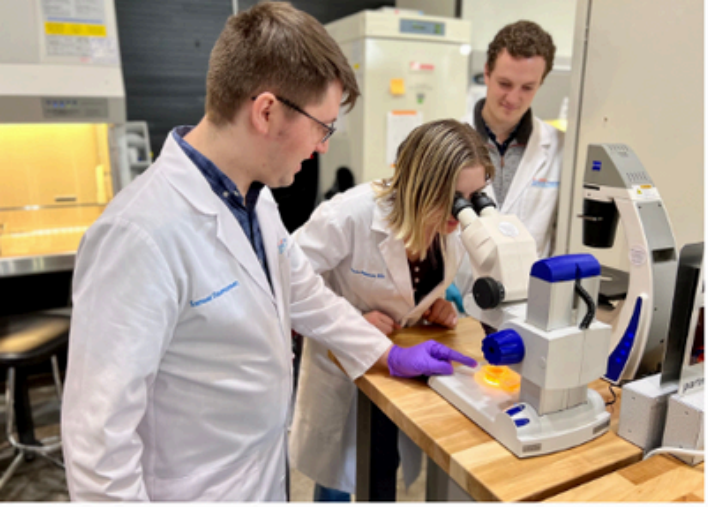




CHILDREN'S CANCER THERAPY DEVELOPMENT INSTITUTE

Impact Report



www.cc-tdi.org

2023

From our founder

Dear Supporters,

2023 was a transformational year for cc-TDI. It is with profound gratitude that we reflect on the remarkable progress made possible through your partnership.

In March we relocated to our **new pediatric cancer R&D laboratory** in the *Silicon Forest* of the Greater Portland Oregon area. This state-of-the-art facility allows for the growth and expansion of cc-TDI's research and would not have been possible without the support from ZGF Architects, R&H Construction, Megan's Mission Foundation, and other long-standing donors and partners committed to our mission.

We made significant strides in our engineering forward initiatives including the application of high-performance computing and artificial intelligence to accelerate our computational drug design. We were honored to receive an impactful $1 million investment from the state of Oregon allocated for equipment and technology during their 2023 legislative session. Additionally, our research team published nine scientific publications and partnered with more than six families on pilot project initiatives. We also proudly founded the *Megan Bugg Global Rhabdomyosarcoma Research Laboratory at cc-TDI*, honoring the life and legacy of **our dear friend Megan Bugg**.

In addition to these accomplishments, our work on PAX::FOXO1 and EWSR1::FL1 protein degraders led to a 2023 CRUK-NCI Cancer Grand Challenges application (*awarded in March 2024!*) in which our global team will receive up to $25 million over five years to further develop protein degraders for rhabdomyosarcoma (RMS) and Ewing sarcoma (EWS).

This prestigious grant not only validates the significance of our engineering-forward approach, but also brings us one step closer to translating our discoveries into clinical trials, ultimately paving the way for **more targeted and personalized treatment** approaches.

As I reflect on the past year with appreciation, I am reminded that our shared vision to make childhood cancer universally survivable, regardless of diagnosis, is only possible thanks to you, our community. Since our inception in 2015, your role as a partner and advocate has been integral to our success. You've helped our team develop two drugs that have moved into three national and international clinical trials and currently we are in the midst of more than four promising research projects for sarcomas, brain tumors and other solid tumors. We know this is just the beginning, and there's a lot more work still to be done.

As we navigate the complexities of drug development and **bring science-justified hope** to families affected by childhood cancer, thank you for entrusting our team to continue pushing the boundaries of what is possible.

With appreciation,

Charles Keller, MD
Scientific Director
Executive Director

Our story so far

Our Mission

cc-TDI is embarking upon a bold scientific course of discovery to send more targeted and less toxic drugs into clinical trials for those childhood cancers that have the most dire outcomes.

Our research team is exploring and testing state-of-the-art treatment options for the most urgent issues facing children with cancer. Biologists and biomedical engineers work closely on teams to identify targets on cancer cells and determine how to safely deliver effective treatments. By proving these methods in the laboratory, we can deliver smart, hope-filled discoveries to be prioritized in clinical trials for kids.

Working in our own, state-of-the-art freestanding research institution allows us to swiftly achieve results—bringing cost control, speed, purpose, and focus to translate effective treatments into the clinic. To get there, we perform basic science and translational research in our modern lab in the Silicon Forest in Hillsboro, Oregon.

Our mission is to translate scientific discovery into clinical trials by understanding and proving new disease-specific treatment options for children with cancer.

cc-TDI fills a crucially needed role created as a result of lack of federal funding for pre-clinical childhood cancer research.

Our Objectives

- Performing **basic science research** that expands our understanding of cancer **at the molecular level** and applying that knowledge in areas of unmet clinical need to guide target-specific and effective drug discovery.
- **De-risking investments in clinical trials** by identifying promising existing adult therapies and testing their potential application to pediatric cancer and developing new therapies 'from scratch' when needed.
- **Developing innovative techniques** to make preclinical testing and clinical trials for pediatric cancer more **efficient and cost-effective** for cc-TDI, academia, and the pharmaceutical industry.
- **Providing a complementary setting** to academia and corporate pharmaceutical labs for **emerging research leaders** to develop new skills, collaborate across disciplines, and create **revolutionary new approaches** to cancer research.

1 in 5

children diagnosed with cancer do not have the lifesaving treatment options they need

Strides forward
in the past year

4
Therapies Advanced

It can take seven years for a therapy to pass through the pre-clinical stage and on to human clinical trials. Each step in moving a therapy further in our pre-clinical pipeline means we are that much closer to improved outcomes for children.

9
Research Publications

Research publications are crucial for advancing science, are a measure of our effectiveness, and impact the field through collaboration with other research institutes. In 2023, we published 9 papers on clear cell sarcoma (CCS), Wilms' tumor, hepatoblastoma, rhabdomyosarcoma, epithelioid sarcoma, and leukemia.

2
Government Grants

Government grants provide funding through a highly selective process. They showcase credibility in the research field, provide the financial power to pursue in-depth NIH supported basic science, and support projects that are critical to drug development.

5+
Family Foundation Collaborations

Family partnerships are the heart of our lab. Through fundraising and advocacy, families have a voice in the fight against childhood cancer and provide ongoing support for research initiatives near and dear to their experience.

7
Next Generation Scientists

We welcome exceptional college and high school students to help further our important mission. Through direct mentorship and guidance by our team, these next generation scientists receive hands-on, real world experience in the field of childhood cancer research.

Key advancements
in childhood cancer research

Entinostat vs mocetinostat studies to support a national clinical trial concept

RMS

A fourth mouse model test of entinostat plus chemotherapy is complete, and the petri dish equivalence of entinostat and mocetinostat has been tested. This step further advanced entinostat as a potentially safe and effective treatment option towards clinical trials for RMS.

DIPG Research on the IL13R Antibody-Drug Conjugate

DIPG

cc-TDI is nearing manuscript completion on reporting test tube and petri dish study results with the first tissue models data. We repeated our tissue studies with another child's Diffuse intrinsic pontine glioma (DIPG) cells for thoroughness and are pursing a commercial path for this DIPG antibody drug conjugate (ADC) drug, which involved small adjustments in the configuration to make human use optimal.

Computational (AI) assisted drug design

Innovation

We have initiated a collaboration with Microsoft High Performance Computing to build an AI program in drug design for Ewing sarcoma (as well as other cancers) to succeed our collaboration with the IBM World Community Grid.

Nanocourse

Education

After the one-week intensive "bootcamp" for families and advocates, participants came away with a metastatic and anaplastic Wilms' Tumor roadmap and vision of creating a PROTAC for FUS-TFCP2 in Spindle Cell Sclerosing RMS.

Research publication: Advances in the clinical management of high risk Wilms tumors

Wilms' Tumor

This peer-reviewed paper takes an in-depth look at "high-risk" Wilms' tumors; those which fail to respond to standard therapies and are highly likely to result in poor outcomes. The paper analyzes current treatment strategies for children with high-risk Wilms' tumor and highlights the need for additional research and new treatments which might benefit these children.

Research publication: Functional genomics of human clear cell sarcoma

Clear Cell Sarcoma

This international collaboration uncovered major genetic differences between CCS for the gastrointestinal tract versus the soft tissues, with the added key observation that both subtypes express HER3 proteins. Using an ADC, patritumab deruxtecan, we aim to show a dose-dependent therapeutic effect on CCS cancer cells.

CRUK-NCI Grand Challenge grant collaboration

RMS & EWS

cc-TDI was honored as part of a shortlisted 10-institution global team for a Cancer Research UK - NCI $25M grant application (awarded in 2024), of which cc-TDI will receive up to $2.5M, to develop novel childhood cancer drugs primarily for RMS and secondarily for Ewing sarcoma.

Relocating to our home in the Silicon Forest

In the spring of 2023 cc-TDI relocated to a new **state-of-the-art laboratory** in the "Silicon Forest" of Hillsboro, OR. As you may imagine, relocating a 7,000 sq-ft lab was a significant task, which required sensitive equipment and research materials to be transported, reinstalled and recalibrated - all in stages.

This relocation has provided for the continued growth and expansion of cc-TDI allowing us to leverage **innovative techniques** and **de-risking investments** in clinical trials. Additionally, it signifies a step forward in our mission, further securing our commitment to advancing childhood cancer research for years to come.

Thank you to our donors, partners, and friends for their impactful support of this project. Special appreciation goes to the cc-TDI team for going above and beyond to ensure critical research continued safely through this transition.

Megan Bugg Global Rhabdomyosarcoma Research Laboratory

On April 29th, 2023 we celebrated the dedication of the Megan Bugg Global Rhabdomyosarcoma Research Laboratory. This initiative, spearheaded by the outpouring of support from the Megan's Mission Foundation, secures Megan's legacy in all current and future rhabdomyosarcoma research projects at cc-TDI.

Without this effort, our new home would not have been possible. Our team continues to carry Megan in our hearts as we work to fulfill our joint mission of making childhood cancer universally survivable through research and advocacy.

Thank you to the Megan's Mission Foundation for their ongoing support in three key areas:

- **Immunotherapy for use in RMS**
- **Citizen Scientist Project**
- **Entinostat for use in RMS**

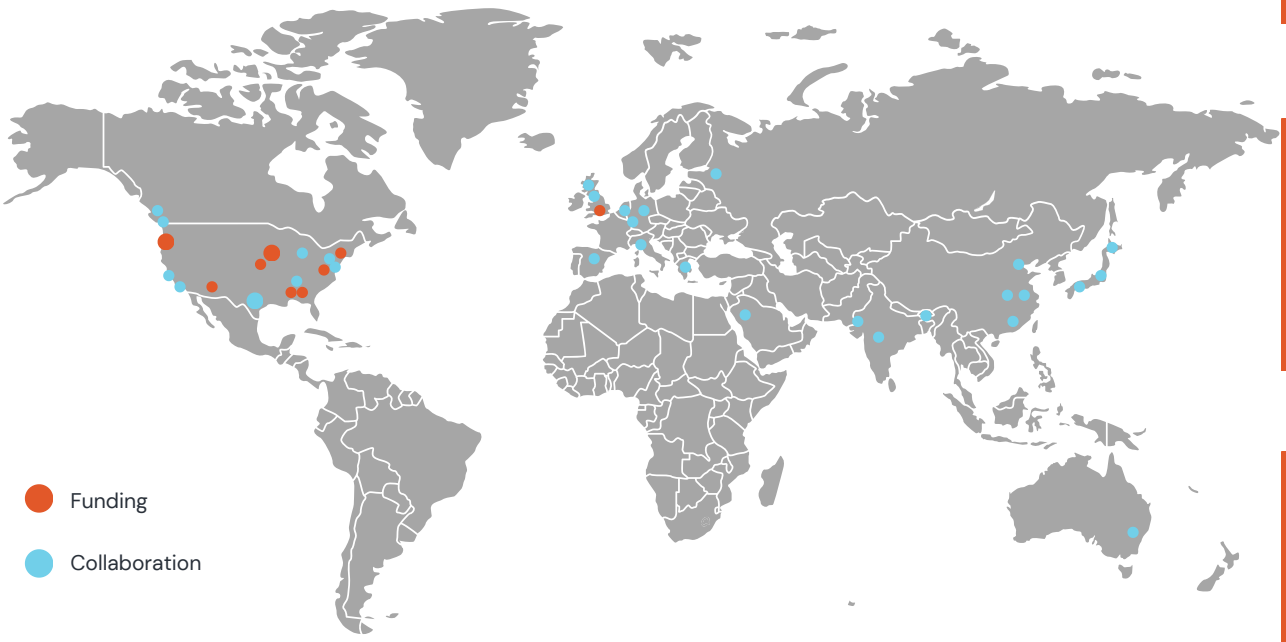
Global collaboration

Extending our reach

10+
Research Facility Collaborations

25+
Corporate Supporters

5+
Pharmaceutical Relationships



Partners & collaborators

Austrian Academy of Sciences
Cancer Research UK
Champions Oncology
Children's Hospital of Philadelphia
Children's Oncology Group
Curie Institute
Genentech
Johns Hopkins School of Medicine
Massachusetts Institute of Technology
National Cancer Institute
National Institutes of Health
Nurix Therapeutics
Rockefeller Institute
Seattle Children's Hospital
Theodor-Boveri Institute
University of Dundee
University of California San Francisco
University of Würzburg

Manuscripts published in 2023

Functional genomic analysis of epithelioid sarcoma reveals distinct proximal and distal subtype biology

Functional genomics of human clear cell sarcoma

CD203c is expressed by human fetal hepatoblasts and distinguishes subsets of hepatoblastoma

BCR-ABL is enriched in S- and G2-cell cycle phases

Translational aspects of epithelioid sarcoma – current consensus

Non-chemotherapy adjuvant agents in TP53 mutant Ewing sarcoma

Piperacetazine directly binds to the PAX3::FOXO1 fusion protein and inhibits its transcriptional activity

Structure-activity relationship of dihydropyridines for rhabdomyosarcoma

Advances in the clinical management of high-risk Wilms tumors

Fueling our mission

A special thank you to our key fundraising partners

$100,000+

- Megan's Mission Foundation
- Rucker Collier Foundation
- Lyla Nsouli Foundation
- Golf Fights Cancer

$50,000+

- Macy Easom Foundation
- Morris Community Foundation
- MJ Murdock Charitable Trust
- Kuni Foundation
- City of Beaverton

$25,000+

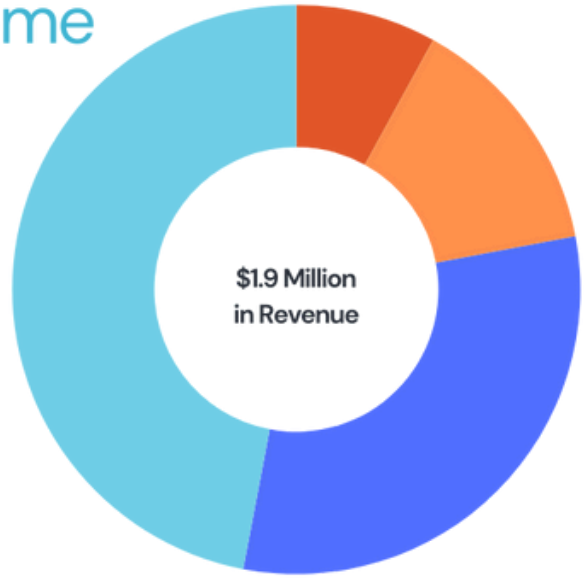
- Hero-Up
- Mello Signs
- Rally Foundation
- Hundt Strong

$10,000+

Sam Biggs Memorial Foundation
Michael Cuccione Foundation
The Brittney Project
Ivory Ella
Cooper Caywood Honor Page
Avery's 'Rhabdo Blast' Project
The Nathan Edwards Family
Cait's Honor Page
Miriam Weiss
Mike Thomas
Coal City Bank
Anonymous Donors

2023 cc-TDI Income

- Other Income 8%
- Philanthropy 31%
- Government Grants 14%
- Foundation Grants 47%



This demonstrates the diverse revenue streams essential for advancing our mission in the fight against childhood cancer

Families inspiring change

> In 2023 our daughter Brittney, a forever five-year-old, earned her wings after bravely fighting rhabdomyosarcoma. Right away we knew our family wanted to further Brittney's legacy, but through our cancer journey, we felt our options for making a lasting impact were limited. This changed when we met Dr. Keller. In his team's embrace, we discovered that we could **have a say in the fight against childhood cancer**.

In memory of Brittney, we launched the Brittney Project, a new research initiative at cc-TDI aimed at validating embryonal rhabdomyosarcoma-specific compounds on a broad range of different embryonal rhabdomyosarcoma cell lines. With the creation of the Brittney Project, we soon became deeply engaged in the research objectives of cc-TDI. As our family has met more of the team, we continue to feel supported, connected and seen. We are not simply donors supporting a mission, we are true partners having found our voice in the childhood cancer research community.

Investing in our bench

In 2023, we focused on increasing capacity in our research team by bringing on four new team members: Mayukha Kashyap, BSc, JiaoJiao Wang, PhD, Zu-Yuan Qian, PhD, and Wil Edwards, BSc. Our research team continues to work tirelessly to develop safe and effective treatment options for some of the most underserved childhood cancers in the world.

In addition to increasing our capacity on the research front, our lab was excited to welcome Claire Newman and Ben Ritt to the operations team as well. As our team continues to grow and develop, we want to say thank you for the ongoing support of our incredible Board of Directors and key supporters that have a great vision for our future!

Meet our team

Board of directors

Leading with purpose

John Grant
Board Chairman

Paul Metzgar
Co-Finance Committee Lead

Jason McGill
Co-Finance Committee Lead

David Dilts
Search & Nominations Committee Lead
Co-Finance Committee Lead

Michele Metzgar
Development Committee Lead

Gary Nagamori
Compliance Committee Lead

Michael Lin

Kenya Robertson

Tina Richards-Lynn

Levi Seed

Chris Rasmussen

Tonya Rogers

Lisa Howard

What makes cc-TDI unique

By focusing our time, energy and talents on filling the pre-clinical trial gap, we can control more than anyone else which drugs for childhood cancer advance to clinical trials.

Working as a freestanding research institution allows us to act swiftly and nimbly to achieve results — bringing cost control, speed, purpose, and focus to translate effective treatments into the clinic.

From our chair

Those of us who have supported cc-TDI over the years are not donors - **we are investors**. We are passionately committed to fighting the scourge of childhood cancer, and each year we dedicate some of our finite resources to advancing this cause. So like good investors, we do our research and we try to identify the organizations and individuals who will make the most effective use of our funding. And like good investors, we expect results.

As you can see in this report, Dr. Keller and his research team have delivered exactly that. In my role as Board Chair, I've had the privilege of witnessing the strides cc-TDI has made in advancing childhood cancer therapies and the team's unwavering commitment to make childhood cancer universally survivable. Whether through moving entinostat a step closer to clinical trials, uncovering the genetic makeup of CCS, joining a global team of researchers to develop novel drugs, or publishing influential research papers pushing out the frontiers of science - cc-TDI is getting results.

We take pride in our distinctive approach as cc-TDI aims to provide science-justified hope for children and families living with this harsh reality. To achieve this, we value strong collaboration between the board of directors and cc-TDI's team, ensuring fiscal responsibility and providing operational leadership, while simultaneously helping steer scientific research toward groundbreaking discoveries. In other words, we are committed to ensuring that cc-TDI is the best investment you can possibly make.

Curing cancer is a slow and complicated process, but our joint **commitment to giving back childhood** remains unwavering and your support is integral in propelling cc-TDI's research forward. As we embark on another year together, I look forward with hope and a resilient spirit, honoring the children and families we serve. Thank you for partnering with us in this important work.

Sincerely,

John Grant
cc-TDI Board Chair

Thank you for your ongoing support of cc-TDI as we work towards a **hopeful future** for the children we love.