
CURESEARCH
FOR CHILDREN'S CANCER
OCTOBER 2021
IMPACT REPORT
#Not1989Anymore

A message from our CEO

Dear CureSearch Supporters,

At CureSearch, we focus on one goal: bringing childhood cancer treatments to the forefront of drug development. Today, the vast majority of therapies given to children diagnosed with cancer were developed and approved before 1990. Simply put, for more than 30 years, many children diagnosed with cancer have had only one option: to receive toxic treatments that likely produce lifelong side effects such as deafness, musculoskeletal problems and even secondary cancers.

If you have volunteered for CureSearch, funded a research project, donated monies, participated in an event or supported us in any of numerous ways, you are helping us to change that paradigm. Together, we are driving the development of promising new therapies that avoid the toxicities of the past. Alongside this important work, we foster collaborations that will lead to every child having a safe and effective treatment option — because it's not 1989 anymore.

In this Impact Report, I'm thrilled to share updates on our prestigious Catapult Award projects, which are actively enrolling glioma and DIPG patients in clinical trials. You'll find updates on the progress of our groundbreaking Young Investigators like Dr. Loretta Li, who is developing a new approach to treating a high-risk subtype of B-cell ALL. CureSearch continues to set the bar in preclinical projects, breaking paradigms by advancing projects into the clinic at five times the average rate and doing so in an accelerated pace that reaches the clinic two years sooner. That speed is critical for families facing cancers with the lowest survival rates and fewest treatment options.

We are committed to leading strategic collaborations, as that is the path to long-term impact. This September, we wrapped up the 2021 CureSearch Summit, a four-part virtual series focused on engaging families, industry and academics on the topic of solid tumor biopsies and their impact in pediatric cancer research. In October, we'll host the second annual CureSearch Pediatric Early Development Symposium, a unique platform where industry, regulatory and academic leaders will discuss new approaches to developing clinical trials.

Excitedly, we resumed in-person campaign events this year. Supporters throughout the country formed teams and enthusiastically raised monies for CureSearch Walks and Ultimate Hikes. DIY Gold events were held in communities across the country to raise funds and awareness in support of our critical mission.

The enclosed report is the impact of our work together. Thank you for your continued support for the children who are counting on us to move one step closer to curing childhood cancers.

Kay Koehler
President & CEO

CURESEARCH-FUNDED CLINICAL TRIALS ARE IMPACTING PATIENTS TODAY

DIPG trial shows encouraging early results

Crystal Mackall, MD
Stanford University

In June 2020, Crystal Mackall, MD, and her team at Stanford University opened enrollment for an early-phase clinical trial to determine whether CAR T-cell therapy is an option for patients with DIPG, a cancer with a dismal five-year survival rate of less than 1%.

According to early results of the phase I study, three of four patients who received an investigational CAR T-cell therapy for diffuse midline glioma showed tumor regression and improvement in neurologic symptoms.

The team presented early findings at the American Association for Cancer Research Annual Meeting in April of 2021.

Dr. Mackall has also modified the protocol to allow additional doses of CAR T-cells through an implanted catheter that allows for direct delivery to the tumor. This delivery method enables patients to skip the conditioning chemotherapy regimen that can lead to toxicity. The clinical trial continues to enroll patients, drawing interest from across the country and internationally.

High-grade glioma trial now open at seven sites

Ranjit Bindra, MD, PhD
Yale University

Ranjit Bindra, MD, PhD, and his team at Yale University began enrolling patients in early 2020 for his clinical trial to test a novel drug in pediatric patients with a specific subtype of glioma that makes it sensitive to chemotherapy. The study is now active at University of California San Francisco, the Dana-Farber Cancer Institute, Washington University St. Louis, Johns Hopkins University, Oregon Health & Sciences University, St. Jude Children's Hospital and Yale University.

Two patients have been enrolled and treated and have entered the observation phase of the trial. In the next six months, Dr. Bindra's team aims to open his trial at five additional Pediatric Neuro-Oncology Consortium (PNOC) sites.

YOUNG INVESTIGATORS REPORT PROMISING NEW FINDINGS, ADVANCE CLOSER TO CLINIC

Research indicates potential new treatment for high-risk B-cell ALL

Loretta Li, MD, studies a high-risk subtype of B-cell acute lymphoblastic leukemia (ALL), which occurs in about 15% of pediatric cancer patients and is dependent on the JAK2 protein, but resistant to classic JAK2 inhibitors.

The Li lab is developing new compounds that can overcome resistance to ruxolitinib, a therapy with demonstrated clinical safety for use in children with relapsed/refractory cancers that harbor the JAK2 mutation. Dr. Li's therapy may offer a new treatment option for leukemias that have become untreatable.

Importantly, Dr. Li has identified the two most potent compounds among a group of JAK2 inhibitors and tested them across four different human cell lines and four different mouse cell lines, demonstrating the ability to inhibit JAK2 and slow growth of these cancer cell models.

Loretta Li, MD
Lurie Children's Hospital / Northwestern University

New method aims to reduce toxicity, increase effectiveness of neuroblastoma treatment

Avery Posey, PhD, developed a novel CAR T-cell therapy targeting polySia for the treatment of pediatric neuroblastoma.

Dr. Posey observed tumor growth delay in patient-derived models of neuroblastoma in response to the CAR T-cell therapy and noticed no changes to body weight or health condition. This indicates that targeting polysialic acid in neuroblastoma may be safe and should not result in neurological complications.

In addition, his lab is studying the combination of a virus designed to destroy cancer cells with cellular immunotherapy. This technique aims to enhance the effectiveness of CAR T-cell therapy by destroying the cancer cells so that they expose more of the polysialic acid target.

Avery Posey, PhD
University of Pennsylvania

YOUNG INVESTIGATORS REPORT PROMISING NEW FINDINGS, ADVANCE CLOSER TO CLINIC

New biomarkers could indicate MPNST treatment efficacy

Kathryn Lemberg, MD, is testing a novel glutamine antagonist that will disrupt cancer cell energy production as a potential treatment for malignant peripheral nerve sheath tumors (MPNSTs) – aggressive tumors that arise from the cells that normally support nerve function.

Dr. Lemberg and her team have identified new biomarkers that could enable her to monitor effectiveness in patients in real-time from a simple blood draw.

Dr. Lemberg has also begun developing combination therapy, combining her drug and a second novel therapy to increase the ability of the treatment to kill MPNST cells. Initial tests have demonstrated that this combination is more effective than either drug alone and Dr. Lemberg will continue to move this combination into more models of MPNST.

Kathryn Lemberg, MD
Johns Hopkins University

New immunotherapy approach could improve survival for AML

In September 2021 – in partnership with the SebastianStrong Foundation – we awarded a new CureSearch Young Investigator grant to Mark Kohler, MD, PhD. Dr. Kohler will develop a new treatment approach for acute myeloid leukemia (AML), a rare blood cancer in children. While improved treatment options for pediatric leukemia have increased overall survival rates, certain subtypes will not be cured with conventional chemotherapy. In fact, AML patients who do not respond to treatment, or experience recurrence after treatment, usually survive fewer than six months.

CAR T-cell therapy is ideal for patients whose disease no longer responds to chemotherapy, as it relies on the immune system to eliminate leukemia cells. Dr. Kohler will develop two CAR T-cell approaches for AML, which will decrease the leukemia cells' ability to avoid treatment and reduce toxicity in children with relapsed AML.

At the conclusion of this three-year project, Dr. Kohler aims to move these new immunotherapy strategies into early phase clinical trials. If successful, this novel approach can potentially be applied to other forms of childhood cancers with poor prognoses.

Mark Kohler, MD, PhD
University of Colorado Cancer Center

RESEARCH FUNDING SUCCESS: PROVIDING CRITICAL FUNDS TO DRIVE NEW TREATMENTS INTO CLINICAL TRIALS

Our Acceleration Initiative projects are five times more likely than average to advance into clinical trials, and they reach the clinic more than two years faster.

New therapies identified for pediatric sarcoma

Andrew Kung, MD, PhD
Memorial Sloan
Kettering Cancer Center

Although overall outcomes for children with cancer steadily improve, survival of children with high-risk sarcoma has remained unchanged over the last 20 years. There is a pressing unmet need for new methods to identify vulnerable targets in childhood sarcomas.

Andrew Kung, MD, PhD, and his team developed a new method to assess the entire signaling network within cancer cells and to identify the critical signaling nodes, or Master Regulators (MRs), that drive malignancy. By using a systems biology approach – where molecular profiling is paired with bioinformatics to identify the key MRs – they set out to analyze single patient samples from children with high-risk sarcomas and identify MRs, and then identify drugs that target the activity of the MRs.

In doing so, the team identified 20 prioritized drugs with the potential to treat a wide range of pediatric sarcoma subtypes.

As of the conclusion of his project, Dr. Kung has:

- ☑ **Analyzed a diverse portfolio of 241 pediatric sarcoma cases**
- ☑ **Developed 124 patient-derived xenograft models for drug testing**
- ☑ **Produced 73 novel cell models from patient tumor cells**

RESEARCH FUNDING SUCCESS: PROVIDING CRITICAL FUNDS TO DRIVE NEW TREATMENTS INTO CLINICAL TRIALS

We're uniquely positioned to drive critical stakeholder collaborations to accelerate the pace of pediatric drug development.

Collaborative funding to accelerate childhood cancer research

Accelerating pediatric cancer drug development requires collaboration among multiple funding organizations. This model allows us to provide significant funding for potentially groundbreaking projects, including a strong co-funding model to support innovative projects, combat duplication of efforts and better leverage a combined funding pool.

Elias Sayour, MD, PhD
University of Florida

In 2020, CureSearch granted $2.5 million to Dr. Elias Sayour at the University of Florida for a first-in-human, phase I/II clinical trial testing an innovative personalized immunotherapy for pediatric high-grade gliomas. This project is supported in part by the Norcross Foundation, Love Your Melon, the Resonance Foundation for Children's Health co-founded by Sheri Sobrato Brisson and Eric Brisson, and by the Rally Foundation for Childhood Cancer Research.

Thank you to our current funding partners:

- ***Resonance Foundation for Children's Health***
- ***The Norcross Foundation***
- ***Anonymous***
- ***Genentech***
- ***SebastianStrong Foundation***
- ***Rally Foundation for Childhood Cancer Research***
- ***John & Maria Laffin Trust***
- ***H.G. Barsumian, M.D. Memorial Fund***
- ***Parker Institute for Cancer Immunotherapy***
- ***James Paul Sutton Medical Research Fund***
- ***Harvey L Miller Family Foundation***

To learn more about co-funding opportunities, please contact Melisse Hunter.

DRIVING CRITICAL COLLABORATIONS TO BRING CHILDREN TO THE FOREFRONT OF DRUG DEVELOPMENT

2020 CureSearch Pediatric Early Development Symposium:
Developing iPSPs and PIPs in an Evolving Regulatory Landscape

Real progress in pediatric cancer drug development requires collaboration among leaders in science, academia, regulatory, funding and industry. The inaugural CureSearch Pediatric Early Development Symposium (PEDS) served as a synergistic platform for driving critical stakeholder collaborations and addressed the challenges in developing initial Pediatric Study Plans (iPSPs) and Pediatric Investigation Plans (PIPs).

In the months following the inaugural symposium, CureSearch worked with global stakeholder and volunteer leaders to execute on the following overarching strategies:

- **Promote global collaboration across all roles in pediatric drug development**
- **Provide pediatric drug development resources to stakeholders**
- **Address areas of unmet need in clinical development for children with cancer**

Read the 2020 PEDS Impact Statement here.

"We are in a period of immense promise for the development of new cancer therapies for children, but with this promise arise inherent challenges. Working together to gain a greater understanding of how to address these challenges and sharing information will allow us to develop, evolve, and implement strategies that not only meet regulatory requirements, but truly advance the care of children with cancer."
- PEDS 2020 Co-Chairs: Samuel C. Blackman, MD, PhD & Brenda Weigel, MD

Stakeholders will convene October 6-8 for PEDS 2021 – **Pediatric Oncology Clinical Trial Development: New Approaches for a Changing World** — to address the unique aspects and challenges of pediatric cancer clinical trial design.

VOLUNTEERS MAKING AN IMPACT

Volunteers and advocates across the country participate in CureSearch fundraising events to support childhood cancer research.

Walking for Caden – 50 miles in 30 days

In 2012, Caden was diagnosed with stage four neuroblastoma, a solid tumor that affects 3.8 percent of all children with cancer. This year, his family walked 50 miles for the CureSearch Mile for Child Challenge, which challenges supporters to walk 10, 30 or 100 miles in 30 days to raise funds and awareness for childhood cancer.

Today Caden is cancer free and a happy, healthy 13-year-old.

"Caden is doing extraordinary today, thanks to the efforts of so many. Cures are so desperately needed and research is the only way we'll get there. We'll always pour our passion into the effort to cure more children." - Pam Shrauger, Caden's Mom

"Fundraising = research = lives saved!"

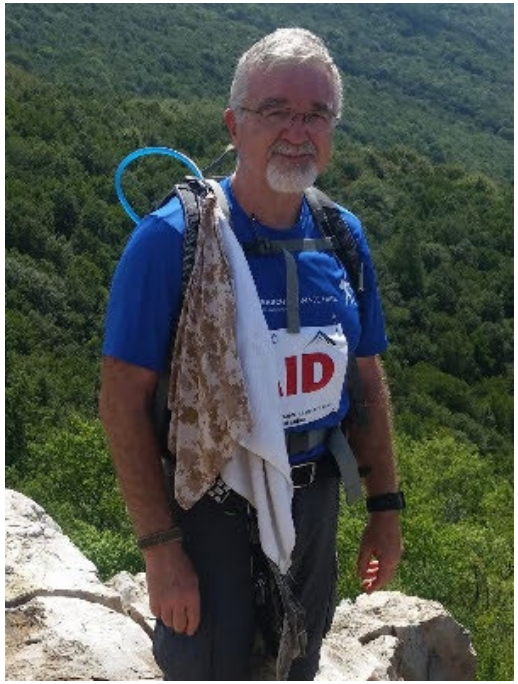
Families, communities and businesses across the country reunited this year for annual CureSearch Walks to support the 17,000 children, adolescents and young adults diagnosed with cancer each year – children like Alex.

Alex was diagnosed with acute lymphoblastic leukemia (ALL) in 2012. Since 2013, Alex and his family have been participating in the CureSearch Walk. Their team — The A Team — has raised more than $127,000. Alex is now 16 years old and thanks to research advancements, he is thriving.

"When we learned that in the 1970's leukemia would've been a death sentence, that really hit us hard. We knew that many of the other cancers didn't have as high of a survival rate as ALL and we wanted to give back. We truly realize that fundraising = research = lives saved!"- Jamie, Alex's Mom

HIKERS GO THE EXTRA MILE FOR CHILDHOOD CANCER RESEARCH

Hikers across the country join us in telling childhood cancer to "take a hike" at the CureSearch Ultimate Hikes. Since its inception, Ultimate Hike participants have raised more than $8 million for childhood cancer research. Individuals who raise $5,000 or more are part of the Ultimate Hike Summit Club.



Mike Owen is a member of the Summit Club and has participated in 14 CureSearch Hikes. He hikes in honor of Daniel, Cameron and Fiona.

"Daniel is a young man, now 21, who survived acute lymphoblastic leukemia (ALL) as a kid. Cameron was diagnosed with medulloblastoma at six years old. In 2011, Cam went to be with Jesus. Six-year-old Fiona has battled retinoblastoma for most of her young life. We are proud to know her and hike in her honor." - Mike Owen

GET INVOLVED!

You can make an impact by fundraising to support the most promising childhood cancer research. Hit the trails for an Ultimate Hike, register to walk with your community, join the team for a race, or create your own fundraising event!

Learn more at curesearch.org/get-involved

PROVIDING EDUCTIONAL RESOURCES FOR FAMILIES

New videos highlight advancements in precision medicine.

Thanks to the generous support of Thermo Fisher Scientific, two new videos are now available in our online video library exploring the evolving science of precision medicine and its impact on patients today. View these videos and more at curesearch.org/video-library.

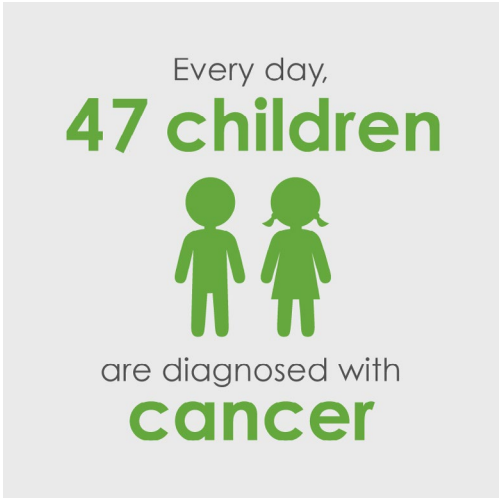
Precision Medicine: The Future of Pediatric Cancer Treatments

Precision Medicine: Joey's Treatment Journey

PROVIDING EDUCATIONAL RESOURCES FOR FAMILIES

Updated childhood cancer statistics released

Key childhood cancer statistics are updated annually and the most recent data is available on our website. CureSearch always cites SEER data from the NIH/National Cancer Institute for all diagnoses and survival statistics. All statistics refer to children and teens ages 0-19.



To view more childhood cancer statistics, visit curesearch.org/childhood-cancer-statistics.