



ALSF Founder Alex Scott

Inside: Fueling young researchers, expanding clinical trial access, helping heroes and more



Edie and Dr. Mossé

From Edie to Alex to **Cures** for all Children with Neuroblastoma

In 2011, 2-year-old Edie Gilger had been fighting neuroblastoma for over half her life. Despite multiple rounds of chemotherapy and surgeries, Edie's cancer persisted. Out of options, Edie went to Children's Hospital of Philadelphia (CHOP).

CHOP doctors tested Edie's blood and found she was harboring a specific mutation called anaplastic lymphoma kinase (ALK). ALK was driving Edie's neuroblastoma — and the trial for a drug called crizotinib, led by Alex's Lemonade Stand Foundation (ALSF)-funded researcher, Dr. Yael Mossé, offered new hope.

The trial worked. By December 2011, Edie was cancer-free. Later, her mother, Emily, would be diagnosed with same type of ALK-driven familial neuroblastoma and find her cure in crizotinib and a similar drug, alectinib.

However, crizotinib is not effective for all types of neuroblastoma-specific ALK mutations. Dr. Mossé discovered that many kids with this disease had tumors that were positive for the ALK mutation, even if the children themselves were not.

Working with her team and using grant funding from ALSF, Dr. Mossé discovered a drug called lorlatinib was the only ALK inhibitor effective against neuroblastoma that expressed the ALK-mutation. Dr. Mossé led the Phase 1 trial for the drug in the New Approaches to Neuroblastoma Therapy (NANT) Consortium.

As patients in the trial showed positive responses to lorlatinib, the Scott family received news that testing had showed ALSF founder Alex Scott's neuroblastoma had been ALK-positive.

Alex, who died at age 8 in 2004 from neuroblastoma, endured chemotherapy, radiation, surgery, MIBG therapy and additional treatments all with harsh, painful side effects. Through it all, Alex always believed that research could help kids, just like her.

Now, lorlatinib will be tested in a Children's Oncology Group (COG) Phase 3 trial as up-front treatment for children with neuroblastoma whose tumor show an ALK mutation. Used in conjunction with chemotherapy, this treatment could substantially improve chances of a cure for children with high-risk neuroblastoma whose tumors harbor an ALK alteration and do so with reduced short- and long-term side effects. This trial is open at the more than 240 COG sites across the United States.

"We expect to significantly improve survival for children with neuroblastoma whose tumors have an ALK mutation. This Phase 3 trial is the last stop before FDA and EMA (European Medicines Agency) registration. We hope that this drug becomes standard of care and available to all kids with ALK-driven neuroblastoma," said Dr. Mossé.

Donors like you have continued Alex's vision of cures for all kids, and every day, you are funding projects that bring us one step closer to that reality.

1996

Alex Scott diagnosed

2004

Alex dies from neuroblastoma

2009

Edie Gilger diagnosed

2011

Edie enrolls in crizotinib trial

2013

Emily Gilger diagnosed with familial neuroblastoma

2014

Emily starts the same treatment Edie had and is cured, like her daughter

2017

Phase 1 trial for lorlatinib opens (no phase 2; going directly to 3)

2021

Scott family receives Alex's tumor genetics

2022

Phase 3 trial opens with lorlatinib for patients with newly diagnosed ALK-driven high-risk neuroblastoma

Fueling Progress, **One Grant at a Time**



Dr. Meenaskhi Hegde

Since ALSF began funding research nearly 20 years ago, researchers have turned their attention to precision therapies that target the genetic drivers of childhood cancer as well as the mutations that fuel growth. This shift has brought promising, curative treatments to the forefront like crizotinib and lorlatinib (mentioned in our cover story). However, given the rarity of childhood cancer and the

diversity of oncogenes and genetic drivers, studying and testing potential treatments is often constrained by the low number of children who qualify for a trial's eligibility criteria.

To accelerate the pace of discovery, ALSF-funded Center of Excellence (COE) researchers and institutions continue to work together to launch multi-site trials that allow more children access to clinical trials, which in turn gives researchers more insight into potential treatments.

Dr. Meenaskhi Hegde, an ALSF-funded researcher from Texas Children's Hospital, is leading a Phase 1 study of CAR T cells for patients with refractory or relapsed ependymoma, a rare brain tumor in children. The study, which opened in early 2022 at two children's hospitals with local approval underway at four more hospitals, will give patients access to treatment closer to home. This is important to move the science along more quickly and is crucial for children's quality of life.

Texas Children's Hospital is one ALSF's Center of Excellence grant-funded institutions. ALSF provides COEs with support to build clinical trial infrastructure. Between 2020-2021, the four COE's have 55 ongoing clinical trials.

"If this kind of treatment is going to make a big difference, it has to be available beyond just a few centers, and we're pushing that envelope," said Dr. Stacey Berg, the co-director of Texas Children's Cancer Center Developmental Therapeutics Program.

Read more about the work at Texas Children's Cancer Center at AlexsLemonade.org/Blog.

Accelerating Early Career Researchers



Dr. Corinne Linardic

Corinne Linardic, MD/PhD at Duke University Medical Center, received her Young Investigator Grant from ALSF to study the genetic cause of rhabdomyosarcoma in 2006. In their research, her team discovered that rhabdomyosarcoma's unique, undruggable DNA mutation switches "on" a fusion protein, which in turn shuts "off" a critical pathway. This critical pathway controlled cell growth, and the "off" mechanism let tumors grow uncontrollably.

This study has since spring boarded several new research directions in her lab. As her work progressed, she also received two ALSF Innovation Awards in 2013 and 2019. These awards have helped accelerate

her team's efforts to identify new therapeutic targets for this childhood cancer today. All the while, she's been inspired to get involved with ALSF in other ways, such as participating as a team member for the Faces of Research Team during The Million Mile, and recently becoming a mentor for the Pediatric Oncology Student Training (POST) Program.

Another researcher, Nicole Brossier, MD/PhD of Washington University, also kicked off her scientific career with her Young Investigator Award in 2019. With her eyes on potential cells of origin for tumors like astrocytomas and optic nerve gliomas, she and her team plan to analyze which cells in the developing brain give rise to these tumors, and how a specific gene mutation functions as a risk factor for brain tumor formations and other pediatric brain cancer predisposition syndromes.

Given the diversity of pediatric cancer research that addresses the undruggable mutations and focuses on developmental origins of cancer, the future appears more and more promising for kids with cancer.



Dr. Nicole Brossier



Dr. Robbie Majzner



Dr. Johanna Theruvath

Two Antibodies Prove Better than One

In 2019, Robbie Majzner, MD, at Stanford University School of Medicine, received an 'A' Award grant from ALSF to study a combination of anti-cancer antibodies, anti-GD2 and anti-CD47, as treatment for two difficult to treat diseases, neuroblastoma and osteosarcoma.

Dr. Majzner and lead author Dr. Johanna Theruvath discovered that alone, these two antibodies did little to improve outcomes in early testing. But together, they eliminated neuroblastoma and prevented cancer from spreading to the lungs for osteosarcoma.

Research revealed this combination of antibodies blocks two deceptive 'don't eat me' signals being expressed by cancerous cells, while anti-GD2 also increased the presence of 'eat me' signals. The result: the killing and removing of dangerous cancer cells.

Dr. Majzner is now serving as principal investigator for a clinical trial that is currently enrolling 80 children and young adults with neuroblastoma or osteosarcoma.



Lemonade Days is Returning This Summer!

Fuel the research that is helping kids win their fight with cancer. Register your stand or event between **June 4-12** and join forces with childhood cancer heroes like Laney! Research into more effective treatments helped 6-year-old Laney achieve no evidence of disease for her uncommon cancer. Last year, she held her first Lemonade Days stand and raised \$3,000! She can't wait to return for Lemonade Days 2022 and help more kids. **Register today at LemonadeDays.org.**



Nate

At 11 years old, Nate is a fighter. Diagnosed with acute lymphoblastic leukemia (ALL) in April of 2021, Nate quickly exhausted his options to treat a cancer that has a 90% survival rate. Today, he is on a clinical trial with hopes it will bring him into remission. He is bravely undergoing chemotherapy, physical therapy and lumbar punctures as part of his treatment. Although he's losing weight due to a loss of appetite and has rapidly fluctuating blood counts from high doses of medication, Nate keeps a positive attitude and is starting to act like a kid again. He and his family dream of a future where easier, safer treatment plans are available for children with cancer.

These Heroes Need Backup



Mary

Mary was 4 years old when she was diagnosed with a rare, deadly brain tumor called diffuse intrinsic pontine glioma (DIPG). This diagnosis comes with many things — fear, a poor prognosis and a loss of hope. Mary's doctors told the family about a clinical trial at Lucile Packard Children's Hospital Stanford. The trial, funded in part by ALSF, uses CAR-T immunotherapy to target the tumor. Mary enrolled and her family began making visits to Stanford, a thousand miles away from their home in Colorado. With help from ALSF's Travel For Care program, Mary's family can make the monthly trip without worrying about travel expenses. They have hope again as Mary continues treatment, fighting every day for a cancer-free future.

“We would love for a cure to be found, or at least an easier treatment plan. Nate is going through something no child, or anyone should have to. He is our little warrior, fighting every day.” — Lindley, Nate's mom

Big Thanks to Our *OutSTANDing* Supporters



Two Sisters Squeeze the Day

As their summer drew to a close, two sisters set up a plastic table in their driveway to sell lemonade and help sick kids feel better. Emily and Alexis raised nearly \$700, proving anyone, big or small, can make a difference with a simple lemonade stand!



A Little Change Goes A Long Way

In September, the River Montessori Charter School in California collected their pennies, dimes, nickels and quarters to change the future of childhood cancer. During their week-long Penny Drive, students brought in or made donations online and helped fund the future of research with every cent!



Making A Stand for Kids Like Her

After Stacy's daughter, Averie, was diagnosed with B cell acute lymphoblastic leukemia, she had never felt more inspired to make a difference. One final round of chemotherapy, a lemonade stand fundraiser and more than \$4,000 later, Stacy, Averie, and their family and friends have funded half a week of research!

Partner Spotlight



Over the last four years, ALDI has been a proud supporter of Alex's Lemonade Stand Foundation and the fight against pediatric cancer. In 2021, ALDI created the ALDI Heroes Fund, where all funds and donations from employees go directly to supporting families traveling for their cancer treatments. ALDI is stepping up the support in 2022, by creating engagement opportunities and raising awareness for ALSF on multiple occasions throughout the year, and announcing a commitment to raise \$10M for ALSF by 2027.



Since 2006, Five Below has raised more than \$8 million to help change the future for kids faced with childhood cancer. From May 23 through June 19, Five Below will once again collect donations for ALSF during checkout at all of its stores nationwide and when shopping online at fivebelow.com, as part of the company's goal to raise another \$2 million this year. This money will make a huge impact for children and their families. Thank you Five Below and their WowCrew for joining us in the fight against childhood cancer.



Northwestern Mutual has funded many new ALSF initiatives to help meet the needs of childhood cancer families. In 2022, celebrating 10 years of the Childhood Cancer Program, they continued that partnership with a commitment of \$1 million to the Crazy 8 Initiative. Along with this commitment, Northwestern Mutual employees at their over 80 network offices go above and beyond each year by hosting fundraising events such as golf outings, galas, cornhole tournaments and more!

The One Cup at a Time Club is more than 800 members strong! Give monthly to join this community **funding research all year long.**



Fernanda

ONE CUP
AT A TIME
CLUB

Join now at AlexsLemonade.org/One-Cup-Newsletter.

The Zest Sale Around!

Score Deals on Childhood Cancer Fighting Gear

Alex's Shop is full of the finest fleeces, swellest shirts and greatest gear you can find. And the best part: **every purchase helps children fighting cancer!** For a limited time, everything in the online store is **30-60% off!** Refresh that wardrobe with something for every season.



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