ST. JUDE

inspire

FALL 2025

Felicity Ever After

A true story of resilience and joy

Hunter's legacy
Bereaved St. Jude dad runs in honor of his son

Transformative research
Pediatric Cancer Genome Project has helped improve treatments for kids

Daddy's girl
Delta's cancer journey at St. Jude and her viral moment with dad

Supporting St. Jude

At Chili's Grill & Bar locations across the country, the long-running support for St. Jude is especially strong each September when guests can visit their local Chili's to purchase a "Create-A-Pepper" coloring sheet as part of Childhood Cancer Awareness Month. When Retirement House, the grandparents of the internet, joined St. Jude cancer survivor Mabry for a meal and a "Create-A-Pepper" coloring competition, it was yet another example of how Chili's strives to provide memorable experiences and make everyone feel special. And the joy so evident on Mabry's face testified to the impact Chili's has made for St. Jude patients and families, raising more than $122 million since 2002.

If there's one thing we enjoy celebrating here at St. Jude Children's Research Hospital®, it's birthdays. And this year, the Pediatric Cancer Genome Project (PCGP) turns 15.

The PCGP has revolutionized pediatric oncology by uncovering genetic alterations that explain why certain cancers develop, return or resist treatment.

Launched in 2010 by St. Jude in collaboration with the Washington University School of Medicine, this groundbreaking initiative has led to more personalized, more effective and less toxic therapies.

We know it is our committed, generous donors who make state-of-the-art research such as the PCGP possible.

We also know that behind the cutting-edge science that leads to treatment and care breakthroughs is a child and a story.

In this issue of St. Jude Inspire, you'll read about Felicity, a little girl utterly enchanted by fairytales and stories of good triumphing over evil.

Or hope over hopelessness.

Felicity's is a story of art imitating life when, diagnosed with aggressive, fast-growing tumors at just 4 months old, she was referred to St. Jude.

For families who find themselves facing a life-threatening diagnosis, these are the darkest days they'll know. A wolf in the woods. A wicked witch in the castle's keep.

At St. Jude, Felicity underwent various therapies: chemo, physical, occupational and speech. But she also marked many firsts — true storybook moments like her first Christmas and first birthday, a confetti-fueled celebration in the Brain Tumor Clinic.

She's blown out birthday candles eight times since her diagnosis and her story keeps getting better and better. Big sister. Energetic. Resilient. All the attributes of a storybook hero.

At St. Jude, we love a good story. And while it may sound like something from science fiction — more than 100 trillion pieces of data produced and made accessible to scientists worldwide — the Pediatric Cancer Genome Project is very real.

It might even be the hero of our story if it weren't for Felicity and thousands of patients like her who will celebrate more birthdays thanks to cutting-edge science and generous supporters like you.

Now that's a happy ending.

Ike Anand
President and Chief Executive Officer, ALSAC

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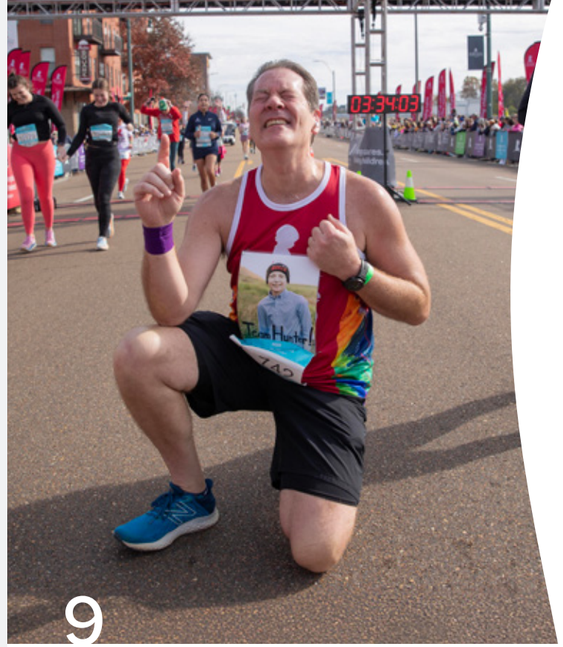

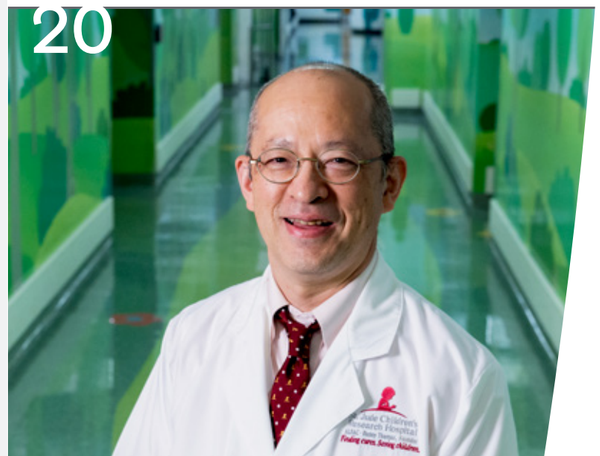

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You can help ensure families never receive a bill from St. Jude for treatment, travel, housing or food — so they can focus on helping their child live. Donate today at **st.jude**.org/ImpactGiving

Daddy's Girl

A glimpse into the family's life at St. Jude went viral, but there was so much more to Delta's story.

By **Betsy Taylor** - ALSAC

Delta had a hitch in her walk, but the 3-year-old willed herself to go faster. Determined, she moved across the parking lot to get to her dad, Hayden.

She wore a backpack emblazoned with the St. Jude Children's Research Hospital® logo. Under her ball cap, she was bald from chemotherapy.

Delta was at St. Jude undergoing leukemia treatment, while Hayden held down his job at the electric company back home in Mississippi.

It was lonely, Hayden said, being away from his wife and two daughters for the work week, but "with some things, you've just gotta do what you've gotta do."

Hayden had driven three hours to be at St. Jude for this reunion.

"I got out of the vehicle, and I heard someone yell, 'Dad! Dad! Dad!' And I look over, and it was Delta," said Hayden.

He hugged his little girl and lifted her into his arms.

Delta's mom, Chelsie, recorded the whole thing with her cell phone and posted it online.

This glimpse into the family's life at St. Jude became a viral phenomenon and has racked up more than 3 million views since March of 2024.

Seeing his little girl, said Hayden, "It just melted my heart."

A deep breath

Delta caught a cold in November of 2023. The symptoms seemed to get worse instead of better, and she felt tired all the time. One day, she fell asleep and woke up with hives from head to toe. Within days, she tested positive for infectious mononucleosis. Then she tested positive for streptococcal pharyngitis, or strep. She just kept getting sick.

The day after Christmas in 2023, Chelsie took Delta back to the pediatrician for bloodwork. The results were abnormal.

The local hospital ran tests, and when the doctor walked into the exam room, Hayden braced himself.

"If someone is going to tell you bad news, usually you can watch their shirt," said Hayden. "There's going to be a deep breath or a light breath. He took a deep breath, so I pretty much knew what he was about to say."

The doctor told them Delta had leukemia.

"You're flooded with all kinds of emotions, and you don't know how to feel in that one moment except to grab your baby and just hold them," said Chelsie.

Delta was referred to St. Jude, where a diagnosis of B-cell acute lymphoblastic leukemia (B-ALL) was confirmed. Delta's doctor explained to Chelsie and Hayden about what it meant to have leukemia and the treatment to come.

"Just having someone sit down and connect with you in a situation where your world is turned upside down and you don't know what tomorrow holds, it gives you peace of mind," said Chelsie. "They care about your daughter, but they also care about you."

At St. Jude, Delta began a multi-year chemotherapy plan to induce remission. Delta's treatment is based on the protocol developed for the TOTAL 17 trial at St. Jude, which personalizes treatment based on analysis of the DNA in both the leukemia cells and healthy cells of each patient while also accounting for other known risk factors for disease recurrence.

This precision treatment approach reflects some of the most recent breakthroughs in more than six decades of progress in treating leukemia at St. Jude, building on lessons from the previous 16 Total Therapy trials at St. Jude and tailoring medicine to eliminate the disease while minimizing side effects.

"You're flooded with all kinds of emotions, and you don't know how to feel in that one moment except to grab your baby and just hold them."

– Chelsie, *Delta's mom*

Still, Hayden knew it was going to be a long road, one that would take them far from their home in the Mississippi country.

A long road

Delta isn't just a product of growing up in the country. She is the country.

She seems to have sprung from the rich, alluvial soil of the Lower Mississippi River Delta where she was born. Like the streams that course through Mississippi like a circulatory system bound for the Gulf and bringing life to the land, Delta is a vibrant and vital part of her family.

Before cancer, Delta spent her childhood outdoors in nature and the huge, inexhaustible expanse. Hot and sweaty from play. Dirty fingernails from digging. Shoes damp from tromping through high grasses. Important missions that had to do with catching frogs or baby chicks or bugs.

Her family had chickens, and she would scoop up the baby chicks and crawl into the hammock with them.

"It was the funniest thing. She could hold them like this right here," Hayden said, mimicking the way she cradled the chicks, "and within five minutes, the chickens would be full-on asleep."

At St. Jude, when Delta's parents viewed her slides under a microscope, they thought the purple leukemia cells looked like bugs. And bugs, this country girl with dirt under her nails, understood.

Hayden sat Delta down.

"Delta's sick," he said. "Delta has these purple bugs in her body. For Delta to get better, you got to take this medicine and this medicine will make Delta's hair fall out."

In fact, Delta's hair was already beginning to fall out with tufts of it on her pillow and left behind on her hairbrush.

"So, Delta's hair fall out?" the little girl asked.

"Yes, baby, your hair is going to fall out," Hayden said.

"OK, but this medicine make Delta feel better?"

"Yes, baby, the medicine is going to make you feel better," said Hayden.

Delta nodded, and that was that.

St. Jude was helping to kill the purple bugs. Her dad had said so. She accepted it.

A few days later, Delta wore her princess dress as the hairdresser shaved her head bald.

St. Jude patient Delta holds a pair of baby chicks in 2023 prior to her diagnosis of B-cell acute lymphoblastic leukemia (B-ALL).

Delta accepted everything.

Not long after chemo began, in January of 2024, Delta suddenly lost all movement in her left arm and leg. Scans showed she had an abscess on her brain. The combination of leukemia and chemotherapy weakened Delta's immune system, putting her at risk for infections anywhere in the body.

"St. Jude was so quick. They started antibiotics immediately and transferred her to the ICU," said Chelsie.

Delta was transferred to the local children's hospital, where she underwent brain surgery to have the abscess drained and cultured. Following surgery, Delta transferred back to St. Jude to continue treatment for ALL and begin physical therapy.

She was just beginning to walk again on the day Chelsie recorded her video.

Girl dad

When Hayden watched the video of Delta, he said, "It hit me hard."

"That was a great distance. She was exhausted the whole time before she got there. But she still managed to push through and get to me."

Hayden thought back to a time before Delta was born. He had wanted a son so badly.

He had dreams of throwing the football with his son. Of going fishing. Of riding the four-wheeler. He wanted a tough kid. He imagined that had to be a son.

So, when Chelsie got pregnant, he wished for that boy. Maybe even prayed for that boy.

"I did not expect myself to be a girl dad," he said. "When we found out we were having a girl, I was sort of bummed out."

His two daughters, Dani and Delta, surprised him at every turn. They threw the football, went fishing, rode the four-wheeler.

But it was more than that.

"You see a 3-year-old that hasn't been dealt the best of cards since Christmas, but not once has she asked why she's here," said Hayden. "She still has the willpower to push through everything."

He thought about Dani, too. At 6 years old, Delta's older sister and protector would have loved to have had more of her parents' attention, but she understands that, right now, Delta needs it.

Dani had persevered and become a great helper by carrying Delta's bags with her chemo pumps or helping pick up toys.

"There's a lot of times we'll sit and talk to her and say, 'Dani, we're proud of you for everything you're doing. You may not realize it, hon, but you're doing very, very good.'"

He had been wrong about what strength looked like.

"It broke me down. It made me feel very humble," said Hayden.

"Daddy, lift me up higher," Delta had said to Hayden that day in the parking lot.

But she and Dani are the ones who have lifted him up.

"The Lord knew what he was doing when he made me a girl dad."

Your support helps give patients like Delta the chance to spend more time with dad.
stjude.org/ImpactGiving

St. Jude patient Delta plays with toys to help her skills during an April 2024 physical therapy appointment.

RUNNING FOR HUNTER

Bereaved dad honors his son by fundraising for St. Jude.

By **Linda A. Moore** - ALSAC

At the finish line of the 2023 St. Jude Memphis Marathon®, John Grusy dropped to his knees in celebration.

He hadn't come in first, not that it mattered. He hadn't broken any records. He wasn't trying to.

John's run was in honor of his son, Hunter, a St. Jude Children's Research Hospital® patient who died on May 31, 2023, months before the big race.

John and members of his family ran the 2022 race while Hunter was still in treatment, and they were hopeful. In 2023, with Hunter gone, they raced in his honor.

Hunter, the youngest of seven, was diagnosed with Ewing sarcoma in 2021 and referred to St. Jude.

While progress has been made in treating many pediatric cancers, Ewing sarcoma that is progressive or has spread to other parts of the body still has a poor survival rate. St. Jude continues to research new treatments in hopes of finding one that will improve the chance of survival.

Unfortunately, Hunter's Ewing sarcoma did not respond well to treatment, and he passed away at home surrounded by those who loved him.

Afterwards, his family made plans to run. Besides the St. Jude Memphis Marathon, they've also run in other events raising thousands of dollars for St. Jude in the hopes of helping other kids.

Celebrating Life

Teen recounts her time at St. Jude filled with love and care.

By St. Jude patient **Gabrielle**

In the early part of 2024, I was living a normal life in Jamaica. As a high school student, I was preparing for my exams and pursuing science subjects, all to achieve my dream of becoming a pediatric surgical oncologist. But then, Wilms tumor thwarted my plans once more.

At 14 years old, I was diagnosed with a tumor that I had no idea would result in a diagnosis again of Wilms tumor, a kidney cancer. I was diagnosed for the first time when I was 7 and had finished treatment many years before. When an ultrasound detected a tumor again, several things went through my mind. I would have to go through chemotherapy for a second time. I would lose my hair and be out of school again.

My parents and my siblings tried to mask their dejection, but I could just imagine what they were going through. I didn't see a way out, but I always maintained a bright smile because I knew that God would not let me down. When I felt sad, I always referred to my name, Gabrielle, which means "God is my strength" and one of my favorite Maverick City songs "Fear Is Not My Future" as a source of encouragement.

When the cancer returned, I was referred to St. Jude Children's Research Hospital®. When I came to St. Jude, despite being unwell, I was thrilled by all the love and great care offered to me. They made it a point to ensure my comfort and happiness, which I appreciate.

Even though I was away from my friends and extended family, I didn't feel homesick because St. Jude provided so many different activities. There is a school there and resources that we can use to our liking.

I will forever love St. Jude, the workers and all the donors.

You can help ensure patients like Gabrielle get the chance to pursue their dreams.
stjude.org/ImpactGiving

St. Jude patient Gabrielle reacts with glee as she rounds a corner to discover one of her favorite gospel artists, award winning performer CeCe Winans, is waiting for a surprise visit. During the encounter the pair sang Winans' song "Goodness of God" together a cappella.

Felicity Ever After

A true story of resilience and joy.

By **Kelly Cox** - ALSAC

The age old story goes like this: The girl is waylaid along the path through the deep, dark woods by a vicious wolf. She falls prey to its cunning plan, but luckily, is rescued in the nick of time and survives, much the wiser.

Or another one: Though it seems only misery lies ahead for the mistreated stepdaughter, she never gives up on kindness or hope, and a surprising twist of good magic leads her to her happily ever after.

Felicity, with her real-life Rapunzel hair and a name that means happiness, is fascinated by these fairy tales. She knows them backward and forward, and her favorite thing is to act them out.

“When we act out these fairy tales, she wants everyone to play a part, it does not matter who it is,” said her mother, Mandy. “And she usually wants Mommy to narrate. As we go through the narration, if a character has an important line, she’ll stop me: *‘Wait, wait, I’ll say it.’* And she’ll act out

that part." She is actress and also director, making sure the fairy godmother knows when to cast her spell, or that the wolf is appropriately vanquished.

Once upon a time, Felicity's life was threatened by something as unforeseen as a wolf from the shadows.

But she doesn't remember that part; she was just a baby then. That story is one her parents remember for her, until she's old enough to really understand.

An unexpected threat

In May of 2017, Mandy took Felicity for her 4-month wellness visit. "Being a first-time mommy, I was so scared about getting her shots," she remembered. She and her husband Eric were completely unprepared for what followed. The pediatrician noticed that in between normal newborn visits, their baby's head went from being average size for her age to being larger than 90% of babies her age. He transferred her to a local hospital that found Felicity had multiple tumors in her brain and spine. After a brain surgery to obtain a biopsy, Felicity was diagnosed with desmoplastic infantile astrocytoma. This very rare type of tumor is typically considered low-grade, but in her case it was fast-growing, aggressive and life-threatening.

Years earlier, when Mandy was in college, her roommate's cousin had been a patient at St. Jude Children's Research Hospital®. To honor that child, their sorority started supporting St. Jude. In high-spirited, college-aged style, they pulled off zany fundraising ideas like a 24-hour see-saw relay, and they raised real money doing it.

Now, in this dire moment, St. Jude was on Mandy's mind again. She and Eric sought a referral.

The location of the tumors and Felicity's young age were factors in the type of treatment that was appropriate for her. At St. Jude, she underwent multiple rounds of chemotherapy. She also received supportive care like physical therapy, occupational therapy and speech therapy.

Meanwhile, many milestones were marked. Felicity experienced her first Christmas while inpatient, dressed in the cutest little red-and-white Santa's helper outfit. There were decorations, St. Jude staff singing carols and gifts delivered by Santa himself. Her 1st birthday was celebrated with balloons and confetti in the Brain Tumor Clinic.

After 6 months of chemotherapy, scans indicated improvement in the tumors and the care team felt it was best for Felicity to stop active treatment but to continue to come for regular checkups at St. Jude. This remains true today, seven years later. And she is thriving.

Everyday magic

People have always been drawn to Felicity, from her babyhood on. "I always prayed that she would have something special about her, and boy, did she," Mandy said. "She does captivate everyone with the way she interacts. You start asking her questions, and that mind, it just goes. There is something about her that's just a little bit different, but it's that factor that everybody loves."

There is a sweetness to their family life, even when things are hectic or stressful, that stems from remembering to take nothing for granted. Christmases and birthdays are full-scale productions, not least of all because Felicity loves a celebration. "After that first Christmas, we don't go shy," said Mandy. "Now Christmases are grandparents, cousins, all of our friends. We make sure to do it big."

> *When we act out these fairy tales, she wants everyone to play a part, it does not matter who it is.*
>
> – **Mandy,** *Felicity's mom*

St. Jude patient Felicity with her mom, Mandy, in February 2018.

"Her favorite thing is putting candles on a cake, someone singing to her, and her just laughing her head off. So, we have to re-light the candles over and over again. And now her baby dolls have to have a birthday as well. Throughout the year, we'll have four or five birthdays for her baby dolls." And Felicity is a big sister now, twice over, so that puts even more parties on the calendar.

When it comes to her diagnosis, "she is very unaware of it," said Mandy. One day, they will want Felicity to know everything she went through. They have documented her journey – the hard times, the fellow St. Jude families who became their dear friends, the staff who became like family – the breadcrumbs leading back in time that show how far she's come.

Mandy hopes there will be lessons in this. "As she gets older and starts to comprehend exactly what's been going on with her, I want her to have compassion for other people, I really do. I hope that she wants to give back. And just to always remember that we came from something hard, and we can get somewhere good."

These fairy tales persist for a reason. Life does take some of us through deep, dark woods filled with danger. It may present us with circumstances that seem insurmountable without a hand from the proverbial fairy godmother. If we are plucky, but mostly if we are lucky, on the other side of these challenges wait earned wisdom, resilience and newfound joy.

It can't be said Felicity is entirely out of the woods. But, said Mandy, "she's becoming the girl that she's meant to be."

Eight years old, unique, imaginative, absolutely brimming with the magic she herself brings into the world.

Your support helps patients like Felicity have a chance to realize their dreams.
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Give them the chance they deserve

St. Jude patient **Miguel**, pictured with his mom

Every child deserves a chance to live their best life and celebrate every moment.

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15 YEARS OF THE

PEDIATRIC CANCER GENOME PROJECT

Launched in 2010 by St. Jude Children's Research Hospital® in collaboration with the Washington University School of Medicine, the Pediatric Cancer Genome Project (PCGP) was the first effort dedicated solely to understanding the genetic changes that give rise to childhood cancer.

By sequencing the genomes of cells from hundreds of children with cancer, the project transformed the understanding of pediatric cancers and has paved the way for new diagnostic tools, targeted therapies and personalized treatment approaches to improve outcomes for children with cancer.

FACTS AND FIGURES:

800 pediatric cancer patients had their genomes sequenced, including tumor and normal cells, which helped identify genetic changes that drive cancer development in children.

23 different childhood cancers were included in the research.

2,000+ patients have now undergone real-time genomic analysis through the St. Jude Clinical Genomics pipeline.

10,570 visits have been made to the Cancer Predisposition Clinic, including 5,256 new patient visits and 5,223 follow-up visits as of Dec. 31, 2024.

100+ trillion data points have been produced by the Pediatric Cancer Genome Project, accessible by scientists around the world.

17% of the new patients seen by the Cancer Predisposition Clinic were found to have an underlying predisposition for cancer.

ge·nome
(noun) [jē nōm]
the complete set of genes or genetic material present in a cell or organism.

"For decades to come, scientists will continue to glean insights into childhood cancer through data generated by the PCGP."

– **James R. Downing, MD**
St. Jude President and CEO

IMPACT:

BETTER UNDERSTANDING OF PEDIATRIC CANCERS:
By cataloging genetic mutations present in pediatric cancers, the PCGP helped researchers understand the underlying causes of tumor development, progression and response to therapy.

IMPROVED DIAGNOSES:
Insights gained led to the development of new diagnostic and prognostic biomarkers that help detect cancers earlier, allowing for timely intervention and improved patient outcomes.

TAILORED TREATMENTS:
The PCGP enabled the development of clinical trials for precision medicine, tailoring treatment to target the specific mutations driving an individual's cancer.

WORLDWIDE COLLABORATION:
St. Jude Cloud now hosts raw genomic data for more than 12,000 pediatric cancer patients, and St. Jude has provided full access to researchers across 300 institutions, accelerating research efforts worldwide.

EDUCATION:
The PCGP has contributed to the education and training of healthcare professionals in interpreting and applying genomic data in clinical settings.

PEDIATRIC CANCER
GENOME PROJECT

St. Jude patient Swayzie and Hiroto Inaba, MD, PhD, share a playful moment during a clinical appointment in October 2023.

IMPROVED OUTCOMES

Over 15 years, the groundbreaking Pediatric Cancer Genome Project has transformed the understanding, diagnosis and prognosis of pediatric cancers.

By **Ruma Kumar** - ALSAC

Dr. Hiroto Inaba was raised in a rural province in Japan to honor his samurai heritage. His parents taught him the "Bushido" that an honorable life is one that upholds "the good fight," Inaba says. After he lost his mother to cancer, he decided his fight would be as an oncologist tackling cancer.

In his 22 years at St. Jude Children's Research Hospital®, his work has involved improving the care and treatment for children with leukemia, specializing in two of the most common childhood cancers, acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML).

"The good fight is to protect and to bring the best outcome for our patients and families," said Inaba, MD, PhD, who joined St. Jude in 2003 and is now the director of the Pediatric Hematology Oncology Fellowship Program at St. Jude, mentoring the next generation of doctors caring for kids with cancer.

In the last 15 years, the work St. Jude has done through the Pediatric Cancer Genome Project (PCGP) has been particularly crucial for Inaba's efforts to improve the diagnosis, treatment and survival for the children he treats.

The PCGP is a groundbreaking collaboration between St. Jude and the Washington University School of Medicine. The primary goal of the project, launched in 2010, was to identify and learn the genetic causes of childhood cancer.

Genomic data from the project has helped doctors like Inaba develop tailored therapies that attack specific abnormalities found in cancer cells, allowing treatments to be more effective with fewer side effects. The project has also allowed researchers and doctors to identify genetic mutations to understand what variations in the DNA cause pediatric cancers to start, grow, become resistant to treatment and even return.

Sequencing the genome for children with cancer has also led doctors to more accurately diagnose and stratify risks of the disease. Better diagnosis and risk stratification have meant more personalized care for each child with cancer and improves overall outcomes, a key step toward raising survival in high-risk leukemia and hard-to-treat brain tumors.

"In many regards, the PCGP came into being because of the need to accelerate progress," said St. Jude President and CEO James R. Downing, MD. "It succeeded because we were willing to chase big ideas and make the most of a unique moment in history."

Genomic sequencing of ALL has improved understanding of the disease which now has a 94% survival rate.

"We can cure most of the patients with this disease. But still, as a physician, we really need 100%; 6% we (still) need to cure," Inaba said. "So, we are working on many new technologies and treatments to improve this."

The PCGP allowed the discovery of previously unknown subtypes of ALL, so doctors are able to further personalize medicine, adjusting chemotherapy based on the molecular and genetic analysis of the tumor cell.

In Inaba's clinic, discoveries and learnings from the PCGP have informed a key clinical trial, TOTAL 17, for newly diagnosed patients with ALL and acute lymphoblastic lymphoma (LBL).

This clinical trial used precision medicine strategies based on the inherited and acquired leukemia-specific genomic features. Researchers want to see if the targeted treatment approaches improve the cure rate and quality of life of children with ALL and LBL.

The active trial has 790 participants, spread across 8 locations (7 in the U.S. and 1 in Australia). Enrolling so many in the study allows researchers to gather large amounts of data more quickly. This research is made possible by the breakthroughs of PCGP that made identifying genetic alterations of importance in ALL feasible. The PCGP has also identified numerous biomarkers that can be used for early diagnosis, risk stratification and monitoring treatment response in pediatric cancer patients.

Over the last 15 years, Inaba said he has been excited to see research in molecular analysis, immunotherapy and genome sequencing conducted in St. Jude laboratories translating into better diagnosis and treatment for patients in clinics. He calls the discoveries "amazing," even as he admits work remains until St. Jude is able to carry out its founder's promise that "no child should die in the dawn of life."

Inaba said he would also like to see more progress made in the treatment and survival of kids with AML. The PCGP has helped doctors like him understand how heterogenous the disease is, making it difficult to treat, because it can affect each child so differently. Eventually, he said, he hopes doctors are able to create individualized therapy for each child with AML. In the 1980s, survival for children with AML was 30%, Inaba said. Today, it is about 70%.

"Significantly, survival is improving, still we have 25 to 30% of patients to save," Inaba said. "In this field, there is new therapy coming such as molecular targeted therapy and also immunotherapies under research now, so I hope AML will also come to the level of acute lymphoblastic leukemia."

Research and treatment at St. Jude are possible because of generous supporters like you.
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PEDIATRIC CANCER GENOME PROJECT

TAILORING THERAPIES *IMPROVES SURVIVAL*

At 22 months old, Aspen, a patient in the Philippines, was diagnosed with stage 4 high-risk neuroblastoma, an aggressive pediatric solid tumor arising from nerve tissues and cells. Despite chemotherapy and surgery, the disease spread to her bone marrow and blood. She received more rounds of chemotherapy, a stem-cell transplant, radiation and retinoids. Still, the cancer persisted.

Aspen was referred to St. Jude Children's Research Hospital® and arrived in Memphis in fall 2019.

At St. Jude, pediatric oncologist Sara Federico, MD, got to work trying to determine what treatment would be more effective, possibly curative, for Aspen. Federico requested tumor tissue samples from Aspen's initial surgery in the Philippines for genetic sequencing. When the samples arrived, St. Jude researchers identified an inherited mutation in one of Aspen's genes.

Inspired by research conducted by her St. Jude colleague, Elizabeth Stewart, MD, Federico prescribed a tailored treatment that combined chemotherapy with a PARP inhibitor, a type of medicine that stops the DNA in a tumor from repairing itself when damaged. Federico was hopeful the combination would target the vulnerability specific to Aspen's cancer.

Aspen began the treatment in 2020, and the cancer quickly responded. She became the first child with refractory high-risk neuroblastoma to be successfully treated with this novel drug combination.

"Some could say she just got lucky, but I don't think that's it," Federico said. "Her cancer had a targetable problem, so we gave her a targeted therapy. She has been healthy and off treatment for over three years, and now our visits focus on what she is learning in school, talking about her friends and looking at her art."

TRANSFORMATIVE *RESEARCH*

How 15 years of the Pediatric Cancer Genome Project has helped improve treatments and identify kids more likely to develop second cancers.

By **Ruma Kumar** - ALSAC

Dr. Kim E. Nichols was a medical student and then a junior oncologist in training when a series of landmark discoveries transformed her field. For centuries, doctors recognized hereditary cancers from family histories, but in the late twentieth century, scientists started to identify the genetic mutations responsible for driving the development of some cancers. In the mid 1980s, scientists identified mutations in the *RB1* gene as drivers in retinoblastoma, a rare eye cancer often diagnosed in children under age 3.

In the mid-1990s, scientists discovered the *BRCA1* and *BRCA2* genes. Mutations in either of these genes were responsible for predisposing women to breast and ovarian cancer. Researchers found that mutations in *BRCA1* could increase a woman's lifetime risk for developing breast cancer by 10 times. Once researchers could identify gene mutations driving these cancers, they next developed genetic testing for earlier detection and management of risk. Doctors started offering women testing for their hereditary risk of breast cancer in 1996, and the results were being used to guide clinical care.

Against this backdrop of discovery, Nichols hoped to capitalize on the emerging understanding of the role that genes and ancestry play in the development of cancer. It made her wonder if she could develop a predisposition program for children with cancer, too.

At the time, her idea was new, and it led to some debate.

"Back in the 1990s my colleagues thought, 'Why would you want to test children for hereditary cancer? There is nothing you can do if you learn that a child tests positive for an underlying predisposition. All that this information might do is cause worry on the part of the parents or the patient.'"

In the beginning "there was much reluctance to even consider genetic testing of children for hereditary cancer risk," said Nichols, MD, who is Director of the Division of Cancer Predisposition at St. Jude Children's Research Hospital®.

Undaunted, she chose that path, starting a cancer predisposition clinic at the Children's Hospital of Philadelphia. But she eventually came to St. Jude in 2014, inspired by the hospital's strong research focus and its emphasis on studying the genetic origins of childhood cancer and seeking new cures.

> **"The PCGP served as a catalyst for transformative research."**
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> **– James R. Downing, MD**
> *St. Jude President and CEO*

The Pediatric Cancer Genome Project (PCGP), a collaboration launched in 2010 between St. Jude and the Washington University School of Medicine, became the world's most ambitious effort to study the genetics of pediatric cancer by mapping out the genomes of both normal and tumor cells of more than 800 children with cancer. This data enabled identification of the genetic changes that drive the development of cancer in many children who are diagnosed with this disease.

"The PCGP served as a catalyst for transformative research," St. Jude President and CEO James R. Downing, MD, said. "St. Jude Cloud, the world's largest storehouse of childhood cancer genomics; pre-clinical resources such as PROPEL and the Childhood Solid Tumor Network; and the St. Jude Cancer Predisposition Clinic can all be traced back to the project."

Discoveries made by the PCGP laid the foundation for the Cancer Predisposition Clinic that Nichols and her team run, which, since 2015, has seen more than 5,200 patients and identified more than 1,100 with an underlying predisposition syndrome.

"I knew there would be a tremendous opportunity to set up a program that could capitalize on the advances of the PCGP to improve the outcomes for children and families with hereditary cancer," Nichols said. "I feel very fortunate Dr. Downing was very keen on having me come help transition genomic testing from the research space that had been established through the PCGP into the clinical space."

Data and insights generated from sequencing the genomes of childhood cancer patients have fueled the work Nichols and her colleagues are doing to determine why some kids are more prone to cancer than others. Those insights have also shown doctors what can be done to catch new cancers early when they can be more readily treated and cured.

The benefits of using insights gained from genetic testing can be seen in patients like Claudia, who was referred to St. Jude in 2015 when she was 8 years old and diagnosed with rhabdomyosarcoma, a cancerous tumor that develops in soft tissue. She was treated on a clinical trial protocol that included chemotherapy and surgery to remove the tumor.

"You're just running on adrenaline at that point. You're not even processing everything you're hearing, but all I was thinking was, 'I've got to get my daughter the best treatment,'" Claudia's mother Amanda said.

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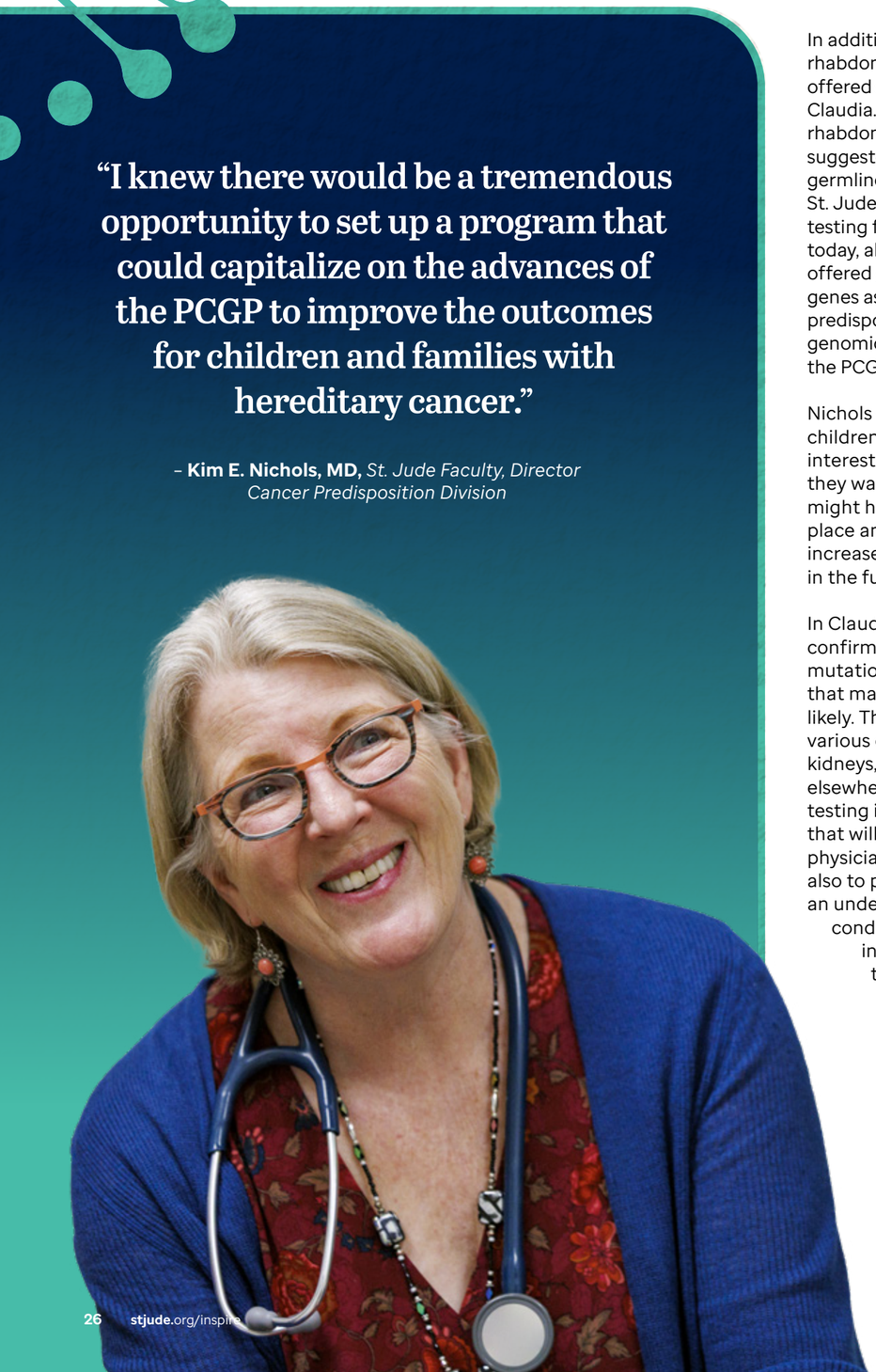
– **Kim E. Nichols, MD,** *St. Jude Faculty, Director Cancer Predisposition Division*



In addition to treatment for her rhabdomyosarcoma, St. Jude offered something else critical for Claudia. Because Claudia’s initial rhabdomyosarcoma diagnosis suggested the likelihood of a germline *DICER1* gene mutation, St. Jude recommended genetic testing for that mutation. Notably, today, all St. Jude patients are offered general screening of 123 genes associated with cancer predisposition as part of clinical genomics testing, a major legacy of the PCGP.

Nichols said most families whose children have cancer express interest in genetic testing because they want to know why their child might have gotten cancer in the first place and whether their child is at increased risk for additional cancers in the future.

In Claudia’s case, the testing confirmed she had a *DICER1* mutation which causes a syndrome that makes developing cancers more likely. These cancers can develop in various organs, including the lungs, kidneys, thyroid, brain, eyes and elsewhere. The goal of the genetic testing is to provide knowledge that will not only guide St. Jude physicians in treating Claudia but also to provide Claudia’s family with an understanding of the hereditary condition so they can make informed choices affecting their own health.

Based on the knowledge of her syndrome, St. Jude doctors recommended surveillance for the development of new tumors. “Surveillance is not going to prevent cancer,” Nichols said. “But the goal is to pick up subsequent tumors at their earliest and most curable

St. Jude patient Claudia in 2023

stages.” Smaller tumors need less invasive surgery, she said, and can sometimes be treated with less or even no chemotherapy.

Surveillance for new cancers led to the discovery of Claudia’s thyroid cancer in 2018 and later an ovarian tumor in 2019. Doctors were able to cure these tumors thanks to the early detection and treatment allowed by earlier surveillance.

“It was such a relief for me that we knew about (the thyroid cancer) so soon,” Amanda said.

“In the past, people with genetic predisposition were identified based on specific clinical features like family history of cancer, physical differences and specific tumor types,” Nichols said. However, these features do not help doctors identify all patients with predisposition.

So, Nichols said, the only way to identify all patients is through broad molecular testing, where clinics like hers offer patients genetic testing for a large number of cancer predisposition genes. In applying this approach, Nichols and her team have identified that almost one in five children with cancer carry a cancer predisposing change in one or more of these genes.

“This information is critical as it may explain why the child got cancer, and it also informs future cancer screening, cancer prevention and testing of other family members,” she said. “For many patients this clinically relevant information would have been missed had one followed the traditional genetic counseling/risk assessment approach.”

In a study published last year, Nichols said her clinic followed 274 patients with an underlying predisposition syndrome for a median of 3 years and found that 10% of those children developed new cancers by screening. They also learned that some of the children already undergoing treatment for an existing cancer had developed a different kind of cancer. Significantly, early discovery through surveillance allowed surgeons to completely remove close to three quarters of the tumors, meaning that the cancer was discovered early enough for good local control, a factor critical for ensuring the best outcomes for patients.

“Previously, oncologists might have waited to screen for second cancers until they had finished treating a child’s first cancer, Nichols said. Now, she said, they know to act quickly and to begin screening as soon as it is determined that a child has an underlying cancer predisposition.

Diagnosis of *DICER1* syndrome through genetic testing, early detection due to surveillance based on cancer predisposition and routine follow-ups at St. Jude helped Claudia survive thyroid and ovarian cancers.

Today, Claudia is 18 and in college, where she plans to study nursing. She is a part-time nanny for a family with young children and spends her free time with friends on the beach, watching movies and painting.

“She’s different from most kids her age,” Amanda said. “She doesn’t have teenage drama…because when you have been through what she’s been through, you don’t let petty things bog you down.”

Your gift helps physicians like Dr. Nichols continue their lifesaving work.
stjude.org/ImpactGiving

St. Jude patient Javier visits with Kim E. Nichols, MD, director of the Cancer Predisposition Division, during a clinical check up at St. Jude in April 2025.

HELPING PATIENTS WITH **GENETIC CANCER RISKS** MANAGE CARE

Amelia lost her son Juan to brain cancer. She's counting on what researchers and doctors at St. Jude Children's Research Hospital® are learning from genetic testing to give her younger son Javier the best possible chance at detecting cancer early and understanding his risk.

With a referral from her local hospital, the Arizona mother brought Juan to St. Jude to receive treatment for a rare brain tumor when he was 9. While he was in treatment, she was diagnosed with breast cancer.

When Amelia told Juan's doctor about her cancer, he asked if she would be interested in genetic testing through the Cancer Predisposition Clinic at St. Jude to look at possible hereditary predispositions to cancer. Juan was tested and the results showed a mutation in a gene called *TP53*, which carries instructions for making a tumor-suppressing protein of the same name. *TP53* mutations are common in many different cancers and are associated with a rare genetic cancer predisposing condition known as Li-Fraumeni syndrome.

People with Li-Fraumeni syndrome have a high likelihood of developing cancer. Half develop some type of cancer by 30. By 60, the risk soars to 80 to 90%. People with Li-Fraumeni syndrome are also more likely to develop multiple cancers.

"Did she want to know?" Amelia asked herself. It could explain Juan's brain cancer. Her breast cancer. What would it mean for Javier?

The results of testing showed that Amelia and Javier had the same *TP53* mutation – as did Juan.

Diagnosed with Li-Fraumeni syndrome, Javier is now a patient in the Cancer Predisposition Clinic, where he is seen for tumor surveillance. Twice a year, he undergoes scans and lab work at St. Jude so if any cancer develops, doctors will catch it early.

Now 16 years old, Javier is working with doctors to transition to managing his own health care. Having a cancer predisposition syndrome increases the risk of developing cancers later in life, so Javier is learning about the importance of continuing health care into adulthood. He is being prepared to tell primary care providers about his Li-Fraumeni syndrome and the risks it poses so that he can be an advocate in his own health care. Javier is learning how regular screenings can help to detect new cancers early, thus improving his chances for a successful outcome. The transition clinic will help him find adult health care providers in his community, transfer medical records to those providers and educate those providers about his cancer predisposition and related health care needs so the transition from St. Jude to adult health care is smooth.

"Cancer predispositions are often lifelong – thus learning how to advocate for one's health to ensure a successful graduation from St. Jude is very important," said Kim E. Nichols, MD, director of the Cancer Predisposition Division. "My team has developed a transition program to help teens and young adults with genetic predisposition and their parents prepare for this process. We are also carrying out several research studies to assess the impact of this transition program. Our hope is that this program will ensure the best outcomes for our patients and their families."

Champions of Hope

Couple's legacy of philanthropy has evolved into enduring support for St. Jude.

By **Yolanda Jones** - ALSAC

In a world where public attention surges and shifts like the tide, Connie and Charles Cotros have remained steadfast – quiet champions for children facing the unthinkable.

Since the earliest days of St. Jude Children's Research Hospital®, the Cotroses have given often and generously. Their support has helped children in treatment for cancer and other catastrophic illnesses find hope, healing and a future.

"This campus is a wonder. It has grown and grown and is still growing," Charles said about their many visits to St. Jude over the years.

They have witnessed this growth firsthand. Connie and Charles both grew up in North Memphis on North Parkway, in the shadow of the St. Jude campus.

The couple met St. Jude founder Danny Thomas many times as they attended fundraisers including the Shower of Stars benefit held for many years at the old Mid-South Coliseum in Memphis, Tennessee.

"Danny used to bring all of his friends from Las Vegas and Hollywood, and we were there that year Wayne Newton literally tore the house down," Charles recalled.

Connie added, "Back then, St. Jude was just getting started, so who would have ever dreamed that it would get to where it is today?"

Charles and Connie embraced Danny Thomas' dream - No child should die in the dawn of life®.

Charles, a retired executive in the restaurant and food distribution industry, and Connie, the pillar for their family, supported St. Jude over the years in many ways.

They have contributed annually, attended and sponsored donor events and were among the earliest St. Jude supporters to donate in the Pediatric Cancer Genome Project, a groundbreaking initiative to uncover the genetic origins of childhood cancers and develop new treatments.

To deepen their legacy, the couple initially mapped out a plan and established a charitable trust to be distributed to several charities with St. Jude receiving the bulk of the funds upon their deaths.

But then Connie and Charles, now in their 80s, changed their minds. "We got to thinking, and said, wait a second, we don't like that plan. God has truly blessed us and been wonderful to us, so we decided we wanted to see our money go toward good while we were still alive," Charles recalled.

That was a decade ago when Charles and Connie released the funds from their charitable trust and made a seven-figure gift to support inpatient facilities in the Kay Research and Care Center at St. Jude.

A year later in 2016, to celebrate their 54th wedding anniversary, they gathered their three children, 11 grandchildren and 13 great-grandchildren together at St. Jude where a wing on the inpatient floor was dedicated to Connie and aptly named, "Connie's Corner."

> *St. Jude is a wonderful place doing a lot of good for so many.*
>
> – **Connie Cotros,** St. Jude donor

"I wanted both of our names on it, but my husband wanted just my name because he knows of my deep love for St. Jude," Connie said. "St. Jude is a wonderful place doing a lot of good for so many."

Charles explained, "Well, she is a very loving person and loves St. Jude. We are retired, and our plans are to continue to support St. Jude as much as we can to the fullest."

Their story is not just one of long-time philanthropy – it's a legacy of love, rooted in compassion and carried forward by an unshakable belief in the St. Jude mission: Finding cures. Saving children.®

"We have a love affair with this hospital," Charles said. "Every time we come here, I feel so much better because I visited and saw these beautiful children."

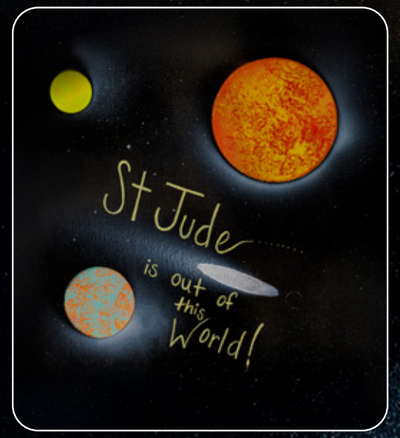
You can join Charles and Connie Cotros in supporting the St. Jude mission.
stjude.org/ImpactGiving

MEET THE ARTIST:

FISHER

Fisher is a kid with passions. He is serious about dirt bike and four-wheeler racing; devoted to his dog, Prisk; and enjoys showing off his creativity through art.

In 2023, when he was 10 years old, Fisher began having headaches that were frequent and severe enough to interfere with some of those passions. Images at his local hospital revealed a brain tumor. After an initial surgery, he was referred to St. Jude Children's Research Hospital® for treatment where he was diagnosed with medulloblastoma, a form of brain cancer.



Fisher faced this challenge with a characteristic mix of good humor and determination. Making sure to have fun is a priority for Fisher, whether he's competing in a race or buckling down for cancer treatment.

One way Fisher found enjoyment during treatment was in making art. For his planet painting, he experimented with a masking technique, using cups, lids and bowls as precise, round barriers between the paint and the canvas. He layered spray paint to create dimension, being careful to control where the spray paint went so it didn't cover aspects of the design. Fisher is great at optimizing tools, even unconventional ones, to create his compositions.

Fisher celebrated his No More Chemo party at St. Jude in October 2024. He is now back at home in Louisiana with his family, his dirt bikes and his dog.

Festive Favorites

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A place for Jasmine

In 2023, Jasmine injured her knee playing softball. Months passed but the pain never went away. Testing revealed she had osteosarcoma – bone cancer. Jasmine, who was 14, was referred to St. Jude Children's Research Hospital®.

Her mom, Ashley, said children from her eastern Tennessee community had been treated at St. Jude, and she felt it was the right place for her daughter. They made the 8-hour drive to St. Jude on Mother's Day, full of emotions.

"The moment we walked through the door, we knew we were coming into a family. Everybody treated us so well and with the utmost respect. They helped us through everything – things we were scared of and what our next steps were," Ashley said.

Her mom describes Jasmine as her "whole world," who likes the outdoors, softball and enjoys spending time with family. "She's very talented, she can sing, and she can draw and she's a natural when it comes to a lot of things," her mom said.

You help bring hope and healing to patients like Jasmine when you support St. Jude. Did you know many ways to give with non-cash assets – like stocks and IRAs – may present unique opportunities to save on taxes while furthering the St. Jude mission? Donate today at **st.jude**.org/ImpactGiving