

2024-2025 IMPACT REPORT



15 Years of Building a Legacy of Hope

A Message from the LFSA President

Dear Friends of LFS Association.

Fifteen years ago, my sisters and I walked into a room at the National Institutes of Health (NIH) in Washington, DC, to participate in a workshop about Li-Fraumeni syndrome (LFS) as part of a group of 100 invited patients.



As someone newly diagnosed at the time, everything was a blur to me. I had no idea what I was doing there or even what questions to ask. I wasn't angry or sad. It was mostly bewilderment. While the medical professionals in the room were there to inform and educate us, it was a new experience for them as well. They had never brought together such a large group of patients

at the same time, and had never met other doctors or researchers involved with LFS. We were all learning from each other.

Despite our collective uncertainty, as the day went on there was an increasing wave of energy moving through the room. Something special was happening as we realized that only by working together could we make a real impact to better understand, treat, and navigate life with LFS. This day marked the beginning of a cross-collaboration that would become a game changer for patients, doctors, researchers, and scientists around the world.

The Li-Fraumeni Syndrome Association (LFSA) was formed one month later in December 2010 with 12 volunteers. Today, we have a global reach with 12 international chapters all working to ensure the most up-to-date tools and resources are accessible and adaptable to LFS patients around the world. Most importantly, no one ever has to feel alone again after a diagnosis of LFS.

In 2016, the LFSA Medical Advisory Board (MAB) was formed to further our collaboration with the LiFE Research Consortium to increase research opportunities that benefit all LFS families. Shortly thereafter, the LFSA Genetic Counseling Advisory Group was created to help serve the needs of LFS patients in understanding genetics, and in 2020, the Scientific Advisory Board (SAB) was established to bring together top *TP53* scientists from around the world to ensure a global approach to LFS research. The MAB and SAB merged in 2022 to create the MSAB, combining medicine and science to more fully impact research and advances in understanding p53 and LFS related cancers.

These dedicated professionals have been our true partners from the very beginning. They have spent years studying the latest science and developing the best treatment protocols for LFS patients. Without them, we would not be where we are today, and the funding and support of their work will always be at the core of our mission.

In 2017, recognizing the importance and worldwide need to inform, support and mobilize young people with LFS, the inaugural LFSA Youth Workshop was held in Salt Lake City, Utah, at the Huntsman Cancer Institute. This biennial workshop provides a space for youth ages 13-26 and their families to connect with others experiencing the same challenges and to learn about science, the latest advances in treatment, and where to go for support. Today, more than 50% of LFSA youth have been inspired to explore professional fields in genetics, medicine, and research, with a united mission to further advances in understanding and treating LFS for the next generation.

Fifteen years ago, genetic testing for LFS was limited by a very exclusive set of qualifying criteria and was cost prohibitive for many. At that time, only 565 families were diagnosed with LFS worldwide. We now estimate that up to 1 in 5,000 individuals have germline variants in *TP53* as testing becomes standard in many countries and easier to access in others. At LFSA, part of our mission is to ensure another 15 years doesn't pass before genetic testing becomes available to all.

LFSA has hosted seven LFSA International Symposiums in the last decade, all dedicated to deepening the partnership between medicine, science, research, and patients that began 15 years ago. We have seen these events grow from under 100 attendees to well over 500 attendees participating in person and virtually from around the world. At the 2024 symposium, 50 esteemed guest speakers and session chairs shared the latest discoveries and advances in their work. The excitement was palpable, and it was awe inspiring to see how far we have come in just 15 years. Even more profound was the feeling of hope expressed by all knowing that we are on the verge of something truly significant and life-changing for those affected by LFS.

As I look back on the last 15 years, I am both proud and humbled by all we have accomplished. I realize that none of it would have been possible without every individual coming together to mobilize into a greater force. I know we can move this over the finish line by continuing the legacy of hope that we started in 2010. From the bottom of my heart, I hope that you will join us to make that happen.

With my deepest gratitude,

Jennifer Perry

LFSA President, Co-Founder & LFS Patient



FROM THE COVER: Attendees at the 2025 LFSA Youth Workshop in Boston explore genetics by extracting DNA from strawberries, enjoying a hands-on activity as part of a weekend of connection and inspiration for youth and families.



Make a difference today!

Scan the QR code or visit **Ifsassociation.org/impact25** to support the LFSA.

Hope and Discovery at 7th International LFSA Symposium

In her opening remarks at the 7th International LFS Association Symposium, LFSA president Jenn Perry noted that "...the most transformational breakthroughs most often come from collaboration..."

There is no better illustration of collaboration at the heart of the fight against Li-Fraumeni syndrome than this biennial gathering where patients and their families spend four days with medical professionals, genetic counselors, researchers, and scientists to strengthen connections, learn about new therapies and treatments, hear about the latest research, and better understand what is most critical for the treatment and ongoing management of LFS.

The 7th International LFS Association Symposium was held in October 2024, hosted by Penn Medicine and Children's Hospital of Philadelphia (CHOP) and in partnership with the LiFE Consortium.

More than 500 attendees from 19 countries joined in person and virtually, gaining a front row seat to learn from over 50 guest speakers and session chairs about new breakthroughs in scientific research, cutting-edge therapies, the latest in treatment, advocacy for LFS families, and much more.

50% of attendees participating in the symposium for the first time were LFS patients, the real people at the core of all research and advancement. In addition to learning about great progress in scientific research, there were also some notable highlights in the areas of early detection tools and prevention.

- Dr. Suzanne MacFarland advocated for liquid biopsy at the clinical level to potentially detect cancer DNA as much as 1-2 years before it shows up on scans.
- Dr. Trevor Pugh discussed the progress of analyzing cell-free DNA (cfDNA) data in the first clinical trial and how future phases could lead to early detection in LFS and other hereditary cancer syndromes.
- Dr. Payal Khincha shared research data on the potential of Metformin, a well-known diabetic drug that shows great promise in reducing the risk of cancer or delaying the onset in LFS patients by disrupting the increase in mitochondrial metabolism that is typically found in LFS patients.

Additionally, this symposium offered opportunities for patients to collaborate in ongoing research, such as the EDISYN/Penn-CHOP Biobank collection of biospecimens and LiFT-UP data collection. Both will help researchers learn more about LFS and facilitate additional research and projects.

Understanding the latest developments in science and research is critical but there is nothing more significant to LFS patients and families than knowing they are not alone. The symposium offered multiple opportunities for families, physicians, scientists, and genetic

counselors to connect with each other through Q&A with the world's leading LFS experts, a dedicated youth panel, mental health awareness discussions, engaging poster sessions, and post-event gatherings at The Inn at Penn, including an international dinner.



I'm used to attending meetings with other scientists. Having families attend and share their stories made a huge impact and provides even more motivation to keep working to solve the problem of p53.

Andrew Giacomelli, PhD



Our heartfelt thanks go out to our REACH 24 hosts and planning co-chairs, Kara Maxwell, MD, PhD, University of Pennsylvania and Suzanne MacFarland, MD, Children's Hospital of Philadelphia and our leaders of the LiFE Consortium, Judy Garber, MD, MPH, Dana-Farber Cancer Institute and David Malkin, MD, Hospital for Sick Children for another successful partnership.



We hope to see you in October 2026!

The 8th International LFS Association Symposium, hosted by MD Anderson Cancer Center in partnership with the LiFE Consortium

Houston, Texas, October 2-5, 2026



Making Cancer History®

2025 LFSA Youth Workshop Inspires Connection and Empowerment

In August 2025, the LFS Association Youth Workshop, hosted by Dana-Farber Cancer Institute and Boston Children's Hospital, brought together 25 youth and their families from around the world for a powerful weekend of connecting, learning, and inspiration.



The weekend kicked off on Friday, giving the youth participants the opportunity to get to know each other in a fun and informal setting. They embarked on a Boston Harbor cruise aboard the Northern Lights Yacht, followed by a visit to Mei Mei Dumplings in South Boston, where they were warmly welcomed by Elaine Shiang and her daughter, Chef Irene Li, the wife and daughter of the late Dr. Frederick Li, co-discoverer of Li-Fraumeni syndrome.

Saturday offered informational sessions from medical professionals and researchers, including topics like updated screening recommendations and tools for living with LFS, the AYA-RISE project, and a special tribute honoring the work of the late Dr. Pierre Hainaut by Professor Arnold Levine, co-discoverer of the *TP53* gene.

Attendees also engaged in interactive panel sessions, special topic breakout groups for young men and women, parent networking time with professionals, and science labs, including a hands-on strawberry DNA extraction! The event culminated with a rooftop dinner overlooking the city skyline.

The LFS Association Youth Workshop is about connection and hope for young people. As was reflected by many who attended in 2025, it also serves to empower LFS youth to be their own advocates, armed with the knowledge, the tools, and the support they will need as we all celebrate the next generation of resilience and discovery.

Discover the LFSA Youth Program.Stay informed. Get involved.



LFSA CLIMB FOR A CURE



The annual Climb for a Cure for LFS provides an opportunity for LFSA teams across the globe to hike, walk, run, or ride to raise awareness and provide support for LFS patients and families. In 2025, LFSA teams collectively raised over \$25,000 for the LFSA Youth Workshop held in Boston in August.

Leading the charge was Erica Kirschner and her team, climbing their way up 199 steps to the top of Cape May Lighthouse in July, and the Weiss family who participated in their third year by walking 1.5 miles through Valley Forge National Historic Park.

Our team is not just raising funds, we are also hunting for hope and raising awareness of Li-Fraumeni syndrome, supporting LFS families, and funding the future.

Hope Hunters for Cody Team

First year team, Hope Hunters for Cody, made a significant contribution by raising over \$5K dedicated to the memory and the spirit of hope lived by Cody Lesko. Even as his own future hung in the balance, Cody never lost sight of the importance of family, kindness, and the strength to keep fighting.

Team LFSA - Fuel the Fight



Jacob Kubetz, founder of Team LFSA-Fuel the Fight, ran the 2025 Chicago Marathon in 3:11:40 as the first leg of his mission to honor the LFS community and fuel critical resources for families, patient support, and research.

Jacob's long-term goal is to build a recognized LFSA presence at major marathons. He hopes to inspire other runners, families, and supporters to join in future events, spreading awareness of LFS while raising much-needed funds to advance the LFSA mission.

Please join us in supporting Jacob at the Boston Marathon in April 2026!

I often tell my family how strong and brave they are in facing LFS head-on, and I often think of them while running. The marathon training miles provide lots of time to think. During my training and races, when I am digging for motivation, I don't need to look further than my wife or my kids.



A New Era in *TP53* Research Brings Hope for the LFS Community

We are experiencing a paradigm shift in *TP53* research, and it couldn't be more profound for the Li-Fraumeni syndrome community.

In the past two years, a sharp increase in studies of the role of *TP53* in Li-Fraumeni syndrome include multiple companies researching drugs and reagents that have potential to treat tumors with *TP53* genetic alterations. Exciting new approaches involve clinical research on the immune system's role in fighting breast cancers in women with LFS, as well as a clinical trial for a drug called Rezatapopt that changes the structure of a genetically altered p53 protein back to normal.

LFSA Supported Research

Together with the Mark Foundation, LFSA supported a clinical research project on breast cancers in LFS patients that asked the question, "Is the immune system involved in fighting the development of breast cancers in women with LFS?"

Led by Dr. Kara Maxwell at the University of Pennsylvania and Dr. Shari Goldfarb at Memorial Sloan Kettering Cancer Center, the study analyzed 58 tumors in 51 patients, with a median age of 34 years. All tumors were sequenced for their genetic changes and spontaneous alterations. The common features were ER+, 68% HER2-positive and *TP53* genetically alterations. Slides of the tumor tissues were stained for immune cells and the expression of proteins that protect the tumor from an immune response. Results showed that the immune system is trying to respond to the tumor, but PD-1 cells protect the tumor from being killed.

Trials are needed to see how women with LFS breast cancers respond to PD-1 antibodies for safety and clinical utility. The first manuscript of these studies is being evaluated for publication.

Drug Development

Using a different approach, biotech company PMV Pharma developed a drug that combines with a specific genetic alteration in the p53 protein, Y220C, to change the protein back to normal. This compound, called Rezatapopt, is in clinical trials and also being tested in mice with LFS. In one published case, a spontaneous triple negative breast tumor that failed all previous therapies was no longer detected in repeated scans over two years in the Rezatapopt trial. This study will be the precursor of a possible clinical trial for prevention of cancers in families who carry a genetic alteration of Y220C.

The Future

Over time, a greater understanding of the origins of cancers has occurred, enabling better assessment of how to prevent some cancers from occurring or to stop their growth and viability when they do. We are working to understand these events in LFS patients specifically, and LFSA's Medical and Scientific Advisory Board (MSAB) will continue to support collaborations in science and research that contribute to the ultimate goal of improving the future for LFS patients.

In 2024–2025, the LFSA has continued its 15-year mission to unite and strengthen the global LFS community of scientists, researchers, clinicians, and patients—all working toward an improved understanding of the complexities of Li-Fraumeni syndrome (LFS). Over the past year, this momentum has accelerated significantly. Expanded efforts are underway to better understand the initiation and progression of common LFS-related cancers, laying the groundwork for improved prevention and treatment strategies. Researchers are also advancing our knowledge of risk modifiers of penetrance, helping to redefine what it means to have LFS and informing more precise screening approaches. LFS investigators are at the forefront in the emerging field of cancer interception—detecting and treating cancer before it becomes clinically apparent. The LFSA's commitment to the LFS community remains steadfast and unwavering, as we continue to drive progress toward a future free from the burden of LFS.

> Robert Lufkin, DO LFSA Medical & Scientific Advisor



Fifteen years ago, there were no clinical trials describing the characteristics of LFS tumors.

Today, a large number of research groups and organizations are developing drugs to treat tumors with p53 genetic and spontaneous alterations. Indeed, we are now thinking of ways to "prevent" tumors from occurring. Testing drugs that will be taken over a lifetime will not be a rapid process, but our level of understanding how to do this improves every time we get a new result, and the challenge of doing this has attracted some of the brightest and best young scientists. We are in good hands for the future.

Prof. Arnold J. Levine, PhD LFSA MSAB Co-Chair



LFS Association Expands Education and Awareness Efforts

The LFS Association and its Education and Awareness Director, Kathy Higgins, represented the organization at major conferences and events throughout 2024 and 2025 to raise awareness of Li-Fraumeni syndrome (LFS). Through presentations and exhibit booths, Kathy shared vital information and resources with healthcare professionals, researchers, and patient advocates.

Key highlights included the American Society of Clinical Oncology (ASCO) Annual Meeting, Rare Disease Week on Capitol Hill, and the National Society of Genetic Counselors (NSGC) Annual Conference, where LFSA helped amplify the voice of the LFS community. Kathy's ongoing outreach ensures that Li-Fraumeni syndrome remains part of critical conversations in cancer research, genetics, and rare disease advocacy—advancing understanding and support for families worldwide.



The Global Reach of LFSA

The international chapters of LFSA are united in the mission to improve life for everyone affected by LFS around the world. Chapters are co-led by local medical professionals and individuals with LFS in Africa, Canada, France, Germany, India, Italy, Japan, Latin America, Netherlands, Saudi Arabia, Singapore, and Sweden. A new chapter in Portugal is coming soon!











Recent activities include:

Africa

Chapter leaders have shared compelling family stories and the work of the LFSA in recently published articles in The Star Kenya and Citizen Digital News to help increase LFS awareness and spread the word about resources in the region.

Canada

Representing in Banff, Alberta, at the Canadian Association of Genetic Counselors, chapter leadership was among 425 genetic counselors and geneticists from across the globe, enabling new connections in Australia and Dubai. LFSA has been involved with the Ontario Hereditary Cancer Research Network, the Canadian Organization for Rare Disorders (CORD) meeting in Ottawa as well as the National Society of Genetic Counselors (NSGC) in Seattle with about 3,500 genetic counselors.

France

The 2nd LFS France Symposium in October 2025 enabled meaningful connections between professionals and families from mainland France, the French West Indies, Tahiti and Belgium, with about 120 participating in person and another 60 virtually. Session topics included the PREVENTABLE Project, assessing the cost of MRI and various screening processes for LFS patient care.

Germany

Active at conferences across Germany, chapter leaders recently presented at the University of Ulm and the German Society of

Psycho-Oncologists to help connect and expand knowledge about LFS. Their LFS Info Day featured lectures on the latest medical advancements and subsequent Family Reunion 2025 supported connections and discussion on topics ranging from nutrition and sports to family planning, social law, and insurance for those with LFS. In addition to participating in the 2025 LFSA Youth Workshop, the chapter supported 2024 youth camps in Kiel and Hannover.

Italy

As a newer chapter working to reach more families affected by LFS in the region, chapter leaders are working to foster conversations and virtual engagements, including a new WhatsApp support group, with a focus on helping young adults get involved in upcoming LFSA events.

Latin America

Highly active at the REACH24 Symposium and LFSA 2025 Youth Workshop in Boston, chapter leadership continues to support awareness of the vast network of LFS medical expertise and family support resources available in the region, including the launch of a quarterly newsletter for the youth program.

Singapore

With a presence since 2018, the chapter is looking to expand connections with young adults and children with LFS, supported by Tas Scriven, genetic counselor from the National Cancer Center in Singapore, who is newly involved with the chapter.