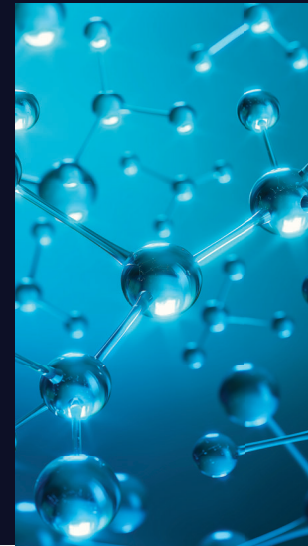




The Legacy of Angels
FOUNDATION



2021

ANNUAL REPORT

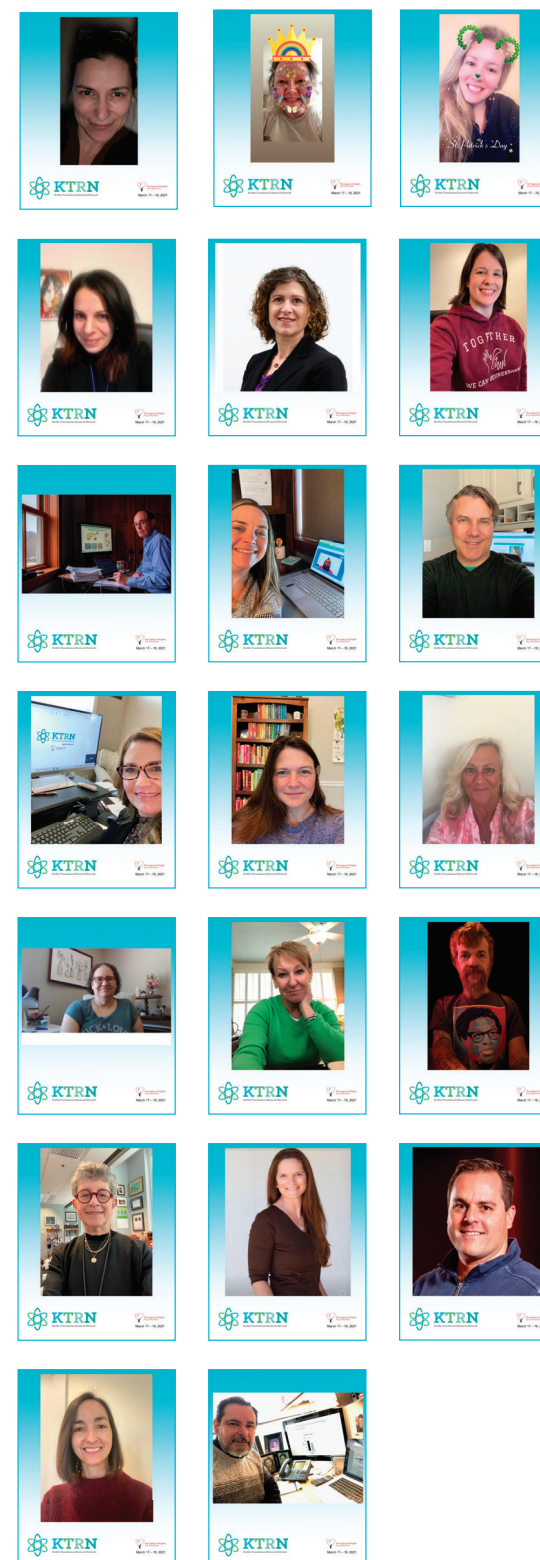


The Legacy of Angels
FOUNDATION

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These mouse and canine KD studies combined with the human KD natural history form the core of information essential for human clinical trials of AAV-GalC gene therapy combined with UCBCT being initiated this year. The improvements in CNS and PNS function, as well as the quality of life from this clinical trial, could be transformational for patients and families affected by KD.

But there is more to do. The basic and clinical research presented at this KTRN meeting highlighted the ongoing needed focus on the mechanisms of KD beyond just the deficient enzyme that can be provided by the combination treatments.

“The 2021 KTRN witnessed progress that has brought into focus a “light at the end of the tunnel” — that is, a potential quantum improvement in treatment outcomes for KD variants

Recognizing this need, over half of the 20+ KTRN presentations were focused on: 1) neuroinflammatory mechanisms and cellular involvement, 2) metabolic pathway abnormalities in KD beyond psychosine, 3) transplantation of potentially corrective cells beyond supplying BMSC and UCBC into the CNS, for example, microglial cells, 4) corrective replacement of cells needed to maintain/improve nerve function, 5) small molecules to inhibit psychosine/GalCer production, and 6) longevity of gene therapy by AAV-GalC or other gene therapy technologies. These research studies derive from the continuing development of detailed understandings of KD clinical effects as well as the toxicity of psychosine on multiple different nervous system cell types.

At the KTRN, the perspectives, experiences, attitudes, access to care, and expectations of KD patients and families are integral to the direction of scientific research and development of treatments as are the disease burdens for families and the health care systems. As was clear from interviews of parents, the KD familial effects are profound and highly disruptive. Mental health is a major and underappreciated effect in KD families as is the chaos of finding appropriate care for their affected children. Additional focus on these aspects of the KD burden is a critical ongoing need.

INITIATIVES

The 2021 Krabbe Translational Research Network Meeting

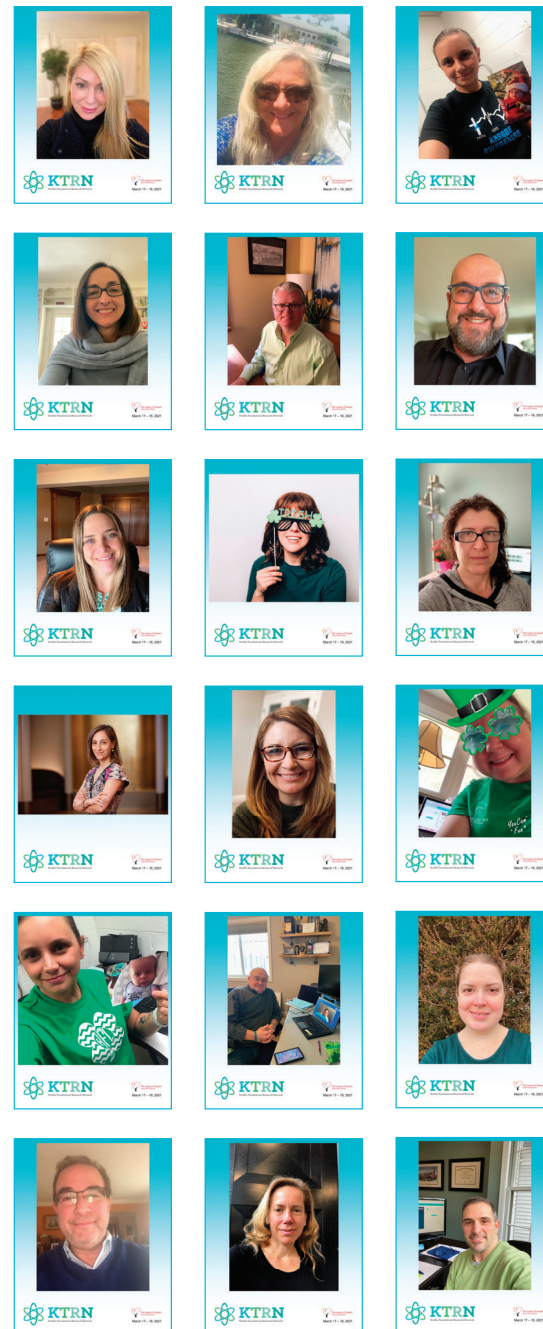
By Dr. Greg Grabowski, MD

In this pandemic year, the TLOAF-sponsored Krabbe Translational Research Network (KTRN) meeting was held virtually on March 17 and 18, 2021. This was also the first time that other organizations and companies helped support this meeting.

The basic and clinical research, as well as patient presentations, showed exciting progress in understanding Krabbe disease (KD) as well as toward improved treatments. Both are major goals of TLOAF research programs. Indeed, for the past decade work funded in part or wholly by TLOAF has expanded our understanding of the basic mechanisms and clinical courses of the different types of KD. These have provided the essential scientific basis to develop and evaluate treatments for KD, including transplantation of normal bone marrow stem cells (BMSCT) or umbilical cord blood cells (UCBCT) either alone or together with gene therapy.

The 2021 KTRN witnessed progress that has brought into focus a “light at the end of the tunnel” – that is, a potential quantum improvement in treatment outcomes for KD variants, based on combining BMSCT or UCBT with gene therapy. As emphasized at this KTRN, the engraftment of normal BMSC into the central (CNS) and peripheral nervous (PNS) systems may take several months to have optimal therapeutic effects by supplying the needed missing GalC enzyme to deficient cells and by dampening inflammation. Gene therapy with a non-disease-causing virus, adenoassociated virus (AAV), containing the GalC DNA provides for rapid expression of GalC in the CNS and PNS for prevention and/or correction of KD during the critical period before BMSC/UCBC CNS engraftment. Mouse and canine KD trials provided solid data of rapid and continued, via gene therapy, and slower sustained, via BMSCT or UCBT transplantation, effects in the PNS and CNS with amelioration of KD when instituted early.

These results together with previous and recent human TLOAF-funded human KD longitudinal natural history studies, clearly show that early diagnosis and intervention provides better neurological outcomes. The human clinical data strongly support the need for universal Newborn screening for KD to identify pre-symptomatic patients. As presented at KTRN, this need is grounded in the irreversibility of many of the pathological consequences of KD, including the interplay of death of nervous system cells and inflammation by specific cells in the CNS and PNS that propagate the disease.



From the desk of the Co-Founder

Another year has rapidly passed, and I can't help but reflect on all that has taken place since 2008. The work is far from done however I am grateful to have played a role in the journey to this point.

The Legacy of Angels Foundation (TLOAF) has worked diligently to uncover crucial scientific insights to improve the diagnosis, treatment, and education for Krabbe disease and Cystic Fibrosis. Our nearly decade and a half of funding work has helped to give patients and caregivers a future free of disease. Our mission is a collective effort. Many instrumental leaders have contributed to systematic advances in both diseases--from researchers, clinicians, statisticians, and patient advocacy organizations to universities, federal agencies, and industry stakeholders. At TLOAF, we value collaboration, and I am proud of the following joint accomplishments supported by TLOAF seed funding:

- » **The implementation of the Krabbe Translational Research Network (KTRN) Consortium**
- » **The discovery of psychosine as a biomarker for Krabbe disease**
- » **The writing of several peer-reviewed articles for Krabbe disease and Cystic Fibrosis by TLOAF-funded grantees**
- » **The identification of second-tier testing and an improved assay to help reduce the false positives in Krabbe disease newborn screening**
- » **The uncovering of many potential advantages of an IRT/NGS screening algorithm for Cystic Fibrosis**
- » **The use of whole-genome sequencing to help identify non-CFTR genetic variants in individual patients to help preserve optimal health for patients with Cystic Fibrosis**
- » **The development of illustrations on the CF-causing mutations identified and their pathologic mechanisms defined**
- » **The creation of an educational handout on CFTR mutations, classes, and potential therapies**
- » **The production of the Save Babies Through Screening Foundation, “Newborn Screening Aves Babies....One Foot at a Time”**
- » **The use of bone marrow transplantation and AAV gene therapy as a new therapy to treat Krabbe disease**

This is an incredible list of accomplishments. Kudos to all of you and many thanks to our savvy scientific advisory board and unyielding board of directors. Now it is time to turn the operation of the foundation over to the next generation. Over the next year, I will be transitioning out of TLOAF. As the only living founder, I will remain the President of the Foundation but will no longer be involved in the day-to-day work. We will name a chair of the board as well as an executive committee that will govern TLOAF on a routine basis.

It is time to travel with Tammy (my wife) and spend time with my grandchildren. Stacy Pike-Langefeld, the Executive Director, Heather Techmeier, the Finance Director, and Dr. Anthony Steyermark, the Medical Director, maintain the same commitment to finding treatments and lessening the impact of disease as Sue and I did. I am confident they will carry our commitment in a meaningful and impactful way.

The Foundation will continue to work towards helping patients live life undefined by Krabbe disease and Cystic Fibrosis. I am eternally grateful for being part of the effort for the past 14 years and look forward to cheering the TLOAF team on as they continue to help cure Krabbe disease and Cystic Fibrosis, two rare diseases that have impacted my family immensely.

Sincerely Yours,
Paul G Rosenau
Co-Founder and President



Who We Are

Our Mission: Improving the lives of patients impacted by Krabbe disease and Cystic Fibrosis through research funding and disease advocacy.

Our Vision: To live life undefined by Krabbe disease and Cystic Fibrosis.

BOARD OF DIRECTORS



STAFF

STACY PIKE-LANGENFELD
Executive Director

ANTHONY STEYERMARK
Medical Director

HEATHER TECHMEIER
Finance Director

HOW TLOAF CAME TO BE:

The Legacy of Angels Foundation (TLOAF) is a private family 501(c)(3) foundation established in 2008 by Paul Rosenau and the late-Sue Rosenau after winning the Powerball on May 4th, 2008. Paul and Sue are passionate about advancing research, improving newborn screening, and expanding awareness for Krabbe disease and Cystic Fibrosis, two rare diseases that affect their family genetics.

RESEARCH FUNDING:

The foundation's grant program drives the organization's mission forward. The foundation is committed to identifying grants to help advance research, education, and newborn screening for Krabbe disease and Cystic Fibrosis. The foundation's grants have grown significantly in size, scope, and stature, allowing the foundation to showcase many results and positive impacts from more than a decade of accomplished funding.

DISEASE ADVOCACY:

The foundation works to expand awareness of Krabbe disease and Cystic Fibrosis by fostering partnerships with patient-focused advocacy organizations that are providing supportive care and developing innovative resources to reduce the burden of the disease on the family and community.

INITIATIVES

The Power of Outside Perspective

By Mary Kay Delvo, ACC, MLS, LSW, INspiring SIGHT



The Legacy of Angels Foundation (TLOAF) became known to me in 2020 when Stacy Pike-Langefeld requested I provide coaching and strategy support to position the foundation for the future.

Two years later, this small family-run foundation has added a medical director, broadened the expertise and size of its board of directors, reorganized staffing structure and roles, implemented a performance evaluation system, and created a strategic plan. The basis of this work began with individual coaching across the organization. TLOAF isn't just positioning itself for the future, the staff and board are creating a purposeful and progressive culture.

TLOAF has never lacked commitment or drive toward its vision but recognized the need for clarity, focus, built-in accountability, and intentionality. To be successful, the team knew outside perspective would be necessary.

A common mindset held by nonprofits is the belief they can save money by doing everything themselves. The saying, "just because you can do something, doesn't mean you should," is appropriate here. Doing everything in-house also means varied ideas, critical inquiry, and experiences are being left out of the equation. TLOAF brought in an outside perspective on purpose; the organization specifically wanted a certified coach versus a consultant.



TLOAF RECOGNIZED THE FOLLOWING BENEFITS OF OUTSIDE PERSPECTIVES:

- » The exposure to fresh thinking
- » The push on comfort zones
- » The freedom from internal baggage
- » The safe place to ask questions that a person might not have been comfortable asking because of close entanglement to the work
- » The sharing of knowledge, relationships, networks & learning from other nonprofit work



HOW COACHING DIFFERS

Coaching practices the idea that people closest to the problem have the solutions, unlike consulting which is designed around expert advice-giving. When people closest to the challenges surface their own solutions, approaches, and strategies, they buy-in, invest and accept responsibility for the results.

Coaching also addresses a primary barrier to change—mindset management. A coaching approach increases self-awareness by challenging limiting beliefs and false narratives.

It digs below the surface and uncovers those limiting beliefs, misalignments, and stories which are no longer relevant. A coaching culture creates safe spaces for candid conversation, risk-taking, accountability, and tackling tough issues. Coaching will help an organization to:

- » Increase emotional wellness
- » Uncover ideas and solutions
- » Improve relationships
- » Increase critical thinking and problem-solving skills
- » Develop strategic mindsets
- » Develop organizational alignment
- » Promote organizational resilience



HOW DO YOU THINK TLOAF IS DOING?

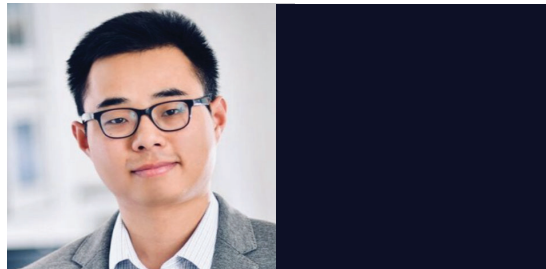
TLOAF has appreciated those who've contributed feedback to improve their work and mission over the past 2 years. If you have some constructive criticism or you would like to tell TLOAF how much you appreciate them, please email me at Mary Kay Delvo at marykay@inspiringsight.com. All feedback is provided to TLOAF anonymously.

FOUNDATION

New Faces to TLOAF

For many organizations, 2021 provided many operating challenges amid navigating the pandemic. However, challenges can bring growth, and, as you've read, TLOAF also used 2021 to evaluate the additional expertise needed on our organization's board. For the next 3 years (2021-2023) TLOAF will work diligently to refresh its governance to ensure the board can effectively steer TLOAF's work toward reaching its goals in the most effective way possible. TLOAF has recently added two new members to its Board of Directors. Dr. Li Ou and Phil Christianson will each bring unique and valuable expertise and perspective to our organization. Dr. Ou provides a scientific and industrial perspective for the strategic planning and operations of TLOAF. Phil Christianson's experience will help guide and advise TLOAF on investments, health services, and information technology. We invite you to learn a little more about these two outstanding individuals below.

DR. LI OU



Dr. Ou is currently the Vice President at Genemagic Bio, a startup focused on gene therapy for neurological and retinal diseases. He received his Ph.D. (major in Genetics, minor in Biostatistics) from the University of Minnesota in 2015; he was an Assistant Professor at the University of Minnesota between 2019 and 2021. Li has over 10 years of experience in leading IND-enabling studies of gene therapy, resulting in 2 IND approvals, 5 pending patents, 23 manuscripts, 62 abstracts, and 23 oral presentations. His previous work on zinc finger nuclease-mediated gene editing for treating MPS I and II diseases led to two Phase I/II clinical trials. These are the first two clinical trials approved for the application of in vivo gene editing to treat a genetic disorder in the world.

In Li's spare time, he enjoys cooking, watching soccer games, playing video games, and hanging out with his son and Corgi.

PHIL CHRISTIANSON



Phil, CEO of California Medical Evaluators (CME) graduated summa cum laude from Cal Poly, San Obispo. He holds a Juris Doctorate from Loyola Law School and an MBA from the University of Southern California. Before joining CME, Phil had served as the President and CEO of HealthSmart, Payment America Systems, Focused Health Solutions, RealMed, and Corporate Benefit Services of America. Phil also has 20 years of experience in being an advisor to and investor in health services and information technology. In May 2019, Phil completed the sale of HealthSmart to Centene Corporation, a \$135B Fortune 25 company.

Phil has been interested in prenatal care and health since the birth of his two children. He has served as the chairman of the Board of Directors for the March of Dimes for the Southern California chapter. Phil volunteered to serve on the board of TLOAF with the hopes that his corporate, fundraising, and benefits experiences could help manage its growth and services.

In Phil's free time, he enjoys playing water sports, traveling, and spending time with family and friends.

Grants Funded in 2021

The TLOAF grant program is at the heart of improving research and advancing advocacy for Krabbe disease and Cystic Fibrosis. Take a moment to learn about our grant guidelines and who received funding in 2021.

2021 GRANTS

Principal Investigator	Institution	Grant Title	Grant Amount
Ernesto Bongarzone, Ph.D.	University of Illinois	Correction of Krabbe Mouse Model to Enable Regulated Expression of Therapeutic GALC Enzyme	\$75,000.00
		Studies of GALC Correction Stability after AAV Gene Therapy for Krabbe Disease	\$180,000.00
Maria Irene Givogri, Ph.D.	University of Illinois	Vesicular Delivery of GALC for ERT of Krabbe's Disease	\$148,723.00
Maria Escolar, M.D.	Children's Hospital of Pittsburgh Foundation	2020 Krabbe Disease Patient Care and Research (NDRD) (*)	\$374,118.00
		2021 Krabbe Disease Patient Care and Research (NDRD)	\$476,000.00
Dawn Laney, MS, CGC	Emory University	Paul M. Fernhoff Memorial Lecture Series	\$5,000.00
M. Laura Feltri	The Research Foundation for SUNY	Support for the Infrastructure of KD & Myelin Research at the University of Buffalo	\$198,156.00
		Innovative Model Systems to Study & Boost Innate Immunity in KD	\$121,666.00

*Approved in 2020 but not paid until 2021.

\$1,578,663.00

GRANT GUIDELINES:

All interested applicants

must be a non-profit and are required to submit a Letter of Inquiry (LOI). The Letter of Inquiry form can be downloaded from our website at tloaf.org. Please note, that we DO NOT fund international applications at this time.

Interested applicants

are encouraged to read The Legacy of Angels Foundation's mission and vision statement plus the list of previously funded grants for information on the type of projects the foundation funds. All projects must align with TLOAF's mission.

Letters of Inquiry

will be evaluated on the subject matter and the potential impact of the proposed research. Letters of Inquiry can be submitted electronically as a word document or a PDF.

Letters of Inquiry should be

no more than 750 words, excluding headers, contact information, biographical sketches, and references. Please answer the questions in the order presented.

No more than 5%

of grant funds can be used for indirect costs.

Insights From the Finance Director

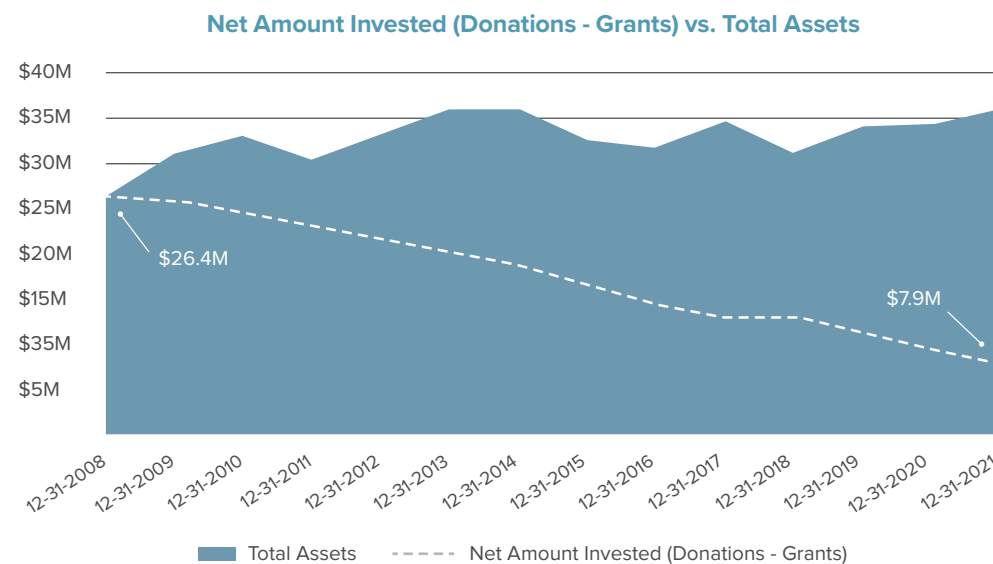
By Heather Techmeier, TLOAF Finance Director



After surviving a tumultuous 2020, there was hope for a return to normalcy following the trauma of the initial phases of the pandemic. Investors looked for signals as to which way the economy was headed. After the development and distribution of vaccines, we saw the easing of lockdowns which was followed by an economic rebound. The market did not disappoint and turned in a solid performance in 2021. Yet, the recovery would be continually tested by labor shortages, supply-chain issues, and rising inflation – sending prices soaring to the highest they had been in nearly four decades!!

In 2021 the foundation continued to maintain a 60% equity and 40% bond investment portfolio with the Foster Group whose philosophy can be summed up as “stay invested and stay diversified” and we couldn’t agree more. As a result of the market performance in 2021, The Legacy of Angels Foundation’s investment portfolio was up 11.70% as of December 31, 2021. We watched our investments flourish from \$26,686,687.81 on December 31, 2020, to \$31,577,092 on December 31, 2021, all the while providing \$1,578,663 in grants to researchers—an astonishing accomplishment! The Legacy of Angels Foundation also completed an in-depth life-insurance evaluation, similar to the one performed in 2018. We currently have 5 insurance policies with a total current death benefit of \$16,775,000.

As we complete another year in the market, we need to remember that past performance does not guarantee future results. Investors can’t predict the timing of the next market fluctuation as new and unexpected challenges will always arise. However, in order to create better investment outcomes, we believe we need to harness the power of capital markets, avoid predictable disappointments like trying to time the market, advance our investments with academic research, and most importantly, embrace uncertainty. Nothing emphasized that more than 2020 & 2021, two years where investors who persevered and stayed invested and diversified, reaped the benefits.



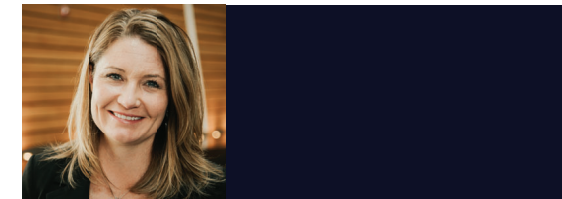
Investing is about endurance. Compounding is powerful and you want to do whatever you can to not interrupt it. This is why it is so important that each investor has a portfolio that is right for them. —Morgan Housel

In 2008, Paul and the-late Sue Rosenau invested \$26.4 million into The Legacy of Angels Foundation. If TLOAF neglected to properly invest these funds, the Foundation’s total assets would have dropped to \$7,906,250.90. Thankfully, through mindful investing, the Foundation’s assets have grown to \$36,124,499.31 in 2021 all while funding \$20,418,477.93 in grants!

FOUNDATION

2021 Recipient of the Sue Rosenau Legacy Award

By Stacy Pike-Langenfeld, TLOAF Executive Director



The Sue Rosenau Legacy award was created to honor the late Co-Founder and Chief Operating Officer of The Legacy of Angels Foundation (TLOAF), Sue Rosenau. To qualify for the distinguished award, the individual recognized must be an inspirational leader who collectively creates memorable and lasting change in the areas of Krabbe disease or Cystic Fibrosis. Just as Sue did, the individual honored must also be making extraordinary contributions to the field, working to propel progress towards better treatment, and providing authentic support to the patient community.

The 2021 recipient was Dr. Maria Luisa Escolar. Dr. Escolar was presented with this award at the 2021 Virtual Krabbe Translational Research Network (KTRN) meeting in recognition of her 20-plus years of work in Krabbe disease. Dr. Escolar was selected for the award based on notable accomplishments;

- Served as the Associate Director for Translational Research at the University of North Carolina Gene Therapy Center.
- She established the Program for the Study of Neurodevelopment in Rare Disorders (NDRD) at the University of Pittsburgh Medical Center in 2000.
- She effectively described the natural history of Krabbe disease through her research at the NDRD clinic and has provided the most robust natural history studies for this condition.
- She initiated the KTRN, a meeting that continues today to bring scientists, clinicians, and patients impacted by Krabbe disease together to collaborate and share resources.
- She assisted Forge Biologics in bringing the 10 years of KTRN work to a company that could facilitate a gene therapy clinical trial for Krabbe disease.

Dr. Escolar is nationally and internationally known for her Krabbe disease research and clinical care of children. The NDRD provides a multidisciplinary full-time team that helps diagnose, treat, and care for children with rare neurological disorders. This is one of the most prominent clinics for the treatment and care of Krabbe disease in the world.

She is the third individual to receive this award: Dr. David Wenger was the 2019 recipient and Dr. Philip Farrell was the 2020 recipient. Congrats Dr. Escolar! We are incredibly thankful you chose to help patients live life undefined by Krabbe disease.



Dr. Maria Luisa Escolar