Kennedy Krieger
Moser Center for Leukodystrophies

March 2026

To the Leukodystrophy Community:

We hope this letter finds everyone well and in the company of loved ones.

We at the Moser Center for Leukodystrophies at Kennedy Krieger Institute have much to be thankful for, including our hard-working team and the trust and support of this inspiring network of patients, caregivers and families.

We would first like to introduce you to the newest Moser Center staff members, who joined us in 2025:

Dr. Sonum Bharil

Antonio Holmes

Madison Yorkowski

Sonum Bharill, MD, MHS, is a pediatric endocrinologist at the Moser Center and an Assistant Professor of Pediatrics at the Johns Hopkins University School of Medicine. Her main interest is in adrenal disease and steroid metabolism in children. She recently joined our Leukodystrophy Clinic to provide endocrine services to children with adrenoleukodystrophy and other leukodystrophies. She often teams up with our other providers to see patients in our Leukodystrophy Newborn Screening Follow-Up Clinic.

Antonio Holmes, BA, joined the Basic Science Research Lab as a Research Assistant and oversees all of our animal model work. He is a recent graduate of the University of Maryland, Baltimore County, and has excelled in all aspects of animal husbandry.

Madison Yorkowski, BA, joined the Moser Center last summer and is also from the University of Maryland, Baltimore County. She is a Research Assistant and has taken to the field quickly, growing and maintaining neuronal and organoid cell cultures for various ALD projects.

GENERAL UPDATES FROM THE MOSER CENTER

Our team members at the Moser Center have been busy with many research activities for various diseases. Despite the tough funding environment, we have been successful in securing several foundation and federal grants. Notably, the Moser Center serves as one of the three lead sites of the Global Leukodystrophy Initiative (GLIA) Clinical Trials Network, which is one of the 21 Rare Disease Clinical Research Networks (RDCRN) funded by the National Institutes of Health (NIH). Last fall, we received a notice of funding renewal for this consortium to continue for five more years. The goal of this network is to conduct the largest natural history study of all leukodystrophies across several expert sites in the U.S., with the aim of developing clinically meaningful outcome measures necessary for clinical trials. In addition to allowing us to conduct a study on all leukodystrophies, this grant also provides funding for a biomarker study for Leukoencephalopathy with Brainstem and Spinal Cord Involvement and Lactate Elevation (LBSL), which will be conducted at Kennedy Krieger in collaboration with Stanford University and Johns Hopkins. We have secured several other grants for research on various diseases—see details below. In total, our investigators published 15 journal articles in 2025 related to leukodystrophies.

We continue to serve as strong advocates for individuals affected by leukodystrophies. One great accomplishment in 2025 was to have metachromatic leukodystrophy (MLD) added to the Recommended Uniform Screening Panel (RUSP). This was the result of hard work by many scientists and advocates, and we were fortunate enough to have our own **Eric Mallack, MD, MBE**, an expert in leukodystrophies, provide a congressional briefing at the U.S. Capitol to emphasize the need for MLD newborn screening.

PROGRESS IN ADRENOLEUKODYSTROPHY (ALD)

While the Moser Center focuses on several leukodystrophies, a great amount of its effort is invested in research related to X-linked adrenoleukodystrophy. It has been a busy year in the research lab, with tireless efforts being made to understand the mechanisms that drive ALD pathology, in men and women, and to identify and test novel—and targeted—therapeutic strategies.

This year was the start of a novel project to grow human cerebral organoids derived from the cells of patients with ALD. These organoids, or “mini brains,” develop similarly to a human brain, including cell types and organizational patterns. As the ALD mouse model fails to develop all phenotypes of ALD, new and humanized models such as these are needed. **Christina Nemeth Mertz, PhD**, from the Moser Center, in partnership with **Annie Kathuria, PhD**, an Assistant Professor of Biomedical Engineering at the Johns Hopkins University School of Medicine, lead this work. We believe these organoids will be useful in helping us clarify genetic differences between different ALD phenotypes and will be useful models for testing

therapies. We are grateful to The Stop ALD Foundation for enabling and supporting this work.

Similarly, in an attempt to glean as much information as possible from the ALD mouse model, **Nadav Weinstock, MD, PhD**, has been leading efforts to fully characterize the ALD mouse using state-of-the-art technologies. This work, including lipid profiling and electron microscopy (EM) of nerve fibers, may reveal how changes to peripheral nerves contribute to many of the symptoms of ALD, including incontinence, numbness and pain. **Chelsey Reed, MD, PhD**, a clinical research fellow at Johns Hopkins, received a grant from ALD Connect to study the female ALD mouse and will perform a similar set of experiments, with high sensitivity, to detect previously unobserved changes in female ALD mice. These studies will be useful in delineating how ALD presents itself in females and how that may be variable across animals. Dr. Reed will present her work at the annual ALD Connect meeting in 2026.

Dr. Chelsey Reed

In other efforts toward advancing disease understanding, **Dr. Mallack**, a renowned clinician and expert in cerebral ALD, has been advancing his novel neuroimaging methods to allow for more precise and early prediction of cerebral disease.

Dr. Christina Nemeth Mertz
at ALD Connect 2025

Quantitative Susceptibility Mapping is a newly developed method to analyze patient MRIs to assess the magnetic properties of brain tissue at a high resolution. Dr. Mallack's work reveals a differential presence of magnetic susceptibility based on ALD phenotype that, if consistent, can be used to aid in clinical assessment. These studies led to a parallel effort by **Dr. Nemeth Mertz** to confirm and validate these findings in ALD patient tissue. Dr. Mallack presented this body of work at the 2025 International Society for Magnetic Resonance in Medicine Annual Meeting and Exhibition and at the 2025 Annual Meeting of the American Neurological Association. Dr. Nemeth Mertz and Dr. Mallack presented their combined work at the 2025 ALD Connect Annual Meeting.

Along with deepening our understanding of ALD progression, we are always searching for targeted and novel ways to treat it. Gene-editing methods, which are small-molecule techniques used to directly edit DNA (to correct disease-causing variants), are in development at the Moser Center. **Greg Newby, PhD**, Assistant Professor in the Department of Genetic Medicine at the Johns Hopkins University School of Medicine, and his team work closely with **Dr. Nemeth Mertz** and **Yousif Alemhza, MS**, to develop and test strategies that directly target DNA. These efforts

involve CRISPR-Cas9 technology to edit specific sites within the DNA of patient fibroblasts or induced pluripotent stem cells (iPSCs) and then phenotyping these cells to look for changes to very long chain fatty acid accumulation. Any phenotypic change is compared to the degree to which the DNA was successfully edited. This work is still in its infancy, but it has the potential to make an impact in the field.

Drug repurposing is also on our mind. When successful, repurposing is an attractive option, as repurposed medications are already FDA-approved and considered safe for other conditions. As ALD and its disease-causing gene, *ABCD1,* share features with other genes and disorders, we have the opportunity to test if drugs proven for use in treating these other disorders will also work in treating ALD. Will to Cure ALD is currently funding efforts to test an FDA-approved compound in patient cell model systems to determine if it, or analogs, can successfully reduce very long chain fatty acid accumulation and result in a meaningful change in disease presentation. This is a new project, and we hope to make significant progress on it in 2026.

In this work, we are grateful for the guidance, wisdom and pure generosity of **Ann Moser, BA**. She is the definition of inspiration and motivation and graces Kennedy Krieger on a daily basis to collaborate, teach and follow through on her own curiosity and dedication to this disease. Thank you, Ann, for being you, and inspiring us all!

In terms of clinical research, our group has been busy recruiting patients and healthy volunteers for our NIH-funded multiomics adrenomyeloneuropathy (AMN) biomarker study, thanks to the efforts of research coordinator **Aditii Makwana, MS**; **Amena Smith Fine, MD, PhD**; and other Moser Center staff members. The goal of this study is to combine advanced large-scale screening techniques looking for blood chemicals (metabolomics) and gene products (miRNAseq) with machine learning tools to develop monitoring and prognostic markers for males and females with AMN. By the end of this project, we expect to have identified a blood test that can be done on a sample collected in the clinic and that will reflect the degree of clinical impairment as a monitoring biomarker. This will be especially useful if patients are no longer able to undergo rigorous clinical tests, such as a fast-paced walk. We also expect this blood test to serve as a prognostic biomarker that predicts the future disease trajectory, thereby guiding clinical care and improving the design and success of clinic trials in AMN. We have enrolled enough study participants for the initial phase of analysis, which will be initiated by **Bela Turk, MD**, in the spring of 2026.

Complementary to this effort, we are also excited to announce that Will to Cure ALD has funded the pilot phase of a new clinical project in AMN, led by **Dr. Smith Fine** and **Dr. Turk**. The project, “Machine Learning Approach to Phenotype AMN Progression,” focuses on the urgent, unmet need for more sensitive clinical outcome measures and biomarkers of disease progression to improve the success of clinical trials in AMN. The project uses machine learning tools to identify phenotypic subtypes and fast-versus-slow trajectories of disease in AMN males and females and then localize these to MRI indices of damage in white matter tracts of the spinal cord. The knowledge gaps addressed are expected to provide new insights about disease prognosis and improved approaches to the conduct of clinical trials.

We are also pleased to report that “Living with adrenoleukodystrophy: adult patient and caregiver perspectives” is now published in the Orphanet Journal of Rare Diseases. This manuscript is a collaborative effort between ALD Connect and senior authors including **Dr. Smith Fine and Dr. Ali Fatemi**. The paper reflects insights from ALD Connect’s Externally-Led Patient-Focused Drug Development meeting in 2022, which included over 250 adults living with ALD, along with caregivers, experts, industry partners and FDA representatives. It highlights the daily impact of adult ALD, treatment limitations and the urgent need for therapies that slow or halt disease progression.

In addition to our work in ALD, our team is also involved with several other leukodystrophies, particularly LBSL, for which we’re focusing on gene-targeted therapies (see our LBSL end-of-year report).

A new collaboration between **Dr. Turk** and the Children’s Hospital of Philadelphia (CHOP) has resulted in an NIH-funded grant to study metachromatic leukodystrophy (MLD) progression. Over the past year, patients with MLD have been recruited at CHOP, which has leveraged the GLIA network and created a machine learning-based predictive model in a landscape of high variability in early disease progression. The goal of the project is to identify clinical assessment markers and predict which individuals are at high risk for developing MLD. This will allow for the development of future monitoring protocols and will help inform clinical trial outcomes and recruitment.

Thanks in part to advocacy by the Moser Center and other leukodystrophy experts, the American College of Medical Genetics and Genomics (ACMG) has added the *ABCD1* gene to its list of secondary findings that are recommended to be reported when people undergo genomic testing for any medical reason. This change means more individuals with unrecognized risk for adrenoleukodystrophy may be identified early, allowing for timely monitoring, treatment and family support. Earlier awareness can make a meaningful difference in health outcomes and in helping families prepare and take action.

CLINICAL TRIALS IN THE LEUKODYSTROPHIES

In addition to our ongoing efforts in understanding disease processes and progression, we are also a site for several clinical trials for the leukodystrophies. We are currently conducting a placebo-controlled trial of Leriglitazone for adults with cerebral ALD and are actively recruiting patients for this study. Additionally, we have an expanded access program for the use of Leriglitazone for men with AMN who were previously in a placebo-controlled trial. In addition, in collaboration with the Johns Hopkins Bone Marrow Transplant Program Team, we treat patients with ALD and *CSF1R*-related leukodystrophy with stem cell transplantation.

Lastly, several additional trials for other leukodystrophies are in a contracting stage, including a collaboration with industry partners to conduct N of 1 trials—which are

highly patient-centric—of antisense oligonucleotides. We are fortunate to have received support from The Dresher Foundation to fund this N of 1' program.

LOOKING AHEAD

We can only hope that 2026 brings peace and joy to all of you. We will continue to be here, working to uncover novel strategies to relieve the burden of ALD. We are grateful for you, the community, for your optimism and trust. Should you be interested, we always welcome participation in research, in any form, or other community engagement. We look forward to seeing you all in 2026, wherever that may be.