PRESS RELEASE

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KIDNEY HEALTH INITIATIVE COMPLETES PROJECT FOCUSED ON CLINICAL TRIAL END POINTS FOR PRIMARY HYPEROXALURIA

Highlights:

- Available evidence supports the use of marked changes in urine oxalate in CKD stages 1-3a and plasma oxalate in CKD stages 3b-5 as surrogate end points for clinical trials in primary hyperoxaluria.
- Worsening kidney function is considered an acceptable clinical trial end point; however in many patients with primary hyperoxaluria, kidney function is not lost at a rapid rate until very advanced stages of disease.
- Kidney stones are clinically meaningful, though lack sufficient standards for measurement and monitoring. Their role as a feasible clinical end point should be reconsidered as more data becomes available.

Washington, DC (March 17, 2020) — The Kidney Health Initiative (KHI), in partnership with the Oxalosis and Hyperoxaluria Foundation (OHF), concluded a collaborative effort to evaluate efficacy end points for clinical trials in primary hyperoxaluria.

The project's conclusions were recently published in *CJASN* accompanied by a Perspective authored by caregivers of people living with primary hyperoxaluria who were involved in the project.

The project workgroup, including clinicians, researchers, people with primary hyperoxaluria and their caregivers, representatives from industry, and the US Food and Drug Administration (FDA), conducted a literature review and evaluation of potential clinical and surrogate end points. As discussed in the paper, available evidence supports the use of marked changes in urine oxalate in CKD stages 1-3a and plasma oxalate in CKD stages 3b-5 as surrogate end points for clinical trials in primary hyperoxaluria. Worsening kidney function is considered an acceptable clinical trial end point; however in many patients with primary hyperoxaluria, kidney function is not lost at a rapid rate until very advanced stages of disease. Kidney stones are clinically meaningful but pose challenges in the clinical trial setting because of insufficient standards for measurement and monitoring. Their role as a feasible clinical endpoint should be reevaluated as the natural history of stone disease in primary hyperoxaluria becomes informed by more robust data.

“Adoption of these end points will help us evaluate the effect of novel therapies in a much shorter timeframe, so that potential benefits can be available to patients as soon as possible,” said Dawn S. Milliner, MD, the lead author on the paper and co-chair of the project.

Primary hyperoxaluria is a rare genetic kidney disease characterized by the overproduction of oxalate by the liver. It causes kidney stones and progression to kidney failure is anticipated by age 33 in 50% of people with type 1 primary hyperoxaluria. "People living with primary hyperoxaluria are faced with the burden of recurrent and painful stone events from a very young age which often results in end-stage kidney disease and the need for intensive dialysis as a bridge to dual liver/kidney transplantation,” said Kim Hollander, the Executive Director of the Oxalosis and Hyperoxaluria Foundation. “Despite the unmet need, there are currently no approved therapies for primary hyperoxaluria on the market.” Additional information regarding the OHF can be found at www.ohf.org.

Growing attention is being paid to this rare disease by the pharmaceutical industry. Clinicaltrials.gov lists more than two dozen studies for primary hyperoxaluria in various stages of progress. Trial sponsors include KHI member organizations Allena Pharmaceuticals, Alnylam Pharmaceuticals, Dicerna Pharmaceuticals, and OxThera.

Agreement between sponsors and the FDA on clinical trial design is critical to approving new therapies. “For many rare diseases, it can be challenging to identify the end points that can be used in clinical trials to demonstrate the efficacy of new treatments and support product approval. Patients, who are the experts in their disease, need to be at the center of such discussions,” said Aliza M. Thompson, MD, Deputy Director of the Division of Cardiovascular and Renal Products in the FDA’s Center for Drug Evaluation and Research. “This project, led by the Oxalosis and Hyperoxaluria Foundation and the Kidney Health Initiative, is an important step forward in identifying suitable end points for clinical trials in primary hyperoxaluria.”

The article, entitled “Endpoints for Clinical Trials in Primary Hyperoxaluria,” appeared online at http://cjasn.asnjournals.org/ on March 12, doi: 10.2215/CJN.13821119.

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Individuals who are interested in learning more about KHI, should contact Melissa West, Acting Vice President for Research, Discovery and Innovation, at mwest@asn-online.org.

The Kidney Health Initiative is a key part of the newly created ASN Alliance for Kidney Health. KHI is uniquely positioned to realize ASN’s vision of a world without kidney diseases. As a public-

private and collaborative partnership with the FDA and more than 100 organizations and companies, KHI catalyzes innovation and the development of safe and effective patient-centered therapies for people living with kidney diseases. Learn more at www.kidneyhealthinitiative.org.

Since 1966, ASN has been leading the fight to prevent, treat, and cure kidney diseases throughout the world by educating health professionals and scientists, advancing research and innovation, communicating new knowledge, and advocating for the highest quality care for patients. ASN has more than 21,000 members representing 131 countries. For more information, please visit www.asn-online.org or contact the society at 202-640-4660.

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