2020

KHI KIDNEY HEALTH INITIATIVE

ANNUAL REVIEW

kidneyhealthinitiative.org

The Kidney Health Initiative (KHI) is a public-private partnership between the American Society of Nephrology (ASN), the US Food and Drug Administration (FDA), and over 100 member companies and organizations committed to **catalyzing innovation and the development of safe and effective patient-centered therapies** for people living with kidney diseases.

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Despite the unique challenges of 2020, KHI and its members stepped up and continued advancing novel therapies for people with kidney diseases. The challenges of this past year crystallized the value of being part of an innovation community where members are at the center of transformative issues. While KHI's 2020 priorities may have changed, the commitment to our mission has not. In fact, the COVID-19 pandemic and its ripple effects throughout the kidney community focused our efforts. Thanks to our partnership with the FDA, leadership from the Board of Directors, commitment of our workgroup chairs, expertise from workgroup members, and participation from our member companies and organizations, KHI continues to catalyze innovation for people with kidney diseases.

As a membership-based organization representing every corner of the kidney community, KHI member companies and organizations experienced challenges and disruptions during these unprecedented times. Patient organizations struggled to address the fears of people with kidney diseases who sift through an avalanche of information about the pandemic and need to know how to keep themselves safe from infection while maintaining their care. CROs adapted quickly to a new landscape and rapidly applied innovations to the design of clinical trials. Dialysis companies were on the front lines from the beginning, since some of the earliest cases of COVID-19 were in dialysis clinics, finding novel ways to protect people with kidney failure and dialysis clinic staff from infection. Pharmaceutical companies saw clinical trials slowed or stopped but also new opportunities to include people with kidney diseases in clinical trials for novel COVID-19 vaccines and therapies. In the face of these challenges, KHI members strove to preserve the research and development gains of previous years and protect people with kidney diseases.

COVID-19 has only increased the urgency of KHI's mission. The pandemic heightened the public's awareness that 37 million Americans with kidney diseases are an especially vulnerable population and the impact kidney diseases have on the underserved minority community who often have less access to healthcare. It is the charge of KHI members to deliver the promising advancements of recent years to the communities that represent the disease.

Addressing the obstacles member companies and organizations faced required a reorientation of KHI as well. The Board of Directors reorganized to better align with the FDA and serve our member companies and organizations. Dividing the Board's efforts among drug, biologics and device development allows KHI to quickly minimize any chance of losing progress because of the pandemic, from the need for more people with kidney failure to utilize home therapies, to the inclusion of people with kidney diseases in non-nephrology clinical trials, to the continuation of existing trials for novel treatments of kidney diseases.

While COVID-19 took up much of the oxygen in 2020, KHI was not distracted from its mission and from executing many important projects that benefit the kidney community. Some of our most important activities undertaken this past year were in close coordination with the FDA and in response to specific requests from the agency. The endpoints for primary hyperoxaluria project informed the FDA approval of the first drug for that rare disease. The Patient Preferences Initiative, a contract with CDRH, continues to progress with the goal of putting a first-of-its-kind survey into the field in 2021. Identifying biomarkers for kidney diseases, a KHI priority area since inception, resulted in a new project to outline a roadmap for AKI biomarkers that can support drug development. Lastly, an inaugural project on pharmacokinetics in people receiving continuous kidney replacement therapy informed an FDA draft guidance and dosing recommendations in a new drug label.

Investigation of treatment and prevention of kidney diseases continue to be an exciting space with much promise. In 2021, we will continue our goal of making that promise a reality by supporting the FDA, promoting the patient perspective in drug and device development, identifying clinical trial endpoints, advancing clinical trial design, developing technology roadmaps, and promoting equity and equality in clinical trials. Thank you for being a part of the important work that KHI is doing. Without the commitment, ingenuity, and persistence of its members, KHI could not meet the demand for patient-centered therapies for people with kidney diseases.

Sincerely,

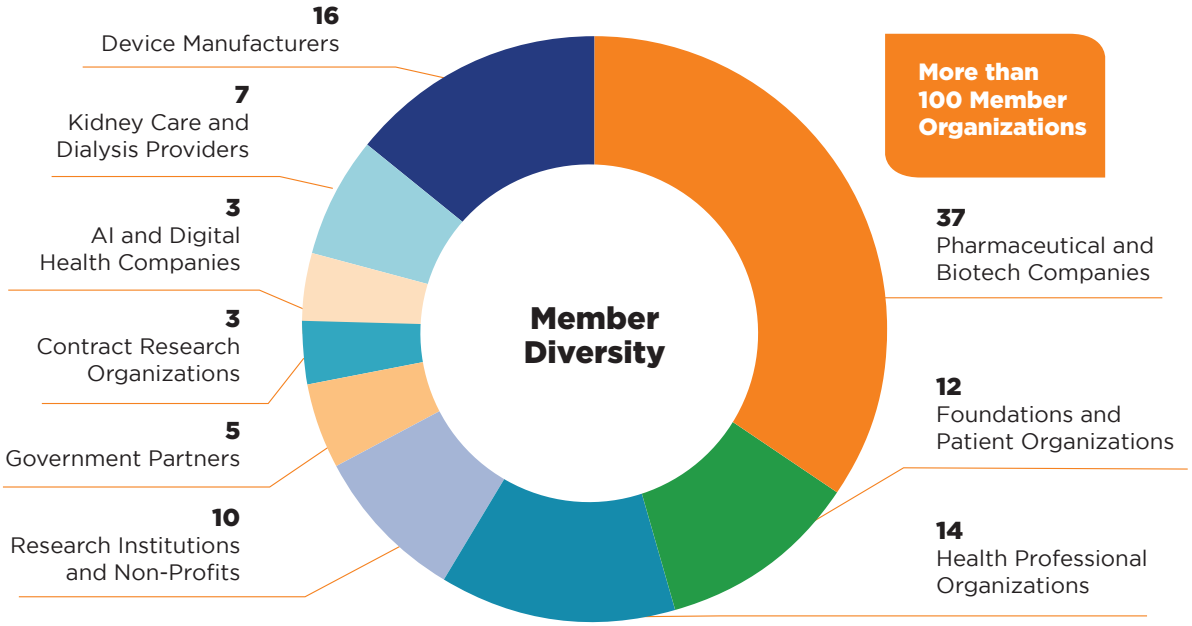
Raymond C. Harris, MD, FASN
ASN Co-Chair for KHI

Roadmap for AKI Biomarkers Begins Work

Throughout the world, 13.3 million people are diagnosed with acute kidney injury (AKI) each year, costing the US healthcare system an estimated $5.4-$24 billion in increased hospitalization costs and 1.7 million deaths worldwide. Traditional AKI detection methods lack sensitivity and specificity and are delayed in showing measurable changes after injury. In 2020, KHI began development of a *Roadmap for Accelerating Development of Biomarkers for Acute Kidney Injury* to outline future biomarkers for drug development that are more specific, sensitive, and measurable earlier in the course of disease. The roadmap will describe key use cases, milestones for success, major challenges, and activities to overcome those challenges, and build momentum for AKI biomarker development.

Progress Continues to Collect Patient Preferences for Novel Kidney Devices

Rigorous patient preference information ensures the next generation of novel kidney devices provide needed solutions for people with kidney failure. 2020 marked the end of the first year of a three-year contract between the FDA and KHI to collect patient preference information on innovative kidney replacement therapies. KHI worked collaboratively with FDA, patient partners, and clinical advisors to complete the initial qualitative work that helped identify the product attributes and define the risks of future wearable dialysis devices. This information was used to develop the survey instrument, which was tested with a small number of patients. A pilot of the programmed electronic survey will begin in early 2021, with full survey dissemination by mid-year.



FDA Revises Guidance on Pharmacokinetics in Patients with Impaired Renal Function

In 2020, the FDA revised its "*Pharmacokinetics in Patients with Impaired Renal Function —Study Design, Data Analysis, and Impact on Dosing and Labeling*" guidance, utilizing the recommendations of an inaugural KHI project. In 2012, KHI convened a diverse workgroup of subject matter experts to critically evaluate key considerations and to propose strategies for facilitating the standardized assessment of pharmacokinetics and the development of drug dosing recommendations in AKI patients receiving continuous kidney replacement therapy (CKRT). The revised guidance document now includes considerations for characterizing a drug's pharmacokinetics and dosing during CKRT and recommends the use of pharmacokinetics from phase 2 and 3 studies to inform kidney dosing recommendations when possible, in lieu of a traditional kidney impairment study.

First Drug Approved for Primary Hyperoxaluria Type 1

The FDA credited the work of KHI and the Oxalosis and Hyperoxaluria Foundation in the approval of the first drug to treat primary hyperoxaluria type 1. Alnylam Pharmaceuticals, a member organization, earned Breakthrough Therapy, Orphan Drug, and Rare Pediatric Disease Designations from the FDA for this new drug. In 2020, KHI completed a multi-year effort to accelerate drug approvals for this rare disease by identifying endpoints for primary hyperoxaluria clinical trials based heavily on patient perspective and the pathophysiology of enteric hyperoxaluria. KHI brought together stakeholders to evaluate potential endpoints to establish efficacy benchmarks of agents that treat primary hyperoxaluria and describe primary hyperoxaluria pathophysiology, causes, outcomes, and therapies.

10 New Member Organizations

3 Completed Projects

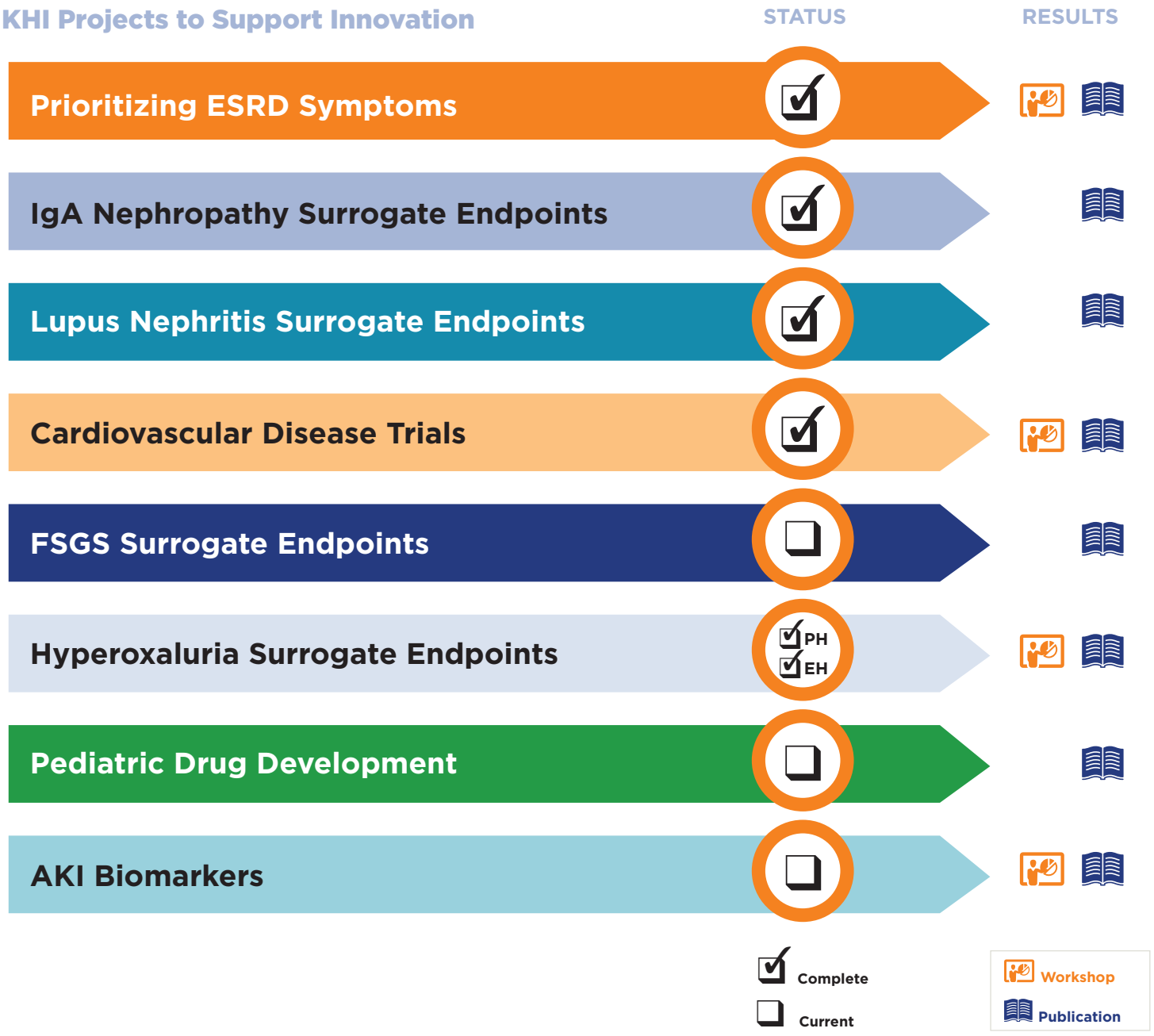
Presented at 9 Meetings

Hosted 5 Member Townhalls

4 Published Manuscripts

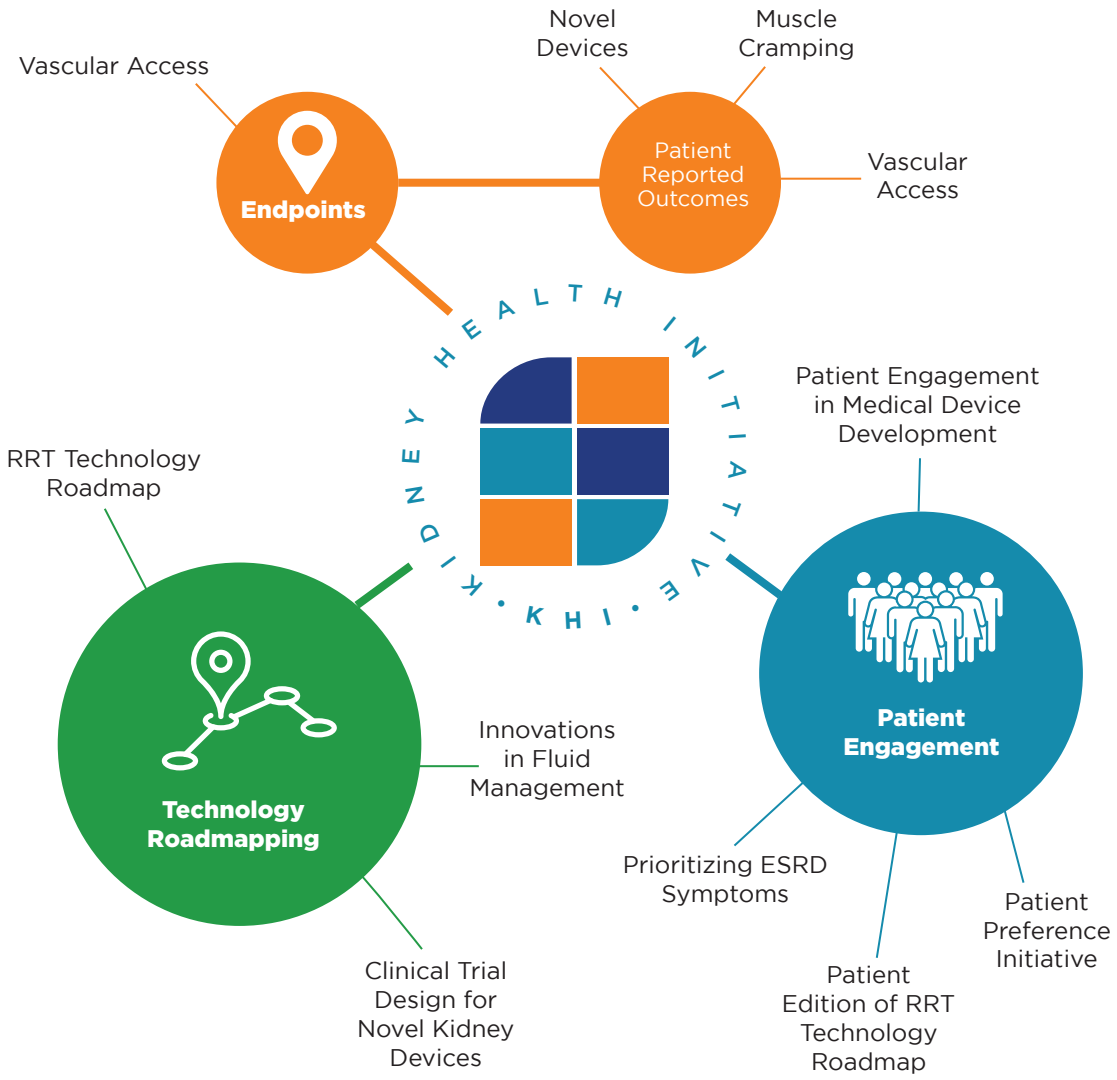
167 Volunteers

Kidney disease drug development has benefited from renewed interest and investment since KHI's establishment in 2012. Member organizations and companies work collaboratively in a pre-competitive community with FDA to address common barriers to innovation in drug development for kidney diseases. KHI's portfolio of drug development projects focus on clinical trial design, clinical trial endpoints, and biomarkers. The results from these projects provide the kidney community the tools needed to deliver novel drugs to people with kidney diseases. In 2020, KHI initiated its first project in the biomarker space and completed projects related to endpoints for primary hyperoxaluria and the inclusion of people with kidney diseases in cardiovascular trials.



KHI member organizations and companies are at the center of transformative device innovation that starts with incorporating the perspective of people with kidney diseases. Our work elevating the patient perspective in device development informed the *Technology Roadmap for Innovative Approaches to Kidney Replacement Therapy*, an effort that connects subsequent clinical trial endpoints and patient reported outcomes (PROs) projects. In 2020, KHI completed a project articulating PROs for novel kidney devices and a project describing clinical trial design and terminology for novel kidney devices. Altogether, KHI's device portfolio provides member organizations and companies the scientific foundation for future alternatives to dialysis and near-term innovations from fluid management to vascular access.

Device Portfolio



In addition to threatening the livelihood and lives of people with kidney diseases with risk of severe disease and infection, the COVID-19 pandemic put in jeopardy the advancement of innovative therapies for people with kidney diseases that have emerged over the past decade. In the early days of the pandemic, the Board of Directors acted quickly to identify the most acute needs faced by member organizations and the broader community.

The Board identified three areas that closely aligned with KHI's mission:

1. Technology advancement to bring more people with kidney failure home for kidney replacement therapy
2. Inclusion of people with kidney diseases in clinical trials for COVID-19 vaccines and therapies
3. Ensuring the resilience of existing clinical trials for novel therapies for kidney diseases during the pandemic

Throughout 2020, the Board met regularly to address these issues by releasing position statements, cultivating relationships with COVID-19 clinical trial sponsors, and sharing resources on novel approaches to clinical trials.

Activity Timeline

MARCH

Launched ASN COVID-19 Response Team

APRIL

Initiated KHI Board of Directors COVID-19 Response

MAY

Published *Accelerating Technology Development During a Pandemic to Bring More People with Kidney Failure Home*

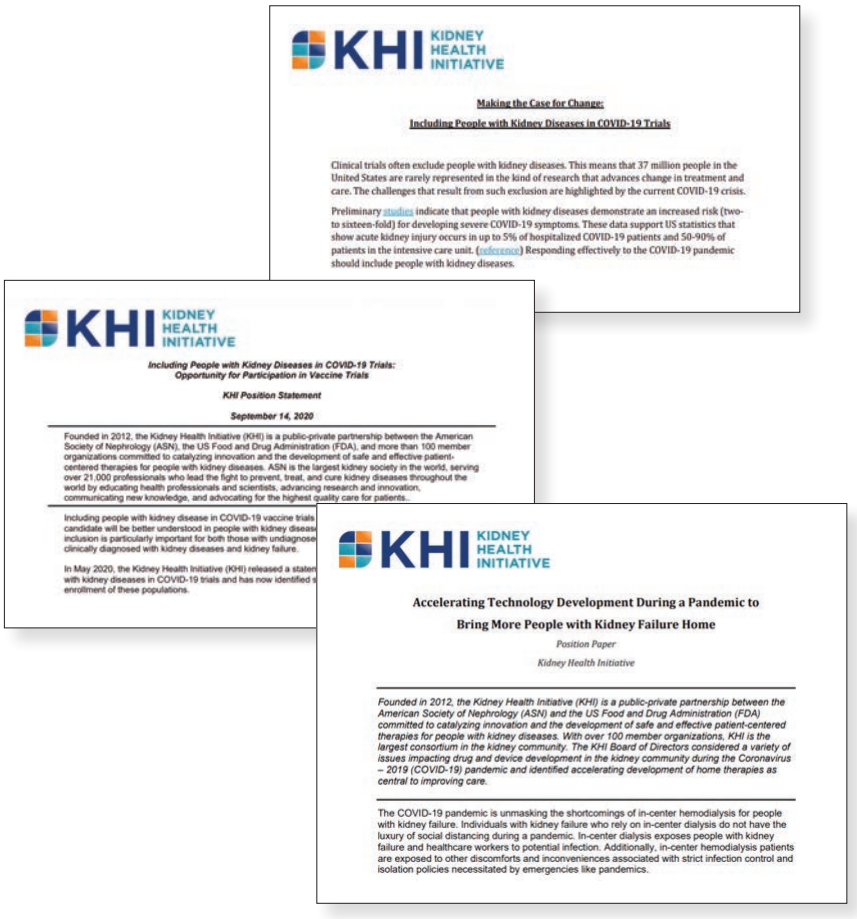
Published *Making the Case for Change: Including People with Kidney Diseases in COVID-19 Trials*

JULY

Hosted Member Town Hall: *Best Practices and Lessons Learned Conducting Clinical Trials During COVID-19: A Fireside Chat with Stakeholders*

Following the emergence of COVID-19, KHI leadership and staff supported the ASN Alliance for Kidney Health's response to the clinical care crisis facing dialysis clinics and hospitals. As the pandemic progressed, KHI began to lead the kidney community by focusing on issues surrounding the conduct of clinical trials and advancement of kidney replacement therapy technology.

Find more information about KHI's response to COVID-19 and resources for members here.



AUGUST

Established KHI COVID-19 Vaccine Trials Task Force

SEPTEMBER

Published *Including People with Kidney Diseases in COVID-19 Trials: Opportunity for Participation in Vaccine Trials*

OCTOBER

Hosted ASN Kidney Week Reimagined Session: *COVID-19 Clinical Trials: The Critical Need to Include People with Kidney Diseases*

Initiated Outreach to Vaccine Developers to Include People with Kidney Diseases in Clinical Trials

DECEMBER

Novavax announced vaccine clinical trial that includes people with kidney diseases

Thank you to all our members. Our member organizations and companies are part of an innovation community at the center of the transformative issues that are catalyzing innovation and the development of safe and effective patient-centered therapies for people living with kidney diseases.

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accp American College of Clinical Pharmacy
ANNA American Nephrology Nurses Association
ASDIN
ASEA
ASN American Society of Nephrology
American Society of Pediatric Nephrology
AST American Society of Transplantation
era edta
nncc 30th Anniversary Nephrology Nursing Certification Commission
RENAL HEALTHCARE ASSOCIATION
RPA Renal Physicians Association
termis.
VASA Access Excellence.

AI AND DIGITAL HEALTH COMPANIES

patientMpower empowering better outcomes
pD pulseData
VASC-ALERT

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HDU
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PKD FOUNDATION Polycystic Kidney Disease
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KIDNEY RESEARCH INSTITUTE A collaboration between Northwest Kidney Centers and UW Medicine
KDIGO Kidney Disease Improving Global Outcomes
Massachusetts General Hospital Kidney Research Center
NAPRTCS North American Pediatric Renal Trials and Collaborative Studies
The George Institute for Global Health
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Thank you to the Board of Directors, Project Workgroup Chairs, and the KHI Patient & Family Partnership Council for making this work possible.

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