

ASN Executive Vice President's Update

The Kidney Health Initiative Has Surpassed Every Expectation

By Tod Ibrahim



This month, the Kidney Health Initiative (KHI) celebrates its first decade, showcases current activities, and articulates a vision for the future. Such an important milestone provides an opportunity to assess KHI's efforts to meet its mission of catalyzing "innovation and the development of

safe and effective patient-centered therapies for people living with kidney diseases" (1).

KHI is the most successful public-private partnership in the history of the kidney community (Figure 1). Having participated in KHI from the initial discussion with nephrology leaders at the U.S. Food and Drug Administration (FDA) on World Kidney Day 2012, I would like to highlight KHI's achievements by describing seven themes that have emerged since its inception.

1. KHI engages living people with kidney diseases meaningfully, equally, and consistently.

Diagnosed as a freshman in college, the late Celeste Castillo Lee lived with kidney diseases for more than 30 years (2). Ms. Lee's life experience sparked a passion for activism, a desire for innovation, and a commitment to collaboration. As one of two patient representatives on the inaugural KHI Board of Directors (with Sam Pederson), she insisted that people with kidney diseases contribute throughout KHI.

With leadership from Ms. Lee and Mr. Pederson, KHI established a Patient and Family Partnership Council (PFPC) in 2015. Serving as Founding PFPC chair, Ms. Lee helped guarantee that KHI workgroups include patients or care partners, that the KHI Board of Directors has three patient representatives, and that the Annual KHI Stakeholders Meeting spotlights real-life experiences of people living with kidney diseases.

Since KHI established PFPC, FDA has held a Patient-Led Drug Development Meeting on kidney diseases, and there have been seven externally led Patient-Focused Drug Development Meetings hosted by patient organizations, such as the Alport Syndrome Foundation, IgA Nephropathy Foundation, National Kidney Foundation (NKF), NephCure Kidney International, and Polycystic Kidney Disease (PKD) Foundation. The success of these interactions helped result in FDA forming the Center for Drug Evaluation and Research (CDER) Patient Engagement Collaborative in 2017 and the Center for Devices and Radiological Health (CDRH) Patient Engagement Advisory Committee in 2018.

PFPC's influence was instrumental at the U.S. Department of Health and Human Services (HHS) when the Kidney Innovation Accelerator (KidneyX) was established in 2018, helping to ensure patient representation on the KidneyX Steering Committee and in the review of all submissions. To date, KidneyX has awarded 25 prizes to people with kidney diseases who developed "ideas and fixes" through "their own everyday experiences and ingenuity" (3). Influenced by PFPC, ASN now includes people with kidney diseases in the planning process and as faculty for Kidney Week, as editors and authors for ASN's peer-reviewed journals, and in initiatives focused on excellence in kidney care. Last year, ASN launched Cele's Champions: Cele Fogarty Travel Support Program for Patients to help people with kidney diseases attend Kidney Week.

2. KHI transforms the lexicon and shifts the focus to kidney health.

From 1972 to 2012, the kidney community focused on dialysis, which the U.S. government made available to every American in 1972, regardless of age, income, or disability. When FDA and ASN discussed KHI as a new public-private partnership 40 years later in March 2012, we knew we needed to build on this commitment to access while prioritizing the protection of kidney health rather than focusing on kidney failure.

Because of this vision, patients are now referred to as people. Chronic kidney disease is now referred to as kidney diseases. End stage renal disease (ESRD) and end stage kidney disease are now referred to as kidney failure (4). In 10 years, the kidney community has moved from acronym-filled, confusing lexicon to language that raises awareness and promotes an understanding of kidney diseases by the public, the media, and policymakers. Ten years later, we now devote ourselves to protecting kidney health—instead of waiting until kidney failure—for people to start to receive treatment.

3. KHI fosters clinical development by standardizing endpoints in kidney diseases to improve trial design.

Developing new therapies is a long, circuitous, and difficult process. Historically, doubling of serum creatinine, dialysis, and death were the standard endpoints for clinical trials in nephrology. In his ASN President's Address in 2012, Ronald J. Falk, MD, FASN, asserted, "It is this reality that has filled our vernacular with words that overflow with negative connotations: 'end-stage,' 'chronic,' 'progressive,' 'inexorable' and the 'three Ds' of doubling of the serum creatinine, dialysis, and death" (5).

Before 2012, many commercial entities (like biotechnology, medical device, and pharmaceutical companies) were hesitant to invest in clinical development for kidney diseases, partly because these endpoints were nonuniform or insufficient for evaluating the efficacy and safety of novel therapies. Not surprisingly, nephrology trailed other specialties in clinical trials in the decades before 2012 (6).

Employing a data-driven approach, KHI workgroups published endpoints for vascular access and lupus nephritis that were defined by consensus across stakeholders. KHI also led efforts to establish surrogate endpoints for primary hyperoxaluria and immunoglobulin A (IgA) nephropathy, prompting the use of the FDA Accelerated Approval Program for these rare diseases, thereby getting therapies to patients sooner. According to FDA, this program allows "for earlier approval of drugs that treat serious conditions, and [to] fill an unmet medical need based on a surrogate endpoint" (7).

In addition to these efforts by KHI, NKF worked with FDA and the European Medicines Agency on changes in albuminuria and estimated glomerular filtration rate slope as surrogate endpoints (8, 9). As a result, the kidney community now has more uniform and appropriate endpoints for clinical trials in kidney diseases.

4. KHI speeds the development of devices and biologics by advancing artificial kidneys and xenotransplantation.

In 2014, then-ASN President Sharon M. Moe, MD, FASN, testified at a U.S. House of Representatives Science, Space, and Technology Committee hearing on the role of prize competitions in promoting innovation. Citing KHI in her testimony, Dr. Moe stated, "If Congress signals to the private sector that you want alternatives to the forms of dialysis currently covered by the [Medicare] ESRD program, then I believe companies, investors, and inventors will produce life-changing and cost-saving technologies" (10).

Explaining that "dialysis was thought of as a bridge to kidney transplantation," Dr. Moe emphasized that "the increase in the number of patients with kidney disease without an increase in the number of available organs has left patients waiting for a transplant for years."

In 2016, the White House convened a summit to address the shortage of organs available for transplantation. There, then-ASN President Raymond C. Harris, MD, FASN (who chaired the KHI Board of Directors from 2019 to 2022); current ASN President Michelle A. Josephson, MD, FASN; and then-ASN Secretary-Treasurer John R. Sedor, MD, FASN, announced three initiatives: the first \$7 million toward a kidney disease prize competition, a partnership with the U.S. Department of Veterans Affairs (VA), and "a commitment to developing a roadmap to achieve the goal of creating a bio-artificial or bioengineered alternative to dialysis" (11).

Working with FDA CDRH—which shared ASN's concern about both the transplant waitlist and lack of innovation in dialysis—KHI published the Technology Roadmap for Innovative Approaches to Renal Replacement Therapy in 2018. Defining the pathway to an artificial kidney, this foundational work was agnostic to the approach (cellular, mechanical, or biohybrid) (12). Led by former ASN President Joseph V. Bonventre, MD, PhD, FASN, the roadmap (updated in 2022 with a Human Centered Design Toolkit for Kidney Failure) stimulated interest from multiple fields and new researchers to solve technical challenges while keeping patient goals front and center.

Since the Technology Roadmap's publication, FDA approved new home hemodialysis machines, funded efforts to evaluate patient-reported outcome measures (PROMS), and developed a patient preference survey about wearable kidney devices. Building on this momentum, the Executive Order on Advancing American Kidney Health in 2019 also committed the federal government to developing "an artificial kidney" and producing "a strategy for encouraging innovation in new therapies" (13). In June 2023, the second phase of the KidneyX Artificial Kidney Prize awarded innovators working in regenerative medicine, cellular engineering, and xenotransplantation (14).

5. KHI promotes investment from commercial entities focused on treating kidney diseases.

By engaging people with kidney diseases; transforming the lexicon to shift the focus to kidney health; increasing the development of drugs to treat kidney diseases by securing surrogate endpoints; and speeding the development of artificial kidneys and xenotransplantation through the development of devices and biologics, KHI has made a case for investing in nephrology and for encouraging politicians and policymakers to value the importance of kidney health.

Advancing this case, KHI participated in several Capital Markets Days for Kidney Health organized by ASN. Starting in 2019 at the London Stock Exchange, capital markets days have brought investors and companies interested in kidney health together with nephrologists, people with kidney diseases, innovators, and government officials from FDA and HHS. Besides changing the narrative and raising awareness about opportunities across nephrology—including prevention, screening, diagnosis, and treatment—capital markets days help emphasize that the kidney community is "open for business."

Rather than summarizing all the recent—and considerable—investment in kidney health, three recent examples illustrate the progress KHI helps facilitate. This year, Novartis agreed to acquire Chinook Therapeutics, "a biopharmaceuti-

tical company with two high-value, late-stage medicines in development” to treat IgA nephropathy and proteinuric glomerular diseases for \$3.2 billion (15). In 2020, Outset Medical’s initial public offering generated more than \$275 million. Since 2016, investors committed more than \$1 billion for companies (such as Evergreen Nephrology, Interwell Health, Monogram Health, Somatus, and Strive Health) to pursue varied strategies for partnering with nephrologists to provide integrated kidney care.

6. KHI convenes the kidney community, federal leaders, and other stakeholders for precompetitive discussions that improve care for people with kidney diseases. Since 2012, KHI has brought together ASN, FDA, and 156 member organizations representing people with kidney diseases (and other patient advocates); health professionals; biotechnology, medical device, and pharmaceutical companies; research organizations; the dialysis industry; and representatives from other government agencies, including the Centers for Disease Control and Prevention (CDC), Centers for Medicare & Medicaid Services (CMS), National Institutes of Health (NIH), and VA (Figure 1).

This remarkable collaboration exists because KHI was founded on a key value: precompetitive inclusivity. From day one, the KHI leadership, staff, and I have fundamentally opposed any effort to play favorites among KHI members, shift to a model that embraces “pay to play,” or indicate that some members of the kidney community are more important than others. KHI’s members, leadership, staff, and I have remained focused on overcoming barriers at a precompetitive level.

KHI is the only precompetitive collaboration focused on kidney diseases that works throughout FDA, including CDRH, CDER, the Center for Biologics Evaluation and Research, and the Center for Food Safety and Applied Nutrition. Prior to KHI, the kidney community interacted within FDA and across federal agencies in a reactive, one-off manner. Because representatives from FDA, CDC, CMS, NIH, and VA participate in KHI, the kidney community can focus on accelerating innovation and helping the 37 million Americans with kidney diseases proactively, strategically, and holistically.

7. KHI produces leaders throughout the kidney community. When ASN leadership and staff met with FDA representatives on World Kidney Day 2012, every participant recognized that the nephrology workforce was struggling. Over time, KHI identified precompetitive barriers to bringing new products to market, advanced the use of PROMS and surrogate endpoints for clinical trials in kidney diseases, and engaged in roadmapping to coordinate a multi-stakeholder community. The therapies and products these gains helped catalyze have also helped renew interest in nephrology as a career and brought new hope to the scientists and health professionals already dedicated to kidney medicine.

Serving on a KHI workgroup or in the leadership requires significant time and effort. Everyone is volunteering their expertise, and the knowledge gap among FDA medical officers, sponsors, nephrologists, and people with kidney diseases has, at times, seemed wide. ASN’s members, leadership, staff, and I applaud the many nephrologists who joined commercial entities to better advise about opportunities in treating kidney diseases or to design appropriate clinical trials. ASN also thanks the many nephrologists who have embraced the regulatory arena to guide KHI projects and educate the greater kidney community on the science, governing framework, or strategies to engage people living with kidney diseases.

More recently, commercial entities have included people with kidney diseases in their efforts. ASN’s members, leadership, staff, and I commend these individuals for their remarkable contributions as well. While Ms. Lee and Mr. Pederson deserve considerable credit for this exciting reality, at least four additional leaders are responsible for KHI’s inclusivity and for setting the overall initiative on a path to exceeding expectations:

▶ Dr. Falk, who first articulated the need for KHI, dedicated

his ASN presidency to making KHI a reality, and served on its inaugural Board of Directors as ASN Council Liaison.

- ▶ Patrick Archdeacon, MD, who is currently Deputy Director, Office of New Drugs, Division of Diabetes, Lipid Disorders, and Obesity, at FDA CDER. Dr. Archdeacon facilitated the meeting in March 2012, helped broker KHI’s establishing Memorandum of Understanding, served as the founding co-chair of its Board of Directors, and positioned KHI for success.
- ▶ Prabir Roy-Chaudhury, MD, PhD, FASN, who served as the founding co-chair of the KHI Board of Directors with Dr. Archdeacon, was then elected to the ASN Council, and served as the ASN Council Liaison to the KHI Board of Directors through 2022. He will become ASN President on January 1, 2025.
- ▶ Melissa R. West, who served as the chief staff executive for KHI for its first 8 years. In 2020, she became ASN Senior Director for Strategic Relations and Patient Engagement and continues to contribute significantly to ASN, KHI, and the broader kidney community. (I sincerely appreciate her considerable help with this editorial.)

Besides highlighting KHI’s achievements, these seven themes summarize how nephrology and the kidney community have changed during the last decade. For example, nephrologists now have powerful, new drugs to treat kidney diseases, FDA recently approved the first de novo prognostic test to predict kidney disease progression, and KidneyX has awarded more than \$18 million (and counting) to innovators.

In his 2012 ASN President’s Address, Dr. Falk announced, “This summer, the US Food and Drug Administration (FDA) commissioner Dr. Margaret Hamburg and I signed a Memorandum of Understanding between the ASN and the FDA that seeks to develop a platform for constructive collaborations between the FDA, academia, patient support groups, and multiple members of industry” (5). Dr. Falk then predicted that KHI would “help write a new and exciting chapter in our fight against kidney disease.”

At the Annual KHI Stakeholders Meeting this month, KHI Board of Directors Chair Uptal D. Patel, MD, will articulate his vision for the next chapter of the initiative. If the second chapter is anything like KHI’s first decade, none of us will recognize nephrology in 2033. ■

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Figure 1. KHI’s first decade by the numbers

