Congenital Kidney Disease Road to Trial Readiness Summit
April 16-17 FDA Campus Silver Spring MD

This inaugural summit serves as the catalyst for a multi-phase initiative dedicated to advancing therapeutic development in congenital kidney disease. As the first in a planned series, this meeting will focus specifically on CAKUT and the mechanisms of kidney dysfunction, integrating patient-informed outcomes, natural history, pathophysiology, data harmonization, and stakeholder requirements.

The primary objectives are to establish a shared understanding of existing evidence, delineate areas of uncertainty, and launch workstreams to enable therapeutic and regulatory science progress.

The Vision:
A future in which foundational clinical care is complemented by safe and effective therapies that target biological drivers of progression, including hyperfiltration, podocyte stress, tubular injury, and fibrosis, to meaningfully alter the life trajectory of children and adults born with CAKUT.

This summit builds upon prior foundational efforts by the community:

- 2022 NIH New Insights into Congenital Kidney Disease Meeting
- 2023 Pathway to SGLT2i for Renoprotection in Pediatric CKD Workshop
- 2025 KHI Advancing Pediatric Kidney Care Through Data Extrapolation Workshop
- 2025 conect4children (c4c) and ERKNet Multi-stakeholder Meeting

Structure: Short anchoring presentations, followed by discussions synthesizing implications for disease progression, trial design, and infrastructure leading to prioritized workstreams.

Core Questions:

- Who are we treating, what outcomes are we trying to change, and how do we measure them?
- What priorities would materially advance therapeutic development and clinical trials in CAKUT?

Moderators:

- Aliza Thompson | U.S. Food and Drug Administration (FDA)
- Bill Smoyer | Nationwide Children’s Hospital
- Jun Oh | University Medical Center Hamburg-Eppendorf (UKE)
- Kirtida Mistry | U.S. Food and Drug Administration (FDA)
- Louise Oni | University College London, University of Liverpool
- Lynne Yao | U.S. Food and Drug Administration (FDA)
- Michelle Rheault | University of Minnesota
- Vincent Ko | KidneyFuture

In-Person Confirmed Participants:
Anna Polczyk-Boroń (Bayer), Anne Rohall (Advocate), Austin Lee (Patient), Brian Becknell (Nationwide Children’s Hospital), David Hains (Riley’s), David Long (UCL), Debbie Gipson (NIH), Franz Schaefer (Heidelberg University), Gordana Atanackovic (Bayer), Howard Trachtman, Jason Greenberg (Yale), Jennifer Charlton (UVA), Jennifer McKenzie (Boehringer Ingelheim), Leighton Borgmann (Patient), Mark Lim (ASN/KHI), Marvin Sinsakul (AstraZeneca), Mary Sweeney (Advocate), Melissa Crimmins (Advocate), Michelle Denburg (Children's Hospital of Philadelphia), Moin Saleem (University of Bristol), Mona Khurana (FDA), Rik Westland (Amsterdam UMC), Shamir Tuchman (FDA), Simone Sanna-Cherchi (Columbia), Tarak Srivastava (Children's Mercy Kansas City), William Stuart Reynolds (NIH), Zubin Modi (University of Michigan), Urologists, Fellows as rapporters.

Opening Remarks and Summit Goals
Vincent Ko | KidneyFuture

Focus:

- Ethos of the meeting and why this convening exists. Goals, ground rules, and expectations.
- Unmet need in CAKUT: progression risk and limited therapeutic options

Session 1: Voice of Patient and Caretakers: Perspectives on Meaningful Outcomes
Panelist: Anne Rohall, Austin Lee, Leighton Borgmann, Mary Sweeney, and Melissa Crimmins
Moderated by Vincent Ko

Focus:

- Lived impact, significant unmet need and what constitutes clinically meaningful benefit.
- Patient and caregiver perspectives on uncertainty, surveillance, and intervention.

Potential Questions:

- What does delaying kidney failure by 10-15 years mean for life trajectory (13 vs 30 y.o.)?
- Which outcomes matter most over time (education, independence, family planning)?
- How do patients and families view clinical trials, including placebo arms, crossover designs, risk-tolerance, participation burden, etc.?

Output: Patient-informed articulation of meaningful outcomes and unmet needs across the CAKUT life course, to inform interpretation of disease progression and trial considerations.

Session 2: Defining the Target and the Outcome
Jennifer McKenzie MD, FAAP, FASN | Senior Clinical Program Leader (Boehringer Ingelheim)

Focus:

- Two Foundational Questions: Clarifying What Is Required to Advance CAKUT Therapeutic Development and Trials: Who and What?
- 1. Who are we trying to treat?
- 2. What outcome are we trying to prevent or delay within a measurable time horizon?
- Translating population definition and outcome selection into development-ready clarity

Session 3: A Foundational Model - Solitary Functioning Kidney (SFK) and Renal Hypoplasia
Moderated by Jun Oh and Louise Oni

Notes: SFK is not the highest-risk CAKUT subgroup, but may provide the clearest and most scalable model to define early injury biology, risk enrichment, and future trial-relevant endpoints

Part A: Defining the High-Risk SFK Phenotype: Longitudinal Evidence and Risk Stratification
Rik Westland, MD, PhD | Amsterdam UMC

Focus:

- Longitudinal outcomes in pediatric congenital SFK across international cohorts
- Differentiating stable versus progressive phenotypes to define the high-risk population
- Risk stratification and implications for early-intervention trial design

Part B: Biological Drivers of Injury – Mechanisms, Evidence, and Knowledge Gaps
David Hains, MD, MBA | Riley Children's Health / Indiana University

Focus**:**

- Integrated pathophysiology linking reduced nephron mass to kidney injury in hypodysplasia.
- Adaptive vs maladaptive responses in hyperfiltration, glomerular, & tubular pathways
- Where biological evidence is strong, emerging, or uncertain across the disease cascade

Part C: Interactive Evidence Review – Assessing Biological Framework and Disease Trajectory

Structure:

1. Community Confidence mapping: Use of a group green–yellow–red framework to illustrate relative strength of biological evidence across the SFK disease cascade.
2. Gap identification: Highlighting areas where evidence is emerging or uncertain, and where additional study may be informative.

Discussants: Brian Becknell, Tarak Srivastava + David Long + Speakers + Audience

Session Output: SFK Risk Enrichment Framework and Evidence-Graded Mechanism Map

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Session 4: Candidate Endpoints and Enrichment Signals from Natural History
Moderated by Vincent Ko and Aliza Thompson

Part A: The European Evidence Base – Endpoints, Biomarkers, and Longitudinal Insight
Franz Schaefer, MD | Heidelberg University Hospital (4C, ERKNet & esCapeKD)

Focus:

- Candidate reasonably likely surrogate endpoints and biomarkers emerging from EU cohorts
- Role of uPCR, uACR, GFR slope, BP, and kidney function trajectories in progression
- Markers including tubule as enrichment and stratification tools
- Longitudinal pediatric-to-adult data addressing survival and late outcomes

Part B: Natural History to Risk Stratification: Insights from CKiD and U.S. Cohorts
Michelle Denburg, MD, MSCE | CHOP and Jason Greenberg MD, MHS | Yale

Focus:

- US cohort confirmation: What CKiD, PEDSnet and related US data reinforce
- Risk stratification signals: How longitudinal measures and paired tubular injury markers may better distinguish stable from progressive trajectories.
- How this may support trial stratification, enrichment, and future endpoint development

Part C: Moderated Synthesis - What Moves Forward

Focus / Discussion Prompts

- Global convergence: Which progression signals appear consistent across cohorts?
- Context of Use: For key measures, what is their role (endpoint, enrichment, exploratory)
- Long-term outcomes: How do pediatric progression relate to adulthood ESKD?
- Readiness gaps: What prevents these data from being used more directly in trials or regulatory decision-making?
- Path forward: Which data & standards, if addressed, would most accelerate progress?

Output: Toolkit framework of globally consistent progression signals in CAKUT and their appropriate context of use for trial enrichment, stratification, and endpoint development.

Additional Output: Assessment of global CAKUT natural history data and consideration of common data elements (CDEs) needed to enable future regulatory-grade analyses.

Session 5: When to Unify and When to Stratify?
Moderated by Michelle Rheault & Kirtida Mistry

Part A: Reduced Nephron Endowment as a Shared Substrate in CAKUT
Jennifer Charlton, MD, MSc | University of Virginia School of Medicine

Focus:

- Reduced nephron endowment as a common biological starting point across CAKUT
- Evidence linking low nephron number to hyperfiltration-driven injury
- Limits of nephron measurement and available clinical proxies

Part B: Shared Progression Pathways in CAKUT: Genetic and Secondary FSGS Mechanisms
Simone Sanna-Cherchi, MD | Columbia University

- Genetic and molecular modifiers influencing progression rate within CAKUT
- Histologic and biological convergence evidence toward shared glomerular injury pathways under hyperfiltration stress
- Use of genetics and histology in stratification and enrichment

Part C: Interactive Synthesis – Unify or Stratify?

Structure: Presentation and evaluation of three parallel classification models to inform a proposed working framework.

Framework 1: Anatomical - Phenotype (Primary Grouping)

A. Kidney Formation / Nephron Endowment Disorders: Small kidneys, hypodysplasia, SFK, cystic dysplasia, etc.
B. Congenital Obstructive Uropathies: UPJO, megaureter, collecting system blockages.
C. PUV & Bladder-Mediated Disorders: PUV, spina bifida, prune belly.

- Modifier (Stratify): Vesicoureteral reflux (VUR), UTI, etc.

Framework 2: Mechanistic - Injury Pathway (The Unifier)

A) Hemodynamic load B) Shear stress C) Podocyte stress D) Inflammation E) Fibrosis.

Framework 3: Risk Stratification - Enrichment for Trials
A) Severity of Nephron Deficit B) Rate of Progression C) Compounding Exposures D) Risk Score

Question: Can you put a PAX2/HNF1B gene and reflux nephropathy child be in the same trial?

Output: Draft conceptual framework clarifying when CAKUT populations may be unified by shared biology versus stratified by modifiers.

Session 6: The Infrastructure Solution – Building a Regulatory-Grade Ecosystem
Moderated by Louise Oni & Jun Oh

Part A: Designing the Infrastructure for CAKUT: Lessons from Other Initiatives
Zubin Modi, MD, MS | University of Michigan

Focus:

- What successful kidney disease communities built to enable therapeutic progress
- The core elements needed to define populations, outcomes, and enrichment
- The infrastructure and coordination needed to make CAKUT studies feasible

Part B: Laying the Tracks from Progress — The CAKUT Infrastructure Landscape
Vincent Ko | Executive Director, KidneyFuture

Focus:

- Translate cross-stakeholder structural constraints into the alignment requirements
- Present a consolidated view of existing CAKUT cohorts, registries, networks, and data assets.
- Surface structural disconnects that limit their collective utility for regulatory-grade execution.
- Define the connective tissue required to align these assets into a trial enabling ecosystem.

Regulatory Perspective: Initial Impressions
Aliza Thompson | FDA

Priority Areas Open Floor Discussion

Day 1 End

Evening Dinner

- Voting on priorities, casual reflection prompts TBD
- Select group will synthesize and set up topics for the next day.

Day 2

Session 7: Synthesis - Where We Landed, Where We're Exposed

Presenters: Vincent Ko and David Hains

Focus:

- Concisely synthesize key areas of scientific and clinical alignment from Day 1
- Surface unresolved tensions that limit near-term therapeutic advancement
- Frame the development-facing exposures most relevant to key stakeholders

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Session 8: Decision - Structured Evaluation of Proposed Priority Barriers

Moderated by Bill Smoyer and Lynne Yao

Note: Based on previous days work and community vote/synthesis priority areas will be shared:

- Proposed Priority Area 1 TBD
- Proposed Priority Area 2 TBD
- Proposed Priority Area 3 TBD

Question: If addressed within 12 months, would this materially accelerate CAKUT therapeutic development or enable trial initiation? If Yes - then move to progress below.

Session 9: Architecture - Framing Priority Workstreams

Moderated by Bill Smoyer and Lynne Yao

Format: Digital Whiteboard

Process Applied to Each:

- Core Development Question: The key uncertainty blocking trial readiness.
- Regulatory Product: The evidence artifact required to reduce uncertainty.
- Minimum Evidence Package: The analytic inputs required to support it.
- 6-Month Deliverable: A defined milestone achievable within six months.

Hypothetical roadblocks/workstreams TBD for example:

1. Risk Definition & Enrichment
2. Endpoint & Context of Use Clarity
3. Regulatory-Grade Data Readiness
4. Trial Design & Control Strategy
5. Infrastructure & Harmonization

Adjorn

Future: Whitepaper, Workstreams, and/or Publication outlining state of CAKUT Community & next steps