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Supplemental Table 1: List of participants who provided sustained input on the Roadmap

This roadmap is dedicated to all patients that have lost their lives to end stage renal disease (ESRD) or are living with ESRD and chronic kidney disease (CKD) and fighting for better treatment options.

Contributor	Affiliation	Role
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Annie Best	Nexight Group	Roadmap Development
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Iain Drummond, PhD	Massachusetts General Hospital	Cellular Working Group
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William Fissell, MD	Vanderbilt University	Mechanical Working Group
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Benjamin Freedman, PhD	University of Washington	Cellular Working Group
Gema Gonzalez, PhD	FDA	Steering Committee
Deborah Hoshizaki, PhD	NIH	Cellular Working Group
Frank Hurst, MD	FDA	Steering Committee, Mechanical Working Group (Chair)
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Bill Murray (in memoriam)	Patient	Vascular Working Group, Patient Advisory Committee

Contributor	Affiliation	Role
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Lindsay Pack	Nexight Group	Roadmap Development
Julianne Puckett	Nexight Group	Roadmap Development
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Murray Sheldon, MD	FDA	Steering Committee
Douglas Silverstein, MD	FDA	Steering Committee
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Roberta (Bobbi) L. Wager, MSN, RN	Patient	Patient Advisory Committee
Jason Wertheim, MD, PhD	Northwestern University	Cellular Working Group
Melissa West	KHI	Roadmap Development
David White	Patient	Patient Advisory Committee (Chair)
Fokko Wieringa, PhD	Dutch Kidney Foundation/ imec-Netherlands	Mechanical Working Group
Caroline Wilkie	Patient	Patient Advisory Committee
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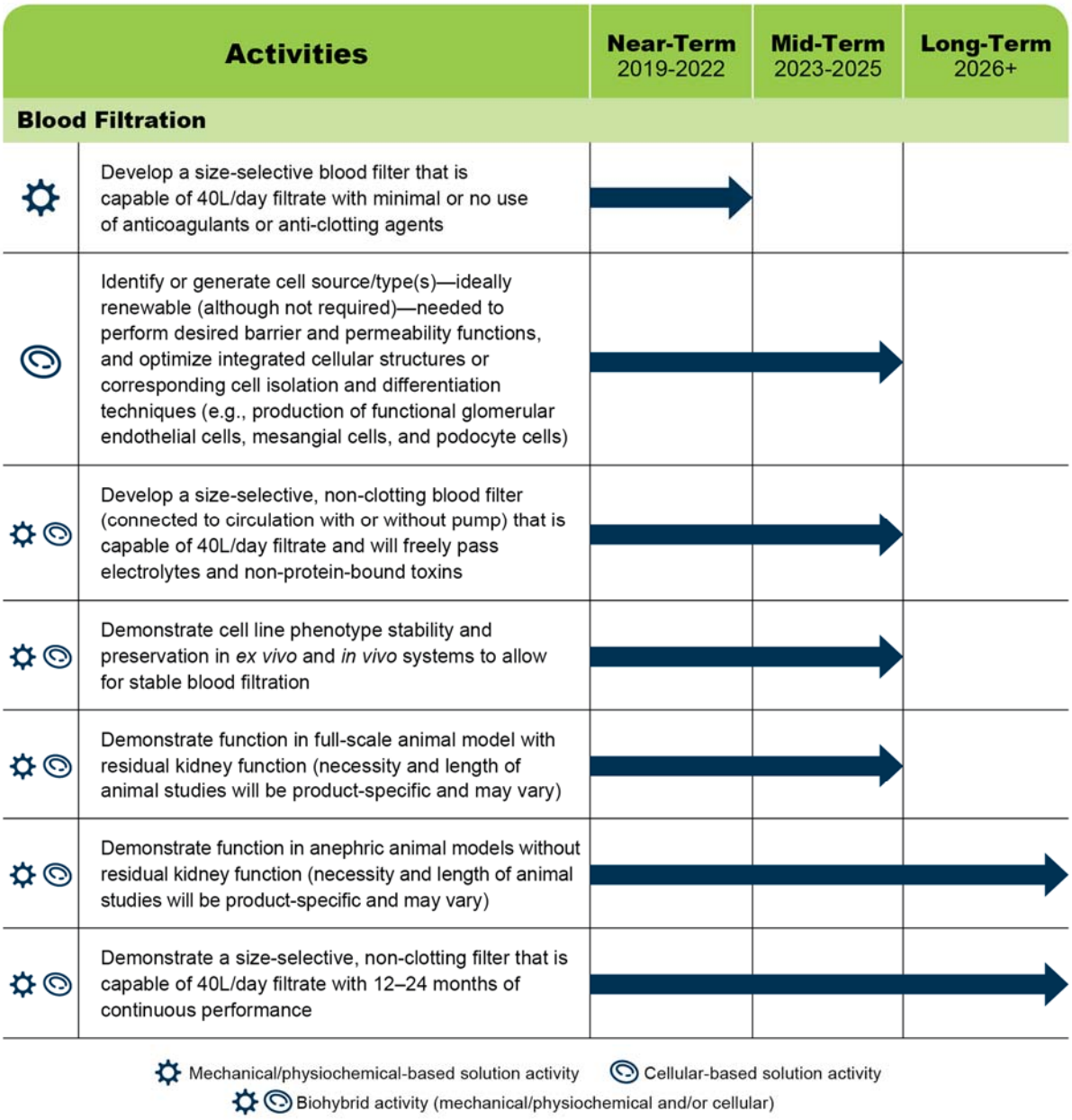
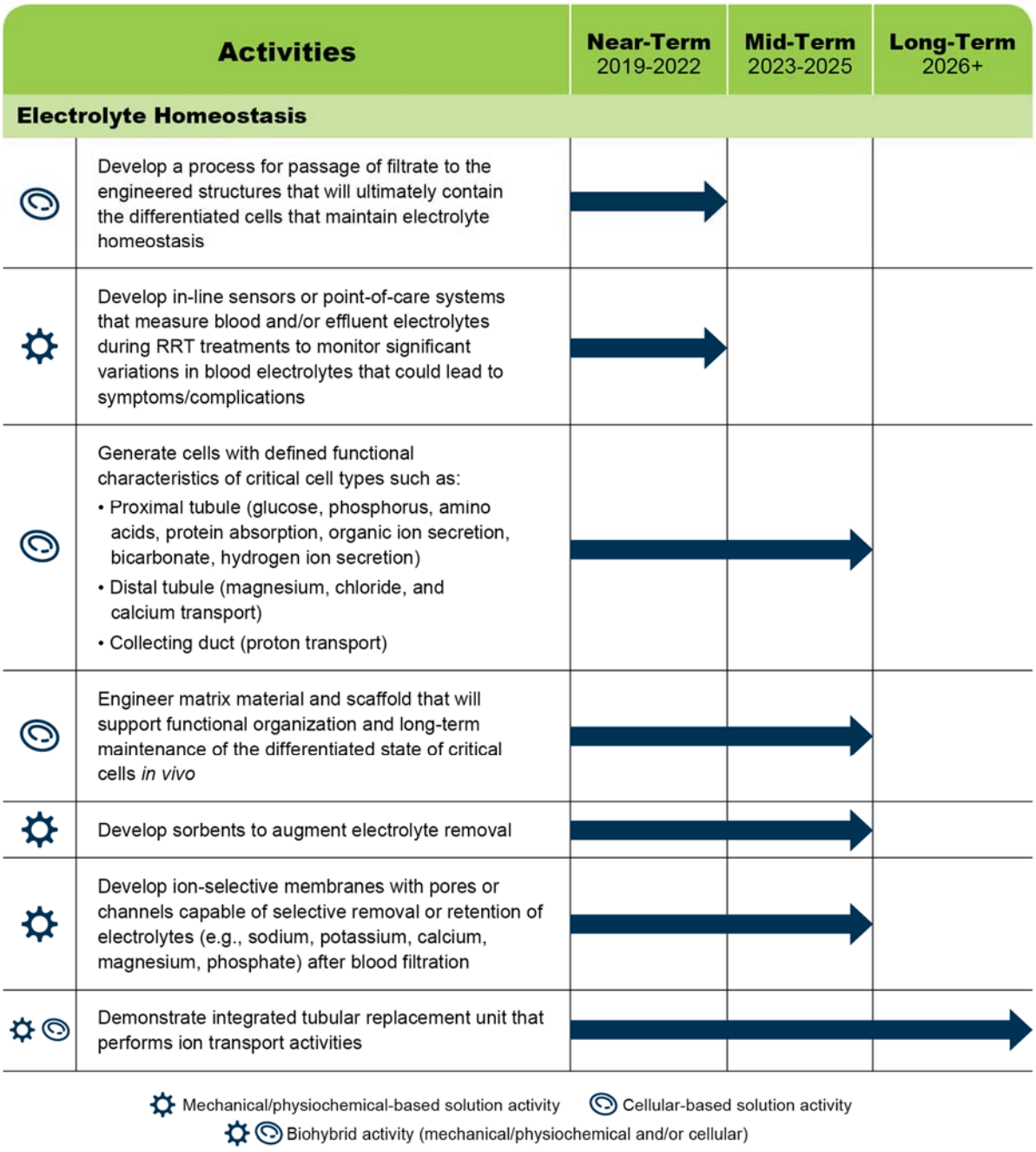
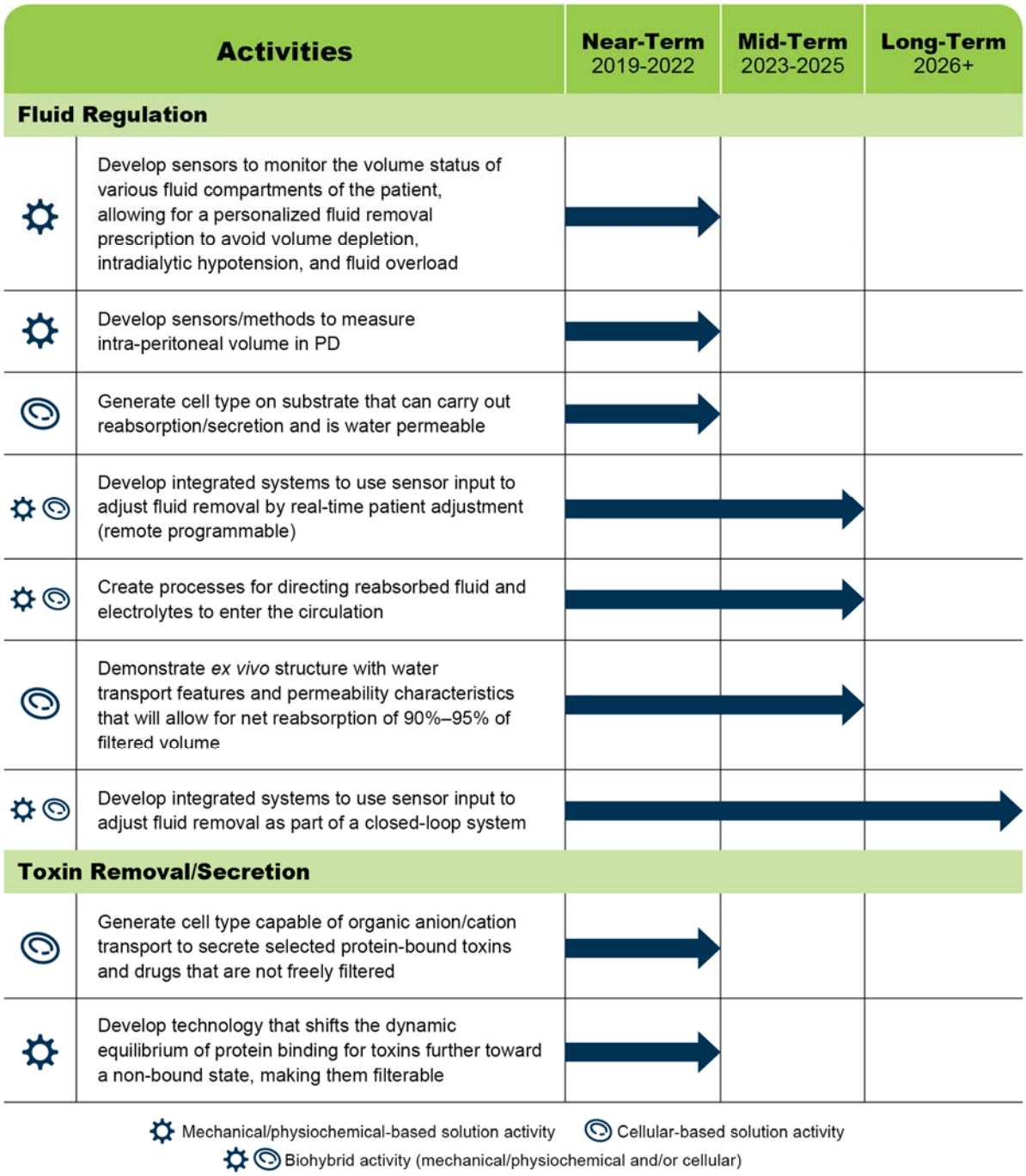
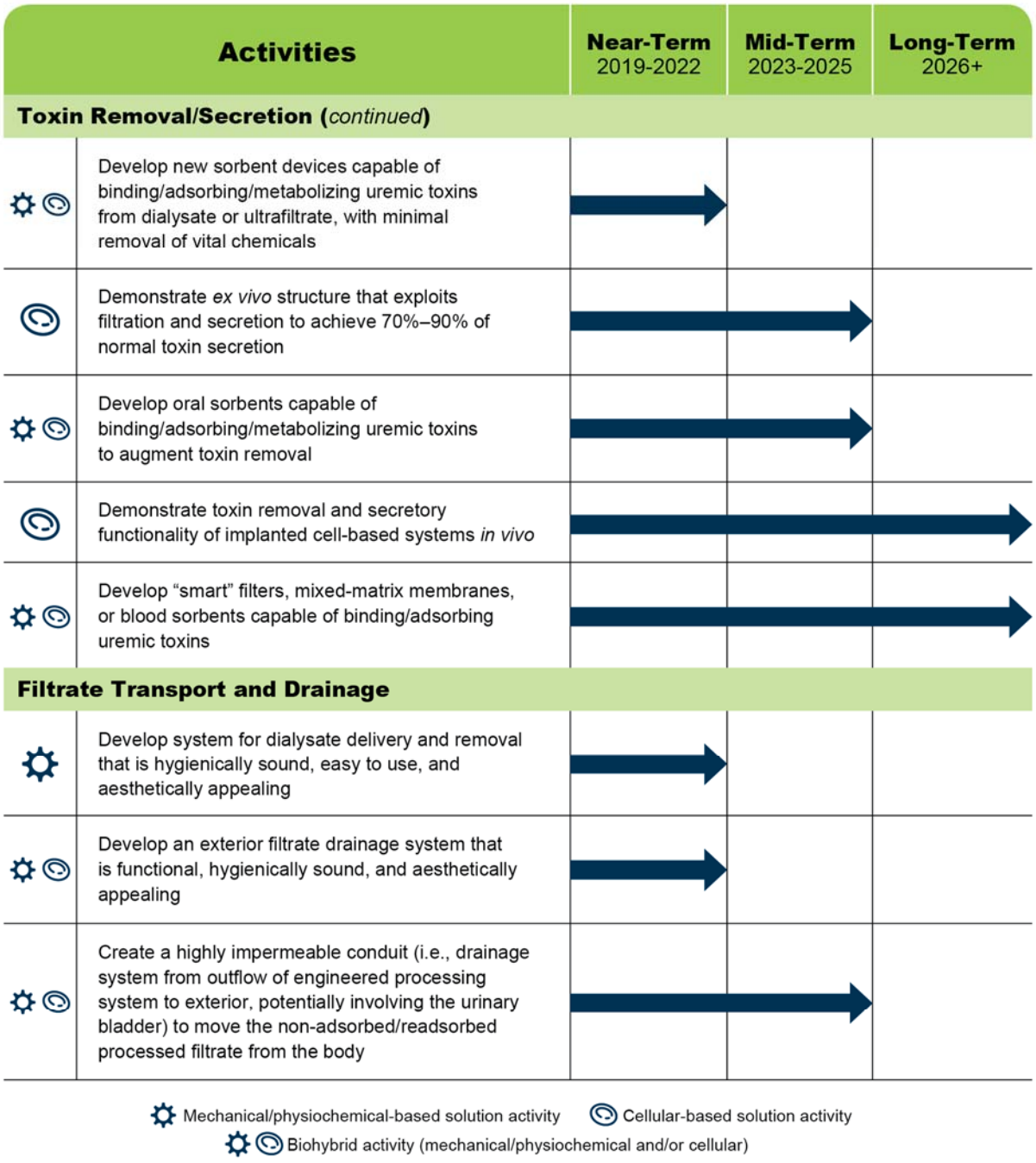
Alex Yevzlin, MD, FASN	University of Wisconsin	Vascular Working Group
Carolyn Yong, PhD	FDA	Steering Committee

Supplemental Figure 1. Kidney function replacement activities

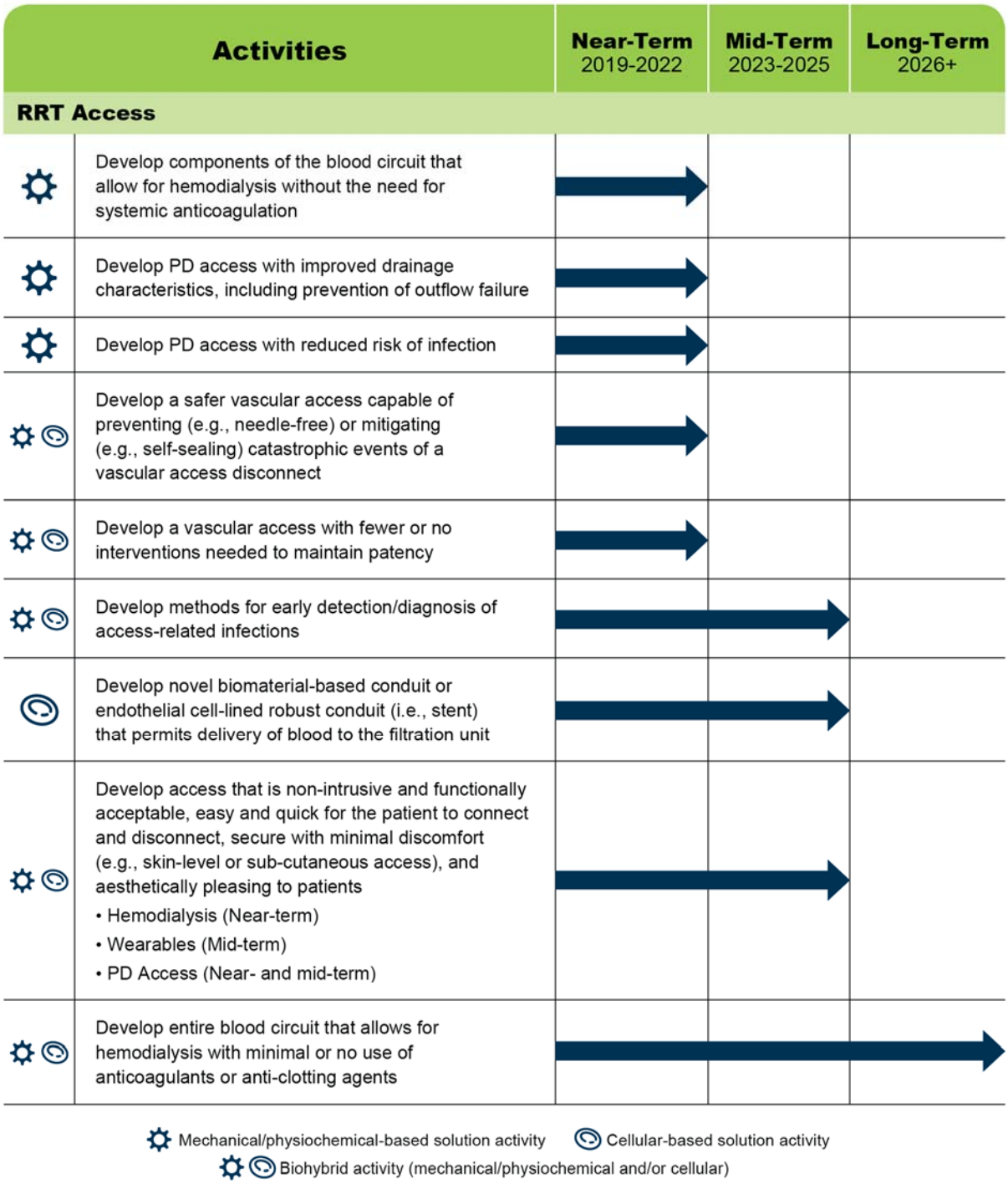


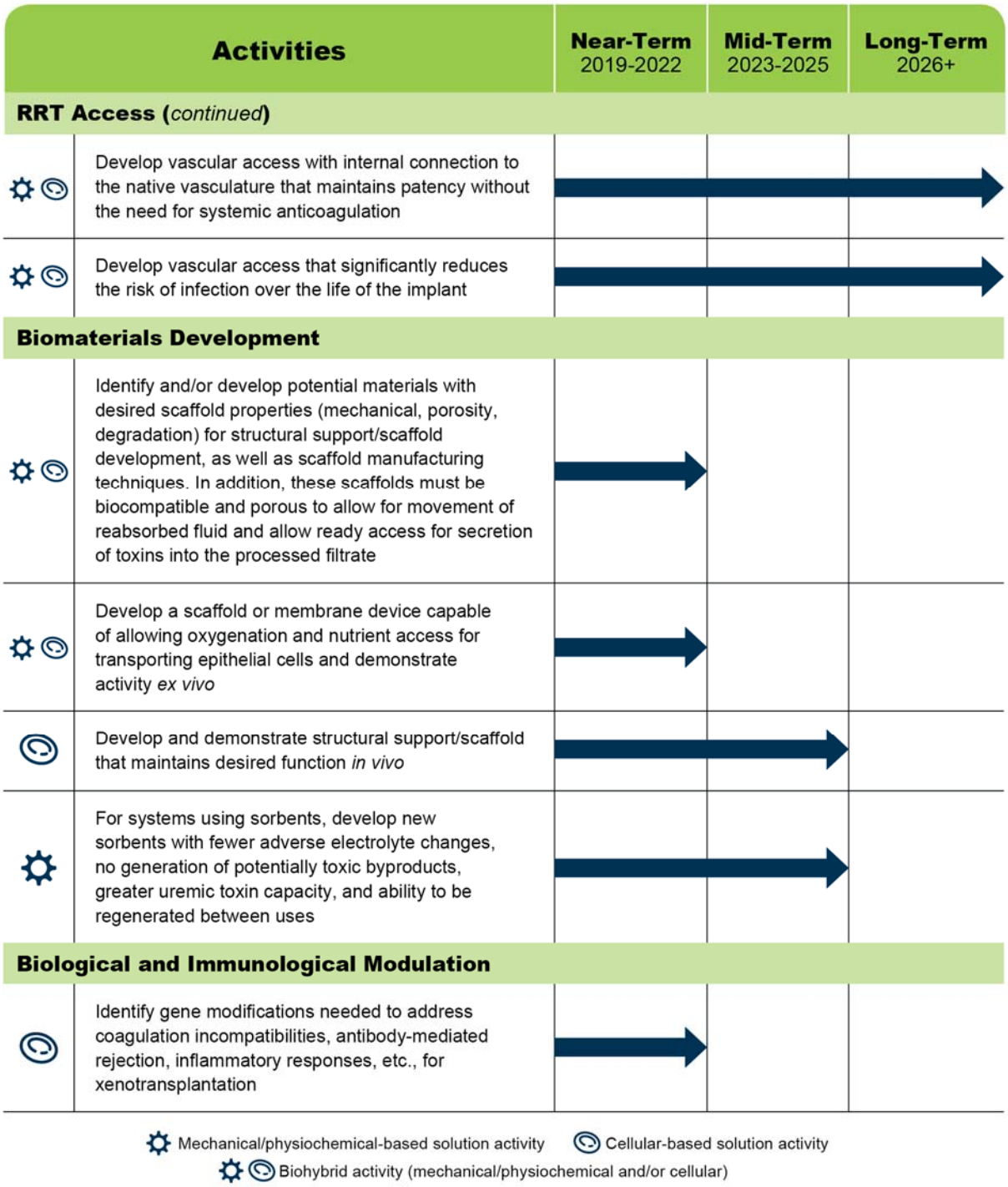


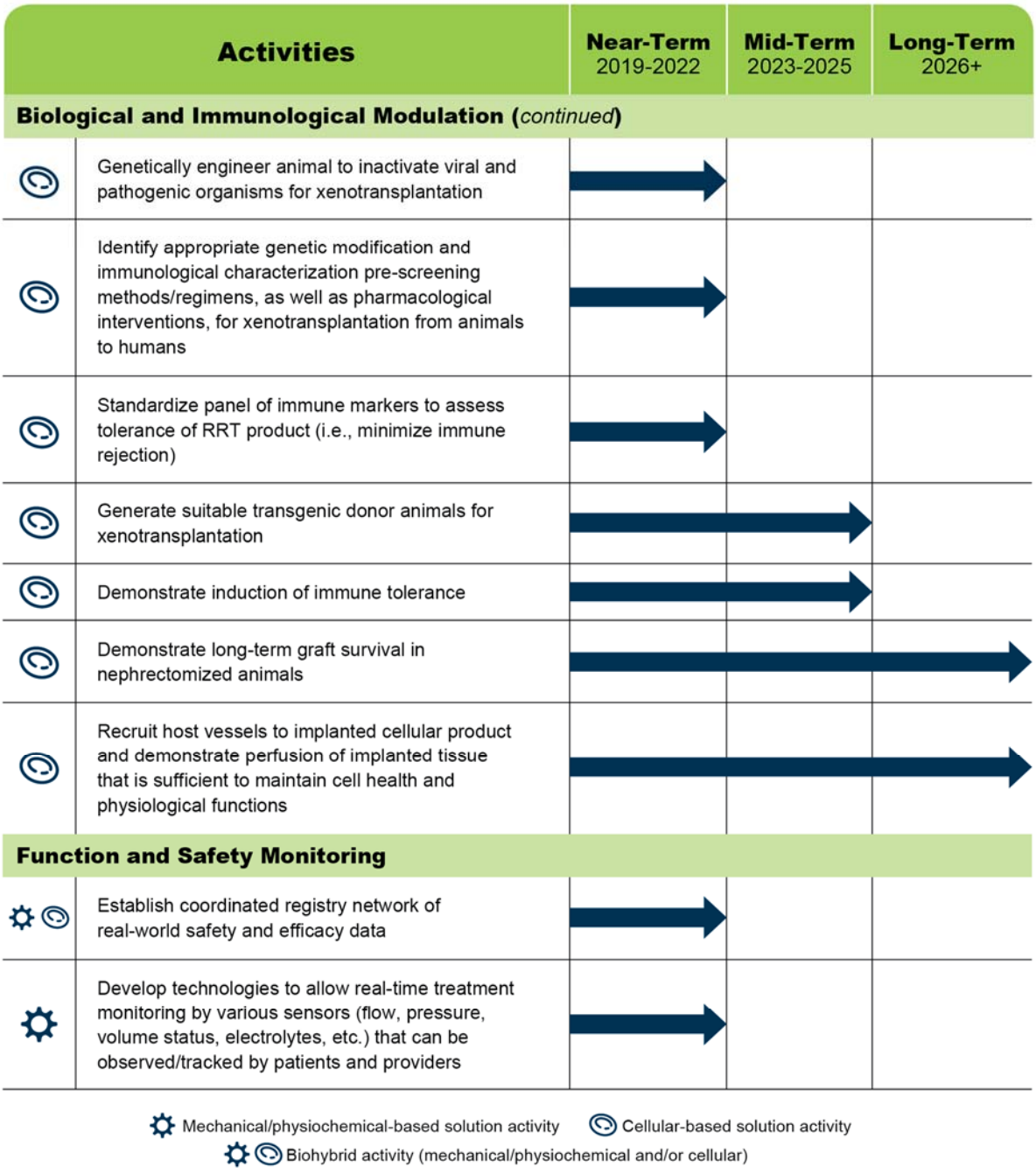


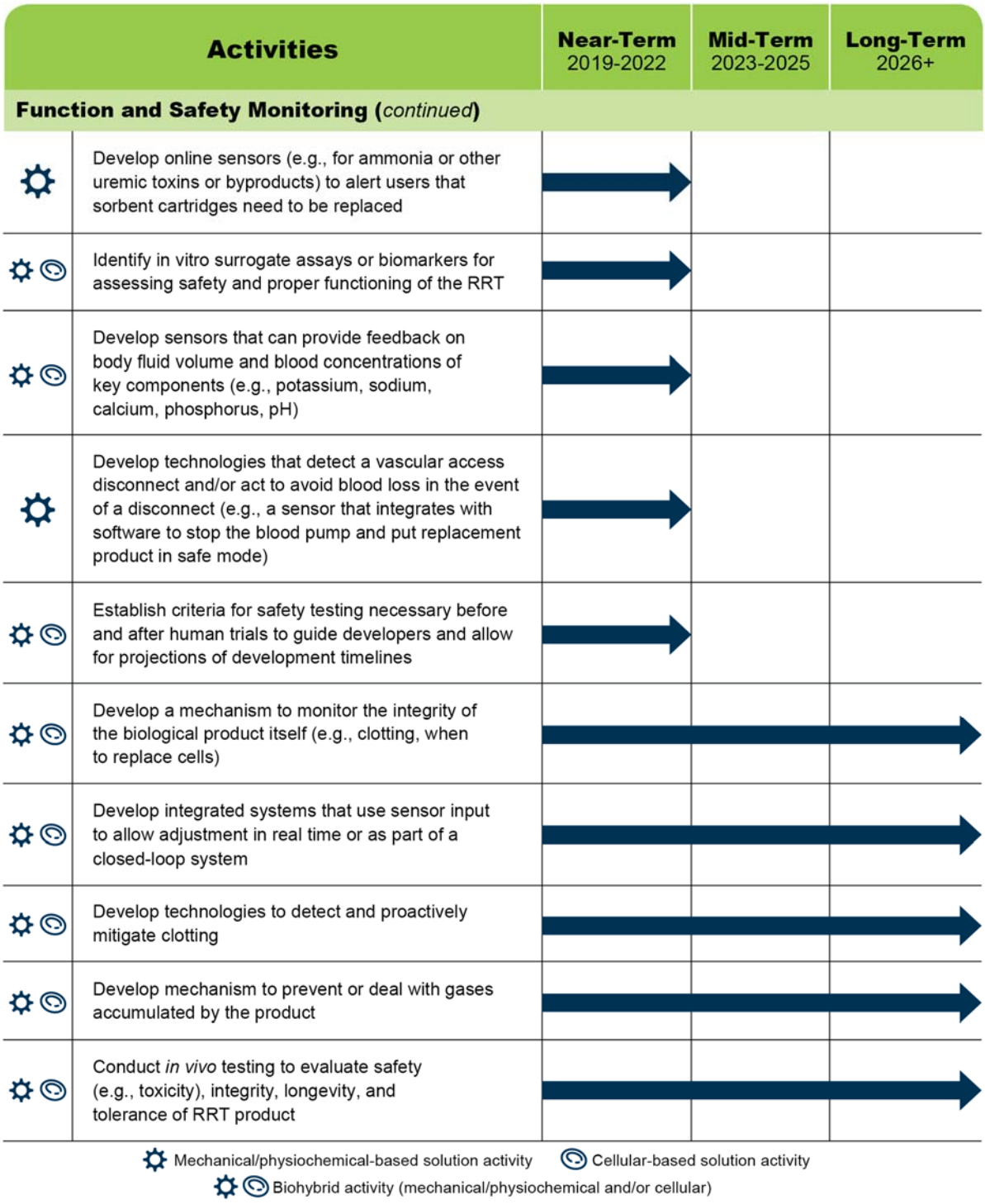


Supplemental Figure 2. System enabler activities









KIDNEY HEALTH INITIATIVE

RRT ROADMAP

TECHNOLOGY ROADMAP

for Innovative Approaches to Renal Replacement Therapy

October 2018

Prepared by
NEXIGHT GROUP

KHI
KIDNEY HEALTH INITIATIVE

Contents

About this Document

Recognizing that more rapid, innovative advancements in the treatment of kidney disease must be made, the Kidney Health Initiative (KHI) was created in September 2012. KHI is a public-private partnership between the American Society for Nephrology (ASN) and the U.S. Food and Drug Administration (FDA) focused on promoting development of safe and effective therapies for kidney disease.

In June 2016, the White House Organ Summit called for an increase in breakthrough research and development to improve outcomes for patients needing transplants. In response, KHI leadership established an initiative on Developing a Roadmap for Innovative Approaches to Renal Replacement Therapy (RRT) to foster a new, multidisciplinary approach to advancing solutions that can improve the lives of millions of kidney patients with end stage renal disease (ESRD).

To help make such a major paradigm shift, this resulting roadmap aims to stimulate the innovation needed to move toward this goal. It outlines the desired future state of improved patient quality of life that innovative RRT solutions aim to achieve, as well as the technical and market challenges that must be overcome, the overarching solution strategy for doing so, and the high-priority research activities with the greatest potential to focus the efforts of the industry and drive the field forward.

WHO SHOULD READ THIS ROADMAP?

While this roadmap was developed by key stakeholders from the kidney community, a broader group of collaborative partners are needed to spur innovative thinking and develop the disruptive solutions required to affect real change and improve patient quality of life.

As the project convener and facilitator, KHI seeks active participation from a diverse group of contributors both within and outside of the medical community, including:

- Patients, care partners, and patient advocacy groups
- Technology developers
- Engineers
- Clinicians, nurses, and allied health professionals
- Regulators
- Researchers
- Payers
- Government agencies (domestic and foreign)
- Entrepreneurs

Call to Action

There are several ways to participate in the implementation of the Technology Roadmap for Innovative Approaches to Renal Replacement Therapy:

- Provide feedback on the roadmap
- Pursue a research and development (R&D) project
- Form collaborative partnerships with those pursuing R&D projects

Please contact the **Kidney Health Initiative** for more information: khi@asn-online.org

The goals of the KHI RRT technology roadmap are to:

- Spur innovation in the RRT field
- Create opportunities to attract industry and academic investment in developing RRT solutions
- Encourage an internationally oriented multidisciplinary approach to solution development
- Accelerate the availability and adoption of commercially viable solutions
- Ensure that patient and care partner preferences are incorporated throughout the RRT solution development life cycle
- Optimize models of reimbursement

To ensure the roadmap's efficacy, KHI incorporated input from a diverse and representative group of stakeholders, including patients, researchers, clinicians, care partners, product developers, entrepreneurs, regulatory agencies, and payers. Additionally, four smaller groups of leaders and experts—including a patient advisory committee and three working groups composed of members of the medical and research communities—provided an integral contribution to the development of the goals, strategies, and activities contained in this roadmap. The members of these groups are listed in Appendix A. The draft version of the roadmap was also available for public comment in August-September 2018. KHI partnered with Nexight Group, a technology and management consulting firm specializing in roadmapping, to assist in building this roadmap.

The inputs from the collaborative work of these key stakeholders created the foundation for this initial roadmap, which will be a living document, updated regularly to ensure its goals and direction remain relevant for the RRT community.

Executive Summary

Chronic kidney disease (CKD) affects about 10 percent of the population worldwide, including an estimated 1 in 7 adult Americans.[1] In the United States, Medicare spending totals more than $64 billion each year to care for Americans with CKD and an additional $34 billion to care for patients with end stage renal disease (ESRD).[2] This high cost of care and limited technology innovation in the renal replacement therapy (RRT) landscape since the introduction of dialysis more than 60 years ago has left all Americans—especially ESRD patients—paying a heavy price.

For the more than 700,000 Americans with ESRD, transplantation remains the best treatment option, yet suitable organs are in short supply;[3] in fact, 12 patients die each day waiting for a kidney transplant.[4] Therefore, the majority of ESRD patients have little choice but to opt for lifestyle-limiting dialysis treatments, the side effects of which often leave them feeling sick and longing for a better existence. While dialysis was initially designed as a temporary treatment rather than a long-term solution, it remains the only viable option for many patients.

The impact of kidney disease extends well beyond the United States; over 2 million people worldwide have ESRD. In higher-income countries, treatment costs are enormous: a 2010 report from the UK National Health Service estimates its annual CKD spending at £1.45 billion—more than half of which was for RRT[5]—while Australia has estimated it will spend over $12 billion on ESRD patients through 2020.[6] At the same time, RRT remains entirely unaffordable to the majority of ESRD patients in low- and middle-income countries throughout the world, with over 1 million people dying annually from lack of treatment.[7]

[1] Nathan Hill et al, "Global Prevalence of Chronic Kidney Disease – A Systematic Review and Meta-Analysis," *PLoS ONE 11*, no. 7, e0158765 (July 2016), doi:10.1371/journal.pone.0158765; United States Renal Data System, *2017 USRDS Annual Data Report*, https://www.usrds.org/2017/download/2017_Volume_1_CKD_in_the_US.pdf.
[2] United States Renal Data System, *2017 USRDS Annual Data Report,* https://www.usrds.org/2017/download/2017_Volume_1_CKD_in_the_US.pdf.
[3] United States Renal Data System, *2017 USRDS Annual Data Report*, https://www.usrds.org/2017/download/2017_Volume_1_CKD_in_the_US.pdf.
[4] Health Resources & Services Administration, Organ Procurement and Transplantation Network National Data Reports, https://optn.transplant.hrsa.gov/data/view-data-reports/national-data.
[5] Vivekanand Jha et al, "Chronic kidney disease: global dimensions and perspectives," Global Kidney Disease series, *The Lancet* 382, no. 9888 (July 2013): 260–272, https://doi.org/10.1016/S0140-6736(13)60687-X.
[6] Kidney Health Australia, "The Economic Impact of Kidney Disease in Australia: Projections to 2020," https://kidney.org.au/cms_uploads/docs/kha-economic-impact-of-eskd-in-australia-projections-2020.pdf.
[7] WG Couser et al, "The contribution of chronic kidney disease to the global burden of major noncommunicable diseases," *Kidney Int*. 80, no. 12 (Dec 2011): 1258-1270.

In response to this current landscape, the Kidney Health Initiative (KHI) committed to **changing the RRT paradigm** by developing a technology roadmap to encourage innovative advances in RRT that will impact ESRD patients not only in the United States but also around the world. Key stakeholders from throughout the RRT community—including patients, researchers, clinicians, care partners, regulatory agencies, product developers, payers, and entrepreneurs—collaborated to develop the **solution strategy and research pathways needed to more effectively and efficiently develop commercially viable RRT alternatives**. An overview of this strategy is presented in Figure 1.

This strategy emphasizes the parallel, rather than sequential, development of solutions with varying complexity and time horizons: enhanced dialysis, portable/wearable solutions, biohybrids/implantables, and regenerated kidneys. This approach will help the community overcome current technical and market challenges to more rapidly deliver meaningful advancements for ESRD patients.

The key strengths of the roadmap approach include:

- **A patient-centered focus,** with a clearly delineated, patient-developed vision of improved patient quality of life that must drive the development of all future RRT solutions
- **Increased opportunities for multidisciplinary collaboration** to attract new innovators, inspire fresh thinking, and leverage technology developments from other industries or fields outside of the kidney domain that could spur disruptive advances
- **Multiple solution pathways with various time horizons,** focused on the prioritized individual kidney functions that must be restored or replaced, to afford greater opportunity for both near-term incremental improvements that patients require as well as longer-term integrated solutions and more disruptive breakthroughs
- **Common design requirements** to ensure that all solutions, regardless of complexity, meet the same minimum technical expectations needed to propel the industry forward

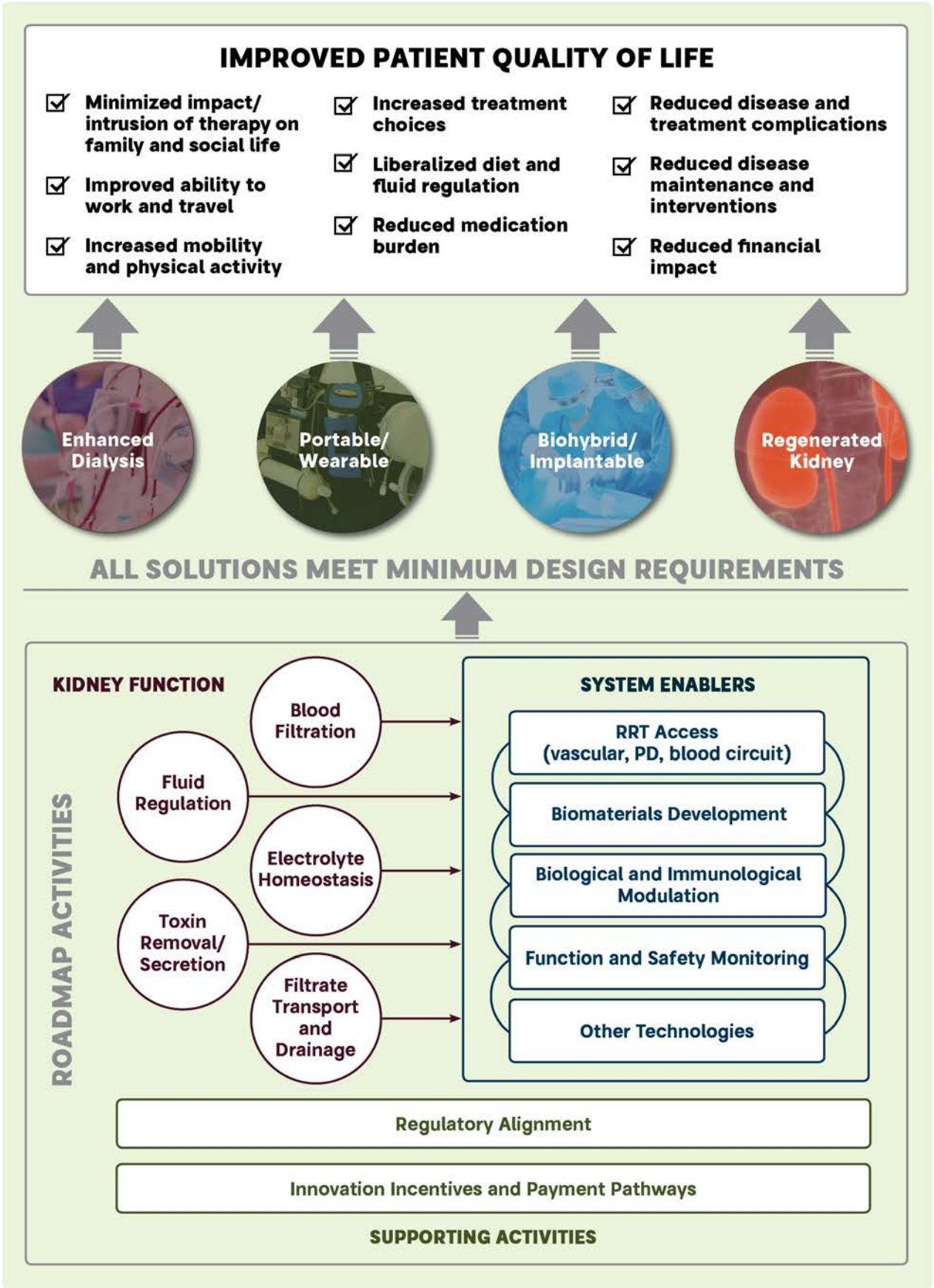
This community-consensus approach will enable the research focus areas and priorities outlined in the roadmap to more effectively:

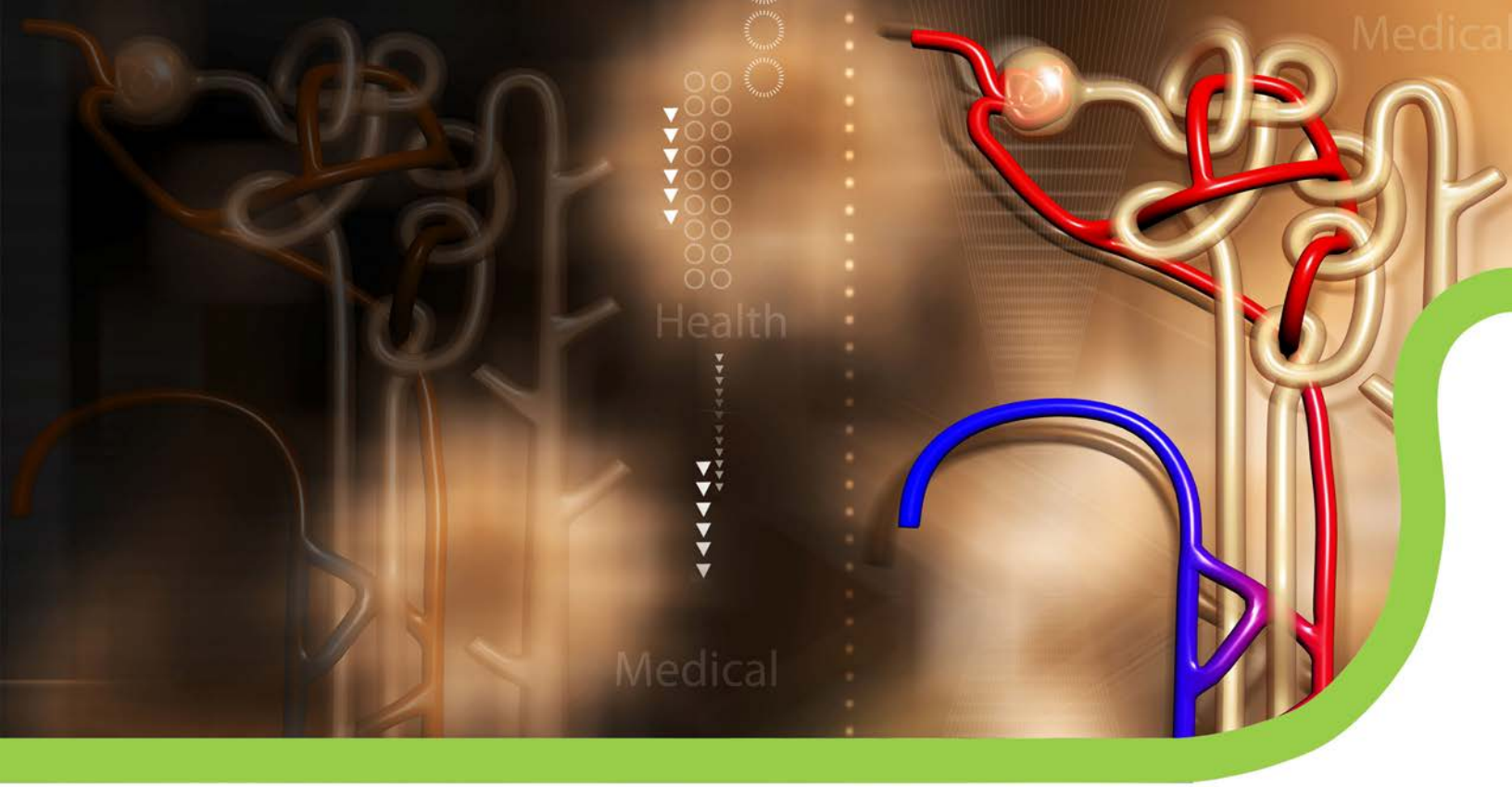
- Foster the creativity and multidisciplinary innovation needed to spur advances in RRT
- Help funding agencies and proposal reviewers assess the relevance and potential impacts of RRT project proposals
- Encourage new interest and investment in the RRT field
- Offer increased treatment options and an improved quality of life to ESRD patients

Achieving a new paradigm for RRT will be challenging but is long overdue. By collectively focusing on the common goals and research pathways outlined in this roadmap, the RRT community can realize real, innovative advances that can **transform the lives of individuals with CKD and ESRD.**

Supplemental material is neither peer-reviewed nor thoroughly edited by CJASN. The authors alone are responsible for the accuracy and presentation of the material.

Figure 1. KHI Renal Replacement Therapy Roadmap Strategy





The Need to Invest in Renal Replacement Therapy

Current State: The Growing Impact of Kidney Disease

An estimated 10 percent of the world's population, including about 15 percent of adult Americans, are living with chronic kidney disease (CKD).[8] Of those in the United States, roughly half a million receive some form of dialysis because their kidney function has deteriorated to the point of end stage renal disease (ESRD). The number of people impacted continues to grow, with more than 100,000 additional Americans beginning some form of dialysis treatment each year,[9] and the number of new patients diagnosed with ESRD worldwide increasing at a rate of 5 percent to 7 percent annually.[10] With its chief risk factors—diabetes and hypertension—on the rise throughout the world, kidney disease has become a serious and under-recognized worldwide epidemic.[11]

[8] Nathan Hill et al, "Global Prevalence of Chronic Kidney Disease – A Systematic Review and Meta-Analysis," *PLoS ONE* 11, no. 7, e0158765 (July 2016), doi:10.1371/journal.pone.0158765; United States Renal Data System, *2017 USRDS Annual Data Report*, https://www.usrds.org/2017/download/2017_Volume_1_CKD_in_the_US.pdf.
[9] Centers for Disease Control and Prevention, Chronic Kidney Disease Surveillance System—United States, http://www.cdc.gov/ckd.
[10] The Kidney Project, "Statistics," https://pharm.ucsf.edu/kidney/need/statistics.
[11] Viswanathan Mohan, Yackoob K. Seedat, and Ragendra Pradeepa, "The Rising Burden of Diabetes and Hypertension in Southeast Asian and African Regions: Need for Effective Strategies for Prevention and Control in Primary Health Care Settings," *International Journal of Hypertension*, 2013: 409083 http://dx.doi.org/10.1155/2013/409083.

Despite this severity and pervasiveness, product development and innovation in the field of renal replacement therapy (RRT) have been relatively stagnant since the introduction of dialysis treatment over 60 years ago. While Medicare spends over $100 billion annually on CKD and ESRD patient treatment, the total National Institutes of Health (NIH) investment in kidney disease research is only about half a billion dollars.[12] Unfortunately, this lack of progress has had the most negative impact on those RRT aims to help: patients.

While dialysis and transplantation remain the primary treatments for ESRD patients, neither offers a permanent solution, with patient outcomes and life expectancies remaining poor. Patients on dialysis experience a 50 percent mortality rate in the first three years of treatment,[13] and 12 patients die in the United States each day waiting for a kidney transplant, as the demand for organs far outweighs the supply.[14] Moreover, because transplanted kidneys only remain functional for an average of 10–20 years (10–15 years for a deceased donor, 15–20 years for a live donor), many patients might require multiple transplants, which often results in the need to return to dialysis treatment while awaiting another new kidney.

Additionally, to date, research efforts in RRT have not been sufficiently patient-centered, as patient and physician priorities often differ. Recent results from the Standardised Outcomes in Nephrology initiative on hemodialysis (SONG-HD), which seeks to establish a set of core outcomes and measures for trials and other research involving HD, indicated that patients prioritize more immediate relief from the burdens of dialysis treatment, while physicians focus largely on improved biochemical and clinical outcomes.

CKD AND ESRD: FAST FACTS

Chronic Kidney Disease (CKD)

CKD is lasting damage to the kidneys that can worsen over time. It occurs when regular kidney function is decreased, from Stage 1 (90 percent function) to Stage 5 (less than 15 percent function). Often called a "silent disease," CKD may remain undetected until it reaches a later, more critical stage because many people exhibit no or few symptoms. In fact, only 10 percent of those at Stages 1–3 are even aware of their CKD.

IMPACT

- 8–10 percent of the worldwide population has CKD
- 1 in 7 adult Americans has CKD
- Medicare spending of more than $64 billion (1 of every 5 Medicare dollars)

End Stage Renal Disease (ESRD)

ESRD or kidney failure occurs when only 10 percent of normal kidney function remains (Stage 5 CKD). At this stage, treatment (dialysis and/or transplant) becomes critical.

IMPACT

- 2 million people worldwide have ESRD
- More than 700,000 Americans have ESRD
- Medicare spending of more than $34 billion

SOURCES:

U.S. Renal Data System. *2017 USRDS Annual Data Report*

National Kidney Foundation. http://www.kidney.org

National Institutes of Health, *Kidney Disease Research Funding and Priority Setting*, GAO-17-121 Report

[12] National Institutes of Health, *Kidney Disease Research Funding and Priority Setting,* GAO-17-121 Report, https://www.gao.gov/products/GAO-17-121.
[13] United States Renal Data System, *2017 USRDS Annual Data Report,* https://www.usrds.org/2017/download/2017_Volume_1_CKD_in_the_US.pdf.
[14] U.S. Department of Health & Human Services, Organ Procurement and Transplantation Network, https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/#.

Future State: Improved Patient Quality of Life

A more effective RRT strategy must focus not only on reducing mortality rates but also on prioritizing the needs of the patient and aiding rehabilitation to improve quality of life. Patients require RRT solutions that address nine key aspects of improved quality of life, which were identified by patients and are described in more detail below.

Minimized impact/intrusion of therapy on family and social life

Patients receiving RRT often feel that they are unable to live a "normal" life due to the impacts of their treatments (e.g., frequency of treatments, fluid management, visibility of vascular access and/or equipment). Additionally, family members must often become care partners at home, which affects their own lives and schedules and changes the nature of their relationships with the patient.

Improved ability to work and travel

More than 70 percent of ESRD patients receive in-center conventional hemodialysis (HD) three times per week.[15] With each treatment lasting approximately 4 hours, patients' flexibility to accommodate a regular employment schedule is often severely impacted; of those patients of working age on dialysis, only 1 in 5 remains employed.[16] Additionally, traveling can be difficult or even impossible for dialysis patients; those receiving in-center HD must arrange for treatment at a facility at their destination, while those dependent on home dialysis machines must find a way to travel with devices that can weigh as much as 100 pounds.

Increased mobility and physical activity

Current RRT treatments can place limitations on patients' ability to be physically active. For example, while exercise is encouraged for patients, peritoneal dialysis (PD) patients must take care not to get their catheters wet. HD patients must avoid any effort that puts pressure or strain on their vascular access area, and anemia may cause activity-limiting weakness and fatigue.

Increased treatment choices

Even though ESRD patients are diverse, often at different stages of life with different lifestyles or daily requirements, they all have the same options among current RRT solutions (i.e., in-center HD, PD, home HD, transplantation)—options that have not substantially changed over the last 60 years. Patients need a variety of treatment options to be able to choose the one that not only improves their kidney function but also best fits their lifestyle and risk tolerance. For example, a patient who must continue to be employed for financial reasons may have enormous challenges trying to accommodate the consuming schedule of in-center HD treatments and could benefit from a more portable or continuous treatment option.

[15] United States Renal Data System, *2017 USRDS Annual Data Report*, https://www.usrds.org/2017/download/2017_Volume_1_CKD_in_the_US.pdf.
[16] Raymond C. Harris, MD, FASN and Marcus Shingles, "Proposed Kidney Disease X Prize Announced at White House Organ Summit."

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Liberalized diet and fluid regulation

Most patients receiving RRT must strictly limit sodium, potassium, and phosphorus as well as closely monitor and regulate their fluid intake to prevent excess fluid and waste from building up in the body. While this regulation is critical for avoiding potential heart failure, bone disease, and changes in blood pressure, it can be quite restrictive to a patient's diet and lifestyle.

Reduced medication burden

In addition to dialysis treatments and a restrictive diet, many ESRD patients must also adhere to a regular medication regimen. One study found that dialysis patients take an average of 19 pills per day, both over-the-counter and prescription (e.g., phosphate binders, anti-hypertensive agents), to protect against treatment complications and compensate for side effects. The study also linked this high pill burden directly to a poorer health-related quality of life (HR-QOL).[17] Similarly, patients who receive a transplant have a lifelong commitment to immunosuppressants, which can put them at greater risk of infections and malignancies.

Reduced disease and treatment complications

While receiving treatment, additional complications—including fatigue, loss of appetite, nausea, vomiting, dizziness, infection, cramping, and pain of cannulation—are common, keeping patients sick, as well as often depressed and unable to see beyond their physical survival.

INCORPORATING PATIENT PREFERENCES INTO INNOVATIVE ALTERNATIVES TO RRT

In addition to receiving patient input to the roadmap from the RRT Roadmap Patient Advisory Committee, KHI conducted a detailed survey to explore patient perceptions and preferences about attributes of new therapies. The purpose of this survey was to ensure that both the roadmap and resulting technology advances keep patient needs and improved quality of life as their overarching goal.

Nearly 250 ESRD and transplant patients completed the online survey, which solicited patient input on the benefits and downsides of new therapies—namely wearable and implantable devices—as well as their interest level in adopting such therapies. While the responses indicated a preference for implantable over wearable devices, these patients expressed keen enthusiasm for all new therapies or advances that would improve their quality of life, citing the ability to travel, return to work, and carry out family responsibilities as preferred attributes of new treatment options.

In short, the survey findings support the aspects of improved quality of life articulated in the roadmap and underscore the importance of considering these patient quality of life improvements in the development of treatment innovations.

[17] Chiu, Yi-Wen et al, "Pill Burden, Adherence, Hyperphosphatemia, and Quality of Life in Maintenance Dialysis Patients," *Clinical Journal of the American Society of Nephrology:* CJASN 4.6 (2009): 1089–1096, http://doi.org/10.2215/CJN.00290109.

Reduced disease maintenance and interventions

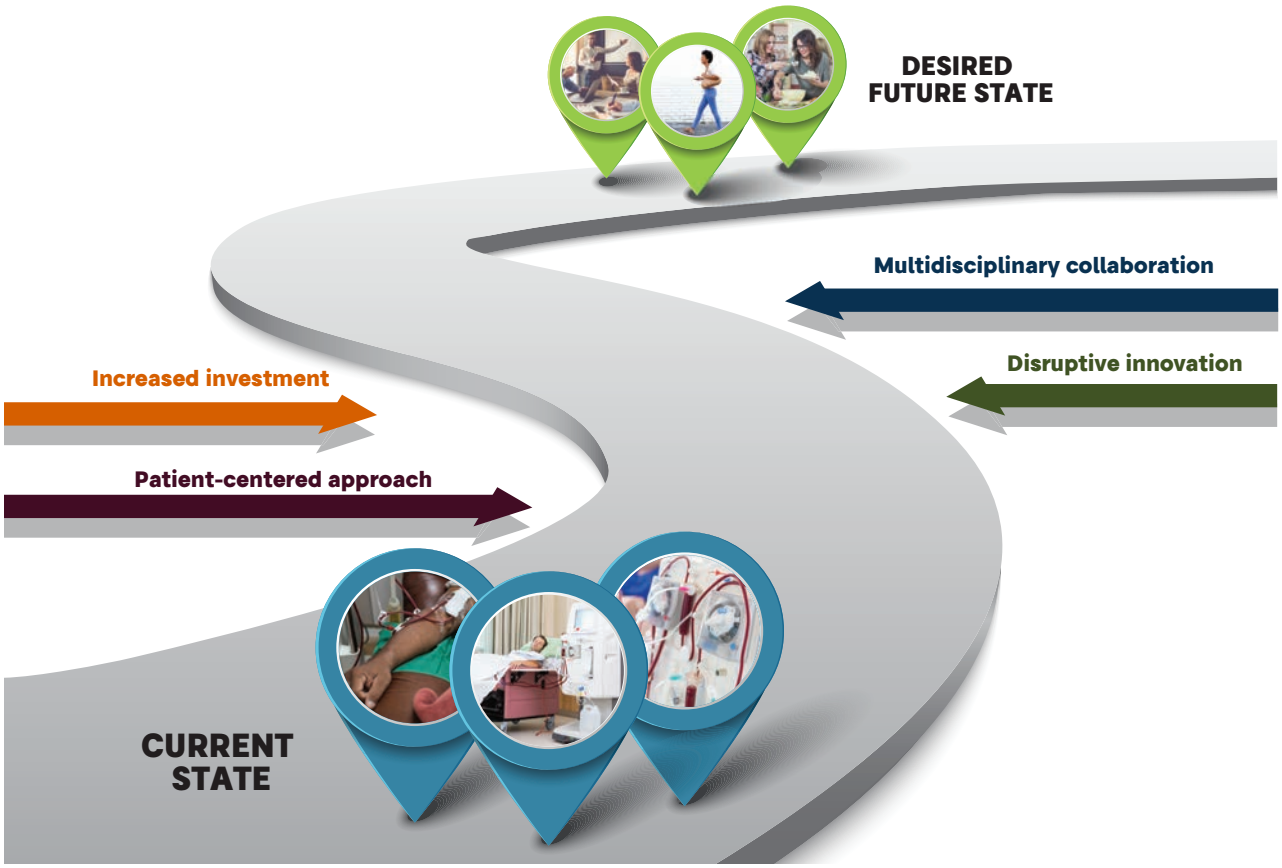
ESRD patients must often undergo repeated hospitalizations, readmissions, or other interventions while managing their disease and treatment. For example, 80 percent of HD patients begin dialysis using a catheter for primary vascular access, with nearly 70 percent still employing a catheter 90 days later.[18] This puts patients at increased risk of infection, which is the second leading cause of death in dialysis patients.[19] Additionally, catheters and other types of access (e.g., arteriovenous fistulas or grafts) can be painful or uncomfortable and often require multiple interventional procedures to maintain patency.

Reduced financial impact

The cost of RRT to Medicare is enormous, but costs also affect individual patients. Many patients have health care expenses related to their treatment that may not be covered by insurance (e.g., transportation to and from HD centers, over-the-counter medications). Others simply cannot afford their private insurance premiums. Additionally, patients not enrolled in Medicare Part D or covered by another prescription plan may find themselves paying large out-of-pocket sums for costly RRT medications.

Figure 2. Pathways for Advancing RRT to Achieve the Desired Future State

Achieving this desired future state for patients is central to the strategies and priorities of this roadmap. By focusing the RRT community's collective efforts on the roadmap's defined solution pathways, the community can address and overcome current obstacles and barriers to achieve the innovations patients need and desire.



[18] United States Renal Data System, *2017 USRDS Annual Data Report*, https://www.usrds.org/2017/download/2017_Volume_1_CKD_in_the_US.pdf.
[19] Centers for Disease Control and Prevention, "Dialysis Safety," https://www.cdc.gov/dialysis/patient/index.html.

Overcoming the Obstacles to Innovative Renal Replacement Therapy

To realize the desired future state of improved patient quality of life, the renal replacement therapy (RRT) community must first overcome a variety of challenges, both **technical** (e.g., accurately reproducing kidney function, leveraging innovative technologies, and developing flexible patient-centered solutions) and **market** (e.g., investment incentives, lack of experience with FDA regulations, representation in clinical trials, and patient risk tolerance).

Addressing these challenges will require a coordinated approach across all RRT stakeholder groups—patients, researchers, clinicians, care partners, product developers, entrepreneurs, regulatory agencies, and payers—as well as a multidisciplinary research focus. The patient-centered solution strategy and research activities of the roadmap offer such a coordinated approach by outlining the focused innovation necessary to overcome identified challenges.

Technical Challenges

Difficulty mimicking all the biological functions of the kidney

- The sheer complexity of integrated kidney function and connectivity (e.g., number of cell types, architecture, variety of functions) makes the task of creating an RRT alternative scientifically challenging within a tenable timeline.
- Lack of success generating functional cells able to transition from *ex vivo* to *in vivo* impacts the ability to develop bioengineered solutions with adequate function and durability.
- Insufficient stable animal uremic models make it difficult to study kidney function and test potential solutions. This difficulty modeling human kidney function and predicting solution performance makes it challenging to meet patient and regulatory requirements for consistent reliability and safety, which can delay the availability of RRT solutions.

Isolated solution development limits innovative, multidisciplinary collaborations that can generate fresh ideas

- The complexity of integrated kidney functions requires multifaceted solutions (e.g., product plus pharmacological intervention), yet there has been a lack of prioritization and consensus about which functions must be replaced through innovative solutions and which can be addressed through conventional medical treatments (e.g., erythropoietin, iron, Vitamin D supplements, phosphate binders).
- Without a multidisciplinary approach, RRT solution development efforts have been unable to adequately leverage disruptive, advanced technologies from other fields (e.g., sensors, nanotechnology, novel materials). Similarly, development teams must be integrated to include a variety of perspectives—including patient and industry together with researcher and clinician—to encourage the most effective and innovative science.

Intrinsic patient variation necessitates customizable or adjustable treatments

- To maximize improvements to patient quality of life, it will be critical to develop solutions flexible enough to accommodate variation in patient biology, cause of kidney function loss, and treatment response as well as psychosocial diversity (e.g., varying needs, preferences, ethnicities, socioeconomic situations, cultural and religious backgrounds, life stages) and differing global care patterns.

Market Challenges

Insufficient investment incentives and established fiscal models hinder innovation

- Potentially lengthy approval processes and time to commercialization for therapeutic products, coupled with the high cost and risk of development, discourage potential funders and investors, who may view the RRT field as not only too time and resource intensive but also too high risk to offer a beneficial return on investment.
- The established end stage renal disease (ESRD) coverage and reimbursement model is focused on dialysis, not disruptive new technologies, making it unclear how new innovative care and treatment options might be rewarded or reimbursed, further disincentivizing research investment.

Lack of experience with government regulations and a lack of relevant industry standards

- Industry stakeholders lack experience with regulations and would benefit from increased interactions with the FDA and other regulatory agencies throughout the world.
- Next-generation RRT solutions are likely to integrate biologics, devices, and/or drugs (i.e., meet the definition of a combination product under 21 CFR § 3.2(e)). These combination products introduce additional complexity because they can require different regulatory pathways for each component.
- There is a lack of sufficient animal models that can recapitulate human kidney dysfunction and model severe chronic kidney disease (CKD) and ESRD.

Underrepresentation of ESRD patients in clinical trials

- Because of the higher health risks associated with ESRD and the length of typical clinical trials, ESRD patients are often excluded from trials of drugs or products for their co-morbidities (e.g., cardiovascular disease, diabetes). As a result, they may be treated with interventions that have not been adequately tested or that have uncertain safety and effectiveness within the ESRD patient population.
- Nephrology has too few randomized controlled trials (RCTs)—the fewest of any internal medicine subspecialty. The lack of a robust clinical trial infrastructure presents challenges to conducting the clinical trials needed to bring a new product to the market. This includes challenges with identification of investigators and clinical sites, patient recruitment and enrollment in trials, clinical trial design, and development of clinical trial endpoints, all of which can impact the feasibility and success of conducting a well-controlled clinical trial.

Varying levels of patient risk tolerance and confidence in solutions

- Patient adoption of new solutions is driven by confidence in reliability, safety, acceptable solution characteristics (e.g., size, weight, appearance), lifestyle impact, and/or extent of maintenance or intervention required from the patient.
- Patients may be split among those who want and would adopt partial or incremental yet near-term solutions (e.g., HD 1x/week versus 3x/week, more frequent at-home treatments) and those who prefer the industry to focus on more disruptive but potentially longer-term solutions.

Solution Strategies for a New Renal Replacement Therapy Paradigm

The roadmap aims to foster opportunities to develop innovative alternatives to dialysis that can help achieve improved outcomes and quality of life for end stage renal disease (ESRD) patients. However, advancing these necessary alternatives and achieving a new renal replacement therapy (RRT) paradigm will take time—time that many patients may not have.

The Need for Multiple Solution Pathways

Accommodating the urgent patient desire for near-term alternative treatment options can be successfully achieved through a solution framework that includes innovative new technologies with increasing levels of complexity. This framework will allow the community to make incremental gains by expanding on some early successes while simultaneously pursuing promising longer-term technologies that more closely replicate kidney function without—or with considerably fewer—complications.

Multiple solution pathways—which may be coupled with pharmacological interventions—allow technologies and advances to be developed in parallel, rather than sequentially, offering greater opportunities to move toward more effective RRT and improved patient quality of life.

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Table 1. Solution Framework

Solution Approach	Goal	Benefits
Enhanced Dialysis Example: interdialytic ultrafiltration device to improve fluid volume management	Encourage incremental improvements to existing dialysis therapy • Remove barriers to home dialysis • Reduce equipment size • Improve transportability • Reduce volume and blood pressure shifts • Increase patient self-care (ease of use)	• Increased treatment flexibility • Reduced disease complications
Portable / Wearable Example: wearable HD or PD with sorbent dialysate regeneration	Provide alternatives to stationary treatment options	• Increased patient independence and freedom of movement (work, travel) • Continuous or near-continuous treatment • Reduced treatment impact (e.g., pill burden, dietary restrictions)
Implantable / Biohybrid Example: implantable hemofilter with filtrate processing and drainage	Develop products that closely mimic normal physiology Develop suitable organs for transplantation (e.g., xenotransplantation, chimeras) Develop bioengineered kidney	• Duplication of kidney functionality • Continuous treatment • Reduced treatment impact for patients (e.g., thirst, diet, work, mobility) • Unlimited, readily available supply of organs when needed
Regenerated Kidney Example: replace fibrosis with normal nephrons and vasculature	Restore endogenous biological kidney function	• Recovered and maintained kidney function • Elimination of disease impact on patients (e.g., unrestricted diet, return to work)

Design Requirements for Ensured Success

Solutions developed as part of the framework implementation must make progress toward the end goals of the future state; ensuring this progress requires a clearly defined set of design requirements. Any technology solution must strive to meet these minimum technical requirements, regardless of approach. While optimal solutions will meet all design requirements, intermediate solutions may offer more immediate patient relief for select kidney functions.

Because integrated function of the kidney is extremely complex, repairing or replacing the various functions will require unique solutions. Therefore, the design requirements have been segmented by kidney function and function-enabling components to better identify the key areas in which focused work and funding can have a significant impact.

Table 2. Common Design Requirements

Function/ Component	Minimum Technical Design Requirements	Patient Impact
RRT Access The vascular, peritoneal, blood circuit, or alternative (e.g., GI tract) access needed for treatment[20]	• Provides access to the blood (either direct or indirect via peritoneal membrane or GI tract) for filtration in a continuous manner • Maintains patency over usable life, reducing incidence of stenosis and thrombosis • Lowers incidence of infectious complications • Patient-friendly (low/no maintenance, easy and quick connection/disconnection, painless access) • Composed of biocompatible materials • Mitigates blood loss or other complications in the event of an unintentional disconnection	Safer, more continuous treatment with fewer complications and reduced need for interventions
Blood Filtration Filtering of blood to remove waste and excess fluid	• Non-fouling and able to maintain continuous performance (duration defined by product and clinical context) • Generates a filtrate of at least 40L/day (~30mL/minute for 24-hour therapy) • Size selective, with no loss of essential blood proteins (e.g., albumin) • Component materials and design must be biocompatible and hemocompatible	Access to a safe, effective, longer-life, easy-to-use filtration system that avoids clotting issues

[20] While really a system enabler, RRT access has minimum technical design requirements and has therefore been included in this table.

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Function/ Component	Minimum Technical Design Requirements	Patient Impact
Electrolyte Homeostasis Maintaining appropriate levels of key components in the blood	• Normalizes and maintains commonly measured or needed electrolytes (e.g., sodium, potassium, calcium, magnesium, and phosphate) within clinically acceptable ranges, potentially with the aid of pharmacological interventions	More comprehensive and effective regulation of electrolytes, resulting in reduced need for dietary restrictions or supplements
Fluid Regulation Regulating the amount of body fluid and/or removing excess fluid	• Has the capacity to remove excess fluid and is adjustable based on the needs of the patient • Allows patient to self-manage and monitor fluid status separate from monitoring of other functions (electrolyte and toxin removal)	Ability to personalize and optimize the amount and rate of excess fluid removal, resulting in stable blood pressure and less thirst and cramping

Toxin Removal/ Secretion
Limiting or preventing toxin accumulation in the bloodstream and throughout the entire body
	• Maintains clearance/reduction of the three categories of uremic toxins:
	  • small, non-protein bound (clearance of 40L/day)
	  • small, protein-bound (reduction in blood concentration)
	  • "middle molecules" (reduction in blood concentration)
	• Capable of secreting non-filtered toxins
		Reduced presence of harmful toxins in the bloodstream that could lead to uremic toxicity and/or drug toxicity

Filtrate Transport and Drainage Removing excess filtrate after processing; connectivity for filtration, processing, and exterior drainage	• Composed of biocompatible materials • Removes remaining processed filtrate—up to 3L/day • Processed filtrate storage/removal apparatus is acceptable to the patient	Drainage processes and equipment that are safe and effective, with acceptable characteristics (e.g., size, weight, comfort, appearance, compatibility with sanitary infrastructure)

Enabling Change through Focused Research and Design

The roadmap strategy provides not only a solution framework but also a set of focused research and development (R&D) activities to accelerate the advancement and availability of innovative and comprehensive renal replacement therapy (RRT) solutions. All the activities are designed to be technology solution-agnostic to encourage the development of the most effective and patient-friendly solutions. Organized into three focus areas, these key activities have the greatest potential to improve patient quality of life by achieving meaningful results in the **near (2019–2022), mid (2023–2025), and long term (2026+):**

- **Kidney Functions:** Activities to pursue unique solutions for replicating or replacing each kidney function
- **System Enablers:** Activities that are broader in scope and serve to connect or integrate a variety of kidney functions or elements of RRT into more comprehensive systems
- **Supporting Activities:** Activities that must occur in parallel with the Kidney Functions and System Enablers R&D activities to ensure the accelerated availability of innovative RRT solutions

With this approach, the activities across focus areas and timeframes can facilitate the development and availability of innovative RRT solutions that can address not only near-term patient demands for alternatives to dialysis but also long-term opportunities for comprehensive and integrated solutions capable of fully replicating or replacing kidney function.

To maximize the impact of these varied solutions and their parallel development, each roadmap activity must be implemented as soon as possible (allowing for any necessary funding or programmatic dependencies), which will require dedicated resources and the development of multidisciplinary teams of researchers, technology developers, clinicians, entrepreneurs, investors, and patients.

Kidney Functions

To advance innovative RRT solutions that can effectively repair or closely replicate the complex functions of kidneys, it is critical to evaluate, understand, and address each function individually. This focused approach can foster fresh solutions for advancing renal replacement technologies. The roadmap kidney function activities aim to achieve solutions capable of the following:

- **Blood Filtration:** Help to more effectively, efficiently, and safely remove waste and excess fluid
- **Electrolyte Homeostasis:** Normalize and maintain appropriate levels of key components in the blood
- **Fluid Regulation:** Regulate the amount of body fluid and/or remove excess fluid
- **Toxin Removal/Secretion:** Limit or prevent toxin accumulation in the bloodstream
- **Filtrate Transport and Drainage:** Remove excess filtrate and address connectivity issues around exterior drainage of processed filtrate

Table 3. Kidney Function Activities

	Activities	Near-Term 2019-2022	Mid-Term 2023-2025	Long-Term 2026+
Blood Filtration				
☼	Develop a size-selective blood filter that is capable of 40L/day filtrate with minimal or no use of anticoagulants or anti-clotting agents	→		
◌	Identify or generate cell source/type(s)—ideally renewable (although not required)—needed to perform desired barrier and permeability functions, and optimize integrated cellular structures or corresponding cell isolation and differentiation techniques (e.g., production of functional glomerular endothelial cells, mesangial cells, and podocyte cells)	→	→	
☼ ◌	Develop a size-selective, non-clotting blood filter (connected to circulation with or without pump) that is capable of 40L/day filtrate and will freely pass electrolytes and non-protein-bound toxins	→	→	

☼ Mechanical/physiochemical-based solution activity | ◌ Cellular-based solution activity

☼ ◌ Biohybrid activity (mechanical/physiochemical and/or cellular)

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	Activities	Near-Term 2019-2022	Mid-Term 2023-2025	Long-Term 2026+
Blood Filtration				
⚙ ◌	Demonstrate cell line phenotype stability and preservation in *ex vivo* and *in vivo* systems to allow for stable blood filtration	→	→	
⚙ ◌	Demonstrate function in full-scale animal model with residual kidney function (necessity and length of animal studies will be product-specific and may vary)	→	→	
⚙ ◌	Demonstrate function in anephric animal models without residual kidney function (necessity and length of animal studies will be product-specific and may vary)	→	→	→
⚙ ◌	Demonstrate a size-selective, non-clotting filter that is capable of 40L/day filtrate with 12–24 months of continuous performance	→	→	→
Electrolyte Homeostasis				
◌	Develop a process for passage of filtrate to the engineered structures that will ultimately contain the differentiated cells that maintain electrolyte homeostasis	→		
⚙	Develop in-line sensors or point-of-care systems that measure blood and/or effluent electrolytes during RRT treatments to monitor significant variations in blood electrolytes that could lead to symptoms/complications	→		
◌	Generate cells with defined functional characteristics of critical cell types such as: • Proximal tubule (glucose, phosphorus, amino acids, protein absorption, organic ion secretion, bicarbonate, hydrogen ion secretion) • Distal tubule (magnesium, chloride, and calcium transport) • Collecting duct (proton transport)	→	→	
◌	Engineer matrix material and scaffold that will support functional organization and long-term maintenance of the differentiated state of critical cells *in vivo*	→	→	
⚙	Develop sorbents to augment electrolyte removal	→	→	
⚙	Develop ion-selective membranes with pores or channels capable of selective removal or retention of electrolytes (e.g., sodium, potassium, calcium, magnesium, phosphate) after blood filtration	→	→	
⚙ ◌	Demonstrate integrated tubular replacement unit that performs ion transport activities	→	→	→

⚙ Mechanical/physiochemical-based solution activity | ◌ Cellular-based solution activity

⚙ ◌ Biohybrid activity (mechanical/physiochemical and/or cellular)

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Activities	Near-Term 2019-2022	Mid-Term 2023-2025	Long-Term 2026+
Fluid Regulation			
Develop sensors to monitor the volume status of various fluid compartments of the patient, allowing for a personalized fluid removal prescription to avoid volume depletion, intradialytic hypotension, and fluid overload	→		
Develop sensors/methods to measure intra-peritoneal volume in PD	→		
Generate cell type on substrate that can carry out reabsorption/secretion and is water permeable	→		
Develop integrated systems to use sensor input to adjust fluid removal by real-time patient adjustment (remote programmable)	→	→	
Create processes for directing reabsorbed fluid and electrolytes to enter the circulation	→	→	
Demonstrate *ex vivo* structure with water transport features and permeability characteristics that will allow for net reabsorption of 90%–95% of filtered volume	→	→	
Develop integrated systems to use sensor input to adjust fluid removal as part of a closed-loop system	→	→	→
Toxin Removal/Secretion			
Generate cell type capable of organic anion/cation transport to secrete selected protein-bound toxins and drugs that are not freely filtered	→		
Develop technology that shifts the dynamic equilibrium of protein binding for toxins further toward a non-bound state, making them filterable	→		
Develop new sorbent devices capable of binding/adsorbing/metabolizing uremic toxins from dialysate or ultrafiltrate, with minimal removal of vital chemicals	→		
Demonstrate *ex vivo* structure that exploits filtration and secretion to achieve 70%–90% of normal toxin secretion	→	→	
Develop oral sorbents capable of binding/adsorbing/metabolizing uremic toxins to augment toxin removal	→	→	
Demonstrate toxin removal and secretory functionality of implanted cell-based systems *in vivo*	→	→	→
Develop “smart” filters, mixed-matrix membranes, or blood sorbents capable of binding/adsorbing uremic toxins	→	→	→

Mechanical/physiochemical-based solution activity | Cellular-based solution activity

Biohybrid activity (mechanical/physiochemical and/or cellular)

Activities	Near-Term 2019-2022	Mid-Term 2023-2025	Long-Term 2026+
Filtrate Transport and Drainage			
Develop system for dialysate delivery and removal that is hygienically sound, easy to use, and aesthetically appealing	→		
Develop an exterior filtrate drainage system that is functional, hygienically sound, and aesthetically appealing	→		
Create a highly impermeable conduit (i.e., drainage system from outflow of engineered processing system to exterior, potentially involving the urinary bladder) to move the non-adsorbed/readsorbed processed filtrate from the body	→	→	

Mechanical/physiochemical-based solution activity | Cellular-based solution activity

Biohybrid activity (mechanical/physiochemical and/or cellular)

System Enablers

While optimal approaches for addressing individual kidney functions can be identified through focused research on each function, ideal solutions will simultaneously address multiple or all functions. To maximize the effectiveness of RRT systems and ensure that they meet the needs of patients, these solution systems must be easy for clinicians and patients to access and maintain and must facilitate real-time monitoring of the mimicked kidney function. Leveraging technologies from other industries, conducting targeted biomaterials R&D, and identifying solutions for biological and immunological modulation will also help improve and accelerate the availability of these systems. The roadmap system enablers activities are organized in the following categories:

- **RRT Access:** Provide connection from the blood circuit to the replacement system
- **Biomaterials Development:** Support blood compatibility and cellular components of the replacement system
- **Biological and Immunological Modulation:** Develop safe and effective, non-immunogenic, sterile products—spanning cell/tissue/organ/organism approaches—for innovative RRT
- **Function and Safety Monitoring:** Ensure system reliability and offer patients peace of mind
- **Other Technologies:** Leverage technologies from other industries and apply them to RRT solutions

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Table 4. System Enabler Activities

Activities	Near-Term 2019-2022	Mid-Term 2023-2025	Long-Term 2026+
RRT Access			
Develop components of the blood circuit that allow for hemodialysis without the need for systemic anticoagulation	→		
Develop PD access with improved drainage characteristics, including prevention of outflow failure	→		
Develop PD access with reduced risk of infection	→		
Develop a safer vascular access capable of preventing (e.g., needle-free) or mitigating (e.g., self-sealing) catastrophic events of a vascular access disconnect	→		
Develop a vascular access with fewer or no interventions needed to maintain patency	→		
Develop methods for early detection/diagnosis of access-related infections	→	→	
Develop novel biomaterial-based conduit or endothelial cell-lined robust conduit (i.e., stent) that permits delivery of blood to the filtration unit	→	→	
Develop access that is non-intrusive and functionally acceptable, easy and quick for the patient to connect and disconnect, secure with minimal discomfort (e.g., skin-level or sub-cutaneous access), and aesthetically pleasing to patients • Hemodialysis (Near-term) • Wearables (Mid-term) • PD Access (Near- and mid-term)	→	→	
Develop entire blood circuit that allows for hemodialysis with minimal or no use of anticoagulants or anti-clotting agents	→	→	→
Develop vascular access with internal connection to the native vasculature that maintains patency without the need for systemic anticoagulation	→	→	→

Mechanical/physiochemical-based solution activity | Cellular-based solution activity

Biohybrid activity (mechanical/physiochemical and/or cellular)

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	Activities	Near-Term 2019-2022	Mid-Term 2023-2025	Long-Term 2026+
☼ ◌	Develop vascular access that significantly reduces the risk of infection over the life of the implant	→	→	→
Biomaterials Development				
☼ ◌	Identify and/or develop potential materials with desired scaffold properties (mechanical, porosity, degradation) for structural support/scaffold development, as well as scaffold manufacturing techniques. In addition, these scaffolds must be biocompatible and porous to allow for movement of reabsorbed fluid and allow ready access for secretion of toxins into the processed filtrate	→		
☼ ◌	Develop a scaffold or membrane device capable of allowing oxygenation and nutrient access for transporting epithelial cells and demonstrate activity *ex vivo*	→		
◌	Develop and demonstrate structural support/scaffold that maintains desired function *in vivo*	→	→	
☼	For systems using sorbents, develop new sorbents with fewer adverse electrolyte changes, no generation of potentially toxic byproducts, greater uremic toxin capacity, and ability to be regenerated between uses	→	→	
Biological and Immunological Modulation				
◌	Identify gene modifications needed to address coagulation incompatibilities, antibody-mediated rejection, inflammatory responses, etc., for xenotransplantation	→		
◌	Genetically engineer animal to inactivate viral and pathogenic organisms for xenotransplantation	→		
◌	Identify appropriate genetic modification and immunological characterization pre-screening methods/ regimens, as well as pharmacological interventions, for xenotransplantation from animals to humans	→		
◌	Standardize panel of immune markers to assess tolerance of RRT product (i.e., minimize immune rejection)	→		
◌	Generate suitable transgenic donor animals for xenotransplantation	→	→	
◌	Demonstrate induction of immune tolerance	→	→	
◌	Demonstrate long-term graft survival in nephrectomized animals	→	→	→
◌	Recruit host vessels to implanted cellular product and demonstrate perfusion of implanted tissue that is sufficient to maintain cell health and physiological functions	→	→	→

☼ Mechanical/physiochemical-based solution activity | ◌ Cellular-based solution activity

☼ ◌ Biohybrid activity (mechanical/physiochemical and/or cellular)

Activities	Near-Term 2019-2022	Mid-Term 2023-2025	Long-Term 2026+
Function and Safety Monitoring			
Establish coordinated registry network of real-world safety and efficacy data	→		
Develop technologies to allow real-time treatment monitoring by various sensors (flow, pressure, volume status, electrolytes, etc.) that can be observed/tracked by patients and providers	→		
Develop online sensors (e.g., for ammonia or other uremic toxins or byproducts) to alert users that sorbent cartridges need to be replaced	→		
Identify in vitro surrogate assays or biomarkers for assessing safety and proper functioning of the RRT	→		
Develop sensors that can provide feedback on body fluid volume and blood concentrations of key components (e.g., potassium, sodium, calcium, phosphorus, pH)	→		
Develop technologies that detect a vascular access disconnect and/or act to avoid blood loss in the event of a disconnect (e.g., a sensor that integrates with software to stop the blood pump and put replacement product in safe mode)	→		
Establish criteria for safety testing necessary before and after human trials to guide developers and allow for projections of development timelines	→		
Develop a mechanism to monitor the integrity of the biological product itself (e.g., clotting, when to replace cells)	→	→	→
Develop integrated systems that use sensor input to allow adjustment in real time or as part of a closed-loop system	→	→	→
Develop technologies to detect and proactively mitigate clotting	→	→	→
Develop mechanism to prevent or deal with gases accumulated by the product	→	→	→
Conduct *in vivo* testing to evaluate safety (e.g., toxicity), integrity, longevity, and tolerance of RRT product	→	→	→
Other Technologies			
Develop lightweight rechargeable batteries capable of powering RRT systems	→		
Develop systems that allow for safe, secure, and efficient two-way communication between the product/implant and the operator	→		
Develop miniaturized systems (e.g., sorbents) capable of regenerating spent dialysate	→	→	
Develop blood/filtrate/dialysate pumps that are miniaturized, low-energy, and hemocompatible	→	→	
Develop lightweight power source capable of powering RRT systems that can be recharged using wireless energy transfer	→	→	
Develop miniaturized, efficient systems to generate sterile water for replacement fluid/dialysate generation	→	→	

Mechanical/physiochemical-based solution activity | Cellular-based solution activity

Biohybrid activity (mechanical/physiochemical and/or cellular)

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Supporting Activities

Efforts to ensure a clear pathway to commercialization or implementation for all solutions can facilitate more widespread availability and adoption of innovative RRT solutions. The roadmap supporting activities are organized in the following categories:

- **Regulatory Alignment:** Facilitate the coordinated effort between regulators and the nephrology community to streamline the product life cycle
- **Innovation Incentives and Payment Pathways:** Facilitate collaborative efforts to examine and inform improvements to current financial investment and reimbursement models

Table 5. Supporting Activities

	Activities	Near-Term 2019-2022	Mid-Term 2023-2025	Long-Term 2026+
Regulatory Alignment				
⚙ ◌	Inform how current standards and regulatory recommendations (e.g., existing guidance documents) can be applied to novel RRT technology, and develop stakeholder working groups to address and publish findings on any identified gaps in testing recommendations (after review of existing standards and guidance)	→		
⚙ ◌	Review existing literature and publish findings on best practices for animal models and animal studies used for testing RRT systems	→		
⚙ ◌	Clarify the different regulatory pathways for device-only systems, cellular/device combination systems, and cell-based/xenotransplantation products	→		
⚙ ◌	Increase understanding and awareness of 1) communication mechanisms (e.g., Pre-Submission, INTERACT) that enable developers to obtain early, non-binding, regulatory advice from the FDA, and 2) expedited programs intended to facilitate development and review of eligible RRT products	→		
⚙ ◌	Develop sources of real-world data (e.g., patient registries) that could be used both to help objectively measure iterative improvements in evolving technologies, as well as garner information to support regulatory decision-making	→		
⚙ ◌	Inform the most appropriate clinical trial designs (including randomized trials and data generation and management) to support product development, safety, approval, coverage, and reimbursement	→	→	
⚙ ◌	Qualify and make publicly available Medical Device Development Tools (MDDTs) that can be used by the community to streamline device development and regulatory evaluation[21]	→	→	

⚙ Mechanical/physiochemical-based solution activity | ◌ Cellular-based solution activity

⚙ ◌ Biohybrid activity (mechanical/physiochemical and/or cellular)

[21] For more information, see "Qualification of Medical Device Development Tools: Guidance for Industry, Tool Developers, and Food and Drug Administration Staff" at https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM374432.pdf.

	Activities	Near-Term 2019-2022	Mid-Term 2023-2025	Long-Term 2026+
Innovation Incentives and Payment Pathways				
⚙ 🫘	Develop uniform technology licensing agreement to broaden participation and facilitate collaboration, while allowing contributors to maintain intellectual property rights	→		
⚙ 🫘	Develop and provide a pre-competitive forum for annual scientific exchange, networking, sharing, and collaboration	→		
⚙ 🫘	Assess scientific advancement and facilitate regular updates to the technology roadmap	→		
⚙ 🫘	Identify gaps and develop necessary educational and scientific tools that may assist innovators with non-nephrology backgrounds to accelerate translation of current technology	→		
⚙ 🫘	Develop and maintain a catalog of research and technology advancements to accelerate efficient and coordinated technology development	→		
⚙ 🫘	Facilitate dialogue with parties that have RRT innovation financing models in place and co-investments from foundations, patient associations, payers, and governments to identify and implement best practices	→		
⚙ 🫘	Conduct thorough assessment of existing and in-development RRT systems and associated technology readiness levels (TRLs) to set a baseline for innovation	→		
⚙ 🫘	Identify potential changes to the current Medicare ESRD Prospective Payment System model that could encourage RRT investment and innovation	→	→	→

⚙ Mechanical/physiochemical-based solution activity | 🫘 Cellular-based solution activity
⚙ 🫘 Biohybrid activity (mechanical/physiochemical and/or cellular)

Next Steps

This roadmap provides a framework for the coordinated development of innovative renal replacement therapy (RRT) solutions that can propel the industry forward and achieve the vision of improved quality of life for patients. The structure of the roadmap's solution strategy encourages multidisciplinary approaches that will necessitate attracting innovators from outside of the RRT, kidney, and medical fields. Connecting current researchers and developers with experts with complementary skills and insight will enable the RRT field to leverage technologies from other industries while infusing the RRT community with fresh, new ideas. Additionally, such a disruptive shift in the RRT paradigm could potentially serve a worldwide market, attracting new thinking and partners from throughout the international community.

The focused research priorities of this roadmap are strategically designed to be patient-centered, outcome-oriented, and solution-agnostic, with a level of specificity that can align with potentially fundable projects. With additional private interest and investment from the corporate, philanthropic, and venture capital communities, short- and long-term advances can be made that will have significant positive implications for the rapidly growing worldwide population of individuals with chronic kidney disease and end stage renal disease (ESRD).

One key near-term funding opportunity is the newly established Kidney Innovation Accelerator (KidneyX), a public-private partnership between the American Society of Nephrology (ASN) and the U.S. Department of Health and Human Services (HHS). The research priorities in this roadmap offer a strategic development and implementation pathway to support KidneyX's emphasis on expediting the development of innovative new therapies across the spectrum of kidney care.

This roadmap is intended to be a living document designed to guide the advancement of innovative RRT. To address current challenges and outline opportunities to advance RRT solutions and continuously improve the quality of life of ESRD patients, the KHI team will consult with key stakeholders to update the roadmap regularly, ensuring that its goals and direction continue to accurately reflect what could become a rapidly changing RRT landscape.

THE KIDNEY INNOVATION ACCELERATOR (KidneyX)

KidneyX is a public-private partnership established to help spur the innovative science needed to develop life-changing solutions for kidney patients.

Focus Areas

- Diagnostics
- Therapeutics (e.g., point-of-care home testing, real-time glomerular filtration rate)
- Next-generation dialysis (e.g., wearable or implantable dialyzers, bioartificial kidneys)
- Tissue engineering (e.g., vascular access technologies to improve the dialysis patient experience)
- Medications (e.g., drugs to slow progression of, reverse, or cure kidney disease)
- Patient-centered tools (e.g., electronic health record tools designed to identify and track disease and applications to empower patients to manage kidney diseases, such as nutrition apps)

SOURCE: http://www.kidneyx.org

Appendix A: Roadmap Contributors

This roadmap is dedicated to all patients that have lost their lives to end stage renal disease (ESRD) or are living with ESRD and chronic kidney disease (CKD) and fighting for better treatment options.

Contributor	Affiliation	Role
Stephen Ash, MD, FACP	Ash Access Technology, Inc.	Mechanical Working Group
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Bill Murray (*in memoriam*)	Patient	Vascular Working Group, Patient Advisory Committee

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