



For Immediate Release

United Therapeutics Corporation Announces FDA Clearance of its Investigational New Drug Application for the UKidney Xenotransplantation Clinical Trial

First-ever human clinical trial of a xeno-organ intended to allow for potential registration through the submission of a Biologics License Application to the U.S. FDA

First xenotransplant is expected to occur around mid-year 2025

SILVER SPRING, Md. and RESEARCH TRIANGLE PARK, N.C., February 3, 2025: United Therapeutics Corporation (Nasdaq: **UTHR**), a public benefit corporation, today announced that the U.S. Food and Drug Administration (**FDA**) has cleared its Investigational New Drug application (**IND**) to initiate a clinical study of the company's investigational UKidney™ derived from a 10 gene-edited source pig. The study will enroll an initial cohort of six end-stage renal disease (**ESRD**) patients, expanding to up to 50 participants, and is intended to support a Biologics License Application (**BLA**) with the FDA.

United Therapeutics expects the first xenotransplant in this trial to be performed around mid-year 2025.

According to the American Kidney Fund, more than 557,000 patients in the U.S. are on dialysis to filter their blood when their kidneys are no longer able to do so¹. A 2009 study estimated that 52% of kidney transplant candidates who were at least 60 years of age when placed on the transplant waitlist die within five years before receiving a transplant². United Therapeutics believes that xenotransplantation offers a therapeutic alternative to dialysis.

"Clearance of our IND for this first-ever clinical trial of a xenokidney represents a significant step forward in our relentless mission to expand the availability of transplantable organs," said **Leigh Peterson, Ph.D.**, Executive Vice President, Product Development and Xenotransplantation at United Therapeutics. "Our goal is to increase the availability of transplantable organs to offer a therapeutic alternative to a lifetime on dialysis for a large population of patients who are unlikely to receive an allogeneic³ kidney transplant."

This first-in-human clinical study aims to assess safety and efficacy of the UKidney in two groups of participants:

- ESRD patients who have been assessed and determined to be ineligible for a conventional allogeneic kidney transplant for medical reasons; and
- ESRD patients who have been on the kidney transplant waitlist but are more likely to die or go untransplanted than receive a deceased donor kidney transplant within five years.

¹ American Kidney Fund 2024 (<https://www.kidneyfund.org/all-about-kidneys/quick-kidney-disease-facts-and-stats>)

² Schold J, Srinivas TR, Sehgal AR, Meier-Kriesche HU. Half of kidney transplant candidates who are older than 60 years now placed on the waiting list will die before receiving a deceased-donor transplant. Clin J Am Soc Nephrol. 2009 Jul;4(7):1239-45. doi: 10.2215/CJN.01280209. Epub 2009 Jun 18. PMID: 19541814; PMCID: PMC2709520.

³Two types of transplants are discussed in this release. *Allogeneic* transplants are human-to-human transplants, while *xenotransplants* are transplants from non-human animals into humans. In this context, we refer to *xenotransplants* specifically from gene-edited porcine (pig) source animals.

“Eliminating the need for dialysis or limiting time on dialysis may improve survival for many patients with ESRD,” said **Noah Byrd, Ph.D., RAC**, Vice President, Global Regulatory Affairs at United Therapeutics. “We appreciate the productive collaboration with the FDA in advancing our efforts to bring this potentially revolutionary therapeutic option to the hundreds of thousands of ESRD patients.”

About the Study

Study Design

The study is a multicenter, open-label, safety and efficacy study and is intended to support FDA approval of a BLA. The study is designed as a combination phase 1/2/3 trial (sometimes referred to as a “phaseless” study) to evaluate safety and efficacy seamlessly without moving through separate phase 1, phase 2, and phase 3 studies that are typically associated with conventional drug approvals. Participants will receive a UKidney transplant followed by a 24-week post-transplant follow-up period, including the evaluation of all study endpoints and safety assessments. After the 24-week post-transplant follow-up period, participants who received a UKidney will continue to be followed for the rest of their lives, including for survival, UKidney function, and monitoring for zoonotic infections⁴.

Efficacy Endpoints

Efficacy endpoints include participant survival rate, UKidney survival rate, change in measured glomerular filtration rate⁵, and change in quality of life in participants⁶ at 24 weeks post-transplant. Overall survival time of participants receiving a UKidney and overall survival time of the UKidneys themselves are also efficacy endpoints.

Safety Endpoints

Safety endpoints include the incidence of adverse events and serious adverse events, all-cause mortality, and the incidence of proteinuria⁷, zoonotic infections, and opportunistic infections⁸.

Cohort-Based Design

The first cohort will consist of six transplants at two centers. There will be a 12-week waiting period between the first and second transplants. After the initial cohort reaches at least 12 weeks post-transplant, safety and efficacy data will be reviewed by an independent Data Monitoring Committee to determine if the study should proceed to the next cohort. In addition, United Therapeutics intends to engage with the FDA after the first six transplants are completed. If safety and efficacy results are supportive, the sample size will be increased to a total of up to 50 participants to enable the study to support registration, with additional transplant centers expected to be added to the study.

Additional Key Participation Criteria

Additional key participation criteria include an age of 55 to 70 years old, a diagnosis of ESRD, and at least six months on hemodialysis. Participants will be screened using a crossmatch assay to assess expected immunological compatibility with the UKidney. Participants must not need multiple organ transplants; must not have severe medical co-morbidities, including but not limited to advanced cardiovascular disease, severe peripheral vascular disease, severe neurological disease, chronic pulmonary disease, and uncontrolled diabetes; and must not have a history of medical noncompliance that may preclude adherence to the demands and requirements of xenotransplantation.

⁴ *Zoonotic infections* are infections transmitted from one species to another.

⁵ The *glomerular filtration rate*, or GFR, measures how much blood passes each minute through the glomeruli, the tiny filters in the kidneys.

⁶ Quality of life will be measured using the following four surveys: the EuroQol 5-Dimension 5-Level, the Standardized Outcomes in Nephrology Life Participant, the Kidney Transplant Questionnaire, and the Patient Global Impression of Change.

⁷ *Proteinuria* is a condition where an excessive amount of protein is present in the urine. This can be caused by multiple factors, including kidney damage.

⁸ *Opportunistic infections* are infections from pathogens that would not normally impact healthy people. Transplant patients, receiving either xenotransplants or allogeneic transplants, must use immunosuppressive medications to prevent rejection of transplanted organs. Opportunistic infections can occur in people with suppressed immune activity.

Full inclusion and exclusion criteria for this study will be provided in a future listing on the clinicaltrials.gov website.

About End-Stage Renal Disease

According to the American Kidney Fund, there are approximately 808,000 patients with kidney failure in the United States and more than 557,000 patients on dialysis, approximately 93,000 of whom are on the U.S. kidney transplant waiting list. Only 21,000 deceased donor kidney transplants occurred in 2023⁹. A 2021 study found that three years after starting dialysis, only 12% of patients had been placed on an Organ Procurement and Transplant Network kidney transplant waitlist while more than 40% died¹⁰.

About UKidney

United Therapeutics' xenokidney, known by the proposed trade name UKidney, is an investigational xenokidney from a pig with 10 gene edits. Six human genes are added to the pig genome to facilitate immunological acceptance and compatibility of the organ in the human recipient, while four porcine genes are inactivated: three that contribute to porcine organ rejection in humans and one that can cause organ growth.

United Therapeutics: Enabling Inspiration

At United Therapeutics, our vision and mission are one. We use our enthusiasm, creativity, and persistence to innovate for the unmet medical needs of our patients and to benefit our other stakeholders. We are bold and unconventional. We have fun, we do good. We are the first publicly-traded biotech or pharmaceutical company to take the form of a public benefit corporation (**PBC**). Our public benefit purpose is to provide a brighter future for patients through (a) the development of novel pharmaceutical therapies; and (b) technologies that expand the availability of transplantable organs.

You can learn more about what it means to be a PBC here: unither.com/psc.

Forward-Looking Statements

Statements included in this press release that are not historical in nature are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include, among others, statements concerning: the timing and enrollment of our planned UKidney clinical trial; our plans to seek FDA approval of the UKidney following completion of the clinical trial; the potential for the UKidney to offer a therapeutic treatment option to ESRD patients; and our goals of innovating for the unmet medical needs of our patients and to benefit our other stakeholders, and furthering our public benefit purpose of developing novel pharmaceutical therapies and technologies that expand the availability of transplantable organs. These forward-looking statements are subject to certain risks and uncertainties, such as those described in our periodic reports filed with the Securities and Exchange Commission, that could cause actual results to differ materially from anticipated results. Consequently, such forward-looking statements are qualified by the cautionary statements, cautionary language and risk factors set forth in our periodic reports and documents filed with the Securities and Exchange Commission, including our most recent Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K. We claim the protection of the safe harbor contained in the Private Securities Litigation Reform Act of 1995 for forward-looking statements. We are providing this information as of February 3, 2025, and assume no obligation to update or revise the information contained in this press release whether as a result of new information, future events, or any other reason.

UKIDNEY is a trademark of United Therapeutics Corporation.

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⁹ American Kidney Fund 2024 (<https://www.kidneyfund.org/all-about-kidneys/quick-kidney-disease-facts-and-stats>)

¹⁰ US Renal Data System 2023 (<https://usrds-adr.niddk.nih.gov/2023/end-stage-renal-disease/7-transplantation>)