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Ultomiris received accelerated approval in the US as first and only C5 complement inhibitor to reduce proteinuria in adults with primary immunoglobulin A nephropathy

Based on I CAN Phase III trial results from prespecified interim analysis in which Ultomiris demonstrated 43.4% reduction in proteinuria vs placebo at 34 weeks

Late-breaking results from I CAN Phase III trial will be presented at American Society of Nephrology's Kidney Week 2026

Alexion, AstraZeneca Rare Disease's *Ultomiris* (ravulizumab) has been approved in the US to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk for disease progression.

This indication is approved under accelerated approval based on reduction of proteinuria. It has not been established whether *Ultomiris* slows kidney function decline in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the ongoing I CAN Phase III trial evaluating *Ultomiris* in adults with IgAN who are at risk of disease progression.[1] The trial is ongoing and will assess the primary endpoint of change from baseline in estimated glomerular filtration rate (eGFR) at week 106, with data intended to support traditional FDA approval.[2]

The approval follows Priority Review by the US Food and Drug Administration (FDA) based on positive results from a prespecified interim analysis of the I CAN trial. Results showed *Ultomiris* demonstrated a 43.4% reduction in proteinuria vs placebo at 34 weeks.[3] *Ultomiris* is administered intravenously every eight weeks in adults (based on body weight), following a loading dose.[1]

IgAN is a rare, inflammatory disease of the kidneys that can lead to chronic kidney disease and progress to end-stage kidney disease (ESKD). It begins when the body develops abnormal IgA proteins resulting in immune complexes that are deposited in the kidneys causing damage. The deposition of these complexes activates the complement system, leading to terminal complement-driven inflammation. This results in damage and loss of essential parts of the kidney, including cells in the glomeruli, the part of the kidneys that filters and cleans the blood.[4] IgAN affects more than 200,000 people in the US.[5,6] Approximately half of people with IgAN who have elevated protein levels in urine or reduced kidney function are at high risk of progression to ESKD, or kidney failure, within 10 years of diagnosis.[7-9]

Richard Lafayette, MD, Professor of Medicine (Nephrology) at the Stanford University Medical Center, Founder and Director of the Stanford Glomerular Disease Center and external scientific committee co-chair of the I CAN trial, said: "For many people living with IgAN, persistent proteinuria remains a significant challenge despite available treatments, signalling ongoing kidney injury and heightened risk of disease progression. With this approval of *Ultomiris*, physicians now have a C5 inhibitor that delivers sustained terminal complement inhibition, targeting a central driver of kidney inflammation to meaningfully reduce proteinuria in patients living with this progressive disease."

Bonnie Schneider, Director & Co-Founder, IgA Nephropathy Foundation, said: "This approval reflects the importance of continued innovation to help improve outcomes for people living with IgAN. With its approved use across several other rare diseases and established safety

profile, *Ultomiris* provides a new treatment option in IgAN that gives patients – and their physicians – more choice as they navigate their care."

Marc Dunoyer, Chief Executive Officer, Alexion, said: "As the first and only C5 inhibitor approved for the reduction of proteinuria in adults with IgAN, *Ultomiris* offers a new treatment option for people living with this serious disease. Many patients continue to face the risk of progression to kidney failure, underscoring the need for more targeted therapies that can slow the course of disease. This approval marks the fifth indication for *Ultomiris*, building on Alexion's pioneering leadership across multiple complement-mediated rare diseases."

In the prespecified interim analysis from the I CAN Phase III trial, *Ultomiris* demonstrated a 46.6% reduction in 24-hour urine protein creatinine ratio (UPCR) from baseline (95% confidence interval [CI]: 39.0%, 53.2%) at week 34, compared to 5.6% (95% CI: -4.9%, 15.0%) in patients receiving placebo, resulting in a placebo-adjusted treatment effect of 43.4% (95% CI: 33.5%, 51.8%; p<0.0001). The reduction in proteinuria was rapid, observed as early as week 10 with *Ultomiris* (36.7% [95% CI: 30.2%, 42.6%]) and sustained through 34 weeks, compared to placebo (8.5% [95% CI: 0.5%, 15.8%]). These results were consistent across patient subgroups, reflecting diverse demographic and baseline clinical characteristics and disease severity.[3]

The safety profile observed in the trial was consistent with the known profile of *Ultomiris* and was generally well tolerated, with no new safety concerns identified. Based on results from the prespecified interim analysis, the most common adverse events (AE) reported were upper respiratory tract infection (11.3%), nasopharyngitis (9.2%) and infusion-related reactions (8.4%) in those treated with *Ultomiris*; and upper respiratory tract infection (10.2%), nasopharyngitis (9.0%) and hypertension (6.6%) in those receiving placebo.[3]

The interim results from the I CAN trial were presented at the 2026 European Renal Association (ERA) Congress, and late-breaking results will be presented at the American Society of Nephrology's Kidney Week on 23 October 2026.[3,10]

Regulatory submissions based on the interim results from the I CAN trial are also under review in Japan and additional countries.

Notes

Immunoglobulin A Nephropathy (IgAN)
Immunoglobulin A nephropathy (IgAN) is a rare, inflammatory disease of the kidneys that can lead to chronic kidney disease (CKD) and progress to end-stage kidney disease (ESKD). It begins when the body develops abnormal IgA proteins resulting in immune complexes that are deposited in the kidneys causing damage. The deposition of these complexes activates the complement system, leading to terminal complement-driven inflammation. This results in damage and loss of essential parts of the kidney, including cells in the glomeruli, the part of the kidneys that filters and cleans the blood. Over time, this damage impacts the ability of the kidneys to function properly, resulting in chronic kidney disease that can progress to end-stage kidney disease.[4]

The signs and symptoms of IgAN can include blood in the urine (haematuria), foamy urine (proteinuria), swelling in hands and feet (oedema) and high blood pressure (hypertension).[11] Most people with IgAN do not experience symptoms in the early stages of the disease, and therefore, it often goes undetected until it has progressed. At diagnosis, irreversible kidney damage may have already occurred.[12,13] Approximately half of people with IgAN who have elevated protein levels in urine or reduced kidney function are at high risk of progression to ESKD, or kidney failure, within 10 years of diagnosis.[7-9]

I CAN (ALXN1210-IgAN-320)
I CAN (ALXN1210-IgAN-320) is a global, Phase III, randomised, double-blind, placebo-controlled trial evaluating the efficacy and safety of *Ultomiris* in adults with immunoglobulin A nephropathy (IgAN) who are at risk of disease progression. Participants were on stable concomitant IgAN treatment(s) consistent with standard of care for at least three months prior to screening.[2]

Participants were randomised 1:1 to receive either *Ultomiris* or placebo, administered intravenously for a total of 106 weeks. Patients in the treatment arm received a loading dose of *Ultomiris* on Day 1, followed by regular weight-based maintenance dosing of *Ultomiris* beginning on Day 15 and then every eight weeks through the 106-week blinded treatment period. Patients who completed the randomised control period had the option to enter an open-label access period.[2]

The primary endpoints are change from baseline in proteinuria based on 24-hour urine protein creatinine ratio (UPCR) at week 34 and change from baseline in estimated glomerular filtration rate (eGFR) at week 106, assessed at the interim analysis and final analysis, respectively. Key secondary endpoints for the final analysis include reduction in 24-hour UPCR ≥ 50% from baseline at week 34, change from baseline in proteinuria based on 24-hour UPCR at week 10, time to sustained ≥ 30% eGFR decline up to week 106 and time to first occurrence of composite kidney event up to week 106. The trial was designed to enrol approximately 510 participants from 28 countries across North America, South America, Europe, Asia and Australia.[2]

Ultomiris
Ultomiris (ravulizumab), the longest-acting C5 complement inhibitor, provides immediate, complete and sustained complement inhibition. The medication works by inhibiting the C5 protein in the terminal complement cascade, a part of the body's immune system. When activated in an uncontrolled manner, the complement cascade over-responds, leading the body to attack its own healthy cells. Following a loading dose, *Ultomiris* is administered intravenously every eight weeks in adults, or every four or eight weeks in paediatric patients (based on body weight).

Ultomiris is approved in the US, EU, Japan, China and other countries for the treatment of certain adults with paroxysmal nocturnal haemoglobinuria (PNH) and is also approved for certain children with PNH in the US, EU, China and other countries.

Ultomiris is also approved in the US, EU, Japan and other countries for the treatment of certain adults and children with atypical haemolytic uraemic syndrome (aHUS).

Additionally, *Ultomiris* is approved in the US, EU, Japan, China and other countries for the treatment of certain adults with generalised myasthenia gravis (gMG).

Further, *Ultomiris* is approved in the US, EU, Japan, China and other countries for the treatment of certain adults with neuromyelitis optica spectrum disorder (NMOSD).

Ultomiris is approved in the US and other countries for adults with primary immunoglobulin A nephropathy (IgAN).

Ultomiris is being assessed as a treatment for additional indications as part of a broad development programme.

Alexion
Alexion, AstraZeneca Rare Disease, is focused on serving patients and families affected by rare diseases and devastating conditions through the discovery, development and delivery of

life-changing medicines. A pioneering leader in rare disease for more than three decades, Alexion was the first to translate the complex biology of the complement system into transformative medicines, and today it continues to build a diversified pipeline across disease areas with significant unmet need, using an array of innovative modalities. As part of AstraZeneca, Alexion is continually expanding its global geographic footprint to serve more rare disease patients around the world. It is headquartered in Boston, US.

AstraZeneca

AstraZeneca (LSE/STO/NYSE: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialisation of prescription medicines in Oncology, Rare Disease, and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca's innovative medicines are sold in more than 125 countries and used by millions of patients worldwide. Please visit astrazeneca.com and follow the Company on Social Media @AstraZeneca.

Contacts

For details on how to contact the Investor Relations Team, please click here. For Media contacts, click here.

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