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Otsuka Sibeprenlimab Phase 3 Data Show a Statistically Significant and Clinically Meaningful Proteinuria Reduction for the Treatment of Immunoglobulin A Nephropathy (IgAN)

- *In the Phase 3 VISIONARY study, sibeprenlimab achieved a statistically significant and clinically meaningful 51.2% (P<0.0001) reduction in proteinuria at nine months of treatment when compared to placebo*
- *The safety profile of sibeprenlimab was favorable and consistent with previously reported data*
- *Immunoglobulin A nephropathy is a progressive, immune-mediated, chronic kidney disease that can lead to end-stage kidney disease (ESKD) over the lifetime of most patients under current optimized standard care*
- *Sibeprenlimab filed its Biologics License Application (BLA) and received Priority Review designation from the U.S. Food and Drug Administration (FDA) with a target action date of November 28th, 2025*

PRINCETON, N.J. and TOKYO, JAPAN – June 6, 2025 – Otsuka Pharmaceutical Development & Commercialization, Inc. and Otsuka Pharmaceutical, Co. Ltd. (Otsuka) today presented results from a pre-specified interim analysis of the Phase 3 VISIONARY study (NCT05248646) evaluating sibeprenlimab, for the treatment of immunoglobulin A nephropathy (IgAN) in adults. Patients treated with sibeprenlimab achieved a 51.2% (P<0.0001) reduction in proteinuria (as measured by 24-hour uPCR [urine protein-to-creatinine ratio]) at nine months of treatment when compared to placebo[1]. The data were presented during a late-breaking clinical trials session at the European Renal Association (ERA) Congress in Vienna, Austria. The study, the largest Phase 3 IgAN trial conducted to date, also showed the safety profile of sibeprenlimab was favorable and consistent with previously reported data[1]. Specifically, 76.3% of patients treated with sibeprenlimab experienced any Treatment Emergent Adverse Event (TEAE) versus 84.5% in the placebo group.[1] Patients who experienced a serious TEAE were 3.9% treated with sibeprenlimab compared to 5.4% treated with placebo.

Sibeprenlimab received Priority Review designation from the FDA last month following its BLA filing in March. Proteinuria reduction is a recognized surrogate marker correlating with delaying progression to kidney failure and has been used as an endpoint in IgAN clinical trials to support accelerated

regulatory approvals[2].

Sibeprenlimab is an investigational monoclonal antibody that selectively inhibits the activity of APRIL (A PRoliferation-Inducing Ligand) in adults with IgAN. APRIL plays a key role in the 4-hit process of IgAN pathogenesis and is an important initiating and sustaining factor in IgAN progression by promoting the production of pathogenic Gd-IgA1 and immune complex formation[3,4,5,6]. By selectively binding and inhibiting APRIL, sibeprenlimab reduces the amount of immunoglobulin A (IgA) and Gd-IgA1 levels[1]. Lower levels of Gd-IgA1 in people with IgAN provide less substrate for immune complex formation[7]. Sibeprenlimab is administered in a single-dose prefilled syringe for subcutaneous injection every four weeks intended for self-administration or administration by caregiver, providing patients the option of convenience at home.

“We are confident about the potential of sibeprenlimab and are grateful to the patients who are helping to further the science by participating in these important trials,” said John Kraus, M.D., Ph.D., executive vice president and chief medical officer, Otsuka Pharmaceutical Development & Commercialization, Inc. “Proteinuria control is an important independent predictor for long-term prognosis, and this interim data reinforces our belief that selectively targeting APRIL has the potential to be an effective and safe approach for this progressive and irreversible kidney disease.”

The VISIONARY study continues in a blinded manner to evaluate the change in kidney function over 24 months as measured by estimated glomerular filtration rate (eGFR) and is expected to be completed in early 2026. Further prespecified and exploratory analyses of the data will be conducted to determine the full potential of sibeprenlimab for the treatment of IgAN[1].

“The VISIONARY phase 3 interim analysis shows a robust proteinuria reduction of 51.2% in the group treated with sibeprenlimab relative to placebo. These results affirm our belief in the efficacy of sibeprenlimab in the largest phase 3 IgAN trial to date. The study enrolled a diverse patient population reflective of the disease epidemiology,” said Dr. Dana Rizk, professor of medicine in the division of nephrology at the University of Alabama at Birmingham. “The safety data emerging from VISIONARY is reassuring and adds to our existing knowledge about sibeprenlimab’s safety profile from prior programs. This is very exciting news for patients and adds a therapeutic option with a novel mechanism of action potentially targeting the immunologic pathogenesis of IgAN.”

ERA presentation on sibeprenlimab will be posted on the following website by 7:00 AM (Japan time) on June 7.
https://visterrainc.com/our-research/conferences/

About the VISIONARY Study

The VISIONARY study is the largest IgAN trial to date, and is a multicenter, randomized, double-blind, placebo-controlled trial consisting of approximately 510 adult patients with IgAN who were receiving standard-of-care therapy (defined as maximally tolerated ACE inhibitor or ARB +/- SGLT2 inhibitor), designed to evaluate the efficacy and safety of sibeprenlimab 400 mg administered subcutaneously every four weeks, compared to placebo[1]. The primary efficacy endpoint is to evaluate the change in 24-hour uPCR at 9 months compared with baseline. The secondary endpoint is to evaluate the annualized slope of eGFR estimated over ~24 months[1].

About Sibeprenlimab

Sibeprenlimab (formerly VIS649) was designed and engineered by Visterra, Inc., a wholly owned subsidiary of Otsuka. Pre-clinical and early-stage trials of sibeprenlimab were also conducted by Visterra. Sibeprenlimab is an investigational monoclonal antibody that selectively binds to and inhibits the activity of APRIL and plays a key role in the 4-hit process. By selectively binding and inhibiting APRIL, sibeprenlimab reduces the amount of immunoglobulin A (IgA) and Gd-IgA1 levels[1]. Lower levels of Gd-IgA1 in people with IgAN provide less substrate for immune complex formation[7]. Decreased immune complex formation should result in diminished deposition in the kidney, and reduced proteinuria and kidney inflammation[8]. By reducing the production of Gd-IgA1, sibeprenlimab may help slow kidney damage and progression toward ESKD[3,4,5,6]. By inhibiting APRIL, sibeprenlimab may help address one of the IgAN-specific drivers for nephron loss.

About IgAN and APRIL

IgAN is a progressive, immune-mediated, chronic kidney disease that typically manifests in adults aged 20-40 years and leads to ESKD over the lifetime of most patients[9,10,11].

IgAN is characterized by the accumulation of Gd-IgA1 complexes in the kidneys. IgAN can lead to progressive loss of kidney function and, eventually, ESKD, imposing a significant burden on patients[10]. Despite supportive care, there is an unmet need for treatments that address the root causes of the condition. Continued research in the disease remains crucial to uncovering opportunities for advancement in our understanding and treatment of patients [5].

APRIL, a cytokine in the tumor necrosis factor (TNF) family, is integral to the pathogenesis and progression of IgAN. It promotes the survival and class switching of B cells to produce IgA, particularly the pathogenic galactose-deficient IgA1 (Gd-IgA1) that forms immune complexes in the kidneys[5].

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