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PRESS RELEASE

Novartis IgAN data in *The Lancet* show clinically meaningful slowing of kidney function decline with Vanrafia® over 2.5 years

- *Phase III ALIGN study results showed reduced rate of kidney function decline by ~34% with Vanrafia vs placebo, based on supportive eGFR slope analysis*[1]
- *Vanrafia reduced protein in urine by 38.3% vs placebo at 9 months, with reductions sustained through end of treatment*[1,2]
- *Patients additionally receiving background SGLT2 inhibitors also consistently showed slower kidney function decline with Vanrafia vs placebo*[1,2]

Basel, June 4, 2026 – Novartis reported final 2.5-year Phase III ALIGN results showing slower kidney function decline with Vanrafia® (atrasentan) versus placebo in adults with IgA nephropathy (IgAN)[1,2]. Results were published in *The Lancet* and presented at the European Renal Association (ERA) Congress.

Estimated glomerular filtration rate (eGFR) change from baseline favored Vanrafia, alongside sustained reductions of protein in the urine through end of treatment. Benefits were consistent across different measures of kidney function and in patients additionally receiving sodium-glucose co-transporter-2 (SGLT2) inhibitors[1,2].

“These results provide robust evidence of clinically meaningful slowing of kidney function decline over more than two years of treatment, reinforcing findings from the earlier analysis of proteinuria reduction,” said Richard Lafayette, MD, FACP, Professor of Medicine, Nephrology, Director of the Glomerular Disease Center at Stanford University Medical Center, and ALIGN Study Investigator and Steering Committee Member. “They highlight the role of a highly selective endothelin A receptor antagonist as part of an evolving treatment approach for IgAN.”

Key efficacy results[1,2]

Endpoint	Vanrafia	Placebo	Effect vs placebo
Main cohort			
Change from baseline in eGFR at end of study* **(Week 136)**	-7.5	-9.9	2.4 (p=0.057)
Change from baseline in eGFR at end of treatment (Week 132)	-6.9	-9.5	2.6 (p=0.039)
Annualized total eGFR slope (Weeks 0-136)	-2.7	-4.1	1.4 (~34% slower decline; p=0.003)
Change from baseline in urine protein-to-creatinine ratio (UPCR) at 9 months (Week 36)†	-39.5%	-1.9%	38.3% relative reduction
Change from baseline in UPCR at end of treatment (Week 132) †	-28.8%	-0.6%	28.4% relative reduction
SGLT2 inhibitor cohort			
Change from baseline in eGFR at end of study* **(Week 136)**	-1.5	-10.6	9.1 (p=0.004)

** Week 132 plus a 4-week off-treatment follow-up*
† UPCR at Week 36 assessed using 24-hour urine collection; UPCR at Week 132 assessed using first-morning void samples.
All p values are nominal except for the change from baseline in eGFR at the end of study in the main cohort; all p values are two-sided;
eGFR change from baseline is expressed in mL/min/1.73 m²; annualized eGFR slope is expressed in mL/min/1.73 m²/year

“ALIGN reinforces Vanrafia’s potential as a foundational IgAN therapy and our commitment to advancing long-term kidney protection through continued innovation,” said Ruchira Glaser, MD, MS, Global Head, Cardiovascular, Renal and Metabolic Development, Novartis. “Together with our broader portfolio, these data strengthen confidence in an evidence-based approach to managing this progressive disease.”

Safety was consistent with prior studies, with adverse events similar to placebo and no new signals observed[1-4].

Vanrafia received accelerated approval in the U.S. and China for reduction of proteinuria in adults with IgAN in 2025[5,6]. Novartis intends to use these data to support submission for traditional approval in 2026.

About IgAN

IgAN is a progressive autoimmune kidney disease, with approximately 25 people per million worldwide newly diagnosed each year[7,8]. IgAN is highly debilitating as it leads to inflammation in the small filters of the kidneys, excess protein in urine, and a gradual decline in eGFR[9]. Up to 50% of patients with persistent protein in the urine progress to kidney failure within 10 to 20 years of diagnosis, often requiring dialysis or kidney transplantation as part of long-term disease management[8-13].

Furthermore, people living with IgAN often face mental and social challenges[9-12]. Supportive care has not addressed the underlying causes of the disease and often fails to slow disease progression, reinforcing the need for more targeted therapies for IgAN[10-15].

About ALIGN[1-4,15]

The ALIGN study (NCT04573478) is a global, randomized, multicenter, double-blind, placebo-controlled Phase III clinical trial comparing the efficacy and safety of Vanrafia vs placebo in patients with IgAN at risk of progressive loss of kidney function. In total, 340 patients with biopsy-proven IgAN with baseline total proteinuria ≥1 g/day despite optimized renin-angiotensin system (RAS) inhibitor treatment were randomized to receive once-daily, oral Vanrafia (0.75 mg) or placebo for approximately 132 weeks. Patients continue receiving a maximally tolerated and stable dose of a RAS inhibitor as supportive care. An additional cohort of 64 patients receiving an SGLT2 inhibitor in addition to RAS inhibitor for at least 12 weeks was also enrolled. The primary efficacy endpoint for the interim analysis (in 270 patients) was change in protein in urine, as measured by 24-hour UPCR from baseline to 36 weeks. The key secondary endpoint for the final analysis is the change from baseline to 136 weeks in kidney function as measured by eGFR. Other secondary efficacy endpoints as well as safety and tolerability are also assessed.

About Vanrafia® (atrasentan)

Vanrafia (atrasentan) is a potent and highly selective endothelin A (ETA) receptor antagonist, which is part of the endothelin system, a key system involved in the progression of IgAN[3,16-18].

Vanrafia is the first and only selective ETA receptor antagonist approved for primary IgAN, a once-daily, oral treatment and can be seamlessly added to, or used alongside, existing supportive care (e.g. RAS inhibitor with or without SGLT2 inhibitor) without the need for titration[5,6]. Vanrafia does not require a Risk Evaluation and Mitigation Strategy (REMS) program. Because some endothelin receptor antagonists have caused elevations of aminotransferases, hepatotoxicity, and liver failure, clinicians should obtain liver enzyme testing before initiating Vanrafia and during treatment when clinically indicated. Vanrafia may cause serious birth defects[5].

Novartis’ commitment to kidney diseases

Building on a legacy of more than 40 years that began in transplant, Novartis is on a mission to empower breakthroughs and transform care in kidney health, starting with kidney conditions that have significant unmet need. Alongside Vanrafia, Novartis is advancing a multi-asset IgAN portfolio that includes Fabhalta® (iptacopan) and investigational compound zigakibart.

Historically, these conditions have had considerably less funding and research, leading to a treatment landscape largely focused on reactive or end-stage disease management, often with significant physical, emotional, and financial burdens. Our portfolio targets the underlying causes of disease, with an aim to protect kidney health and delay or prevent dialysis and/or transplantation. Our goal is to help patients get back to living life on their terms -

whether at work, in school, or with loved ones, and by partnering with patients, advocates, clinicians and policymakers, we aim to raise awareness, accelerate diagnosis, and get patients the right care, sooner.

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This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements can generally be identified by words such as "potential," "can," "will," "plan," "may," "could," "would," "expect," "anticipate," "look forward," "believe," "committed," "investigational," "pipeline," "launch," or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved products described in this press release, or regarding potential future revenues from such products. You should not place undue reliance on these statements. Such forward-looking statements are based on our current beliefs and expectations regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that the investigational or approved products described in this press release will be submitted or approved for sale or for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that such products will be commercially successful in the future. In particular, our expectations regarding such products could be affected by, among other things, the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; regulatory actions or delays or government regulation generally; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures and requirements for increased pricing transparency; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political, economic and business conditions, including the effects of and efforts to mitigate pandemic diseases; safety, quality, data integrity or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Novartis

Novartis is an innovative medicines company. Every day, we work to reimagine medicine to improve and extend people's lives so that patients, healthcare professionals and societies are empowered in the face of serious disease. Our medicines reach more than 300 million people worldwide.

Reimagine medicine with us: Visit us at **https://www.novartis.com** and connect with us on **LinkedIn**, **Facebook**, **X/Twitter** and **Instagram**.

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